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ABSTRACT BOOK

Valencia, Spain

PLENARY LECTURE 3

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KIDNEY STEM/PROGENITOR CELLS CAN BE ISOLATED FROM THE URINE OF NEONATES INDEPENDENTLY OF THEIR GESTATIONAL AGE AT BIRTH

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Aims/Purpose: In the human kidney, nephron structures derive from a population of kidney stem/progenitor cells which express SIX2, a transcription factor responsible for cell survival and self-renewal. These SIX2+ kidney stem/progenitor cells are only present during nephrogenesis, which is reported to terminate at 36 weeks of gestational age (GA).(1) We have previously described a strategy to isolate kidney stem/progenitor cells from the urine of neonates born before 36 weeks of GA, named the neonatal kidney/stem progenitor cells (nKSPC).(2) In preterm neonates, nephrogenesis is still ongoing at the time of birth, enabling isolation of kidney stem/progenitor cells from the voided urine. In this study, we aimed to determine the efficiency of nKSPC isolation from the urine of neonates and which GA results in the highest yield of nKSPC.

Methods: Thirty-seven fresh urine samples were obtained from 36 neonates shortly after birth at the University Hospitals Leuven (Belgium). Five urine samples were collected from extreme preterm (< 28 weeks GA), 6 samples from very preterm (28–32 weeks GA), 18 samples from moderate-late preterm (32-37 weeks GA) and 8 samples from term neonates (> 37 weeks GA). When a sample yielded cell growth, cell colonies were subcultured to achieve clonal expansion. Cell lines were characterized for SIX2 using RT-qPCR and immunostaining. SIX2+ cell lines were further evaluated for their potential to differentiate into kidney epithelial cells (proximal tubular epithelial cells (PTEC) and podocytes) in 2D cultures using our established protocols.(2)

Results: From the 37 urine samples collected, 28 samples yielded cell growth (76%). After subcloning, 147 cell lines were characterized for the expression of SIX2, of which 42 were SIX2+. Four SIX2+ cell lines were from extreme preterm, 12 from very preterm, 13 from moderate to late preterm and 13 from term neonates. SIX2+ cell lines isolated from term neonates exhibited similar cells growth and differentiation potential compared to those isolated from extreme preterm neonates. Additionally, we observed a dose-response effect regarding expression levels of SIX2 and the differentiation potential: cell lines with higher levels of SIX2 maintained their undifferentiated state while lower levels of SIX2 enabled successful differentiation to PTEC and/or podocytes.

Conclusion: This study demonstrates that SIX2+ nKSPC can be isolated from the urine of neonates, independently of their GA at birth. This could indicate that nephrogenesis persists longer than what has previously been reported. Furthermore, the nKSPC exhibit a dose-response effect with regard to levels of SIX2 and induction of differentiation.

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PLENARY LECTURE 4

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APRIL IS ACTIVATED IN CHILDREN IGAN TRIGGERED BY CD89

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Aims/Purpose: IgA nephropathy (IgAN), characterized by the renal deposition of IgA, involves a multi-hit development process with the formation of circulating immune complexes (CICs) containing Galactose-deficient IgA1 (Gd-IgA1) and sCD89, contributing to renal inflammation. A Proliferation-Inducing Ligand (APRIL) is implicated in the immune response. The aim of this study is to investigate APRIL implication, particularly in children with IgA nephropathy (cIgAN), who often exhibit more inflammation than adults.

Methods: First, we evaluated APRIL levels in human mesangial cells (HMCs) after exposing them to various stimuli, including soluble CD89 (sCD89) or plasma from cIgAN patients. Subsequently, we conducted a comprehensive international cross-sectional study involving 86 pediatric IgA nephropathy (cIgAN) patients and 48 control subjects recruited from France and Canada. Our investigation included the quantification of APRIL plasma levels and circulating immune complexes (CIC), which were then compared with the biological, clinical, and histological characteristics of the disease. Additionally, we performed immunohistochemistry analysis on kidney biopsies obtained from cIgAN patients to visualize APRIL staining patterns.

Results: First, we demonstrated that stimulations with cIgAN plasma and recombinant sCD89, induced inflammation in human mesangial cells (HMCs), leading to increased APRIL mRNA and protein production. In our cross-sectional study, we observed elevated levels of Gd-IgA1, sCD89-IgA1, sCD89, and circulating soluble APRIL in the plasma of cIgAN patients compared to control subjects ($p < 0.05$). Moreover, we found evidence suggesting that APRIL may be trapped within circulating immune complexes (CICs), colocalizing with IgA in same-size complexes in Western blot experiments. Additionally, IgA-APRIL and CD89-APRIL complexes were detected in cIgAN samples using ELISA and immunoprecipitation techniques. Levels of CICs correlated with plasma APRIL levels, and the presence of IgA-APRIL and CD89-APRIL complexes in CICs was associated with histological inflammation, particularly in active cIgAN cases with endocapillary proliferation ($p < 0.01$). Immunohistochemical staining of cIgAN biopsies revealed the presence of APRIL deposits within the glomerulus in the mesangium and near the Bowman capsule.

Conclusion: Our research highlights the role of APRIL in the pathways of cIgAN, with sCD89 identified as a potential inducer of APRIL activation in HMCs. APRIL hold promises as a valuable biomarker, offering a non-invasive means to detect active forms of cIgAN, thereby potentially reducing reliance on kidney biopsy. APRIL inhibition as a therapeutic strategy presents an exciting opportunity for cIgAN treatement.

PLENARY LECTURE 5
AND BEST ABSTRACTS

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UROMODULIN INDUCES CELL DEATH AND FIBROSIS IN THE NEONATAL MOUSE MODEL OF OBSTRUCTIVE UROPATHY

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Aims/Purpose: Urinary tract obstruction during renal development leads to inflammation, tubular cell death (apoptosis and necrosis), and interstitial fibrosis. Uromodulin (UMOD), also known as Tamm-Horsfall protein, is produced and released by tubular epithelial cells of the thick ascending limb of the loop of Henle. Once secreted, UMOD undergoes polymerization within the tubular lumen, where it modulates salt transport and protects the kidney from bacteria and stone formation. Under pathological conditions, polymerized UMOD can accumulate within the tubular lumen, migrate to extratubular locations and induce leukocyte recruitment and inflammation in the kidney. We studied the role of UMOD in the neonatal mouse model of obstructive uropathy.

Methods: Newborn transgenic mice (UMOD-/-) and wildtype-mice (C57BL/6; WT) were subjected to either unilateral ureteral obstruction (UUO) or sham operation at day 2 of life. Whole kidneys were harvested at day 3, 7, and 14 of life. The kidneys were analyzed by immunohistochemistry for signs of inflammation (F4/80, CD3), cell death (TUNEL), atrophy (PAS), fibrosis (MT, -SMA), as well as for protein expression using Western blot (PARP, RIPK3, -SMA).

Results: Neonatal UMOD-/- mice showed decreased apoptosis and necroptosis in the neonatal UUO kidney in comparison to WT. Following UUO UMOD-/- mice showed a reduction of fibrosis compared to WT. UMOD-/- kidneys after UUO displayed more atrophy in distal tubules, but no difference in atrophy in proximal tubules compared to WT. Immunohistochemical staining of F4/80 and CD3 did not show differences in inflammation between UMOD-/- and WT UUO kidneys.

Conclusion: Neonatal UUO kidneys of UMOD-/- mice showed a reduction of cell death and renal fibrosis in comparison to WT. Contrary to expectations, no difference in inflammation between neonatal UMOD-/- and WT mice was detected. The inhibition of UMOD or the corresponding signaling pathways may have a beneficial effect on neonatal kidneys with urinary tract obstructions.

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INSL3 VARIANTS AND INSL3 DEFICIENCY IN HUMAN AND MURINE CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT

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Aims/Purpose: Variants in the insulin-like 3 (INSL3) gene encoding a ligand of relaxin family peptide receptor 2 (RXFP2) and Insl3 deficiency cause cryptorchidism. Here, a cryptorchidism-associated INSL3 missense variant co-segregated with the CAKUT phenotype in females of an index family, instigating the investigation of the role of INSL3 in human and murine CAKUT.

Methods: Whole-exome or targeted INSL3 sequencing was done in 312 CAKUT families. Variant carriers were subjected to reverse phenotyping. INSL3 expression was determined in human fetal and adult tissues and the developing murine kidney by qRT-PCR. A tubulo-morphogenesis assay was done on CRISPR/Cas9-derived Insl3-deficient mIMCD3 cells. Insl3 knock-out mice were characterized morphologically and histologically with respect to urogenital anomalies.

Results: Very rare (minor allele frequency ≤0.0005) INSL3 variants predicted to be deleterious were identified in 6 of 312 (1.9%) CAKUT families, significantly more frequently than in controls (0.4%, p =0.003). The four different INSL3 variants detected were heterozygous, and almost exclusively maternally inherited. Cryptorchidism was significantly more frequent in male CAKUT patients with versus without INSL3 variants (2/3 males, 67% vs. 17/198 males, 9%; p =0.02). INSL3 was expressed in the fetal and adult human kidney. Insl3 and Rxfp2 transcripts were present in the developing murine kidney. In Insl3+/- and Insl3-/- mIMCD3 cells, fewer tubular structures were observed indicating impaired tubulogenesis processes. The CAKUT spectrum in Insl3+/- and Insl3-/- mice included kidney hypo(dys)plasia, fusion, segmental nephron losses, hydronephrosis, duplex ureter, a narrowed ureteric lumen.

Conclusion: Heterozygous INSL3 variants associate with human CAKUT, and heterozygous and homozygous Insl3 knock-out can cause CAKUT in mice.

MINI LECTURE 1

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EXOME SEQUENCING IN A COHORT OF INDIVIDUALS WITH MICROSCOPIC HEMATURIA AND CLINICAL SUSPICION OF TYPE-IV-COLLAGEN-RELATED-NEPHROPATHY

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Purpose: Type-IV-collagen-related nephropathy is an umbrella term comprising thin basement membrane nephropathy (TBMN) and Alport syndrome (AS). The effects of the phenotype range from isolated microscopic hematuria to end-stage kidney failure with possible extrarenal involvement. Disease-causing variants in COL4A5 are linked to X-linked AS (XLAS) and lead to full AS phenotype in males, while females (heterozygous) are variably affected. Monoallelic variants in COL4A3/COL4A4 are associated with TBMN/autosomal dominant AS (ADAS), whereas biallelic variants cause autosomal recessive AS (ARAS). The aim of this study was to establish a genotype-phenotype correlation in 289 patients with clinical suspicion of type-IV-collagen-related nephropathy.

Methods: Phenotype assessment was conducted using a standardized questionnaire. Exome sequencing (ES) was performed for genetic analysis and variants were evaluated according to AC mg/ACGS criteria.

Results: TBMN was clinically suspected in 210/289 (73%) individuals (median age: 6 years; extrarenal involvement: 4%) and AS in 79/289 (27%) (median age: 8 years; extrarenal involvement: 43%). Overall, disease-causing variants in COL4A3-5 were identified in 144/289 (50%) of the individuals: Genetically, 53% had XLAS with variants in COL4A5 and 7% had ARAS due to biallelic variants in COL4A3. The remaining 38% had monoallelic variants in COL4A3/COL4A4, genetically associated with TBMN/ADAS. 2% of individuals had variants in other genes (MYH9, INF2, COQ6). Overall, 71% of all identified variants in COL4A3-5 were non-truncating; 83% of these were missense variants causing substitution of glycine residues.

Conclusion: Despite precise phenotypic characterization, only 50% of the individuals in this study were found to have disease-causing variants. It should be noted that ES is not covering all genomic regions. Furthermore, a large proportion of the cohort showed clinical suspicion of TBMN, which offers the possibility of new insights into TBMN/ADAS: Thus, the frequency of extrarenal manifestations was increased in individuals with TBMN compared to the literature. However, on closer inspection, there appears to be no recognisable causal relationship with TBMN in many individuals. The next step will involve carrying out a burden analysis to identify possible further variants influencing the phenotype.

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COGNITIVE PROFILE ASSESSMENT ADAPTIVE FUNCTIONING AND EMOTIONAL-BEHAVIOURAL ASPECTS IN A COHORT OF X-LINKED AND AUTOSOMAL ALPORT SYNDROME PATIENTS

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Aims/Purpose: Collagen IV subunits may be implicated in synaptic differentiation and stability. Studies have suggested that the dragnet (col4a5) gene activity is required for normal axon targeting. In addition, familial cases of chronic kidney diseases (CKD), as frequently observed in Alport Syndrome (AS) may affect psychological wellbeing and alter intra-familiar relationships. To assess the cognitive profile, the adaptive functioning, and the emotional-behaviour of a cohort of X-linked AS (XLAS) and autosomal AS (AAS) patients followed in our Paediatric Nephology Division.

Methods: Patients were included in the study if they were diagnosed with XLAS or AAS before the age of 18 years. The mean age at the psychological evaluation was 14.1 years (range 4.4-24.5 yrs). All patients were assessed for:

eGFR, proteinuria (UPCR) and hearing function - cognitive and behavioural performance.

The following scales and tests were used: Wechsler Scale of Intelligence (WIPPSI III, WISC IV, WAIS IV) for cognitive profile; Adaptive Behaviour Assessment System-Second Edition (ABAS-II) for adaptive functioning; Child Behaviour Checklist (CBCL) for emotional-behavioural aspects; K-SADS PL test for psychopathological evaluation.

Results: Fifty-seven patients were included in the study. Demographic characteristics and kidney function are reported in table 1. Cognitive Profile: the mean Intelligence Quotient (IQ) was 97,8 ± 17,2 (median 98; range 40-131), similar to the general population. A negative correlation was observed between IQ and age (p =0,04). The Verbal Comprehension Index (VCI) score was significantly lower in patients with hearing aids (p =0,019). Adaptive Functioning assessment: the General Adaptive Composite (GAC) score was lower in AS patients (P =< 0,001) compared to the general population; similarly, specific scores related to social skills (p =0,002) and to everyday life abilities (< 0,001) were also low. Psychopathological evaluation, was performed only in 19/57 patients. The prevalence of anxiety and depression (53%) was high, compared to the general population (p =0,006). No genotype-phenotype correlations was observed.

Conclusion: the cognitive profile of this cohort of children and young adults with XLAS or AAS was similar to the general population, while Adaptive Functioning was slightly impaired. Anxiety and depression were the main observed psychological disorders.

Table 1

Patients (N°)	57
Mean age (yrs)	14.1±5.6 [4.4-24.5]
M:F	35:22 (57)
eGFR	116.2 ± 36.9
Proteiuria	74%
Onset of Proteinuria (yrs)	8.1 ± 4.8
CKD5	10.5% (5.3%)
Hearing Loss	47.4%
Onset Hearing Loss (yrs)	11.8±4.6

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CARDIAC MANIFESTATIONS IN CHILDREN WITH ALPORT SYNDROME: A SINGLE CENTER STUDY

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Aims/Purpose: Valvular dysfunction and aortic dilatation seem to be associated with Alport syndrome (AS). There are no cohort studies on cardiac involvement in children with AS. The aim of study was to define prevalence and spectrum of cardiac manifestations in children with AS.

Methods: In a single cohort study we evaluated 138 children (96 X-linked AS;77M) with genetically confirmed AS (age 10.2 ± 4.3 yrs, eGFR 101,9 ± 17,2 ml/min/1.73m2). The aorta was measured at level of the sinus of Valsalva (SoV), aortic dilatation was determined by z-score > 2 for BSA. Clinical (body mass index (BMI, kg/m2), mean day blood pressure (zMBP)), laboratory (proteinuria (Pr, mg/m2/day), eGFR (ml/min/1.73m2), echocardiograms (z-scores of left ventricular mass index (zLVMI) and left ventricular end diastolic diameter (zLVEDD), relative wall thickness of the left ventricle (RWT, N < 0,42)) data were obtained.

Results: Mitral regurgitation, mitral and tricuspid regurgitation without hemodynamic disorders were revealed in 22% and 4,2% of children, respectively; prevalence of valvular dysfunction depended on age (r = 0.45, p =0.0012). SoV dilatation was identified in 16 children (11.6%) with AS (including 1 pts with heterozygous COL4A3 variant, 3 pts with homozygous/compound heterozygous COL4A3 variants and 12 pts with X-linked AS; 0.17 vs 0.38 vs 0.1, respectively, p > 0.05). SoV dilatation was associated with male gender (1 = 0.31, p =0.02), BMI (1 = -0.27, p =0.03), Pr (1 = 0.23, p =0.04), LVMI (1 = 0.26, p =0.02), LVEDD (1 = 0.21, p =0.04). No statistically significant effect of SBP, DBP, MBP, Pr, eGFR on aortic dilatation has been demonstrated.

Conclusion: Prevalence of valvular dysfunction and SoV dilatation in children with AS is higher than in general population but appears comparable to that in children with CKD. Dilatation of SoV is associated with male gender, low BMI and left ventricular remodeling.

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"MORE THAN HALF OF CHILDREN WITH NONFAMILIAL HEMATURIA HARBOR COLA3-5 MUTATIONS. RESULTS FROM A POLISH NATIONAL ALPORT SYNDROME / THIN BASEMENT MEMBRANE NEPHROPATHY REGISTRY"

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Aims/Purpose: Pathogenic variants in COL4A3-5 genes are a frequent and characteristic finding in subjects with familial hematuria. The frequency of COL4A3-5 mutations in children with a negative family history has not been well established. The aim of the study is to assess the frequency of pathogenic variants in COL4A3-5 in an unselected national cohort of children with nonfamilial hematuria.

Methods: Research design: multicenter open cohort study. Between 2017-2023 over 500 children from 14 pediatric nephrology centers were registered into a National Alport Syndrome/Thin Basement Membrane Registry. A cohort of 125 subjects with a negative family history of hematuria was established. Genetic testing was performed by a NGS panel for COL4A3-5 pathologic variants. The anonymized clinical data of the children and their families were entered into an on-line platform. (Bioethic Comittee approval nr NKBBN 59/2021)

Results: The cohort included 80 girls (64%) and 45 boys (36%). The median age at genetic analysis was 11 years. 68/125 (54%) of the studied cohort were found to have an underlying genetic defect in COL4A3-5 genes. They included pathogenic variants in XLAS in 39, digenic mutations in 4, heterozygous variants in 25 and ARAS in a further 5 subjects. The clinical manifestation of children with COL4A3-5 gene defects and that of children without any identified pathogenic variants were similar: proteinuria 53% v. 42%, albuminuria 33% v. 18%, macroscopic hematuria episodes 13% v. 19%, hearing loss 12% v.5%, positive family history of a different/unknown kidney disease 31% v.14%. Forty three children underwent kidney biopsy; in thirty two (nineteen subjects with a COL4A3-5 variant and thirteen without a recognized genetic background) BM changes characteristic of AS/TBMN had been described.

Conclusion: Pathogenic variants in COL4A3-5 genes are present in over half of children with persistent nonfamilial hematuria. The most frequent are pathogenic variants of XLAS. NGS studies enable a rapid diagnosis of COL4A3-5 defects in children with nonfamilial hematuria, whose clinical presentation is not characteristic.

Key words: Hematuria, nonfamilial, Alport Syndrome, Thin Basement Membrane Nephropathy, collagen IV, COL4A3, COL4A4, COL4A5

Additional information:

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PREDICTIVE VALUE OF IMMUNOHISTOCHEMICAL WORKOUT AND ELECTRON MICROSCOPY ON RENAL TISSUE IN PATIENTS WITH ALPORT SYNDROME: PRELIMINARY DATA

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Aims / Purpose: Alport syndrome (AS) is a progressive hereditary glomerular disease. Genetic testing is the most accurate method for diagnosis, but a strong genetype-phenotype correlation has never really been demonstrated. So, an accurate prognostic test is lacking. Histology is a useful aid in the diagnosis of renal diseases. The purpose of this study is to verify the diagnostic value of immunohistochemistry (IHC) and electron microscopy (EM) on renal biopsy (RB) in patients with AS.

Methods: We conducted a retrospective monocentric observational study (1998-2023) on patients who eceived a RB and NGS test suggestive for AS and availability of frozen renal tissue to perform IHC analysis for alpha-3-4-5 chains of Collagen type IV. Bowman's capsule, GBM and TBM were considered as target structures. Staining intensity was scored: 0 if the antigen was present in less than 25% of the structures considered, 1 if from 25 to 75%, 2 if greater than 75%. In addition, histologic features suggesting the diagnosis of AS at EM (GBM thinning, lamellation, basket-weave lesions, alternating thickening/thinning, sclerosis, podocytopathy) were re-evaluated. The following score was assigned: 0 if the item was absent, 1 if focal, 2 if moderate, 3 if diffuse. A total score was related to age at biopsy for both IHC and EM. Data about proteinuria during follow up were collected. Finally, the predictive value of single items and total scores on developing proteinuria was assessed by the Cochran Armitage test.

Results: A total of 135 patients with AS were diagnosed by RB and genetics. The analysis was performed on the 27 patients who met all the inclusion criteria. Alfa-3 chain was not used due to technical problems. The total IHC score resulted significantly lower in the group of patients developing proteinuria.(p =0.003). This score is equally predictive of the occurrence of proteinuria if patients were divided in groups according to the type of AS (p =0.65). The total EM score is higher in case of proteinuria, but not significantly (p =0.10). It becomes significant when corrected for age at biopsy (p =0.01). The predictivity of the individual items of the two tests is shown in the following table.

	p values for proteinuria
Presence of alfa4 chain on GBM	0.001
Presence of alfa5 chain on GBM	0.001
Distribution of alfa5 chain on Bowman capsule	0.046
Presence of alfa4 chain on TBM	0.15
Thinning of GBM	0.02
Lamellated GBM	0.02
Basket weave lesions	0.053
Thinning/tickening GBM	0.08
Podocitopathy	0.87
Sclerosis	0.6

Conclusions: IHC seems to have a good predictive ability for the occurrence of proteinuria in patients with AS. This feature seems to be superior to that of ME. The patient group is limited, and genetic techniques are now very advanced. However, there is still no clear genotype-phenotype correlation. Application of IHC on larger populations could help to better define the risk and speed of evolution to the proteinuric phase of the disease.

MINI LECTURE 2

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SOCIOECONOMIC CHALLENGES IN MANAGING PAEDIATRIC MINERAL BONE DISEASE IN END STAGE RENAL DISEASE

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Aims/Purpose: The aim of this study was to investigate the impact of socioeconomic factors on mineral bone disease (MBD) in children with end-stage renal disease (ESRD) secondary to quality of life (QoL).

Methods: Of a total of 51 patients with ESRD, 44 met the inclusion criteria (15 PD, 14 HD and 15 Tx). Patients' quality of life of was assessed using Paediatric Quality of Life Inventory Version 4.0 Generic Core Scales both child self-report and parent proxy report, while socioeconomic status was assessed using indicators such as household income, financial problems, education level, and occupation of their primary caregiver. The research was approved by the Ethics Committee of the University Children's Hospital (ID No. 017-16/16).

Results: The age range of study cohort was 2–20 years, with predominance of males (70.5%). The group of transplanted patients was significant older compared PD group ($p < 0.05$) (15.5 ± 4.8 vs 9.2 ± 4.9). Majority of caregivers are married (87.2%) and most of them have completed high school (62.8% mothers vs 61.4% fathers). High percentage of mothers (40.9%) are unemployed, while 83.3% of fathers are employed. One third of families are on the poverty line with a total monthly income of less than EUR 500. A third of the respondents replied that they have some financial difficulties ("We can copy with most of the expenses but no money left every month") 46.7%, 35.7% and 33.3% of the PD, HD, and Tx patients respectively. The astonishing data is that 25.6% of parents were forced to leave their jobs, and 4.7% of them were fired due to the employer's lack of understanding of parents needs to be with the sick child during HD or during hospitalization. Regarding the control of MBD-CKD in context of QoL, the value of the Pearson coefficient was found to be - 0.32 for PTH level, and -0.121 for CaxP product, which means that the lower the values of the total quality of life score are (PedsQL), values of PTH and CaxP product are the higher. There is evident correlation between poorly regulated secondary hyperparathyroidism and financial difficulties ($p < 0.05$), and this correlation is stronger the more pronounced the financial problems are.

Conclusion: The financial situation of families of children with ESRD is challenging. It is necessary to expand the involvement of social workers in helping patients' families. Parents who primarily take care of sick children devoted their entire time to them, neglecting work self-realization. MBD-CKD can affect normal growth and development leading to significant lifelong health burdens and lower QoL, but also represent risk factor for cardiovascular disease development with shortening of life span. This integrated approach with periodic assessment of sociodemographic factors and QoL in children with ESRD could lead to more effective and tailored interventions to improve the overall well-being of these children.

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CALCIMIMETICS IMPROVE IMPAIRED CARDIAC FUNCTION AND CARDIOMYOCYTE CONTRACTILITY IN MICE WITH KIDNEY FAILURE VIA ACTIVATION OF THE CASR/CAMP SIGNALING PATHWAY

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Aims/Purpose: A high phosphate load stimulates the synthesis of PTH and FGF23 and is associated with increased cardiovascular (CV) mortality. In hemodialysis patients, the administration of calcimimetics led to a reduction of PTH and FGF23 and the latter was associated with a lower rate of CV events. We have previously shown that mice with a diet-induced phosphate overload have high PTH and FGF23 levels and develop impaired systolic cardiac function, which could be improved by calcimimetics. Mechanistically, calcimimetics are allosteric activators of the calcium sensing receptor (CaSR) and it has recently been shown that phosphate (Pi) inactivates the CaSR at concentrations > 1.4 mM Pi. Whether calcimimetics contribute to CV event reduction indirectly via lowering PTH and FGF23 or directly via CaSR activation at the heart is not clear.

Methods: Wild-type mice were fed a high phosphate diet (HPD) ± etelcalcetide (Etl) or a normal phosphate diet (NPD), cardiac function was assessed by echocardiography and Millar catheterization, and cardiac tissue was harvested for histology and RNAseq analysis. In addition, isolated adult mouse cardiomyocytes (AMCM) were stimulated ex vivo with PTH, FGF23 or Pi, contractility and calcium handling were measured with the addition of Etl and activity analyses were performed.

Results: In addition to the positive effect on HPD-induced systolic cardiac dysfunction, Etl improved impaired LV contractility and reduced fibrosis. RNAseq analyses revealed reduced Ca, PKA and cAMP signaling by HPD. Ex vivo stimulation of AMCM with PTH and FGF23 had no functional effect, whereas Pi significantly worsened contractility and Ca handling. Both could be almost normalized by Etl co-stimulation. Downstream of CaSR, Pi reduced the synthesis of cAMP, which led to PKA-dependent dephosphorylation of PLN and subsequently to lower Serca2a activity, which was ultimately responsible for the reduced contractility. Etl improved cardiomyocyte contractility via increased cAMP synthesis and increased PLN phosphorylation and Serca2a activity.

Conclusion: In addition to the positive secondary effects of FGF23 reduction on the heart, Etl effectively improves the Pi-induced pathological cardiac phenotype despite hyperphosphatemia, at least in part due to direct activation of the CaSR/cAMP signaling pathway, resulting in improved cardiomyocyte contractility.

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CORRELATES OF IRISIN WITH MINERAL BONE PARAMETERS AND INSULIN RESISTANCE IN CHILDREN WITH CHRONIC KIDNEY DISEASE

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Aims/Purpose: The myokine irisin is released after physical activity, promotes promyogenesis, myogenic differentiation, glucose uptake and improvement of mitochondrial function in skeletal muscle. Moreover, recent in vitro studies suggest and interplay between irisin and parathormone (PTH). The aim of this study is to investigate serum irisin levels in children with chronic kidney disease (CKD) and to explore its association with mineral bone disorders and insulin resistance.

Methods: Serum irisin was measured in 53 patients with CKD stage 3-5D. Body composition was assessed with bioimpedance spectroscopy. The following serum mineral bone parameters were measured: calcium, phosphorus, parathyroid hormone (PTH), 25-hydroxy-vitamin D (25(OH)D), fibroblast growth factor-23 (FGF23) and Klotho. The myokines myostatin, follistatin and insulin growth factor-1 (IGF-1) and IL-6 were also measured. Finally, HOMA-IR was calculated as an index of insulin resistance.

Results: Serum irisin levels were lower in CKD 5D patients but the difference from the other stages was not significant (p =0.161). No correlation was observed between irisin and body composition indices or other myokines levels. Serum irisin was negatively correlated to PTH (rs = -0.287, p =0.039) and 25(OH)D (rs = -0.282, p =0.042) after adjustment for CKD stage. Serum irisin was negatively correlated to HOMA-IR (rs = -0.294, p =0.038) and was negatively associated with high HOMA-IR (34% of patients) independently of fat mass percentage and CKD stage (OR 0.802, 95% CI 0.565- 0.981, p =0.032). No significant correlation was observed between HOMA-IR and IL-6.

Conclusion: The myokine irisin decreases with the progression of CKD in children. Its negative correlation with PTH and HOMA-IR suggests a possible pathogenic role of this myokine in mineral bone disorders and glucose metabolism.

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EPIDEMIOLOGICAL AND CLINICAL DATA FROM SPANISH PEDIATRIC PRE-DIALYSIS CHRONIC KIDNEY DISEASE REGISTRY (REPIR II)

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Purpose: To report the epidemiology, clinical status and prescribed treatments of children with pre-dialysis chronic kidney disease (CKD) 2-5 stages in Spain through analysis of the Spanish pediatric pre-dialysis chronic kidney disease Registry (REPIR-II)

Methods: Data were obtained from REPIR II by a REDCap (Research Electronic Data Capture) database that records annually, since 2007 to nowadays, demographic, clinical, laboratory and treatment data of children and youth under 18 years with non-dialysis CKD 2-5 living in Spain.

Results: 2916 patients (68% males) have been included. Mean age on first visit was 8.18 ± 5.32 years (16% < 2 years old). The incidence was 25.2 per million of pediatric population (pmpp) and the prevalence was 134.9 pmpp. Tubulointerstitial diseases-including structural anomalies-were the primary cause of CKD (62.4%) while glomerular diseases accounted for only 3.4%. Associated extrarenal anomalies were described in 38.4%. Patients were registered predominantly in early CKD stages: 54% stage 2, 19% stage 3a, 13% stage 3b, 11% stage 4 and 3% stage 5. The average time of evolution of CKD was 5,71 ± 4,64 years. Mean height Z-Score was -0.67 ± 1,86 (-1.04 in infants) and 17.5% had a mean height Z-Score < -1.88; 9% have been treated with recombinant growth hormone. Malnutrition (BMI Z-Score < 1.88) was present in 3.8%, reaching 29% in < 2 years old group; 2,7 % required gastrostomy or nutritional supplementation. Overweigth (BMI Z-Score > 1.88) was present in 6.35%, reaching 48% in adolescents.The prevalence of anaemia was 32% (10% on erythropoietin therapy), hypertension 16.6% (98% receiving antihypertensive drugs, 68% angiotensin converting enzyme inhibitors or angiotensin II receptor antagonists), and hyperparathyroidism 50% (52% of children treated with vitamin D and 13% with calcium-based phosphate binders). All of these pathologies were more prevalent in 4 and 5 CKD stages. 13,4% received allopurinol to treat hyperuricemia. 13% of patients at 5 years and 23% at 10 years progressed to end-stage renal disease. Progression of kidney disease, defined as either initiation of renal replacement therapy (dialysis or transplant) or a 50% reduction of GFR was achieved in a median time of 14 years (95% CI 0,47-0,54). Younger children, more advanced CKD stages on first visit, uncontrolled proteinuria, acidosis, hypertension, anemia and those with a glomerular disease showed a greater progression rate (p < 0,05). Mortality since the Registry was created was 3.11%.

Conclusions: Few data are available in CKD in children, mostly in early stages. REPIR II is one of the largest registries available in the world and provides relevant epidemiological data that may be a useful quality clinical tool to analyze risk factors allowing in the future appropriated interventions to slow the progression of renal disease.

MINI LECTURE 3

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THE ADVERSE EFFECTS OF KETOSIS DURING PREGNANCY ON NEPHROGENESIS AND OFFSPRING KIDNEY HEALTH

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Aim/Purpose: Maternal nutrition profoundly influences embryonic development, including nephrogenesis, which lays the groundwork for future susceptibility to chronic kidney disease. Understanding intrauterine factors, such as maternal ketosis, is vital in comprehending and potentially mitigating these risks. This study aims to investigate the effects of maternal ketosis during pregnancy on nephrogenesis and reveal the underlying mechanisms.

Methods: Two mouse experimental models were utilized to assess the impact of maternal ketosis on kidney development: a ketogenic diet and beta-hydroxybutyrate supplementation. Nephron count in adulthood was evaluated using acid maceration and immunofluorescence staining of nephrin. Serum urea levels were measured to assess kidney function. Nephron progenitor cells were isolated via FACS from transgenic mice, and RNA sequencing was conducted to analyze gene expression profiles. Immunofluorescent staining, western blotting, and RT-PCR validated alterations in altered pathways.

Results: Analysis of two maternal ketosis models revealed diminished nephron numbers at birth and in adulthood, indicative of impaired kidney development. Long-term consequences included compromised kidney function in adulthood. Examination of gene expression profiles in nephron progenitor cells unveiled decreased proliferation and downregulation of the Myc pathway, alongside an increase in an inflammatory response. These findings were corroborated by immunofluorescent staining, qPCR validation, and western blot analysis. Notably, there was an increase in the expression of genes associated with inflammatory processes, elevated protein levels of P65, reduced levels of the proliferation marker KI67, and decreased Myc protein levels.

Conclusions: This study provides compelling evidence of the adverse effects of maternal ketosis during pregnancy on nephrogenesis and subsequent kidney function in adulthood. Reduced proliferation and diminished Myc signaling within nephron progenitor cells emerge as potential mechanisms for these effects, offering critical insights for pediatric nephrologists in understanding and addressing prenatal factors contributing to chronic kidney disease susceptibility.

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POPULATION SURVEILLANCE STUDY IN WALES OF INFANTS PRESENTING WITH LOW SODIUM AND HIGH POTASSIUM

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Aims/Purpose: Infants presenting with life threatening hyponatraemia and hyperkalaemia present a diagnostic conundrum that can reflect abnormally low aldosterone production such as congenital adrenal hyperplasia, renal resistance to aldosterone associated with infected urinary tract malformations, or single tubulopathy salt wasting gene disorders (pseudohypoaldosteronism). Although incidence figures for individual conditions are available, no overall data exists for its presentation and causes. We aimed to report the incidence, aetiology and outcome of infants presenting with hyponatraemia and hyperkalaemia.

Methods: Prospective population-based surveillance study over 24 months (July 2021 to June 2023). Cases were identified though monthly Welsh Paediatric Surveillance Unit emails to all paediatricians in Wales (population 3.5 million). Hospital biochemists and endocrinologists were also recruited to optimise ascertainment. Inclusion criteria were term infants < 12 months with sodium < 130 mmol/L (< 2.5 SD) AND Potassium > 5.5 mmol/L (> 2.5 SD).

Results: In total 10 cases were identified over two years across Wales. This yields an annual incidence of 1.7 per 10 000 infants/year. There was 99% return rate of monthly surveillance emails. Infants presented at median 14 days old (1 hour to 3 months). 4 were shocked or with > 10% weight loss. All received 0.9% normal saline fluid boluses with only one receiving insulin for hyperkalaemia. Serum sodium and potassium corrected by median one day after admission (range 0-3 and 0-2 days respectively). Eventual diagnoses were: 3 congenital adrenal hyperplasia, 4 transient pseudohypoaldosteronism (3 with urinary infection and urinary tract malformation), 1 maternal hyponatraemia, 2 transient electrolyte imbalance. Patients were discharged after median 6 days (range 3-17). One infant represented after one week with a seizure with normal neuroimaging. No deaths occurred.

Conclusions: In this first ever population surveillance study, infants presenting with low sodium and high potassium were rare. Normalisation of biochemistry was rapid and short-term outcome favourable.

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GENOTYPE PHENOTYPE CORRELATION IN RENAL AND GONADAL DISEASES OF PATIENTS WITH WT1 GERMLINE VARIANTS: RESULTS FROM THE FRENCH GONADVENIR'S STUDY

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Aims/Purpose: Germline variants of WT1 are known to generate kidney and gonadal diseases, including variation in genital development (VGD), chronic kidney disease and early kidney and gonadal tumors. The genotype phenotype correlation in renal disease has already been described opposed to gonadal disease but never in a large cohort as GONADVENIR.

Methods: GONADVENIR is a French national, retrospective, observational study designed to investigate, the gonadal function over time in a wide cohort of patients with WT1 germline variants, but also the genotype phenotype correlation in renal and gonadal diseases according to variant and genetic groups designed thanks for the literature knowledge.

Results: Eighty patients were included, at a median age of 14.2 +/-5 years. Among those, 33 (41.3%) had a missense variant of exon 8 or 9 (MS E8-9) corresponding to Denys-Drash Syndrome, 24 (30%) had a variant generating WT1 truncated protein (TP), 14 (17.5%) had a donor splice site variant of intron 9 (DSS I9) with Frasier Syndrome, and 9 other rare variants. More than 90% were diagnosed with WT1 disease before 5 years old. The median age of renal disease onset was 1 year (0.4-2.4), respectively 0.7 years (0.1-1.4) in MS E8-9 group, mostly (73%) with congenital (CNS) or early steroid-resistant nephrotic syndrome (SRNS), 1.2 years (0.7-1.6) in TP patients, mainly with Wilms' tumor (83%) and significantly later : 4.5 years ($p < 0.0001$) in patients with DSS I9 variant, mostly with SRNS (64%) or proteinuria (23%)In addition, 35 patients (43.8%) developed Wilms tumor, at a median age of 1.3 years (0.8-1.8), 26.3% from the TP group with 87.5% patients concerned against 12.5% from MS E8-9 with only 30% patients concerned ($p < 0.0001$). Histologically, among patients with kidney biopsy, 25% had focal and segmental glomerulosclerosis (FSGS) and 61% diffuse mesangial sclerosis (DMS). Finally, 6 patients (7.5%) had CAKUT without variant predisposition observed. Regarding gonadal disease, 95% of XY patients had VGD, significatively more severe in MS E8-9 and DSS I9 groups ($p = 0.01$) than in TP group, as gonadal function impairment happened earlier and inversely correlated to the Wilms tumor risk. Furthermore, 39% of XX patients had uterine malformation including 72% of MS E8-9 XX population, appearing like a protector factor against gonadal function impairment ($p = 0.02$).

Conclusion: WT1 germline variants generate, rather than syndromes, a spectrum of renal and gonadal damages. Our study is the largest cohort reported to date and contributes to a better knowledge of the genotype-phenotype correlation, which may help practitioners to better understand their patients' diseases and provide a more individualized follow-up according to their genetic variant.

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GONADAL FUNCTION IN PATIENTS WITH GERMLINE VARIANTS OF WT1 : RESULTS FROM THE FRENCH GONADVENIR'S RETROSPECTIVE STUDY

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Aims/Purpose: Germline variants of WT1 are known to generate kidney and gonadal diseases, including variation in genital development (VGD), chronic kidney disease and early kidney and gonadal tumors. However, the state of gonadal function, its evolution over time, and the impact of WT1 disease on puberty and fertility in this population have never been studied.

Methods: GONADVENIR is a French national, retrospective, observational study designed to investigate, the gonadal function over time, according to karyotype and genotype, in a wide cohort of patients with a germline variant of WT1.

Results: Eighty patients were included, at a median age of 14.2 +/- 5 years. 30% had XX karyotype, 95% of whom were female and 39% had uterine malformation (moderate VGD). 70% had XY karyotype, 14% of whom were female, 27% male with or without bilateral cryptorchidism and 59% non-female with severe or moderate VGD. 30% of XX and 87% of XY patients had gonadal dysgenesis and 3 developed gonadal tumors. 94% of XX and 60% of XY patients had spontaneous non delayed onset of puberty. 57% of XY patients were treated primarily or secondarily with hormonal replacement treatment (HRT). 90% of patients in the cohort had gonadal disease by the age of 15, 67% had impaired gonadal function at the age of 12.6 and 83% at the age of 16.2 years old. Gonadal function impairment was significantly earlier in XY patients than in XX, in XY patients with severe VGD/DSD and XY patients with a missense variant of exons 8 or 9 (MS E8-9) compared with patients with a truncating variant (TP), who develop more moderate gonadal disease inversely correlated with the development of nephroblastoma. There was no significative difference in proportion of gonadal failure between patients with renal insufficiency prior or after gonadal failure (p-value = 0,37) and there was less gonadal failure in patients transplanted before the appearance of gonadal failure (p-value < 0,0001). In addition, increased FSH, LH and decreased AMH and Inhibin B are observed with or without gonadotoxic treatment in most of patients as soon as childhood or onset of pubertal time.

Conclusion: In conclusion, patients with a germline variant of WT1 are mostly affected by early gonadal insufficiency of variable severity depending on karyotype and genotype. Patients and their practitioners are largely misinformed about the impact on fertility and sometimes on initiation of physiological puberty. Regular follow-up by an endocrinologist, from the average physiological age of puberty onset is essential for both XY and XX patients, as well as providing clear information about gonadal function and fertility, and evocating fertility preservation and risk of transmission.

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LONG-TERM KIDNEY OUTCOME FOR WILMS TUMOR: A RETROSPECTIVE COHORT STUDY

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Aims/Purpose: Wilms tumor is the most common kidney tumor of young children. The survival rate of children with Wilms tumor is higher than 90%, however, most children end up with an important kidney parenchyma loss. It is known that patients with a decreased nephron mass may be subject to hyperfiltration injury leading to proteinuria, hypertension and CKD. To date, there are limited data on the long-term kidney outcome after treatment of Wilms tumor and no clear recommendation for follow-up. However, early identification of individuals with reduced kidney function increases the opportunity for interventions aiming to preserve kidney function and to reduce the morbidity and mortality associated with CKD. Our goal is to assess the kidney outcome after treatment for Wilms tumor in order to guide surveillance recommendations in our population, prevent kidney disease and optimize long-term health.

Methods: We retrospectively identified all patients presenting with a diagnosis of Wilms tumor at University Hospital of Leuven from October 1976 until December 2003. Patient demographics, tumor-related characteristics and data to evaluate kidney function at presentation and at last follow-up were collected.

Results: We included 40 patients. At diagnosis, patients have a median age of 3.5 years. 57% of patients are female. 95% of patients have unilateral Wilms tumor and 7 patients have metastasis. We assessed blood pressure and kidney function with more than 15 years mean follow-up. One patient has kidney failure and 26% of patients have an eGFR < 90 mL/min/1.73 m^2. The most common comorbidity is hypertension: 45% of patients have hypertension stage 1 or 2 and 10% of patients are taking antihypertensive medication. 8% of patients have proteinuria.

Conclusion: In our study, a notable number of Wilms tumor survivors have signs of kidney function impairment. Given the excellent survival rate of patients with Wilms tumor, it is essential to prevent and slow down the progression to CKD in order to improve morbidity and mortality. To achieve this goal, patients with risk factors of progression must be detected early to start nephroprotective measures. Therefore, we are convinced that patients need to be seen in pediatric nephrology to make them aware of the related risks. We suggest an annual screening at pediatric oncology with blood pressure measurement, urine and blood analysis and at least two counselling visits by a pediatrician nephrologist. Annual follow-up should be maintained on the very long term.

SESSION 1

NEWS IN NEPHROTIC SYNDROME

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EFFICACY OF PEGCETACOPLAN IN CHILDREN WITH C3 GLOMERULOPATHY

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Aims/Purpose: C3 glomerulopathy (C3G) is a rare chronic kidney disease caused by a dysregulation of the alternative complement pathway leading to glomerular deposition of complement component 3 (C3) followed by inflammation and tissue damage. Pegcetacoplan is an inhibitor of both C3 and of its active fragment C3b, that can prevent their glomerular deposition. A phase III registration protocol is currently ongoing in patients (adolescents and adults) with C3G, with promising results. Herein we describe our recent experience with Pegcetacoplan in 5 pediatric patients with C3G.

Methods: This retrospective, observational study presents the efficacy and safety of Pegcetacoplan in pediatric patients with biopsy proven C3G over a 12-week treatment period. The drug was administered subcutaneously, twice a week for the first month, then weekly. The primary endpoint was the change in urinary protein-to-urinary creatinine ratio evaluated by the mean of 3 samples collected on different days before each visit at baseline, 8 and 12 weeks. The changes in serum C3, albumine, creatinine and urinary erythrocytes (number/µL) were also evaluated.

Results: Detailed results are shown in Table 1. Median C3 level increased of more than 600% while proteinuria decreased to 30% of baseline value. Some of the patients with decreased renal function exhibited an improvement of eGFR. No adverse event has been recorded except for some transient discomfort at the injection site.

Table 1

Patient	Gender	Age at diagnosis (Yrs)	Age at Peg (Yrs)	C3 (mg/dl)		eGFR (ml/min/1.73m2)		Proteinuria (mg/mg)		sAlbumin (g/dl)		Urinary RBC (n/microL)	
				Wk0	Wk12	Wk0	Wk12	Wk0	Wk12	Wk0	Wk12	Wk0	Wk12
1	M	7.6	12.5	45	364	26	41	7.7	2.8	1.8	3.9	1380	29
2	F	2.2	13.1	113	429	45	46	3.5	3.4	3.8	3.5	65	40
3	F	19.1	20.0	67	335	45	46	5.0	1.3	3.0	4.0	395	27
4	M	9.0	10.8	28	222	104	114	3.5	1.3	3.7	4.4	99	41
5	F	8.7	9.5	18	185	63	61	7.1	1.5	2.3	3.6	425	315

Conclusion: All our patients showed a rapid over-normalization of the C3 levels, a significant reduction of proteinuria and a significant increase in albuminemia. We think that the present case series, although small and with a short follow up period, may be important to support other physicians to consider this treatment as an opportunity for their C3G patients.

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SAFETY OF OBINUTUZUMAB IN PEDIATRIC STEROID-DEPENDENT AND FREQUENT-RELAPSING NEPHROTIC SYNDROME

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Aims/Purpose: B-cell depletion with rituximab has become increasingly used to treat children with steroid-dependent or frequently relapsing nephrotic syndrome (SD/FRNS), with a relatively safe profile. Obinutuzumab (OBI) is a 2nd generation anti-CD20 antibody, initially designed to overcome resistance or intolerance to rituximab in B-cell malignancies. OBI is currently under evaluation in two randomized controlled trials (RCT) in pediatric SD/FRNS (NCT05786768, NCT05627557), but data on short- and long-term adverse events are still scarce in children. The aim of this study is to report side effects after OBI in a large cohort of patients with SD/FRNS.

Methods: Retrospective monocentric study at Robert-Debré Hospital, Paris, France including all children with SD/FRNS treated with at least one infusion of Obinutuzumab between April 2018 and March 2024. The Infusion protocol included premedication with paracetamol, methylprednisolone and dexchlorpheniramine, pneumocystis prophylaxis and a routine monthly monitoring of immunoglobulin levels and white blood cell counts until B-cell repletion.

Results: We analyzed 168 infusions in 99 patients, including 109 low-dose infusions (300 mg/1.73m2) and 59 standard dose infusions (1000 mg/1.73m2). B-cell depletion was achieved in all patients after one infusion, including 17 with anti-rituximab antibodies. No serious adverse event occurred during infusions while mild infusion-related reactions were reported during 38 (23%) infusions in 35 patients, mainly digestive symptoms (12.5%), headache (3.6%) or fever (3.6%). No case of serum sickness disease were reported. Neutropenia < 1000/mm3 was reported in 12 patients, at median delay of 3.7 months. Severe infectious complications were pneumonia in 3 patients (including 1 related to COVID) and 1 case of sepsis secondary to panaritium during severe neutropenia. Reversible Acute-Lung-Injury occurred in 1 patient. There was no correlation between low vs standard dose and the occurrence of these adverse events.

Conclusion: This study reports on the tolerance profile during and after Obinutuzumab in a large cohort of children with SD/FRNS treated with a single low- or standard-dose infusion. These results suggest a relatively safe profile, comparable to that of rituximab, supporting the use of obinutuzumab in case of failure and/or intolerance to rituximab in children.

1254

EFFICACY AND SAFETY OF ORAL TOLVAPTAN VERSUS INTRAVENOUS FUROSEMIDE IN CHILDHOOD NEPHROTIC SYNDROME WITH EDEMA - AN OPEN LABELLED RANDOMISED CONTROLLED TRIAL

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Aims/Purpose: To evaluate the efficacy and safety of oral tolvaptan versus intravenous (IV) furosemide in nephrotic syndrome (NS) patients with oedema aged 5 to 14 years.

Methods: This prospective, open-label superiority trial was conducted from October 2022 to October 2023. Children of NS aged between 5 and 14 years with moderate to severe oedema who did not respond to oral furosemide for up to 24 hours (< 3% weight loss or urine output < 1 ml/kg/hour) were enrolled. Patients were stratified based on disease course (steroid sensitive or steroid resistance). Variable block randomization in a 1:1 ratio was done using computer-generated random numbers to receive oral tolvaptan or IV furosemide over 48 hours. Efficacy was assessed primarily by urine output (ml/kg/hr) over 48 hours. Percentage of weight loss, trends of serum sodium, serum osmolality and urine osmolality were also observed along with adverse effects. Data were analysed using standard statistical tests on the intention-to-treat model.

Results: Of the 209 children with oedema, 112 patients were excluded. While on furosemide therapy, 58 patients with weight loss of < 3% and/or urine output < 1 ml /kg/hr over 48 hr were included in the study. This was a superiority trial where the calculated sample size was taken as 35 in each arm; however, till now, only 29 patients could be enrolled in each arm. No patient was lost to follow-up. The median (IQR) age of the study group was 69.5 (64-96) months. There were 31 (53.4%) boys. The median (IQR) of urine output over 48 hours in the furosemide group was 2.25 (1.8-2.4) ml/kg/hr as compared to 2.31 (1.7-2.7) ml/kg/hr in the tolvaptan group and the difference was not significant (p =0.689). The mean difference between the two groups was 0.07 mL/Kg/hour, with a 95% CI of -0.25 to 0.39 mL/kg/hr, indicating that at worst, tolvaptan will underperform furosemide by only 0.25 mL/Kg/hr which is indicative of comparable response between two arms. The difference in the weight loss percentage was not statistically significant between the two groups. There was a significant increase in serum sodium levels and increased serum osmolality in the tolvaptan group. On the contrary, urinary sodium excretion and urinary osmolality were significantly decreased in tolvaptan with higher free water clearance. Two patients in the tolvaptan group developed hypernatremia and two mild transaminitis. The incidence of life-threatening hypokalemia requiring IV correction was much higher in the furosemide group.

Conclusion: A comparable response of monotherapy with tolvaptan for diuresis and weight loss in children with NS as to the widely used IV furosemide regimen with the advantage of fewer episodes of life-threatening hypokalemia was seen. Tolvaptan also has the added benefit of earlier correction of hyponatremia, which is a frequent electrolyte disturbance in NS. While the therapy is safe, careful monitoring of serum sodium is essential.

1389

CORD-BLOOD DERIVED MESENCHYMAL STROMAL CELLS FOR THE TREATMENT OF CHILDREN WITH STEROID-DEPENDENT NEPHROTIC SYNDROME: RESULTS OF AN OPEN LABEL PHASE II STUDY

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Aims/Purpose: The management of children affected by steroid-dependent nephrotic syndrome (SDNS) requires prolonged doses of steroids or other immunosuppressive (IS) drugs with a major impact on the quality of life. Mesenchymal Stromal Cells (MSCs) are multipotent non-hematopoietic stem cells with proven immunomodulatory activity.

Methods: We designed an open label, single-arm, phase 2 trial to evaluate the efficacy of cord-blood derived MSCs (CB-MSCs) in maintaining remission in children with SDNS. We planned to enroll 11 children with SDNS, aged 3-18 years, in remission for > 6 months with IS therapy. Patients received 3 intravenous infusions of CB-MSCs at the dose of 1.5 x 106/kg at a time interval of 1 to 2 weeks. IS has been tapered by 50% at each administration, with complete withdrawal after the 3rd administration. The primary endpoint was relapse-free survival 6 months after IS discontinuation. A planned interim analysis at the end of the first part failed to meet the efficacy threshold (remission rate < 4/11 patients) and an anticipated rescue phase was implemented. In the second part with the same sample size, IS treatment was tapered off with complete withdrawal before the 1st infusion. Patients received 3 CB-MSCs infusions at the dose of 2 x 106/kg at a time interval of 1 to 2 weeks. Children in remission at the first follow-up, received a 4th infusion. A historical population of SDNS children, tapering IS according to standard care and with a follow-up > 12 months, served as control.

Results: Population. In the first part, 9 patients (7 males), with a median age of 6 years (IQR 5-13) were enrolled. Enrolled patients had been previously treated with a median of 3 lines of IS therapy (IQR 2-4) and 7 (77.8%) were on combined IS therapy. In the second part, 11 patients (7 males) with a median age of 11 years (IQR 10-13.5) were enrolled. These patients had been previously treated with a median of 2 IS drugs (IQR 1.5-3). 5/11 (45.4%) were on combined IS therapy. Primary endpoint: In the first part, 7/9 (77.8%) patients relapsed within 6 months after IS withdrawal. At the 12 months follow-up, relapses were reported in 8/9 patients (88.8%). In the second part, 9/11 (81.8%) patients were in remission at the first follow-up visit and received the 4th CB-MSCs infusion. 5/11 (45.4%) patients were in remission 6 months after IS discontinuation. Twelve months after IS withdrawal, 7/11 (63.6%) patients had experienced at least a relapse, with 3 children having multiple relapses. No treatment-related adverse events were reported. From the revision of all digital medical records, 95 SDNS patients (56 males) were selected as historical controls.

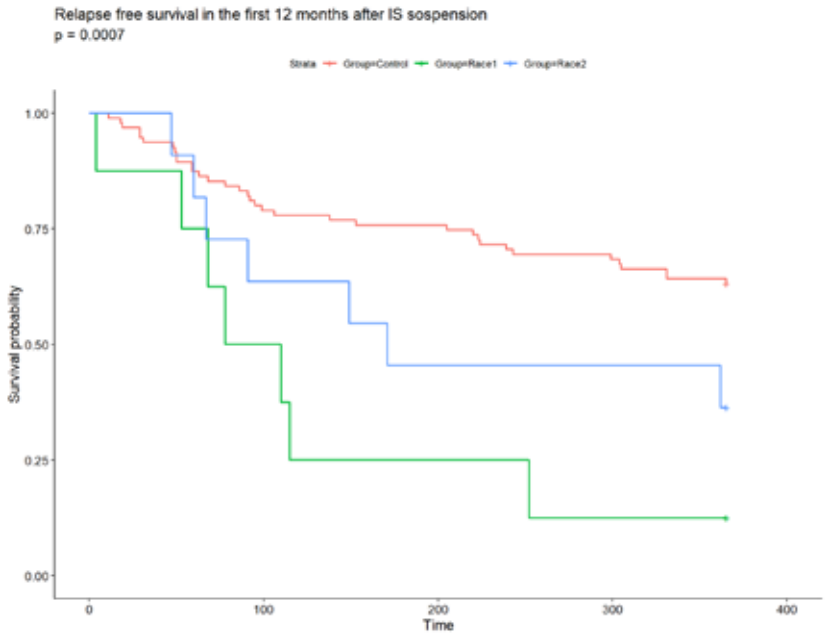

Figure 1 shows the relapse free survival of SDNS children enrolled in the 3. Despite the prolonged IS, relapse-free survival was better in controls (p = 0.0007).

Conclusion: In children with SDNS, a novel therapy with CB-MSCs was not able to maintain remission 6 months after IS withdrawal.

1025

MANAGEMENT EXPERIENCE IN NEPHROTIC SYNDROME DIAGNOSED IN THE FIRST YEAR OF LIFE

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Infantile nephrotic syndrome (iNS) is defined by the presence of nephrotic range proteinuria, hypoalbuminemia with or without intrauterine edema in the first year of life. If it appears in the first 3 months of life it is denominated congenital nephrotic syndrome with the most frequent cause being a genetic mutation affecting the podocyte, although it can also be caused by congenital infections or autoimmune conditions. The aim of our study was to describe the initial treatment and long-term prognosis of children with a clinical or genetic diagnosis of congenital or infantile nephrotic syndrome between 1973 and 2023 in our centre.

A descriptive, retrospective study by chart review was conducted.

There were 29 patients (18 females/11 males) with a median age at diagnosis of 13 days (IQR 88.25). Thirteen had a mutation in NPHS1 (Finnish type, NSf) and 16 other mutations (non-Finnish type, NSnf): WT1 (4), PLCE1 (3), LAMB-2 (2), NPSH2 (1), 2 had negative genetic testing, 4 unknown. Fourteen (61% NSf and 37% NSnf) required periodic infusions with IV albumin. Pre-transplant nephrectomy was performed in 8 patients (5 NSf and 3 NSnf) at a median age of 1.2 years (IQR 3.02), 2 children underwent nephrectomy at the time of transplantation and another 2 after transplantation. The median age of dialysis initiation was 2.4 years (IQR 2.3, 0.7-4.6) in NSf and 0.85 (IQR 2.29, 0.03-14.2) in NSnf (p 0.39). Median time on dialysis until transplantation was 6 months in NSf vs. 17 months in NSnf ($p < 0.005$). Eighteen patients received a renal transplant, at a median age of 2.56 years (IQR 1.93) in NSf and 3.57 (RIQ 3.97) in SNnF (p 0,14), 9 in each group. There were no differences in graft survival, neither between both groups nor comparing with our overall sample. Nine children died: 2 NSf and 7 NSnf. Three died before 3 months of age, and another 3 due to post-transplant complications.

INS is a therapeutic challenge and requires a multidisciplinary management. Although mortality was high in the first months, especially in tNSnf, after transplantation patient and graft survival was satisfactory. 2/3 of the children did not require nephrectomy prior to transplantation.

1074

SERUM TUMOUR NECROSIS FACTOR-ALPHA AS A MARKER OF DISEASE ACTIVITY IN CHILDREN WITH NEPHROTIC SYNDROME

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Aims/Purpose: Idiopathic nephrotic syndrome (NS) is a common glomerular disease in children; however, the exact pathogenesis of the disease remains unknown. There is evidence of immune dysfunction in steroid-sensitive NS patients. Studies have shown that tumour necrosis factor-alpha (TNF-), a proinflammatory cytokine, plays a significant role in the pathogenesis of NS. The literature lacks sufficient data to establish the relationship between TNF- and NS. Our study evaluated the relationship between TNF- level at initial presentation and response to steroid therapy in children with idiopathic NS.

Methods: This prospective study was conducted on children aged 1 to 14 years diagnosed with idiopathic NS. Children with secondary NS or deranged renal function at diagnosis and an estimated glomerular filtration rate of < 60ml/minute/1.73m2 were excluded. All enrolled individuals were followed up from disease onset or relapse of NS until remission or at least 42 days with steroid therapy if remission was not achieved. Serum TNF- levels were measured at presentation and remission or after 42 days of steroid therapy if remission was not achieved. The role of TNF- levels in response to steroid therapy in NS was also assessed.

Results: One hundred and twelve children (68% boys) with idiopathic NS were enrolled. The median age (IQR) at enrollment was 58.5 (37-84.7) months, while the median age at symptom onset was 47.5 (24-60.7) months. The median TNF- level at presentation was 7.5 (3.5-12.1) pg/mL, and that at remission was 5.25 (1.62-8.8) pg/mL. The median TNF- levels among first-episode NS at presentation were 3.98 pg/mL and 1.88 pg/mL (p =0.04) at remission, whereas in steroid-resistant NS (SRNS), it was 6.59 pg/mL at presentation and 9.02 pg/mL at 42 days (p =0.45). The mean fall in TNF- levels among remission cases was 9.1(-14.7 to 149.6) pg/mL versus 2.27 (-0.4 to 5.4) pg/mL in SRNS cases. There was a significant negative correlation between the duration of steroid therapy and TNF- levels, with a correlation factor of -0.021 and R2 of 0.154 (P =< 0.001).

Conclusion: Serum TNF- levels decrease with steroid therapy in children with steroid-sensitive NS, which correlates clinically with the achievement of remission. These findings suggest that TNF- may play a role in glomerular dysfunction and proteinuria in NS. Identifying TNF- as a biomarker for disease activity can benefit patients by identifying more tailored therapeutic approaches.

Keywords: Children, Nephrotic syndrome, Tumour necrosis factor-alpha

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RISK FACTORS FOR SPONTANEOUS RESOLUTION VERSUS PERSISTENCE OF CHILDHOOD IDIOPATHIC NEPHROTIC SYNDROME- A POPULATION-BASED STUDY

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Aims/Purpose: Childhood idiopathic nephrotic syndrome (INS) responds to corticosteroids (CS), but tends to relapse, requiring steroid sparing agents (SSA), until a long-standing treatment-free remission evolves in most patients. We aimed to determine the duration of illness in childhood INS, the age of the last relapse and its possible relation to puberty.

Methods: Children (age 2-10 years) with a new INS diagnosis and a CS prescription between 2000-2010 were included and followed until March 2024 based on computerized medical records database. Disease length was determined as the period between last and first CS or SSA prescription. "Single episode" was defined as CS treatment for < 6 months without a subsequent prescription. A state of less than 1 year follow up since the last prescription was defined as "disease continuation".

Results: Out of 1,669,977 eligible children, 887 were diagnosed with NS, but 608 also received CS at diagnosis and comprised the study group. A single episode occurred in 84 (14%) patients. In the remaining 524 [347 (66%) of them males], diagnosis age was 4.8 ± 2.2 years. SSA were prescribed to 182 (35%). Median (IQR) CS or SSA purchases count was 21 (11-48). Comparing the first 3 with the 4th quartile for purchases [n = 132 (25%)], the latter had longer disease course and older age at last relapse (13.3 ± 5.7 vs 6.4 ± 5.3 and 17.9 ± 6.3 vs 11.3 ± 5.9 years respectively, $p < 0.001$), more SSA use (78.8% vs 20%, $p < 0.001$), without difference in diagnosis age or male: female ratio. At the end of follow up period (15.5 ± 5.1 years) 113 (21.6%) continued to relapse at an average age of 19.3 ± 6.3 years. In the others (n = 409), last relapse age was 11.2 ± 5.7 years, close to the age of pubertal stage 2. There was no difference between males and females (11.2 ± 5.7 vs 11 ± 5.5 years, p =0.62).

Conclusion: In this population-based study, NS remission occurred around pubertal stage-2 age in most cases. A fifth of the patients continued to relapse into adulthood. More studies are needed to determine the factors related to spontaneous long-term NS remission.

SESSION 2
ADVANCES IN DYALISIS

1322

TIMING AND CHOICE OF KIDNEY REPLACEMENT THERAPY IN CHILDREN AND ADOLESCENTS

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Aims and Purpose: The optimal time to initiate kidney replacement therapy (KRT) cannot be clearly defined. In everyday clinical practice, clinical parameters, feasibility, family preferences and clinicians´ attitudes will influence the decision. In addition to the timing, these issues will also influence the modality of KRT. We investigated the factors associated with KRT modality and timing in the multicenter, multinational prospective pediatric 4C cohort study.

Methods: 695 pediatric chronic kidney disease patients enrolled into the 4C study at age 6 to 17 years with estimated glomerular filtration rate (eGFR) 10 to 60 ml/min/1.73 m2 were investigated. Competing risk regression was performed to identify factors associated with initiation of dialysis or preemptive transplantation (Tx), including primary renal diagnosis, demographic data, clinical and laboratory parameters.

Results: During the 8-year observation period, 342 patients (49%) started KRT. Dialysis was the first KRT in 200 patients, whereas 142 patients underwent preemptive Tx. eGFR at initiation of KRT did not differ in children who started dialysis (11.8 ml/min/1.73 m2) from those who underwent preemptive Tx (11.1 ml/min/1.73 m2). A lower eGFR at enrolment (HR (hazard ratio) 0.76 [95% confidence interval 0.74-0.78], a steeper eGFR slope (HR 0.90 [0.85-0.95] and a higher systolic blood pressure standard deviation score (SDS) (HR 2.07 [1.49-2.87]) increased the likelihood of KRT initiation. Patients with glomerulopathies were more likely to start dialysis than children with CAKUT (HR 3.81 [2.52-5.76]). Lower BMI SDS (HR 0.73 [0.6-0.89]) and lower hemoglobin (HR 0.8 [0.72-0.9]) were associated with higher likelihood of dialysis. Patients with tubulointerstitial diseases were more likely to receive a pre-emptive Tx than CAKUT patients (HR 1.79 [1.11-2.88]). A significant center effect was observed, accounting for 6.8% (dialysis) to 8.7% (pre-emptive Tx) of explained variation.

Conclusion: We observed that next to eGFR and the rate of eGFR loss, underlying diseases and CKD related factors like anthropometrics, blood pressure and anemia influence the decision of modality and of the time point to start KRT in children.

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THE BENEFITS OF ICODEXTRIN USE FOR CHRONIC PERITONEAL DIALYSIS - DATA FROM PEDIATRIC PERITONEAL DIALYSIS NETWORK (IPPN) REGISTRY

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Aim: Experience on icodextrin use in children on chronic peritoneal dialysis (PD) is limited. We describe international icodextrin prescription practices and their impact on clinical outcomes.

Methods: Icodextrin was prescribed in 783 (18%) of 4439 patients enrolled in the prospective IPPDN Registry between 2007-24. Volume status, technique survival and peritonitis rates were assessed in 312 patients with icodextrin use for > 6-months. Icodextrin users and non-users (glucose-based dialysate) were propensity score matched based on demographics, region, etiology, urine output, and dialysis vintage. We compared outcomes in icodextrin users and non-users, and also in patients who started icodextrin early (within 1-yr of PD start) and late (> 1-yr).

Results: Icodextrin use varied across regions, ranging from 61% in Western Europe to 21% in East and Central Europe, and was associated with older age, glomerular disease, longer dialysis vintage, lower urine output, and higher membrane transport characteristics ($p < 0.001$ for all). Next, we compared a matched cohort of 245 icodextrin users and non-users with > 6-mo follow-up, having similar rates of hypertension, ultrafiltration (UF), glucose exposure and biochemical parameters at baseline. Over a median follow-up of 2.3 (1.4, 3.7) yr, icodextrin users showed a positive linear increase in UF adjusted for body surface area (= 2.5 ± 0.8; $p = 0.004$) and reduction in diastolic BP SDS (= -0.5 ± 0.2; $p = 0.003$) compared to icodextrin non-users. Change in glucose exposure, urine output, biochemical parameters, risk of peritonitis and technique failure were similar in both groups. At the time of starting icodextrin, 120 "late starters" (median 1.7, IQR 1.2, 0.5 yr) were significantly stunted, had lower albumin, higher PTH, higher phosphate binder and lower diuretic use ($P < 0.001$, for all), compared to 192 "early starters" (median 0.2 IQR 0.1, 0.5 yr). Both groups were similar in age, sex, ethnicity, disease etiology, prevalence of hypertension and glucose exposure ($P > 0.5$, for all). After median 1.5-yr of icodextrin use, 'late-starters" had significantly more uncontrolled hypertension (38% vs. 20%; $P < 0.001$) and anti-hypertensive agent requirement (68% vs. 55%; $p = 0.03$), increase in glucose exposure from baseline (median 5.4 vs. 4.8 gm/kg/day; $p = 0.05$) without an improvement in UF rates, and trend towards a higher incidence of peritonitis (0.27 vs. 0.37/person-years; $P = 0.06$). Adjusting for demographics, region, etiology and PD vintage, late-start was independently associated with increased risk of technique failure (HR 4.72, 95% CI 1.35-16.6; $p = 0.02$).

Conclusions: Icodextrin use varied across regions, with preference for early icodextrin use in Western Europe. Early use of icodextrin was independently associated with improved volume status and an almost 5-fold greater technique survival.

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INCIDENCE AND MANAGEMENT OF CULTURE-NEGATIVE PERITONITIS IN CHILDREN ON CHRONIC PD: INSIGHTS FROM THE INTERNATIONAL PEDIATRIC PERITONEAL DIALYSIS NETWORK (IPPN) REGISTRY

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Purpose: To assess the incidence and treatment outcomes of peritoneal dialysis (PD) associated culture-negative peritonitis (CNP) in children.

Methods: Analysis of peritonitis episodes reported to the IPPN registry between 2007 and 2023. Outcome parameters include full functional recovery as defined by PD continuation without ultrafiltration problems, adhesions or uncontrolled infection, PD discontinuation and peritonitis relapse rate.

Results: Of 2589 peritonitis episodes, 781 (30%) were culture-negative, with an incidence of 0.1 per patient year. The fraction and incidence of CNP assessed in 50 centers reporting > 10 peritonitis episodes and > 20 pt year observation time varied significantly between centers (range 0-87% and 0 to 0.41/yr, respectively) and world regions, being lowest in North America (15%, 0.07/yr) and highest in Latin America (LA) and Turkey (43/40%, 0.18/0.16/yr; NA vs. LA/Turkey all $p < 0.0001$). The cumulative treatment duration was shorter than 14 days (median 10, IQR 8-12 days) in 91, 14 days in 418 and longer than two weeks (median 20, IQR 17-21 days) in 272 episodes. Full functional recovery /FFR) was achieved in 71%, 91% and 86% for ' < 14', '14' and ' > 14' days, respectively ($p < 0.0001$, adjusting for age and disease severity at onset). PD was discontinued in 11%, 2.6% and 4.8% for ' < 14', '14' and ' > 14' days, respectively ($p = 0.007$, adjusted for age and disease severity). 82 (11%) episodes were followed by relapse (59% again culture-negative, 23% gram-negative, 15% gram-positive, 2% fungal and 1% multiple organisms), without significant differences between treatment duration groups. In 318 episodes treated for 14 days, empiric therapy with either vancomycin/ceftazidime (n = 180) or cefazolin/ceftazidime (n = 138) was applied. In 276 (87%) of these, the initial antibiotic scheme was continued unchanged after receiving negative culture results. Among these cases, FFR was observed in 94% of vancomycin and 90% of cefazolin treated episodes ($p = 0.19$). PD was discontinued in 1 vancomycin and in 3 cefazolin treated episodes ($p = 0.24$). 14% of vancomycin and 11% of cefazolin treated episodes were followed by relapse ($p = 0.32$). In 42/318 patients cefazolin was changed to vancomycin and 9 from vancomycin to cefazolin, with full functional recovery rates 79% vs, 67%, $p = 0.45$ and 1 PD discontinuation and in each group. 6 relapses were reported in patients who were switched from cefazolin to vancomycin.

Conclusions: Rates of culture-negative peritonitis are still common, particularly in lower resource areas and show significant regional and center-related variation. Antibiotic treatment of gram-negative peritonitis should not be shortened to below 14 days. Since similarly good outcomes were observed with vancomycin and cefazolin, in view of emerging antimicrobial multiresistance the latter should be considered once culture-negative results are obtained.

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EUROPEAN SURVEY ON PEDIATRIC LONG-TERM HEMODIALYSIS FACILITIES

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Introduction: Pediatric hemodialysis (HD) is a constantly evolving practice. However, clinicians' resources are not always adapted to pediatric use. We therefore feel it is important to take stock of the situation of pediatric HD across Europe. We wanted to describe the activity, the human and material resources available for pediatric HD in Europe in 2021-2022, with the aim of improving practices and equipment availability.

Method: Data were collected via a validated questionnaire about HD centres' infrastructure and staff, patients' demographics and HD-specific details describing dialysis practices over a 2-year period. A national representative was identified from all European countries with the support of ESPN and each national society. These representatives sent out the questionnaire to all centers practicing long-term pediatric HD in their countries.

Results: We obtained responses from 85 centers in 32 countries, among the 183 European pediatric HD centers identified. One-fifth of these centers were mixed adult-pediatric. Ultrapure water was available in 86% of centers and there was a median of five in center dialysis station per facility. 10% and 4% of centers offered home HD and nocturnal HD respectively. At the time of the survey, these centers were caring for 504 children, with a median number of five dialyzed children per center. Half of children weighed less than 20 kg at HD start in the two studied years and 55% of centers were faced with a child weighing less than 10 kg in the same period. At the time of the survey, an arteriovenous fistula was used in 43% of children, hemodiafiltration mode was used in 53% and 19% of children dialysed more than three time a week. As far as equipment is concerned, Fresenius 5008 and 6008 were the devices most frequently present in the units: in 62 and 30% of the centers respectively, while Medcomp has a monopoly on the European market for pediatric double lumen long term HD catheters at the date of the survey. In addition to HD, other extra-corporeal purification technique offered were plasmapheresis (97%), immunoadsorption (53%) and LDL apheresis (40%).

More than half of practitioners surveyed felt that available equipment (devices and catheters) was not optimal for pediatric HD, particularly for children weighing less than 10 kg. Our results showed also that HD centers differ in terms of HD anticoagulation and dialysate baths.

Conclusion: Our study describes infrastructure, staff and activity of 85/183 (46%) pediatric HD centres in Europe. These centers are heterogenous and half of practitioners felt that available devices and catheters are not optimal for children. Pediatric HD is a rare treatment with a median of five children per-center and children median weight at HD start is 20 kg.

Acknowledgements

We would like to thank all colleagues who have already participated in the survey and the members of EPDWG.

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ASSOCIATION OF EARLY ACUTE KIDNEY INJURY AND POSITIVE RENAL ANGINA INDEX SCORE WITH THE NEED FOR CONTINUOUS KIDNEY REPLACEMENT THERAPY AND MORTALITY IN PATIENTS WITH INFECTION ADMITTED TO PEDIATRIC INTENSIVE CARE UNIT: A MULTICENTRIC COHORT STUDY

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Aims/Purpose: In the Pediatric Intensive Care Unit (PICU), critically-ill children face a high risk of acute kidney injury (AKI), which greatly increases mortality. Recently, the use of predictive scores has been proposed to detect early onset of severe AKI and associated outcomes. Patients with infection and sepsis are at high risk of renal dysfunction of vary degrees due to the inflammatory process, hemodynamic changes or direct tissue damage. In this study, we examined the relation between early AKI and a positive Renal Angina Index score (RAI ≥8) with mortality and the need for continuous kidney replacement therapy (CKRT) in pediatric patients admitted to the PICU with infection.

Methods: We performed a secondary sub-analysis of data from a prospective, multicenter cohort study involving pediatric patients with infection admitted to nine Italian PICUs between February 2022 and January 2024. We investigated the association between each increase of AKI stage within the initial 24 hours and the requirement for CKRT during the entire hospital stay. Furthermore, we assessed the relationship between a positive RAI score in the initial 24 hours and the development of severe AKI (stage 2 and 3) in the first 48 hours, need for CKRT and mortality.

Results: We enrolled 581 patients with a mean age of 713 days, among whom 22 (4.1%) died. The presence of infection was verified in 370 patients (64%), whereas cultures were negative in the remaining patients. During the first 48 hours, 102 patients (18%) developed AKI, including 34 (33%) with stage 1, 19 (19%) stage 2, and 49 (48%) stage 3. Each increase in the AKI stage during the first 24 hours showed an increased odds ratio (OR) for mortality (2.61 interquartile range [IQR] 1.88-3.83, $p < 0.001$) and need for CKRT (OR 7.73, IQR 4.02-24.29). A positive RAI score was detected in 50 patients (8.6%), and it was associated with an increased risk of severe AKI (OR 12.23, IQR 6.29-23.82), need for CKRT (OR 10.64, IQR 3.58-31.05), and mortality (OR 13.80, IQR 5.55-34.48).

Conclusion: Children admitted to the PICU with infections who develop AKI or have a positive RAI score on the first day of admission have an increased risk of severe AKI, need for CKRT and mortality.

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INDOXYL SULFATE CONTRIBUTES TO IMPAIRED HEIGHT VELOCITY IN (PRE-) SCHOOL CHILDREN

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Aims/Purpose: Growth failure is considered the most important clinical outcome parameter in childhood chronic kidney disease (CKD). Central in the pathophysiology of growth failure is the presence of a chronic pro-inflammatory state, presumed partly driven by the accumulation of uremic toxins. In this study, we assessed the association between uremic toxin concentrations and height velocity in a longitudinal multicentric prospective pediatric CKD cohort of (pre-)school aged children and children during pubertal stages.

Methods: In a prospective, multicentric observational study, a selection of uremic toxin levels of children (0-18y) with CKD stage 1-5D was assessed every 3 months (max 2 years) along with clinical growth parameters. Linear mixed models with a random slope for age and a random intercept for child were fitted for height (in cm and SDS). A piecewise linear association between age and height was assumed.

Results: Data-analysis included data from 560 visits of 81 children (median age 9.4 years; 2/3 male). In (pre-)school aged children (2-12 years), a 10% increase in concurrent indoxyl sulfate (IxS, total) concentration resulted in an estimated mean height velocity decrease of 0.002 SDS/year ($p < .05$), given that CKD stage, growth hormone, bicarbonate concentration, and dietary protein intake are held constant. No significant association with height velocity was found in children during pubertal stages (> 12years).

Conclusion: The present study demonstrated that especially IxS contributes to a lower height velocity in (pre-)school children, while we could not find a role for uremic toxins with height velocity during pubertal stages.

SESSION 3

PRECISION MEDICINE FOR MONOGENIC NEPHROPATIES

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NPHS2 A242V AND E264Q: NOVEL INTERALLELIC INTERACTION-DEPENDENT VARIANTS

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Purpose: NPHS2 is the most frequently mutated gene in monogenic podocytopathies. The encoded podocin, a key component of the slit diaphragm, oligomerizes via two C-terminal oligomerization sites. We have formerly described the first human variant with a mutation-dependent pathogenicity, NPHS2 R229Q. It is only pathogenic when associated to specific 3' variants in trans. Recently, we showed that podocin decreases the distance between neighbouring nephrin molecules, reducing the size of the glomerular pore, that pathogenic R229Q oligomers fail to exert.

To date, apart from R229Q no other NPHPS2 variant is known to be dependent on interallelic interactions in its pathogenicity. Recently, patients with FSGS were found to be compound heterozygous for the pathogenic V260E and a rare benign variant, either A242V or E264Q, raising the possibility that A242V and E264Q become pathogenic when trans-associated to V260E. Therefore, we aimed to explore their potential interallelic interactions.

Methods: To assess the effect of podocin heterooligomers, nephrin constructs tagged with Förster Resonance Energy Transfer (FRET) pairs were transiently coexpressed with HA- and V5-tagged podocin variant(s) in HEK293 cells. FRET efficiency between the tagged nephrin constructs was measured by time-correlated single photon counting in living cells 48 hours after incubation. We formerly showed that this method can distinguish pathogenic and benign associations with a high specificity (97%). Their subcellular colocalization was confirmed in podocyte cell culture under confocal microscopy.

Results: In accordance with their benign nature, the wild-type and the E264Q and A242V podocin variants reduced the distance between the nephrin molecules, i.e. increased the FRET efficiency. In contrast, the FRET efficiency was significantly reduced in the presence of the V260E podocin (vs wt: p =4.01 x 10-4), in line with its pathogenicity. The E264Q or A242V podocin variants failed to reduce the nephrin-nephrin distance in the presence of the V260E podocin (p vs. wild-type podocin = 3.78 x 10-6 for both), indicating the pathogenic interaction of a benign and the pathogenic V260E variant. Confocal images confirmed the colocalization of these pathogenic variants in podocyte cell culture.

Conclusion: Besides NPHS2 R229Q, A242V and E264Q are also subjects of interallelic interactions. These benign variants become pathogenic in trans with V260E. This has direct consequences in the therapy and genetic counselling.

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CELLULAR MODELS OF DENT DISEASE 1 FOR TESTING THE THERAPEUTIC POTENTIAL OF CHEMICAL CHAPERONES

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Aims/Purpose: Dent disease 1 (DD1) is a rare X-linked renal tubular disorder caused by CLCN5 gene variants. CLCN5 encodes for the electrogenic 2Cl-/H+ exchanger ClC-5, involved in tubular proximal endocytosis. The main manifestations are related with proximal tubule dysfunction, including low-molecular-weight proteinuria, hypercalciuria, nephrolithiasis, nephrocalcinosis, and progressive renal failure. The treatment of DD1 patients is aimed at alleviating the symptoms and delaying the progression of kidney disease. A fraction of variants associated with DD1 have been shown to produce mutant ClC-5 proteins that are retained and degraded in the endoplasmic reticulum (ER). Chemical chaperones are small molecules that enhance the folding and/or stability of the abnormal protein, thus being able to leave the ER and reverse the effect of the mutation. Our objective was to generate cell models that stably express mutated ClC-5 proteins and study the effect of two chaperones; 4-phenylbutyric acid (4-PBA) and tauroursodeoxycholic acid (TUDCA), on the expression and localization of ClC-5.

Methods: A ClC-5-EGFP fusion was generated by introducing the ORF of the CLCN5 gene into the pEGFPN1 vector. Variants previously identified in DD1 patients p.G466D, p.G462S, p.G65R and p.V523del were introduced by site-directed mutagenesis. The expression levels and localization of ClC-5 proteins were determined by flow cytometry and live-cell confocal microscopy. TUDCA and 4-PBA doses were stablished by cell viability assays. Cells were treated with each drug for 24 h and the changes in expression levels, localization and aggregation of the ClC-5-EGFP protein were determined.

Results: Compared to the control ClC-5-EGFP protein, all 4 selected mutations altered protein expression levels, aggregation, and localization. Treatment with 4-PBA and TUDCA increased the expression of ClC-5-EGFP with the p.V523del mutation, its localization was recovered, and protein aggregates decreased, showing similar patterns to the control protein ClC-5-EGFP. For the rest of the mutations, no significant changes were observed as result of the treatment.

Conclusion: The 4 cellular models generated show altered phenotypes. Treatments with both chemical chaperones reversed the phenotype observed for the p.V523del variant, as we had previously observed in an animal model with the same mutation. Therefore, the development of cellular models of DD1 could be very useful for pre-clinical screening of molecules with therapeutic potential. This research was co-financed by grant PI23/01609 from "Instituto de Salud Carlos III-Subdirección General de Evaluación y Fomento de la Investigación" and the European Regional Development Fund "Another way to build Europe", grant PI23/18 from Fundación Canaria Instituto de Investigación Sanitaria de Canarias and by "Asociación de la enfermedad de Dent" (ASDENT).

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NOVEL THERAPEUTIC FOR CRESCENTIC GLOMERULONEPHRITIS THROUGH TARGETING CLDN1 IN PARIETAL EPITHELIAL CELLS

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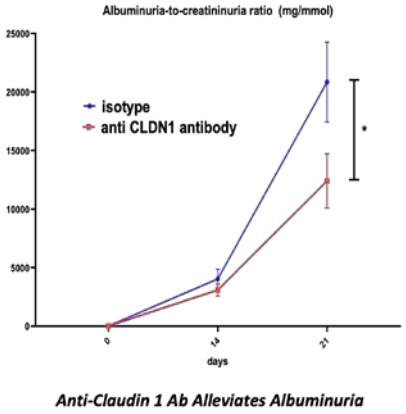
Aims/Purpose: Crescentic glomerulonephritis (CrGN) is the final mode of kidney injury common to several immune-mediated kidney diseases. CrGN is characterized by extensive glomerular parietal epithelial cells (PECs) proliferation forming crescents, which is then progressively replaced by fibrosis. Currents therapies for CrGN do not directly target the deleterious response of resident kidney cells. In a pathological context, claudin-1 (CLDN1), a transmembrane protein involved in epithelial tight junctions, can be exposed outside the tight junctions and mediate pro-fibrotic pathways. Lixudebart (formerly ALE.F02) is a first-in-class monoclonal antibody that specifically targets and blocks exposed CLDN1 in injured epithelial cells. A phase II clinical trial is under way for patients with antineutrophil cytoplasmic antibody-associated vasculitis (AAV) (RENAL-F02, NCT06047171). CLDN1 is highly expressed by glomerular PECs. This study investigated the functional role of CLDN1 in CrGN and the potential benefit to target CLDN1 in CrGN.

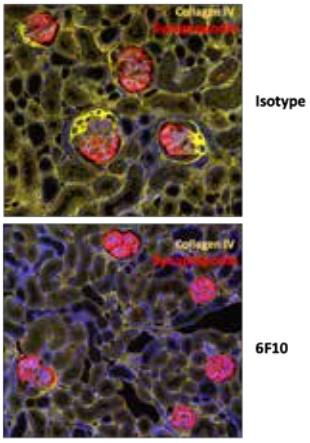
Methods: CLDN1 expression in renal tissues of CrGN patients was analyzed using multicolor immunofluorescence staining and spatial transcriptomics. Correlation between CLDN1 expression and clinical endpoints (eGFR, proteinuria), disease biomarkers and crescent evolution were studied. A spatially resolved molecular roadmap from CLDN1+ crescentic glomeruli was conducted. Proof-of-concept studies using anti-CLDN1 mAb were performed in preclinical models of CrGN.

Results: In tissues (n = 150) of patients with AAV and IgAN, multicolor immunofluorescence revealed up-regulated CLDN1 expression by crescents. At the time of diagnostic kidney biopsy, glomerular CLDN-1 expression was correlated with podocyte loss (as measured with P57 staining) and fibronectin area. The extent of dual expression of CLDN1 and CD44 at the surface of active PECs was associated with poor renal outcome (eGFR < 30 ml/min) in AAV and IgAN patients with a median follow-up of 2.5 and 3.7 years respectively. Spatial transcriptomics analysis highlighted the association between CLDN1+ crescentic glomeruli and ECM genes. Treatment with anti-CLDN1 mAb reduced albuminuria and decreased fibrosis biomarkers in nephrotoxic serum-induced CrGN in mice.

Conclusion: Our results suggest a functional role of CLDN1 in the pathogenesis of CrGN, providing preclinical proof-of-concept for anti-CLDN1 antibodies as a novel therapeutic approach in patients with CrGN.



Anti-Claudin 1 Ab Alleviates Albuminuria



Anti-CLDN1 Ab Blunted Glomerular Scarring

Figure 1. Decreased ACR and Collagen IV expression in mice treated with anti-CLDN1 antibody.

A. ACR in mice treated with anti-CLDN1 antibody or isotype in glomerulonephritis mice model (induced with nephrotoxic serum)

B. Representative immunofluorescence images of collagen IV (yellow) and synaptopodin (red) expression in the glomerulus from mice developping cGN treated with anti-CLDN1 antibody (6F10) or isotype.

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UNLOCKING THERAPEUTIC POTENTIAL: MTOR INHIBITORS ALLEVIATE GLOMERULAR INFLAMMATION IN IGA NEPHROPATHY THROUGH TRANSFERRIN RECEPTOR 1

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Background: IgA nephropathy (IgAN) stands as the predominant primary glomerulonephritis. Our recent findings reveal a compelling impact of the soluble myeloid receptor sCD89 on mesangial cell expansion via the PI3K/Akt/mTOR axis in vitro. Recognizing the mTOR pathway's involvement in the transferrin receptor 1 mesangial IgA receptor, our investigation explores the potential of the mTOR inhibitor, everolimus, in 1KI-CD89Tg mice expressing human IgA1 and CD89, inducing an IgAN-like disease. Additionally, we examine its impact in 1KI mice expressing human IgA1 with recombinant CD89 injection to thwart disease onset. Innovatively, we utilize single-cell kidney biopsy techniques to delve further into TfR1 and mTOR expression in mesangial cells from kidney biopsies of both IgAN and healthy patients at the single-cell level

Methods: Eight 1-KI -CD89-Tg and eight 1-KI mice with CD89 injection constituted two groups. The treated arm (eight mice) received the mTOR inhibitor everolimus (2 mg/kg), while the control arm (eight mice) underwent a placebo water treatment for 8 weeks. Weekly urine collections monitored mouse proteinuria, and after 8 weeks, the mice were sacrificed for renal function, circulating immune complex analysis, and histological examination. Using single cells, we quantified mTOR and TfR1 expression in five IgAN and one healthy patient kidney biopsy.

Results: Everolimus treatment demonstrated a reduction in mesangial IgA1 and C3 deposits observed by immunofluorescence in mouse kidneys. It also decreased in-situ proliferation, as indicated by diminished Ki67 staining in glomerular cells (a marker of cell mitosis) ($p < 0.05$). The treatment led to a decrease in proteinuria ($p < 0.05$), preventing kidney failure (Fig. 1). Levels of immune complexes (sCD89-IgA1 and IgG-IgA) were slightly impaired by everolimus treatment. sCD89 induced the activation of mTOR pathway with PI3K/Akt/mTOR phosphorylation in human mesangial cells. Most of all, using singles cells in cIgAN kidney biopsy, we found and overexpression of TfR1 and mTOR in IgAN human mesangial cells compared to healthy patients in kidney biopsies patients (Fig. 2).

Conclusion: Our study suggests that everolimus treatment holds promise in preventing and treating IgAN by targeting mesangial injury through the TfR1 receptor. This could potentially reduce IgA1 deposits and glomerular inflammation in the kidney, opening new avenues for IgAN treatment.

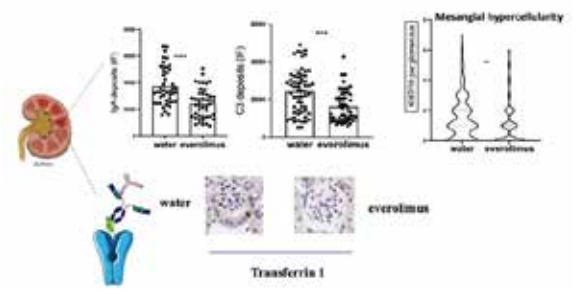

Figure 1

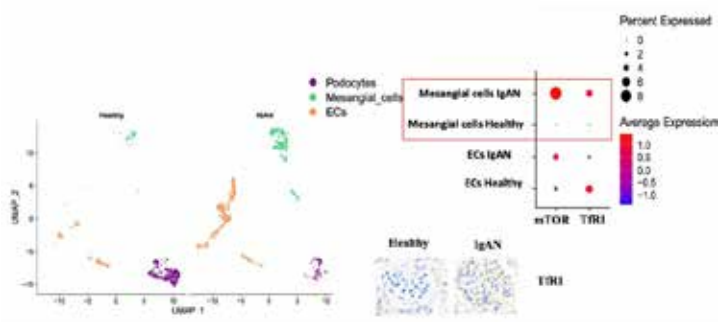

Figure 2

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SOLUBLE CD93 MEDIATES PODOCYTE INJURY IN IDIOPATHIC NEPHROTIC SYNDROME

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Aims/Purpose: Idiopathic Nephrotic Syndrome (INS) is traditionally categorized as a disorder centered around podocytes, but growing evidence suggests the possibility of an endothelial contribution. Yet, its impact in INS remains to be elucidated. CD93, an endothelium produced protein that facilitates cell adhesion and migration, exists in both membrane-bound and soluble forms. The objective of our research is to investigate if soluble CD93 sourced from endothelial cells plays a contributory role in podocyte damage associated with INS.

Methods: We analyzed soluble CD93 in urine and serum from 70 children with idiopathic nephrotic syndrome either at disease onset, during relapse or remission. We also evaluated the presence of CD93 in human kidney tissue in 15 patients and 10 controls. Furthermore, a variety of experimental techniques, including co-immunoprecipitation, migration and permeability assays, were utilized to investigate the impact of soluble CD93 on the functionality of human podocytes and the regulation of albumin permeability, as well as to identify its cellular origin.

Results: Soluble CD93 levels were higher in urine and sera from ~90% patients during relapse and ~30% during remission compared to controls. Immunofluorescence studies revealed a pronounced expression of CD93 in the glomerular endothelium of INS patients, while immune cells expressing CD93 were notably absent within the glomeruli. Sera from these patients stimulated in vitro human glomerular endothelial cells to release CD93. Soluble CD93 bound to podocyte 1 integrins and led to podocyte FAK activation and migration via 1 integrin signaling (Figure 1). Additionally, patients' sera caused podocyte injury and albumin leakage in a glomerulus on a chip system, but remarkably, these effects were mitigated by a CD93 antibody (Figure 1).

Conclusions: Soluble CD93 is novel endothelial-derived mediator of podocyte injury in INS and emerges as candidate therapeutic target for these patients.

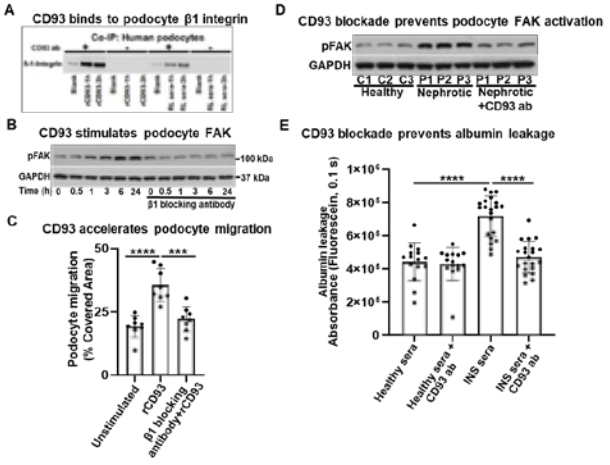

Figure 1. Soluble CD93 mediates podocyte injury

SESSION 4
HYPERTENSION & CARDIOVASCULAR RISKS

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AUSES OF DEATH IN A NATIONAL COHORT OF CHILDREN RECEIVING KIDNEY REPLACEMENT THERAPY

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Aims: Limited information exists regarding the causes of death for children on kidney replacement therapy (KRT). In the UK, data are not regularly reported due to a high proportion of missing data and small numbers of child deaths annually. This study aimed to describe the causes of death for children receiving KRT in England and Wales captured by the UK Renal Registry (UKRR) and compare this to Civil Registration (CR) records.

Method: Children aged ≤18 years, receiving KRT between 01/01/2001-21/12/2021 in England and Wales were included. Causes of death reported by nephrology centres to the UKRR were compared with the primary cause of death (ICD-10 codes) from CR records. The kappa statistic was used to assess agreement between UKRR and CR cause of death and chi-squared tests examined frequency differences between groups. Causes of death were analysed by age group, sex, and treatment modality.

Results: During the study period, 2,657 children received KRT in England and Wales. The UKRR identified 294 deaths, with 62.6% having a cause of death reported. CR records showed 292 deaths with 98.3% having a cause of death listed. There was reasonable agreement between datasets regarding dates and number of deaths. Cause of death agreement was substantial for malignancy (0.70), moderate for cerebrovascular disease (0.43) and fair to slight for cardiac disease, infection, and other causes (0.06-0.19). In UKRR records, 25.5% of deaths were due to infection, 10.9% from cardiac disease, 10.9% from malignancy, 10.3% treatment withdrawal and 29.9% due to other causes of death (table 1). In CR records, the majority of deaths were due to genitourinary conditions (21.3%), congenital anomalies (15.3%) and malignancy (11.9%, figure 1). For those with a missing cause of death or recorded as death due to treatment withdrawal in UKRR records, CR records suggested deaths were due to genitourinary, congenital, or endocrine conditions. No differences were found between cause of death by age group, sex, or treatment modality in UKRR records. Using CR records, deaths due to malignancy were more frequent (17.1%) in transplanted children compared to those on dialysis (15.6%), while infections were more frequent for children on dialysis (43.9%).

Conclusion: This is the first study to examine causes of death for a national cohort of children receiving KRT from two robust data sources. Infection and cardiac disease are common among children receiving KRT, with malignancy more frequent than previously reported, particularly among transplant recipients. Frequency and timing of deaths are similar in both datasets although agreement between causes of death was variable. While UKRR data suggests more granular information regarding cause of death, data completeness limits its epidemiological use.

Table 1: Causes of death in paediatric patients receiving KRT 2001-2021 (UKRR data).

Causes of death	Number	%
Cardiac disease	20	10.9
Cerebrovascular disease	8	4.4
Infection	47	25.5
Malignancy	20	10.9
Treatment withdrawal	19	10.3
Other	55	29.9
Uncertain aetiology	15	8.2
Total	**184**	**100.0**
Missing	110	37.4

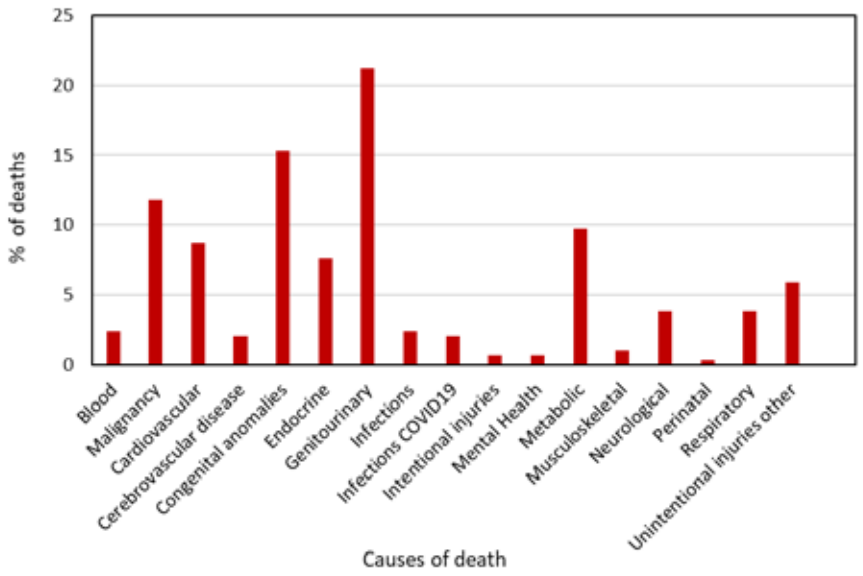

Figure 1: CR causes of death for the study cohort.

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INFLUENCE OF METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE AND OF ITS GENETICS ON KIDNEY FUNCTION IN CHILDHOOD OBESITY

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Aims/Purpose: Metabolic associated steatotic liver disease (MASLD) has been linked to several extrahepatic outcomes including kidney dysfunction. A critical pathogenic role for the I148M variant of the Patatin-like phospholipase containing domain 3 (PNPLA3) has been also suggested. We aimed at investigating the relationship of MASLD and of its genetics with kidney function in children with obesity.

Methods: A comprehensive assessment including genotyping for the I148M PNPLA3 polymorphism was performed in 1037 children with obesity. Presence of hepatic steatosis (HS) was assessed by liver ultrasound. The estimated glomerular filtration rate (eGFR) was calculated by using the original Schwartz equation and then normalized to the ideal body weight-derived body surface area. The cohort was clustered based on MASLD criteria. As a highly selected population such as children with obesity was examined, BMI (or BMI Z-score) was excluded from diagnostic criteria. Therefore, patients with obesity and with HS presenting ≥1 of the remaining metabolic features were classified as MASLD. According to their metabolic status, subjects with obesity but without HS were included in group 1, while patients with obesity and HS (encompassing one MASLD criterion) were clustered into group 2. Group 3 included patients with obesity, HS, and evidence of metabolic dysregulation (encompassing > 1 MASLD criterion).

Results: Alanine transaminase (ALT) levels significantly increased while eGFR significantly reduced from group 1 to group 3. Group 3 showed a higher percentage of carriers of the I148M allele of the PNPLA3 gene compared to other groups ($p < 0.0001$). Carriers of group 2 and of group 3 showed reduced eGFR levels than noncarriers of group 2 ($p = 0.04$) and of group 3 ($p = 0.02$), respectively. A general linear model for eGFR variance including gender, duration of obesity, BMI-SDS, PNPLA3 genotypes, and metabolic dysfunction was performed in the study population. It showed an inverse association of eGFR with both MASLD and PNPLA3 genotypes ($p = 0.011$ and $p = 0.02$, respectively). An inverse association of eGFR with MASLD was also confirmed only in carriers ($p = 0.006$).

Conclusion: The coexistence of more than one MASLD criterion in children with obesity adversely affects kidney function. The PNPLA3 148M allele further impacts on this association. Given the multisystemic nature of MASLD and its clinical and prognostic relevance on metabolic health, this research area deserves further emphasis.

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THE ASSOCIATION OF SERUM URIC ACID-TO-CREATININE RATIO AND HYPERTENSION IN CHILDREN WITH OBESITY

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Aim / Purpose: Childhood obesity is a global health problem with increasing prevalence, leading to long-term cardiovascular complications. Research conducted on adults has established a correlation between serum uric acid to creatinine ratio (SUA/Cr) and metabolic syndrome (MetS) as well as its components. The study investigates the relationship between SUA/Cr and hypertension (HT) and MetS components in children with obesity.

Methods: A total of 103 children (aged 6-18 years) with obesity who underwent ambulatory blood pressure measurement (ABPM) were included in the study. According to ABPM results, patients were divided into two groups "HT" (n = 60) and "Normal" (n = 43). Demographic, anthropometric, and laboratory features were retrospectively analyzed.

Results: The study included 103 children (42 female, 61 male) with a mean age of 13.7 ± 2.9 years. HT prevalence was significantly higher in patients with severe obesity, MetS, and dyslipidemia (p =0.045, p =0.000, p =0.01, respectively). Males exhibited significantly higher SUA/Cr than females (p < 0.001). However, SUA/Cr showed no significant differences between patients with and without HT, MetS, dyslipidemia, or hyperglycemia (p =0.69, p =0.64, p =0.90, p =0.37). Univariate logistic regression analysis did not establish a significant impact of SUA/Cr on HT (B = 0,097, OR: 1.1, p =0.65).

Conclusion: In our cohort, no significant positive association was found between SUA/Cr and HT, as well as MetS components in children with obesity. These findings highlight the necessity for more research into the complex mechanisms that regulate uric acid metabolism, obesity, and cardiovascular risk in children. The study contributes valuable insights to the limited data on this topic in pediatric populations.

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COMBINED USE OF SRAA BLOCKERS AND SGLT2 INHIBITORS FOR REDUCTION OF PROTEINURIA IN PAEDIATRIC PATIENTS WITH CHRONIC KIDNEY DISEASE

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Aims/Purpose: To assess the reduction of proteinuria and tolerability of iSGLT2 in paediatric patients with CKD.

Methods & Results: Retrospective observational study, patients aged 8-21 years with CKD grade 2-3 and proteinuria > 0.5 mg/ mg. Excluded patients with uncontrolled baseline disease, UTI in the last 3 months and orthostatic proteinuria. Dapagliflozin was administered, single daily dose of 5 mg for patients ≤30kg and 10 mg for patients > 30kg. Statistical analysis was performed using T-student, assessing the reduction in proteinuria and its effect on glomerular filtration rate, potassium, haematocrit, changes in weight or adverse effects at 6 months. Six patients were studied, of whom one patient was excluded after 3 months due to comorbidities that worsened the progression of CKD. Mean age was 14.8 years, four of six were female. All with RAAS blockage, none diabetic. The most frequent diagnosis was nephrotic syndrome (50%). Mean proteinuria reduction was 42.8% (initial proteinuria 2.8 mg/ mg and 1.6 mg/ mg at 6 months). Mean eGFR at baseline was 72.4ml/min/1.73m2 and at 6 months was 112.6ml/min/1.73m2. Mean potassium at baseline was 4.53 mg/dL and at 6 months 4.13 mg/dL. Mean haematocrit at baseline and 6 months was 35.6% and 39% respectively. Mean weight at baseline was 46.3kg and at 6 months 44.6kg (3.6% reduction). No patients reported adverse effects (urinary symptoms, digestive symptoms, dyslipidaemia).

Conclusion: iSGLT2 is considered one of the gold standard treatments for CKD in adults. In combination with RAAS blockade, they have been shown to be effective in reducing proteinuria regardless of the underlying renal disease mechanism. In our cohort, with the combined use of RAAS blockade and iSGLT2, an added reduction in proteinuria was observed. No deterioration of renal function was observed, as described in the literature. In addition, an increase in haematocrit was observed, which may be of added value in the management of anaemia in paediatric patients with CKD, and must be monitored to avoid hyperviscosity phenomena. No adverse effects were reported with the use of iSGLT2, as demonstrated by Paige, G. and Robert, B. in 2022 in a paediatric diabetic population. Therefore, the combined use of these drugs appears to be well tolerated and effective. It is important to mention that due to the number of participants it is not appropriate to draw conclusions. Undoubtedly, this study can be a starting point for future research. We consider necessary and urgent to conduct multicentre studies.

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RISK OF LONG-TERM CHRONIC KIDNEY DISEASE AND HYPERTENSION IN CHILDHOOD CANCER SURVIVORS: A MATCHED COHORT STUDY

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Introduction and Aim: The improvement in childhood cancer survival seen over the last decades has resulted in adverse effects, including chronic kidney disease (CKD) and hypertension. However, the incidence and timing of CKD and hypertension in childhood cancer survivors (CCS) compared with other at-risk populations or the general population are unclear. We used administrative healthcare data to study our hypothesis that CCS are at increased risk for long-term CKD and hypertension.

Methods: We performed a population-based retrospective matched-cohort study of all CCS in 1993-2020 in Ontario, Canada, using linked provincial administrative databases. The CCS (exposed) cohort included children (< 18 years) who received and survived treatment for cancer. There were two comparator cohorts (matched on a 1:4-ratio by age, sex, rural/urban, income, index year, and hospital admissions): the at-risk cohort included children who were hospitalized; the general pediatric population (GP) cohort included all other children from Ontario. Follow-up started at cancer-treatment end and terminated in 2021, outcome acquisition, death, or new/relapsed cancer. Exclusions: history of previous cancer, transplant, CKD, dialysis, or hypertension. The outcomes were defined using administrative healthcare diagnostic and procedure codes. The primary outcome was a composite of CKD or hypertension. We calculated cumulative incidences of the outcomes, and performed Cox proportional hazards modeling, accounting for competing risks (death; new cancer diagnosis/relapse), and adjusting for cardiac disease/liver disease/diabetes, to determine the association between cancer treatment and the outcomes.

Results: The CCS, at-risk, and GP cohorts (median [IQR] age 7 [4-13] years, 54.5% males) included 10,182, 831,214, and 2,145,854 participants, respectively, and median [IQR] follow-up time was 7.8 [2.4-14.8], 14.9 [7.8-21.5], and 8.6 [4.6-13.6] years, respectively. The leading cancer types were leukemia (29.0%), central nervous system neoplasms (20.9%), and lymphoma (15.5%). During observation of up to 27 years, 20.85% (95% CI 18.75-23.02) of CCS acquired CKD or hypertension compared with 16.47% (CI 15.21-17.77) of the at-risk cohort; 19.24% (CI 15.99-22.73) of CCS acquired CKD or hypertension compared with 8.05% (CI 6.76-9.49) of the GP cohort. The CCS cohort had an increased risk of CKD or hypertension compared the at-risk cohort (aHR 2.0 [CI 1.86-2.14], $p < 0.0001$), and the GP cohort (aHR 4.71 [CI 4.27-5.19], $p < 0.0001$).

Conclusions: This large retrospective matched cohort study shows that CCS have an increased risk for long-term CKD and hypertension compared with hospitalized children and with the general pediatric population. As CKD and hypertension are strongly associated with mortality and are treatable, early detection and treatment of these outcomes in CCS may decrease late mortality.

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CLINICAL OUTCOMES OF PEDIATRIC CHRONIC KIDNEY DISEASE STAGE 5 DUE TO HEMOLYTIC UREMIC SYNDROME IN THE PAST AND IN THE FUTURE - THE POLISH REGISTRY STUDY

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Backgroud: Hemolytic uremic syndrome (HUS) is a life-threatening disease with a poor prognosis and high mortality in children receiving long-term renal replacement therapy (RRT). The aim of this study was to analyse the incidence and outcome of chronic kidney disease stage 5 (CKD5) in children due to HUS, differentiating between STEC-HUS and atypical HUS (aHUS), compared to controls with CKD5 due to other primary kidney diseases, and to assess the influence of currently available treatment for aHUS on incidence and outcome.

Methods: The study included 1,488 children undergoing renal replacement therapy in Poland, who were enrolled in the national RRT registry between 2000 and 2023. Thirty-nine patients with aHUS and 18 with STEC-HUS were identified and analysed for incidence, RRT methods used and their impact on survival.

Results: The incidence rate of CKD5 was 0.09 cases/million age-related population (marp) for STEC-HUS and 0.23/marp for aHUS in the pre-eculizumab era, while no patients subsequently started RRT for this reason. Patients with aHUS started RRT at a significantly younger age compared to STEC-HUS and controls (median 6.0 years vs. 10.9 and 10.9 years, respectively) and remained under nephrological care for a significantly shorter time from first manifestation of disease to initiation of RRT. aHUS was associated with a higher risk of death (HR 1.92, 95% CI 0.9 - 4.13), and cardiovascular complications were significantly more common causes of death compared to other causes of CKD. Five-year renal graft survival was significantly worse in the aHUS group compared to STEC-HUS and the control group at 77%, 93% and 90%, respectively, ($p < 0.001$).

Conclusions: Children diagnosed with CKD5 due to STEC-HUS have significantly better long-term survival, shorter waiting times for kidney transplantation and better kidney graft survival compared to other causes of CKD. Patients receiving renal replacement therapy for aHUS prior to the availability of eculizumab had significantly higher mortality, longer waiting times for renal transplantation and significantly worse graft survival. The introduction of eculizumab into the treatment of aHUS has revolutionised the course of the disease and means that aHUS is likely to remain only a marginal cause of CKD5 in children.

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PROGRESSION OF ARTERIAL STIFFENING IN CHILDREN WITH EARLY STAGES OF CHRONIC KIDNEY DISEASE IS ASSOCIATED WITH BLOOD PRESSURE BUT NOT KIDNEY FUNCTION: INSIGHTS FROM THE HOT-KID STUDY

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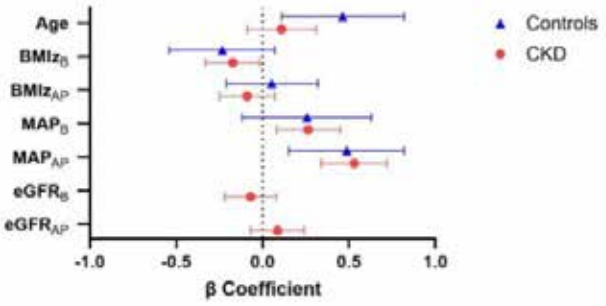
Aims/Purpose: The extent of an association between arterial stiffening and kidney function independent of the blood pressure (BP) in childhood chronic kidney disease (CKD) is not clear. The aim of this study was to examine the longitudinal associations between BP, kidney function and progression of arterial stiffness in children with early CKD and to compare the rate and determinants of pulse wave velocity (PWV) progression between children with CKD and healthy controls.

Methods: Children who attended for two measurements (mean interval 3.1 ± 1.4 years) of carotid-femoral PWV as part of the HOT-KID study1 were included (n = 151, mean age 10.5 ± 3.2 years). Annual progression of PWV (PWVAP) was compared for children with CKD stages 1-3 (n = 106) versus healthy controls (n = 45), using multivariable linear regression analyses and adjusting for mean arterial pressure (MAP), estimated glomerular filtration rate (eGFR) and other risk factors at baseline and follow-up.

Results: When adjusted for age, sex, BMI z-score and MAP, there was no significant difference in PWVAP between healthy children and those with CKD (0.12 ± 0.05m/s/year vs 0.12 ± 0.03m/s/year, P =0.977). In healthy children, annual progression in MAP (MAPAP) was independently associated with PWVAP (= 0.49, P =0.006), whereas in children with CKD, PWVAP was strongly associated with both baseline MAP and MAPAP (= 0.26, P =0.007 and = 0.53, P < 0.001) but not baseline or change in eGFR, see Figure.



Results were similar when analysed with PWV z-scores. However, elevated PWV z-scores at baseline were associated with female sex (OR: 4.43, P < 0.001). Mean PWV z-score at baseline for girls was 1.22 ± 0.14, compared to 0.75 ± 0.13 for boys, (P =0.014), when adjusted for age, BMI z-score and MAP.

Conclusion: In children, there is no demonstrable difference in progression of arterial stiffening between children with early CKD and those without. In children with CKD, progression of arterial stiffening appears to be associated with BP rather than kidney function. However, the strong associations between PWVAP and baseline MAP and MAPAP reiterates the need for careful BP control in children with CKD. Identifying groups at high risk of arterial stiffening may be particularly important to reduce long-term risk of cardiovascular disease.

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FEASIBILITY OF IDENTIFYING PEDIATRIC PATIENTS WITH CHRONIC KIDNEY DISEASE AND SEVERE PROTEINURIA USING US ELECTRONIC HEALTH RECORDS: A RETROSPECTIVE ANALYSIS AND DESCRIPTIVE OUTCOME ASSESSMENT

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Aims/Purpose: Chronic kidney disease (CKD) in children, while rare and of diverse etiology, has significant long-term effects on growth, quality of life, and lifespan. To date, no approved treatments exist for delaying pediatric CKD progression. By applying the adapted selection criteria of the 'FInerenone for the treatment of children with chrOnic kidNey disease and proteinuriA' (FIONA) clinical trial, this study aimed to assess the feasibility of identifying a pediatric population with CKD and proteinuria using US Optum electronic health records (EHR) data between 01/2013 and 12/2022.

Methods: Eligible patients (aged 6 months to 18 years at index) had to have at least two lab values indicating CKD stages 1 to 3 (estimated glomerular filtration rate [eGFR] ≥30 ml/min/1.73m2) and two lab values indicating severely increased urine protein/creatinine ratio ([UPCR] ≥0.5 g/g). Qualifying eGFR and UPCR values were considered in pairs, separated by 89 days at most; a gap of 90-365 days between the first and second pairs of eGFR/UPCR values was required to ensure disease chronicity (index date = last qualifying lab value in the second pair). Baseline characteristics were assessed descriptively, outcome incidences were expressed as cases per 100 patient years (PYs).

Results: We included 778 patients, with 60.8%, 28.2% and 10.9% being in the predominant age categories 12-18 years, 6-12 years, and 2-6 years, respectively. 55.9% of patients were categorized as CKD stage 1, 25.6% as stage 2, and 18.4% as stage 3. Median UPCR at index was 1.63 g/g. Dominant baseline comorbidities were hypertension (27.4%) and anemia (11.8%). ACE inhibitors (45.0%), corticosteroids (48.8%), immunosuppressants (39.0%) and ARBs (8.5%) were commonly prescribed drugs at baseline. During a median follow-up of 3.8 years, incidence rate for the end-stage renal disease (ESRD) composite endpoint was 2.68 cases per 100 PYs (95% CI, 2.11-3.34), with 0.80 (0.51-1.17) for chronic dialysis and 1.58 (1.16-2.09) for kidney transplant as sub-components of ESRD; 1.69 (1.25-2.22) and 6.52 (5.56-7.57) cases per 100 PYs for sustained ≥50% eGFR decline and acute kidney injury, respectively. Subgroup analyses demonstrated that cumulative incidence rates of these outcomes were notably higher in patients with a baseline eGFR < 60 ml/min/1.73 m2.

Conclusion: Our study demonstrated the feasibility of characterizing a pediatric population with CKD and increased proteinuria using US EHR data. The findings underscore the substantial burden of CKD in children and the resulting unmet medical need, by showing considerable rates of disease progression and associated comorbidities in a population eligible to the FIONA study.

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PERINATAL RISK FACTORS OF CARDIOVASCULAR-RENAL OUTCOME IN FORMER EXTREMELY LOW BIRTH WEIGHT NEONATES

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Background: Extremely low birthweight (ELBW, i.e., birthweight below 1000 grams) children are at increased risk of developing adverse cardiovascular and renal outcomes in later life. Their improved survival necessitates more focused research on long term outcome aspects. According to the Developmental Origins of Health and Disease concept, kidney insults in early life may lead to altered organ function and morphology and eventually lead to chronic kidney disease (CKD). Little is known about additional perinatal risk factors and their similarity for these adverse outcomes.

Methods: We compared cardiovascular-renal outcome between ELBW children and controls, to find perinatal risk factors for poorer renal and cardiovascular outcome and to unveil associations between kidney function and blood pressure. This study included 93 ELBW children and 87 healthy controls. We measured cystatin C-based estimated glomerular filtration rate (eGFR) and blood pressure. Blood pressure and eGFR levels were compared between cases and controls. We subsequently investigated perinatal risk factors for adverse outcome amongst ELBW children. The most significant perinatal determinants for an unfavorable renal outcome in ELBW children were used to create a model that could illuminate their risk of a lower eGFR by age 11, defined in the study as a single measurement of eGFR < 90 ml/min/1.73m2. A point was assigned for sex (male), ventilation therapy (> 10 days) and intraventricular hemorrhage IVH (any), representing vulnerability through sex, exposure to intensive treatment and the occurrence of neonatal comorbidities.

Results: ELBW children have significantly higher blood pressure and lower eGFR. Elevated blood pressure did not correlate with perinatal characteristics. ELBW children with eGFR < 90 ml/min/1.73m2 were ventilated longer (17 vs. 9 days, p =0.006), more frequently male (OR = 3.33, p =0.055) and tended to suffer more from intraventricular hemorrhage (40% vs. 15.8%, p =0.056). There was no association between blood pressure and kidney dysfunction. As a proof of concept, we modelled the risk for kidney function, using the criteria sex (male), ventilation (> 10 days) and IVH (any). Amongst ELBW children 34.5% progressed to kidney function decline. This risk progresses linearly between 0% and 80% varying on the points scored in the model.

Conclusions: Understanding risk profiles for unfavorable outcomes may help to identify children at increased risk for kidney or cardiac dysfunction. These risk profiles could be different for renal and cardiovascular outcome. Poorer eGFR was associated with longer ventilation, male sex, and intra-ventricular hemorrhage. This knowledge can lead to safer neonatal therapeutic regimens for ELBW infants, a more intensive follow-up and earlier treatment initiation for children at highest risk.

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RWE OF LISINOPRIL IN PEDIATRIC HYPERTENSION AND NEPHROPROTECTIVE MANAGEMENT AND THE VALUE OF RAAS BIOMARKERS: A 10-YEAR COHORT STUDY

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Background: Over the last 20 years, pediatric hypertension (pHTN) prevalence in Western society has risen from 3.5% to 9% due to childhood overweight, obesity, and secondary kidney and cardiological conditions. Few studies have assessed commonly used antihypertensive medication lisinopril's (ACE-inhibitor) long-term efficacy and long-term value of renin-angiotensin-aldosterone system (RAAS) biomarkers.

Methods: A retrospective cohort study at Ghent University Hospital, Belgium, aggregating electronic health record data on 106 young patients (1-18 years) treated with lisinopril due to hypertension (HNT) without CKD(1), hypertension or proteinuria associated with CKD (eGFR < 90 ml/min/1,73m^2) (2), and proteinuria (PRT) without CKD or hypertension (3), assessed for treatment outcomes against clinical benchmarks over 10 years.

Results: Lisinopril was mainly initiated for secondary hypertension or nephroprotection (89%) due to kidney causes. The study revealed a starting dose across groups of half the population starting at lower than 0.7 mg/kg, with notable long-term follow-ups showing varied treatment outcomes. Hypertensive patients without CKD showed a reduction in systolic blood pressure below the 95th percentile within 2 years, but efficacy is lost after 2.5 years. CKD patients had a steady treatment response, achieving systolic blood pressure targets by 40 months, with diastolic pressure control also improving steadily in this group over 70 months. Proteinuria reduction had a median UPCR to 0.57 g/g at 6 months. Proteinuria reappearance is noted to reach 2 g/g creatinine after 40 months. Aldosterone showed an initial decline in the first 6 months; however, an aldosterone breakthrough is noted from 6 months onwards in all groups. The ARR showed a gradual decline in the 3 different groups. Aldosterone and ARR progression significantly differ in the children with kidney impairment when compared to the children without kidney impairment over 70 months.

Conclusion: Systolic blood pressure treatment efficacy is lost after 2.5 years in hypertensive patients without kidney impairment, and proteinuria treatment efficacy is lost after 3 years in children with impaired kidney function, highlighting the need for dosage recalibration according to guidelines and/or the need for alternative treatments. Biomarkers aldosterone and aldosterone-renin-ratio (ARR) should be considered in an impaired population.

SESSION 5
FUTURE OF PEDIATRIC TRANSPLANTATION

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DONATION AFTER CIRCULATORY DEATH, A VALID ALTERNATIVE IN PEDIATRIC KIDNEY TRANSPLANTATION

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Aims/Purpose: The use of donation after circulatory death (DCD) in kidney transplant (KT) may be a valid alternative in pediatric patients with end-stage kidney disease (ESKD). The aim of the study is to describe the outcome of a cohort of pediatric KT recipients from DCD donors.

Methods: Retrospective descriptive multicenter study including 1123 patients under 18 years of age who received a deceased donor (DD) kidney transplantation between 2013-2024 in Spain. Among them, we collected demographic, clinical, biochemical, pharmacological characteristics and outcome of all transplanted patients with DCD Maastricht type III donors by reviewing electronic medical records. Statistical analysis was performed with IBM-SPSS 29.0.

Results: 54 patients received a DCD kidney transplantation. Mean age of recipients was 9.9 years (SD: ± 5.28), 68.5% were male and 75.9% Caucasian. The main cause of ESKD was congenital anomalies of the kidney and urinary tract (35.2%) followed by focal and segmental glomerulosclerosis (13%). 18.5% of patients received a preemptive KT, whereas 33.3% were on peritoneal dialysis vs. 48.1% on hemodialysis (p 0.02). In 88.9% of cases it was a first transplantation, and in 9.3% it was the second KT. In our series, 1.9% were hypersensitized. The median waiting time on the transplant list was 3 months (IQR: 1, 8). 16.2% had 0 mismatch in DR, 31.1% 1 mismatch and 25.7% had 2 mismatches (p 0.1). The median age of donors was 24.5 years (IQR: 11.7, 40.5), and 44.4% of donors were under 18 years old. Median donor serum creatinine before death was 0.51 mg/dl (SD: ± 0.27). The mean total warm ischemia time was 20.3 minutes (SD: ± 7.09) and functional warm ischemia was 11.1 minutes (SD: ± 6.6). The mean cold ischemia time was 12.8 hours (SD: ± 5.3). Extraction was normothermic in 90.9%. It was a multiorgan donation in 90.4% of cases. Of our patients, 13% had delayed graft function. Graft survival at 1 year was 95.5%. There were 4 graft losses due to immediate arterial thrombosis, acute cellular rejection (8 days post-transplant), antibody-mediated (3 years post-transplant) and mixed rejection (5 years post-transplant).

Conclusion: Despite the limitations of this study, the use of DCD donors shows a favorable short-term outcome. In our study graft survival in DCD kidneys was similar to what is previously described in DD after brain death. To our knowledge, this is the largest study published so far in Europe with DCD donors and pediatric recipients. The use of DCD donors may help to reduce the waiting time for transplantation.

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IS THERE A DIFFERENCE IN OUTCOME BETWEEN DCD AND DBD DONOR KIDNEYS IN PEDIATRIC TRANSPLANT RECIPIENTS?

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Aims/Purpose: Although pre-emptive living kidney donation is the first-choice treatment modality for pediatric patients with end stage renal disease in the Netherlands, we still have the need for a post-mortal kidney donor program. Despite the fact that brain dead heart beating donors (DBD) are scarce, we are cautious to use non-heart beating donors after circulartory death (DCD) because of the risk for delayed graft function and reduced graft survival. Since 2000 the DCD program has evolved from static cold storage of the kidney ('kidney on ice', similar to the DBD protocol) towards a successfull nation wide machine perfusion protocol. We questioned whether our cautiousness to use DCD donors is still justified and aimed to evaluate the outcome of DCD kidneys compared to DBD and living donor kidneys in pediatric recipients.

Methods: All children who received a kidney graft between 2012 till 2024 were included. The recipients were analysed based on the donor type (living-, DBD- or DCD donor). Graft recovery in the first week after transplantation and at 3 months as well as graft survival and dialysis waiting time were evaluated.

Results: In total 261 pediatric recipients received a kidney transplantation. Of them 192 (74%) received a living donor and 69 (26%) a post mortal donor. Of the 69 post-mortal donors, 15 (22%) were of DCD origin while 54 (78%) were from a DBD donor. Graft recovery of the living donor kidneys was superior to the DBD group which was again superior to the DCD group. Nevertheless at 3 months post transplantation the kidney function was similar irrespective of the organ type used. The 10 year graft survival was for living-, DBD and DCD donors respectivity 94%, 60% and 70%. (P =< 0,05) Thus, a significant graft survival benefit when using a living donor, but no difference in graft survival between DBD and DCD donors. Importantly, we saw that by implementing the different kidney transplantation programs we were able to lower the dialysis waiting time for an organ from 3 years to less then 1 year at the moment.

Conclusion: Although a slower graft recovery the outcome of DCD kidneys is similar to DBD kidneys and therefore these organs can safely be used in pediatric recipients who don't have the opportunity for living donation. In the Netherlands this program (togheter with other programs) has resulted in a substantial decline in dialysis waiting time.

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INCIDENCE AND TIME-VARYING DETERMINANTS OF GRAFT FAILURE AFTER RE-TRANSPLANTATION IN PEDIATRIC PRIMARY KIDNEY TRANSPLANT RECIPIENTS IN THE EUROTRANSPLANT AREA

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Aims/Purpose: The majority of patients who underwent kidney transplantation (KTx) during childhood and adolescence are expected to outlive their initial transplant, and most of them will be eligible for re-transplantation. Little is known about factors associated with graft failure (GF) after re-transplantation in pediatric primary kidney transplant (KTx) recipients.

Methods: We investigated the incidence and determinants of GF after re-KTx in Eurotransplant countries between 1990 and 2020. Piecewise exponential additive mixed models were used to investigate determinants of GF after re-KTx in Eurotransplant countries and to detect time-varying associations.

Results: We report on 5987 KTx (1990-2020), of which 4528 were primary pediatric KTx, while 1153, 259 and 41 were second, third, and fourth KTx, respectively, with 5-year GF probabilities of 16%, 27%, 33% and 55%. The rate of GF in the first month was 58% higher in the second, 84% in the third and 143% in the fourth allograft compared to the primary KTx. LD KTx, recipient age 12-24 years, donor age above 42 years and PRA 1-100% were time-varying determinants of GF after the second KTx. LD KTx was associated with a lower risk of GF in the first 2 years from 2nd KTx (aHR at 1 month posttransplant: 0.56, 95%CI: 0.34-0.91). Between 1 and 6 years posttransplant, increasing recipient age up to 24 years was associated with a higher rate of GF. Between 10 and 14 years posttransplant, recipients aged 18 to 28 years at 2nd KTx had a lower rate of GF. KTx with donors older than 42 years had a higher GF rate during the entire follow-up period. Sensitized recipients displayed a progressively increasing rate of GF with time posttransplant compared to non-sensitized recipients (respective aHR at 5 and 10 years posttransplant: 1.41 vs. 1.97, 95%CI: 1.12-1.77 vs. 1.38-2.8). In non-sensitized recipients, the risk of GF was higher with a shorter primary graft survival over the follow-up period (respective aHR 1 and 15 years: 1.71 vs. 0.61, 95%CI: 1.13-2.59 vs. 0.42-0.87, reference = 5 years). The association between dialysis vintage before second KTx and higher rates of GF was stronger with increasing waiting time at primary KTx (P =0.007).

Conclusion: The rate of GF increased with each subsequent KTx, especially in the first months post-transplant. GF after the second KTx was associated with recipient and donor age, donor source, sensitization status, and graft survival of the first KTx.

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MANAGEMENT OF CHILDREN WITH FAILING KIDNEY ALLOGRAFTS: RESULTS FROM ESPN CKD-MBD, DIALYSIS AND TRANSPLANT WORKING GROUPS

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Introduction: Kidney allograft survival in children is limited due to several factors, with up to 15% of children receiving another transplant prior to transition to adult services. Medical management of children with failing kidney allografts is poorly understood and likely varies across centres in Europe. The aim of this study is to describe the cohort of children with a failing kidney allograft and to provide insights into the different management practices across Europe.

Methods: An initial survey was sent to all members of the ESPN CKD-MBD, Dialysis and Transplant Working Groups to determine the number of patients transplanted under the age of 18 years with poor allograft function. Through an iterative delphi process a failing kidney allograft was defined as an eGFR < 30 ml/min/1.73m2 for more than 3 consecutive months. A 3- year observational review of all children identified as having a failing kidney allograft, with at-least one-year follow-up, was undertaken. Data were collected through the CERTAIN registry and a fully anonymised data sheet for detailed data collection on 4 domains: CKD-MBD, cardiovascular, immunosuppression changes and future kidney replacement planning.

Results: 123 children (115 with first kidney transplant) form 27 centres were included. Median age at transplant was 8 years (IQR 3.4-12.9) with allograft loss at a median 5 years (IQR 2.5-9) post-transplant (Graph 1). 35% (43/123, 40 first kidney transplant) had a living kidney donation with 18% (21/115) pre-emptive transplants. 50% (45/90) children were acidotic (bicarbonate < 21 mmol/L), 20% (18/92) were hyperphosphatemic (phosphate > 1.8 mmol/L) and 67% (63/94) were anaemic (haemoglobin < 11 g/L) at the time of allograft failure. 91% (105/115) were on medication for management of acidosis, anaemia and CKD-MBD at last follow-up. 77% (89/115) patients were hypertensive or on anti-hypertensive agents at the time of allograft failure. Only 61% (70/115) had surveillance echocardiography with 39% (27/70) of these developing left ventricular hypertrophy. Immunosuppressive medications were not altered after allograft failure in 20% (23/115) patients. When immunosuppression was altered; CNI monotherapy was continued in 36% (24/66), anti-metabolite doses were halved with CNI continued in 6% (4/66), 6% (4/66) stopped all medications and other combinations were used in 36% (24/66). 12 patients had transplant nephrectomies. 9 patients developed new-onset post-transplant diabetes. At last follow-up 40% (46/115) children were back on dialysis (74% on HD, 20% on PD and 6% on home HD).

Conclusion: Management of children with failing kidney allografts is complex, poorly understood and highly variable even across European centres. This study is the first step towards understanding this cohort, and following prospective interventional strategies that may attenuate kidney allograft failure.

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UNREAVELING INTERINDIVIDUAL DIFFERENCES AND FUNCTIONAL CONSEQUENCES OF GUT MICROBIAL METABOLISM OF IMMUNOSUPPRESSANTS

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Aims/Purpose: A major challenge in kidney transplantation (KT) is the large interpatient variability in the pharmacokinetics of immunosuppressants. Here, we aim to provide a comprehensive understanding of the interindividual differences, functional consequences and underlying mechanisms of gut microbial metabolism of immunosuppressants.

Methods: We studied 25 drugs commonly used in KT, including 16 immunosuppressants, for their metabolism by 38 different human-derived gut microbial communities, including 10 from kidney transplant recipients, and 45 representative gut bacterial species. Drug degradation and identification of microbial drug metabolites were assessed by liquid chromatography coupled to mass spectrometry-based metabolomics. The influence of microbial drug metabolism on enteric absorption was measured by assessing transport rates of drugs and drug metabolites across a gut epithelial monolayer. Molecular mechanisms of gut microbial metabolism were evaluated by a gain-of-function genetic screen. Random forest-based machine learning models were used to predict drug degradation in the tested microbial communities.

Results: Analysis of fecal communities revealed significant interindividual and drug-specific differences in the metabolism of immunosuppressants. In particular, 15 of 16 immunosuppressants tested were metabolized by at least one microbial community, and specific bacterial species were identified as potent metabolizers. We identified 18 different drug metabolites, including two newly identified ones for sirolimus and everolimus. Our study reveals the functional impact of microbial metabolism on key immunosuppressants, including inactivation of tacrolimus, activation and potential increase in toxicity of mycophenolate mofetil (MMF), and shows that the microbial metabolite of methylprednisolone exhibits a 2.6-fold increase in epithelial permeability compared to the parent drug. In addition, we identified the B. uniformis enzyme RS05305 as responsible for MMF activation. Abundance features of prevalent species predicted the biotransformation of some drugs well, while for others, experimental information on bacterial genes and enzyme protein structures led to better predictions.

Conclusion: Our research highlights the potential of gut microbiome features to explain interindividual variability in metabolism of immunosuppressants and sets the stage for clinical trials to identify microbiome-encoded signatures predictive of drug metabolism in KT patients.

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LONG-TERM OUTCOMES OF RIGHT VERSUS LEFT KIDNEY TRANSPLANTS OVER A 33-YEAR PERIOD IN THE USA - A COMPARATIVE STUDY

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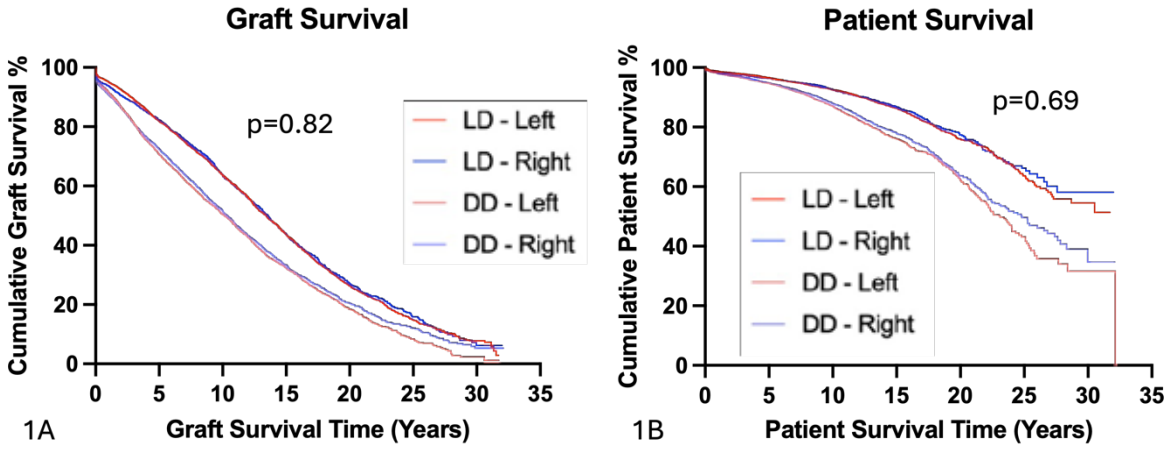
Aims/Purpose: Right kidneys have shorter renal veins than left kidneys. This may make the transplant surgery more challenging and complex. We reviewed the use of right versus left kidneys transplanted in children over a 33-year period in the USA.

Methods: Data were retrieved and analysed on right versus left kidney transplants performed in paediatric recipients (younger than 18 years old) from October 1987 until September 2020, from the United Network for Organ Sharing. En-bloc kidney transplants were excluded as we have previously reported on those. SPSS v29 was used for statistical analysis. Data were compared using chi-square test, t-tests and Kaplan-Meier survival analysis.

Results: kidneys being used more often in organs coming from deceased donors (DD) (42% of DD kidneys, and 25% of living donor (LD) kidneys, $p < 0.01$). Right kidneys had significantly more delayed allograft function than left kidneys (11.1% vs 7.5%, $p < 0.01$) even when accounting for donor type (5.8% vs 4.6% $p = 0.01$ in LD transplants, and 15.0% vs 12.8% $p < 0.01$ in DD transplants). However, there was no significant difference in primary non-function ($p = 0.37$). In DD transplants, right kidneys were more likely to develop a thrombus (1.8% vs 2.6%, $p < 0.01$). Throughout the study period, right kidneys retrieved from LD were more likely to lead to allograft loss than left kidneys retrieved from LD (46% vs 44%, $p = 0.01$). Kaplan-Meier analysis also showed that right kidneys had a worse allograft survival (median survival 11.3 years vs 12.2 years, $p < 0.01$). However, when accounting for donor type and transplant era, this difference is no longer significant (Fig. 1A). The same findings were found for patient survival (Fig. 1B).



Conclusion: Left kidneys are more frequently used in LD as the choice of a longer renal vein makes transplantation easier. Using right kidneys for transplantation, where the vein is shorter and may require extension, carries an increased risk of delayed allograft function, thrombus formation and allograft failure. However, when adjusted for donor type and transplant era there was no significant difference in allograft or patient survival when using right kidneys compared to left kidneys.

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CHILDREN AFTER KIDNEY TRANSPLANTATION SHOW SEVERE CARDIAC ALTERATIONS

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Aims/Purpose: Sudden cardiac death is among the most common causes of death in patients after pediatric kidney transplantation (KTx), but defined diagnostic procedures identifying children at risk are not established. Echocardiographically detectable damage in CKD has been described, fewer data exist after KTx in childhood. The aim was to characterize alterations on cardiac MRI (cMRI) and by echocardiography and elucidate the significance of diastolic dysfunction in children after KTx.

Methods: 46 KTx recipients (mean age 16 years) and 46 age-/sex-matched healthy controls were examined with non-contrast cMRI (parameters: native T1 time, nT1; left ventricular mass z-score, LVMIz; ejection fraction, EF; global longitudinal strain, GLS). KTx recipients underwent also echocardiography: EF, mitral inflow (E-, A-wave), TDI: e', E/e'-ratio, isovolumetric relaxation time (IVRT), pulmonary venous flow (PVFsys, PVFdia), atrial reversal (PVF-AR), left atrial volume index (LAVI), left ventricular mass z-score (LVMz).

Results: In cMRI KTx recipients had a siginficant higher nT1 (1198ms vs. 1155ms, $p < 0.0001$), a higher LVMIz (0.1g/m2 vs. -0.3g/m2; $p = 0.026$) and a lower GLS than healthy controls (-19% vs. -20.3%, $p = 0.01$). While based on cMRI 2 patients were diagnosed with left ventricluar hypertrophy (LVH), 11% (n = 5) displayed LVH on echo. EF was preserved in all patients. Based on echocardiography, 90% (n = 40) showed diastolic parameters out of the normal range (Fig.1) with changes in ≥4 parameters in half of the cohort. Multivariable linear regression analysis revealed associations of nT1 on cMRI with the following echo parameters: septal E/e´ (ß = 8.415, $p = 0.042$), A-wave (ß = 1.037, $p = 0.045$), LAVI (ß = 3.347, $p = 0.002$), PVF-AR (ß = 2.945, $p = 0.021$) (Fig. 2).

Conclusion: Young KTx recipients show a high prevalence of diastolic dysfunction with preserved EF. Impaired diastolic function was associated with structural alterations reflecting myocardial fibrosis. Our findings suggest that a large number of children after KTx suffer from heart failure with preserved EF – an entity not yet defined in children but described for adults, in whom it is associated with sudden cardiac death. Further studies are needed to describe the clinical relevance of these findings, which gain explicit importance, as the prognosis of HFpEF in adults is improved by SGLT2i, a treatment option not yet considered in our high-risk patient group.

SESSION 6

RENAL TUBOLOPATHY - WHATS NEW?

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PATIENTS WITH FAMILIAL HYPOMAGNESEMIA WITH HYPERCALCIURIA AND NEPHROCALCINOSIS WITH DIFFERENT DISEASE PROGRESSION HAVE A DIFFERENTIAL EXPRESSION PROFILE OF URINARY MIRNAS

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Aims/Purpose: To identify the pathophysiological mechanisms underlying the progression of Familial Hypomagnesemia with Hypercalciuria and Nephrocalcinosis (FHHNC) and the phenotypic variability observed in patients. For this purpose, we have isolated urinary extracellular vesicles (uEVs) from our FHHNC cohort in order to obtain a differential profile of miRNAs between patients and controls, and between patients with different disease progression.

Methods: The classification of FHHNC patients was carried out according to the evolution of their estimated glomerular filtration rate (eGFR) over time, resulting in three groups of disease progression: fast (loss of eGFR ≥10 mL/min/1.73 m2/year), moderate (< 10 mL/min/1.73 m2/year) or slow (stable eGFR). Only patients with native kidneys were included in this study. The uEVs were isolated and characterized using a technique optimized in our group based on differential ultracentrifugation. Total RNA was isolated and miRNA profiles were obtained using two high-throughput technologies, microarray and openarray. The results were validated by qPCR. Finally, the data were analyzed using artificial intelligence to identify pathological mechanisms associated with the miRNA profiles obtained.

Results: Our cohort includes 6 control subjects (healthy siblings) and 30 patients with FHHNC. 90% (n = 27) of patients carry mutations in CLDN19, of which 92% (n = 25) have the so-called Hispanic mutation, p.G20D, (67% (n = 20) of them, in homozygosis). Regarding disease progression, most patients (63%, n = 19) have a moderate eGFR decline, while 17% (n = 5) have a fast decline and 20% (n = 6) slow. Our results identified two profiles of miRNAs differentially expressed in uEVs that discriminate between patients and healthy controls, and between patients according to the severity of the renal phenotype. These miRNA profiles are associated with processes related to endoplasmic reticulum stress, tight junctions and renal fibrosis.

Conclusion: In conclusion, patients with FHHNC present different profiles of urinary miRNAs that are associated with the pathological characteristics of this disease and allow patients to be discriminated according to the evolution of the loss of kidney function. We propose that selected miRNAs could constitute non-invasive biomarkers of progression and represent potential therapeutic targets for this orphan disease.

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EVIDENCE FROM A NOVEL CYSTINOTIC CRISPR/CAS9 COLLECTING DUCT MODEL LINKS SECONDARY NDI OBSERVED IN CYSTINOSIS TO AUTOPHAGY-MEDIATED AQP2 DEFICIENCY

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Aims/Purpose: Cystinosis, an autosomal recessive lysosomal storage disease, is caused by mutations in the CTNS gene, encoding for cystinosin, leading to the accumulation of cystine. Kidneys are the first and most affected organs, with severe tubular dysfunction and glomerular damage. Secondary Nephrogenic Diabetes Insipidus (NDI) has been reported as a complication of cystinosis, due to the resistance to vasopressin, a key hormone regulating collecting duct water reabsorption through the activation of the water channel Aquaporin-2 (AQP2). The lack of a cystinotic collecting duct in vitro model has however limited the research on the mechanisms involved in the impairment of urine concentrating ability. The aim of this study was to establish a new collecting duct cystinotic in vitro model to investigate the molecular mechanism causing the vasopressin resistance associated with cystinosis.

Methods: By CRISPR/Cas9 technology, CTNS was efficiently knocked out in MCD4 cells, a mouse renal collecting duct cell line stably expressing the human AQP2 and the vasopressin receptor 2 (V2R). Sanger sequencing, qPCR and mass spectrometry were performed to validate the editing efficiency and assess cystine accumulation. Osmotic water permeability measurements were carried out to evaluate water transport in response to desmopressin, the synthetic vasopressin analogue. AQP2 expression and localization were evaluated by Western blotting and immunofluorescence.

Results: The CTNS KO cell line showed a strong reduction of AQP2 expression. In CTNS KO cells, dDAVP treatment did not increase osmotic water permeability, likely due to reduced AQP2 expression. Interestingly, inhibition of the autophagic pathway by chloroquine treatment resulted in a significant increase in AQP2 expression, indicating that the observed AQP2 reduction in CTNS KO cells is mediated by enhanced autophagic degradation.

Conclusion: In conclusion, we established the first collecting duct in vitro model for the study of secondary NDI associated with cystinosis, demonstrating that vasopressin resistance associated with cystinosis depends on reduced expression of AQP2 due to autophagy-mediated degradation.

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KETOGENIC DIET FOR NEPHROPATHIC CYSTINOSIS

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Aims/Purpose: Nephropathic cystinosis is a rare inherited lysosomal storage disorder caused by mutations in the CTNS gene that encodes for cystinosin, a lysosomal cystine/H+ symporter. Nephropathic cystinosis causes early-onset renal Fanconi syndrome and progressive kidney failure. Current therapy can reduce the amount of cystine in lysosomes, but it does not prevent progression of kidney failure.

Methods: We have tested the effects of ketogenic diet on renal disease in two animal models of nephropathic cystinosis, using biochemical and histological methods.

Results: When Ctns-/- mice were fed with ketogenic diet from the age of 3 to 12 months, we observed a near complete protection against the development of Fanconi syndrome, including low molecular weight proteinuria, glycosuria and polyuria ($p < 0.001$). Compared to wild-type animals, BUN at 12 months of age was significantly higher in cystinotic mice fed with standard diet ($p < 0.001$). At sacrifice, the kidneys of knock out mice fed with ketogenic diet appeared macroscopically similar to those of wild type animals, which was reflected microscopically by a significant reduction of interstitial cell infiltration (CD3 and CD68 positive cells, $p < 0.01$), of interstitial fibrosis (Masson and -SMA staining, $p < 0.001$), and of apoptosis (cleaved caspase 3 levels; $p < 0.001$), and by indirect evidence of restoration of a normal autophagic flux (SQSTM1/p62 and LC3-II expression, $p < 0.05$). The beneficial effects of ketogenic diet on tubular function (i.e. stabilization of biochemical parameters) were also observed after mice were fed with this diet from the age of 6 months to the age of 15 months, after they had developed proximal tubular dysfunction. Although slightly less pronounced, these data were replicated in Ctns-/- rats fed with ketogenic diet from 2 to 8 months of life.

Conclusion: These results indicate a potential therapeutic effect of ketogenic diet to mitigate the renal phenotype in human subjects affected by nephropathic cystinosis.

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ELEVATED BLOOD PRESSURE IN PEDIATRIC PATIENTS WITH X-LINKED HYPOPHOSPHATEMIA IS ASSOCIATED WITH BMI AND TREATMENT MODALITY: AN ANALYSIS OF THE GERMAN/SWISS XLH REGISTRY

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Purpose: X-linked hypophosphatemia (XLH) is the most common genetic cause of hypophosphatemic rickets with a prevalence of 1.7 - 4.8/100,000 children. Mutations in the PHEX gene lead to an increase in intact fibroblast growth factor 23 (FGF23) and consecutive renal phosphate wasting. The resulting main symptoms are rickets, osteomalacia, disproportionate short stature, and tooth abscesses. XLH patients were found to have an increased body fat percentage and around 30% of them were classified as overweight. Preliminary small studies suggest that XLH patients are at risk for elevated blood pressure. Conventional treatment, consisting of active vitamin D and phosphate salts, has limited efficacy for healing of rickets and leads to the adverse effects of nephrocalcinosis and hyperparathyreoidism. Burosumab, a monoclonal anti-FGF23 antibody, was shown to be superior to conventional treatment in healing of rickets. The impact of overweight and treatment modality on blood pressure in XLH patients is largely unknown.

Methods: We conduct a prospective observational multicenter study in Germany and Switzerland to identify long-term comorbidities in children with XLH. Patients receive conventional therapy or burosumab. Clinical and biochemical data, blood and urine samples are collected annually.

Results: To date, 130 patients (77 girls, median age 10.6 years) from 40 centers are included. 23% of patients have been treated conventionally for a median period of 5.1 years, 75 % of patients have received burosumab for 1.3 years with 4.5 years of prior conventional treatment. 33% of patients showed nephrocalcinosis. The median systolic blood pressure (SBP), diastolic blood pressure (DBP) and BMI of children with XLH were significantly increased by 0.74, 0.24 and 0.57 z-score, respectively. Overweight (BMI > 90th percentile) and arterial hypertension (systolic blood pressure > 95th percentile) were each found in approximately 21% of patients. SBP tended to be associated with BMI ($p = 0.091$), DBP was significantly associated with BMI, while nephrocalcinosis was no correlate. In the multivariate analysis SBP was significantly associated with treatment modality after adjusting for BMI z-score ($p = 0.01$), indicating higher blood pressure in children on conventional compared to burosumab treatment.

Conclusion: Children with XLH present with elevated blood pressure which is associated with BMI and conventional therapy. Monitoring of cardiovascular health and its risk factors in children with XLH appears to be important.

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HEALTH-RELATED QUALITY OF LIFE OF CHILDREN WITH X-LINKED HYPOPHOSPHATEMIA IN GERMANY IN THE BUROSUMAB ERA

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Purpose: X-linked hypophosphatemia (XLH) is a rare inherited phosphate-wasting disorder associated with bone and dental complications. Health-related quality of life (HRQoL) is reduced in XLH patients on conventional treatment with phosphate supplements and active vitamin D. Here, we investigated HRQoL of patients treated with burosumab.

Methods: HRQoL was assessed in 63 pediatric XLH patients participating in a prospective, observational study and patient registry in Germany using the KIDSCREEN-52 survey instrument and standardized qualitative interviews.

Results: The median age of the XLH patients was 13.2 years (interquartile range 10.6 – 14.6). At the time of the survey, 55 (87%) patients received burosumab and 8 (13%) conventional treatment. Forty-six patients (84%) currently treated with burosumab previously received conventional treatment. Overall, HRQoL was average compared to German reference values (mean ± SD: self-report: 53.36 ± 6.47; caregivers' proxy: 51.33 ± 7.15) and even slightly above average in some dimensions, including physical, mental and social well-being. In general, XLH patients rated their own HRQoL higher than their caregivers. In qualitative interviews patients and caregivers reported that, compared with conventional therapy, treatment with burosumab reduced stress, bone pain, and fatigue, improved physical health and increased social acceptance by peers and the school environment.

Conclusion: In this real-world study in pediatric XLH patients, HRQoL was average or even slightly above that of the general population, likely due to the fact that the vast majority of patients had their treatment modality switched from conventional treatment to burosumab resulting in improved physical health and well-being.

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ADENOSINE MONOPHOSPHATE ACTIVATED PROTEIN KINASE ACTIVATORS ARE A NOVEL POTENTIAL THERAPY FOR X-LINKED CONGENITAL DIABETES INSIPIDUS

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Aims/Purpose: X-linked congenital NDI presents in infancy and is characterized by production of very large quantities of dilute urine. This results from kidney unresponsiveness to vasopressin due to inactivating mutations in type-2 vasopressin receptors (V2R). Patients can produce up to 20 L/d of dilute urine. Current therapy is to drink an equal quantity of water to avoid dehydration. Failure to maintain adequate water intake can cause cognitive impairment due to repeated episodes of severe dehydration. The necessity for frequent and high-volume urination can lead to bladder dysfunction, reflux nephropathy, and chronic kidney disease. V2R mutations prevent vasopressin-mediated activation of PKA, resulting in decreased phosphorylation of aquaporin-2 (AQP2) water channels and UT-A1 urea transporters, and an inability to concentrate urine. We showed that metformin increases AQP2 and UT-A1 phosphorylation, plasma membrane accumulation, and urine concentration in rodent models of NDI. However, metformin is a weak AMPK activator and the dose given to rodents far exceeds what can be given to people. The aim of this study was to design highly potent, selective, orally active AMPK activators that may become a therapy for X-linked NDI.

Methods: NephroDI Therapeutics successfully synthesized several AMPK activators from our proprietary library. We generated a rat model of X-linked NDI by gavage feeding male Sprague Dawley rats with tolvaptan, a V2R antagonist, for 1 week. Rats were housed in metabolic cages and urine collected daily to determine urine osmolality and volume. After verifying tolvaptan-mediated NDI (reduced urine osmolality), rats continued to receive tolvaptan and were gavage fed for 1-2 weeks with NDI-5001 or vehicle. Blood glucose was measured at the end of the study.

Results: Tolvaptan reduced urine osmolality and increased urine volume. Subsequent daily oral dosing with NDI-5001 significantly increased urine osmolality and decreased urine volume compared to vehicle. The improvement in urine osmolality and volume was maintained over the entire study. Blood glucose was normal in all groups.

Conclusion: We conclude that NDI-5001, a potent, selective, orally active AMPK activator, improves urine concentration in a rat model of X-linked NDI and holds promise as a potential therapy for patients with V2R mutations. NephroDI Therapeutics is completing pre-clinical studies with the goal of obtaining regulatory authorization to begin phase 1 human studies.

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ECYSCO, A EUROPEAN CYSTINOSIS COHORT

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Aims/Purpose: Cystinosis is a rare multisystem lysosomal storage disease due to variants in the CTNS gene, causing cystine accumulation. Specific treatment by cysteamine decreases renal and extrarenal complications frequency in cystinosis patients but data on long-term manifestations of the disease are lacking. The aim of the ECYSCO cohort is to describe the natural history of the disease and the effect of treatments.

Methods: We set up a European, multi-centre, longitudinal, non-interventional cohort, ECYSCO, that uses observational study methods to collect uniform data. 243 patients with a confirmed diagnosis of cystinosis and followed in 25 French and 5 European centers (Belgium, Italy, Spain and Germany) were included. Data are collected on the secure RaDiCo platform, via an e-CRF (REDCap).

Results: Data from 177 patients (50.8% male) were analyzed. Median age at diagnosis was 1.3 years [IQ 0.9; 1.8], with earlier diagnosis since the 1990s. Genetic analysis was available for 158 patients: 46 (31.9%) presented with homozygous 57kb deletion in the CTNS gene, 57 (39.6%) with heterozygous 57kb deletion associated with another variant and 46 (26.4%) with other variants. The type of variant had no impact on the age at diagnosis. Median age at cysteamine start was 1,6 years (IQ 1.0-3.0). All but 7 patients were treated with cysteamine. Sixty-seven patients received immediate release formulation (Cystagon®) and 103 received extended release formulation (Procysbi®). Median white blood cell cystine level was 1.2 nmol ½ cystine/ mg protein (IQ 0.6; 2.2). The median duration of treatment was 21.5 years [IQ 11.7; 31.1]. 165 (93,2%) patients also received cysteamine ocular gel, Cystadrops®. Median age at inclusion was 18.4 years (IQ 10.4; 30.6). At that time, 104 patients (57.8%) had reached kidney failure (KF). There was no impact of genotype on age at KF. Median age at KF was 12.9 years [IQ 9.9; 18.0]. A 5-year gain in renal survival was observed after the 1990s. 102 patients (56.7%) received a kidney transplant. Extrarenal manifestations included hypothyroidism in 29 (16.4%) patients, diabetes mellitus in 15 (8.4%), skeletal manifestations in 89 (53.6%), myopathy in 28 (17.9%), and neurological disorders in 21 (13.5%).

Conclusion: Cystinosis is a good example of a pediatric disease with multiorgan involvement extending into adult care. The high frequency of extra-renal manifestations demonstrates the importance of a multidisciplinary follow up of these patients.

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LONG-TERM CLINICAL OUTCOMES OF DRTA PATIENTS TREATED WITH SIBNAYAL, AN ORAL TWICE-DAILY FIXED AND PROLONGED-RELEASE COMBINATION OF POTASSIUM BICARBONATE AND POTASSIUM CITRATE

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Aims/Purpose: Distal renal tubular acidosis (dRTA) is a rare disease characterized by hyperchloremic metabolic acidosis affecting growth, bone and kidney health. The aim of the study was to evaluate the long-term safety and efficacy of Sibnayal®, a prolonged-release alkalizing formulation with twice-daily dosing, in children and adults with dRTA.

Methods: Patients with inherited dRTA, were followed for an average of 6 years in a multicenter open-label extension trial (B22CS1) to evaluate the long-term effect of Sibnayal® on safety, anthropometric and pubertal evaluations, on evolution of tubular damages including metabolic acidosis, kidney function, and lumbar BMD. At baseline visit (last visit of phase II/III trial, B21CS2), all patients were already treated by Sibnayal®.

Results: A total of 30 patients (24 children, 6 adults, mean age: 10.6 ± 6.0 years), entered the long-term study, 27 of whom had data collected beyond Month 30. Sibnayal® was well tolerated over the study duration. In terms of efficacy, Sibnayal® allowed a sustained control of metabolic acidosis as plasma bicarbonate level was 22.0 ± 3.2 mmol/L at baseline versus 22.6 ± 2.5 mmol/L at the End of Follow-up (EoF), p =NS. Mean height Z-score significantly increased from baseline (-0.6 ± 1.0) to EoF (-0.3 ± 0.9), p =0.03, without significant change in weight and BMI. It was significantly greater in patients with abnormal EAS (Estimated Adult Stature) at baseline as compared to normal EAS at baseline, ($p < 0.001$). Kidney function remained stable from baseline to EoF: eGFR = 105 ± 17 and 104 ± 20 mL/min/1.73m2 respectively, p =NS. Most of patients (87%) had KDIGO CKD stage 1 at baseline and there was no difference in patients' CKD stages between baseline and EoF. Urinary ratios UCa/UCr, UCi/UCr, UCa/UCi were maintained between baseline and EoF (p =NS). Both percentages of patients with nephrocalcinosis and with nephrolithiasis remained stable between baseline and EoF (p =NS). Mean lumbar BMD Z-score underwent a significant increase from baseline (-1.1 ± 1.0) to EoF (-0.8 ± 1.0), p =0.005. There is a significant improvement of mean lumbar BMD Z-score between baseline and EoF in pre- and post-pubertal patients (respectively, p =0.035 and p =0.0007) whilst it was maintained in patients in pubertal phase (p =NS).

Conclusion: Long-term data support the good safety and efficacy profile of Sibnayal® in the treatment of dRTA with adequate control of metabolic acidosis, stable kidney function and significant positive long-term outcomes, notably on growth, lumbar spine BMD and bone metabolism in patients with dRTA treated over 6 years in average.

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SESSION 7
UNMET NEEDS IN CHILDREN ON DIALYSIS

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A STUDY INVESTIGATING THE PHARMACOKINETICS OF A SINGLE DOSE OF INTRAVENOUS DIFELIKEFALIN IN ADOLESCENTS AGED 12 TO 17 YEARS ON HAEMODIALYSIS

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Aims: Difelikefalin is a novel therapeutic agent that was recently approved for the treatment of moderate-to-severe pruritus associated with chronic kidney disease kidney (CKD) in adults on haemodialysis (HD)1. The aim of this study was to evaluate the PK profile, safety, and tolerability of a single dose of difelikefalin administered as an intravenous bolus injection to adolescents on HD.

Methods: KOR-PED-201 (EudraCT number: 2021-000894-94) was a multicentre, open-label, single-arm, single-dose study in adolescents (12 to 17 years) who had been on HD for at least 3 months and were on HD at least 3 times per week. After a screening period of up to 21 days, subjects were administered a single dose of difelikefalin of 0.5 µg/kg, based on their estimated dry body weight, at the end of the dialysis. Blood samples were collected over a 3-day period for difelikefalin plasma concentration. A safety follow-up visit was performed at 7 to 10 days after difelikefalin administration.

Results: A total of 8 subjects (3 males and 5 females) were enrolled and completed the study per protocol. Mean age at informed consent was 15.0 years (minimum age: 12 years; maximum age: 17 years). The mean (SD) time since first HD was 3.3 (3.09) years. One subject was excluded from the PK Analysis Set because of non-quantifiable difelikefalin concentrations at all time points. The mean (95% confidence intervals) and median for the most relevant PK parameters were: Cmax 6.03 (4.36 to 7.71) ng/ml and 6.57 ng/ml; AUC0-48 63.4 (47.4 to 79.5) h*ng/ml and 62.8 h*ng/ml; AUCinf 72.5 (50.6 to 94.4) and 73.0 h*ng/ml. A pre-specified numerical comparison of Cmax, AUC0-48, and AUCinf values (median and 95% confidence intervals for the mean) in the adolescent HD population (KOR-PED-201 study) with the corresponding values from a previous study CR845 CLIN2005 (NCT02229929) in an adult HD population showed that the overall exposure following administration of a single dose of difelikefalin was comparable between adolescents and adults. Overall, 2 mild treatment-related adverse events were reported in 1 (12.5%) subject (1 event each of headache and dizziness). There were no serious treatment-emergent adverse events (TEAEs) and no TEAEs led to study withdrawal.

Conclusion: Following administration of a single difelikefalin dose of 0.5 µg/kg in adolescents on HD, the overall exposure was found to be comparable with previous data in adults on HD; the safety profile in adolescents was consistent with the known safety profile of difelikefalin in adults and no new safety signals emerged. The difelikefalin dose of 0.5 µg/kg was found to be appropriate for the adolescent HD population and will be further investigated in adolescents with CKD-associated moderate-to-severe pruritus.

Summary of Product Characteristics. Kapruvia 50 micrograms/mL difelikefalin (as acetate). https://www.ema.europa.eu/en/medicines/human/EPAR/kapruvia.

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RISK FACTORS AND CONSEQUENCES OF LONG-TERM DIALYSIS IN CHILDREN: DATA FROM ERKREG REGISTRY

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Introduction: The overall mortality rate is higher among dialysis children than in general pediatric populations. Cardiovascular disease increases with the time spent on dialysis; cardiovascular events and infections remain the leading causes of death in pediatric dialysis.

Methods: We performed a multi-centre, descriptive study using data from the ERKReg registry, including all patients who started dialysis before the age of 18 years. Patients were divided into three groups according to time spent on dialysis: less than 3 years, between 3 and 5 years and more than 5 years. We collected the 9 Key Performance Indicators (KPIs) previously identified in the registry for pediatric dialysis. A linear mixed-effect modelling was used to study longitudinal progression for clinical and biological parameters. To analyze more deeply patients' characteristics and quality of life, we also sent a questionnaire to healthcare professionals of patients on dialysis for more than 3 years.

Results: In April 2023, 370 patients were included, with 284 pediatric patients on dialysis for less than 3 years, 55 between 3 and 5 years and 31 for more than 5 years. No association was found between the cause of kidney failure and dialysis duration, but patients on prolonged dialysis started dialysis at a significantly younger age. They were also more likely to receive growth hormone therapy and had lower diastolic blood pressure. Linear mixed-effect modelling analysis showed a decreasing trend for height, serum phosphate, systolic and diastolic blood pressure; and an increasing trend for haemoglobin and serum bicarbonate with the time spent on dialysis. The survey was completed for 39 patients on dialysis between 3 and 5 years and 20 for more than 5 years: approximately 20% of patients or families had refused kidney transplantation whilst more than 40% had at least one medical contraindication to transplantation.

Conclusion: KPIs are reassuring in children undergoing long-term dialysis in ERKReg. These data allow to better understand reasons, management and complications of long-term dialysis in children.

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LONG-TERM KIDNEY FAILURE FOLLOWING ACUTE KIDNEY INJURY IN A NATIONAL COHORT OF CHILDREN

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Aim: There is growing evidence of the consequences of paediatric AKI but little is known about the risk of developing long-term kidney failure. Adult studies show risk increases in a graded manner with AKI severity. In NHS laboratories in England, electronic AKI alerts generated by relative rises in serum creatinine are sent to the UK Renal Registry for reporting; subsequent linkage to the kidney failure dataset provides a unique opportunity to explore AKI outcomes nationally. Our aim was to examine a cross-section of children in England with AKI and determine the demographic and clinical factors associated with subsequent long-term kidney failure.

Methods: All children aged < 18 years old for whom an AKI e-alert was received by the UK Renal Registry between 1/1/16-31/12/19 were included and linked to Hospital Episode Statistics and the UK Renal Registry kidney failure dataset. Children already established on long-term (> 90 days) kidney replacement therapy (KRT) and those who died before 90 days were excluded. The outcome of interest was the need for long-term KRT between 1/1/16-31/12/21 following an AKI episode. Characteristics of the study cohort are presented and differences in demographic and clinical characteristics between children who did and did not develop established kidney failure were compared.

Results: 48,932 AKI episodes were received for 37,660 children in England during the study. Following exclusions, 42,706 AKI episodes in 32,581 children were included for analysis. 276 children (0.8%) who received an AKI alert were identified in the kidney failure dataset. Children who developed long-term kidney failure were older (median age 10.8) and more likely to be of Asian ethnicity (25%); they also experienced more AKI episodes during the study period compared to those who did not. Stage 3 AKI was more common among children later requiring long-term KRT, both at start and peak, with four-times longer median duration of AKI. Of those who had an AKI stage 3 at start, 7.1% required long-term KRT. Among first AKI episodes, higher proportions of community-acquired AKI were noted for those requiring long-term KRT compared to those who did not (46.0%). For the 276 children requiring long-term KRT, the median time from last AKI episode to KRT start was 83 (IQR 25, 352) days. The most common underlying kidney diagnosis was tubulointerstitial disease(37.0%) and glomerular disease(30%). Most children commenced KRT on dialysis (86.2%).

Conclusion: Over a 5-year period, the risk of developing long-term kidney failure following AKI for children in England was 0.8%. Duration and severity of AKI were associated with subsequent kidney failure development. This is the first national study to be able to examine these associations and will support clinicians in assessing long-term prognosis following AKI. Interventions to reduce AKI disease progression may help lower the incidence of long-term kidney failure.

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SHORT-TERM OUTCOMES OF CONTINUOUS KIDNEY REPLACEMENT THERAPIES IN NEONATES AND INFANTS - RESULTS FROM THE EURAKID REGISTRY

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Aims/Purpose: In recent years, technological advancements and increasing clinical experience have enabled the application of continuous kidney replacement therapies (CKRT) even in the youngest patients. The aim of this study was to identify factors influencing short-term outcomes of CKRT in neonates and infants.

Methods: The study involved children up to 12 months of age, included in the EurAKId registry (European Registry of Dialysis in Pediatric Acute Kidney Injury), who underwent CKRT treatment. We analyzed clinical, anthropometric, biochemical data, and CKRT parameters. The primary endpoint was mortality. Secondary endpoints were proteinuria, hypertension, and the need for chronic dialysis at hospital discharge. The predictors were identified using decision tree models, and confirmed with stepwise general regression.

Results: The analysis comprised 95 children (32 neonates, 63 infants, median age 1 month, IQR 0-7), who underwent a total of 24,382 hours of CKRT (median 148h per patient, IQR 71.5-371). In 85.8% of cases CKRT was performed using Prismaflex system. Median prescribed dialysis dose was 108.5 (IQR 75.0-133.3) mL/kg/h and was the highest in patients with inborn errors of metabolism (274.3, IQR 111.2-671.6 mL/kg/h; $p < 0.001$). Overall mortality was 46.3% and did not differ significantly regarding the primary disease. With the decision tree model, we identified age ≤7 months, urine output at dialysis start ≤2.135 mL/kg/h, and urine output at hospital admission of > 0.145 mL/kg/h as dependent prognostic factors for mortality. Model accuracy was 68.8%, with 85.7% specificity, and 40.1% sensitivity. In children meeting all the above criteria, median urine output decline until dialysis initiation was higher than in the rest of the patients (2.3, IQR 0.8-4.4 vs 0.0, IQR -1.3-0.7 mL/kg/h, $p = 0.002$). Children with urine output at hospitalization < 0.145 mL/kg/h initiated CKRT immediately. Proteinuria was present in 32.6% of survivors. Primary kidney disease was a strong predictor of proteinuria, and in children with other primary diseases potassium ≤5.7 mg/dl was a protective factor. Decision tree model accuracy was 89.1% (specificity 100%, sensitivity 66.7%). Hypertension was noted in 26.1% of cases. We identified no factors influencing its occurrence. Only one patient required chronic dialysis at hospital discharge.

Conclusion: CKRT in children up to 12 months is associated with high mortality, but comparable to overall pediatric population. Young age and low urine output may predict mortality in neonates and infants requiring CKRT. Larger urine output decline until dialysis initiation might also be predictive of death in the youngest patients. Kidney disease and serum potassium levels could be associated with the occurrence of proteinuria in short-term observation.

1050

A LITTLE GOES A LONG WAY. OUTCOMES OF CHILDREN UNDER TWO YEARS OF AGE WITH END STAGE RENAL DISEASE - A RETROSPECTIVE, MULTICENTER ANALYSIS

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Aims/Purpose: The aim of this study was to assess the clinicopathological outcomes of children under two years of age, with ESKD that were dialysed in three Australian paediatric centers, across two states, New South Wales, and Queensland. We further assessed whether these outcomes were affected by the presence of anuria and hypotension and whether they were comparable with national and international data.

Methods: All children less than 2 years of age at the commencement of chronic RRT at one of the three centers (center A, B, C) from January 2001 to December 2021, were included in the study. Children dialysed for acute kidney injury were excluded, but those who initiated dialysis with a long-term plan, were included even if they died within the first 3 months. Data was collected retrospectively from the patient medical record and from the Australia and New Zealand kidney registry (ANZDATA). The study was approved by Human Research Ethics Committees in NSW and QLD (2021/ETH11586).

Results:

Table 1: Patient characteristics and outcomes

(n)	TOT (54)	A (22)	B (19)	C (13)
Age at initiation of dialysis-months(range)	10.4 (0.1-23.9)	11.3 (0.1-23.1)	10.7 (0.3-23.9)	8.6 (0.3-20.1)
Weight at initiation of dialysis – kilograms (range)	8.1 (3-17)	9 (3.9 – 17.0)	7.9 (3-13)	6.9 (3-10)
Transplant (%)	42 (78%)	16	16	10
On Dialysis (%)	3 (5%)	1	1	1
Demised (%)	9 (17%)	5	2	2

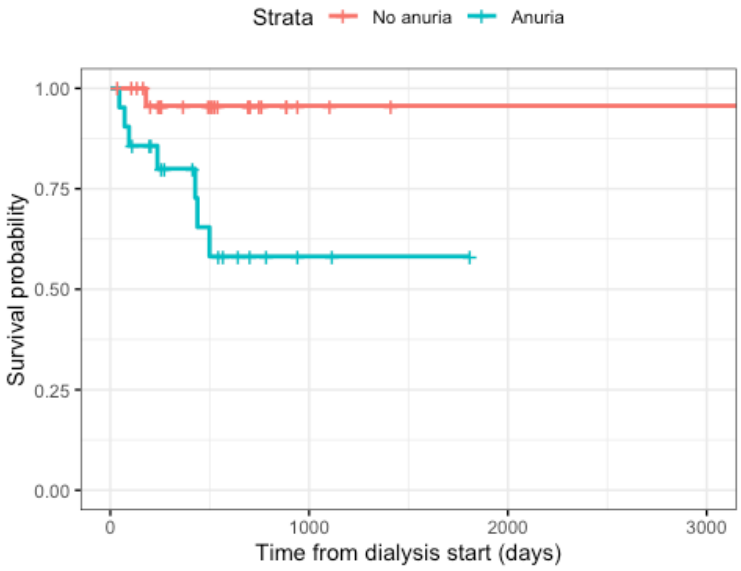
At initiation of dialysis, 32 patients commenced on APD (58%), 14 on IHD (26%) and 9 on CVVH (16%). Fifty-two children (96%) had long-term APD and two patients received chronic HD (including one that was ICU dependent and alternated IHD with CVVH). Three more patients on APD switched to IHD for long term dialysis.

Table 2: Dialysis and transplant characteristics

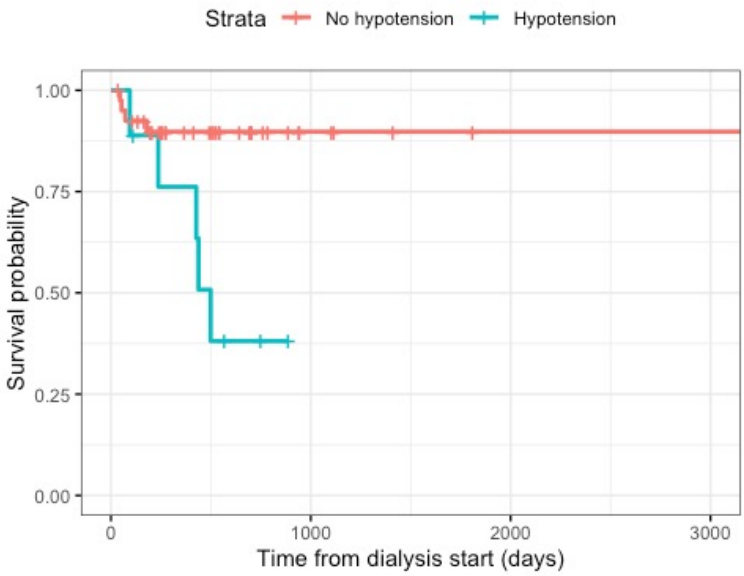
(n)	TOT (54)	A (22)	B (19)	C (13)
Anuria within one month of dialysis	21 (39%)	10	5	5
Anuria after one month of dialysis	25 (46%)	15	9	1
Hypotension	11 (20%)	7	2	2
Midodrine	11 (20%)	7	2	2
Age at transplant-months(range)	32.2 (11.9-112.8)	28.3 (11.9-41.1)	35.4 (13.3-63.9)	31.5 (16.6-112.8)
Weight at transplant – kilograms (range)	12.1 (7.2-28.5)	10.9 (7.2-13.7)	12.8 (10-17)	12.5 (9-28.5)
Length of time on dialysis – months (range)	22.4 (1.1-112.5)	14.8 (1.2-31.3)	23.5 (13.3-63.9)	24.5 (1.1-112.5)

Characteristics of patients that demised: Of the 9 patients that demised, 5 succumbed to sepsis (56%), 2 had pulmonary oedema and 2 cardiac arrests. 7 were on long term APD and 2 IHD. 2 patients (22%)

started dialysis in the first month of life.



Graph 1: Kaplan Meier survival curve of children under two years on RRT with anuria (blue) vs no anuria (red)



Graph 2: Kaplan Meier survival curve of children under two years on RRT with hypotension (blue) vs no hypotension (red)

Conclusion: Our study aligns with national and international data in demonstrating that more infants under two years of age are accessing RRT and survival is improving. However, we note that anuria and hypotension significantly affect mortality in this group of patients.

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IMPROVING INTRADIALYTIC SYMPTOM MANAGEMENT IN PEDIATRIC HEMODIALYSIS PATIENTS THROUGH BLOOD VOLUME MONITORING AND MACHINE LEARNING

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Aims/Purpose: Intradialytic symptoms (IDS) arise from the imbalance between ultrafiltration (UF) and plasma refilling during hemodialysis (HD) sessions, leading poor clinical outcomes. New generation HD machines equipped with blood volume monitors demonstrate the relative changes in blood volume (RBV) during HD sessions. It has been shown that steeper RBV fall is associated with IDS. The aim of our study is to evaluate the role of RBV to avoid IDS and also to establish a machine learning model for predicting the 2nd hour RBV values.

Methods: This single-center retrospective study analyzed 255 HD sessions with complete data of 11 pediatric patients (4 males, all anuric) in a standard chronic HD program (four hours and thrice weekly). The dataset included pre-dialysis weight, dry weight (DW), interdialytic weight gain (IDWG)/DW, UF/DW, at the start of dialysis systolic and diastolic blood pressure (BP), heart rate, hemoglobin, albumin values and RBV at the 2nd hour. A regression task employed the XGBoost algorithm for model training and testing, optimized for the dataset using the Python programming language via the SPYDER IDE.

Results: The median (25th and 75th percentile) age of the patients was 17.4 (9.4; 20.6) years, with a median HD duration of 32.2 (18.3; 61.3) months. IDS were noted in 37.5% of the sessions (n = 95). Symptomatic patients exhibited significantly higher hemoglobin increase (%19.9 vs. %13.6, p =0.011) and RBV decrease (%-12.7 vs. %-10.8, p =0.005) at the 2nd hour, while IDWG/DW, UF/DW, systolic, and diastolic BP did not differ. The XGBoost model achieved 95% training and 79% testing success in predicting 2nd hour RBV, with IDWG/DW, UF/DW, and hemoglobin identified as the most influential features.

Conclusion: Blood volume monitoring seems to be promising tool to avoid IDS. Machine learning models may effectively predict the 2nd hour RBV, guiding the adjustment of the dialysis prescription before starting HD treatment. Large scale data sets are needed to validate our findings.

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THE BURDEN OF HOSPITALIZATION IN CHILDREN ON DIALYSIS: THE EXPERIENCE OF THE ITALIAN REGISTRY OF PEDIATRIC CHRONIC DIALYSIS (IRPCD)

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Aims/Purpose: Children undergoing kidney replacement therapy often experience complications leading to frequent hospitalizations. This nationwide retrospective observational study, performed within the Italian Registry of Pediatric Chronic Dialysis (IRPCD), aims to describe complications requiring hospitalization in children on chronic peritoneal dialysis (PD) and hemodialysis (HD); we also sought to compare hospitalization rates between the two dialysis modalities.

Methods: Patients receiving HD or PD aged less than 18 years were recorded from January 2000 to December 2019 by the IRPCD. Hospitalization was defined as an admission involving at least one overnight stay, excluding hospitalizations for dialysis initiation and kidney transplantation. Reasons for hospitalization were categorized into infections related to dialysis, non-infectious complications related to dialysis, other infections, other non-infectious medical conditions, diagnostic tests, procedures or surgery, and other complications related to end-stage kidney disease (ESKD).

Results: 847 incident dialysis patients (493 PD, 354 HD) were enrolled. The median age at dialysis initiation was 5 (1.0-10.7) years for PD and 13 (9.6-15.3) years for HD, with the majority being females in both groups (59.6% and 54.8%, respectively). The primary cause of ESKD was CAKUT in both groups (41.6% in PD, 32% in HD); among the other causes, a significant difference was noted for glomerulonephritis, with a higher prevalence in the HD group (25.4 vs. 16.1%). Of the 847 patients, 418 (49.3%) required hospitalization, predominantly in the PD group (314 [75%] vs. 104 [24%] in the HD group). Median hospitalization duration was 6 days in both HD (IQR 4.5-11) and PD (4-9) patients. Infections related to dialysis were the main cause of hospitalization (35%), followed by other non-infectious medical conditions (18%) and other ESKD-related complications (14%). The hazard of hospitalization over time was significantly lower for HD compared to PD patients (aHR 0.54[0.42;0.70]). Moreover, it decreased with increasing patient age (aHR 0.97[0.95;0.98]) and calendar year since dialysis initiation (aHR 0.97[0.96;0.98]). The hazard of hospitalization was not related to the primary renal disease but increased significantly with the number of complications. Children on PD for over 1 year had a higher aHR (1, ref) for changing treatment compared to HD patients (0.29[0.10;0.81]).

Conclusion: Our nationwide data reveal a significant burden of hospitalization in children on chronic dialysis. Risk of hospitalization is linked to younger age at dialysis initiation and decreases in more recent calendar years. Children on PD face a higher risk of hospitalization over time compared to HD. This resulted in a higher chance of switching dialysis modality.

SESSION 8

KIDNEY DEVELOPMENT: BASIC AND NEWS

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ELUCIDATING THE CATALYTIC AND NON-CATALYTIC ROLES OF KMT2D IN CAKUT IN KABUKI SYNDROME

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Aims/Purpose: Environmental and metabolic factors are associated with congenital anomalies of the kidney and urinary tract (CAKUT) and are hypothesized to function at the epigenetic level. Yet, the underlying mechanisms are largely undefined. Histone lysine N-methyltransferase 2D(KMT2D), a major epigenetic modifier, catalyzes H3K4me1 at prime enhancers via its SET domain and acts non-catalytically as a scaffold protein, utilizing its tertiary structure to catalyze H3K27ac at enhancers and activate gene transcription. Mutations in KMT2D are frequent in Kabuki Syndrome (KS); 40% patients exhibit CAKUT, particularly those with variants in the Coiled Coil (CC) domains, crucial for protein folding. This project aims to elucidate KMT2D catalytic and non-catalytic functions in kidney development and the impact of CC domains mutations on kidney malformation.

Methods: A meta-analysis of 737-KS patients from 34 publications elucidated the spectrum of CAKUT in KS-patients. KMT2D-deficient human kidney organoids were generated using CRISPR-edited iPSCs targeting the SET domain (KSSET), and from urine-derived iPSCs of KS patients with CC domains variants (KSCC). Artificial Intelligence tool (ALPHAFOLD) was used to examine mutated KMT2D-CC protein structures in KSCC patients.

Results: A meta-analysis of 737 KS patients found 35% with CAKUT and positively correlated KMT2D-CC mutations with a higher CAKUT risk ($P \leq 0.01$). ALPHAFOLD analysis revealed altered protein structures in recruited KSCC patients. Immunostaining of human kidney organoids ($n = 2$) revealed KMT2D expression in control intermediate mesoderm (IM) and in SIX2+ nephron progenitors but not in PBX1+ renal stroma. Histologic analysis revealed a dysplastic phenotype with complete absence and dilated nephron-like structures in decreased numbers, in KSCC and KSSET kidney organoids ($n = 5$), respectively. qPCR of both KSCC and KSSET IM-RNA demonstrated upregulation in the IM markers, OSR1 and LHX1 ($n = 3$, $P \leq 0.0001$) and downregulation of SIX2 ($n = 3$, $P \leq 0.001$). qPCR of mature KSCC and KSSET kidney organoids showed downregulation in nephron segment differentiation markers ($n = 3$, $P \leq 0.001$) and upregulation in stromal markers ($n = 3$, $P \leq 0.001$).

Conclusion: Our results indicate that KMT2D catalytic and non-catalytic functions are required for formation of human kidney organoids and provide a basis for determining underlying molecular mechanisms that control epigenetic regulation in the human embryonic kidney.

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REANALYSIS OF GENETICALLY UNDIAGNOSED PATIENTS WITH CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT USING WHOLE-EXOME SEQUENCING DATA AND OPTICAL GENOME MAPPING FOLLOWED BY REVERSE PHENOTYPING

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Aims/Purpose: Congenital anomalies of the kidney and urinary tract (CAKUT) are the predominant cause of chronic kidney disease in children. Today, over 60 genes are known to cause CAKUT if mutated. Nevertheless, causative aberrations are commonly identified in only ~16% of patients. To increase the diagnostic yield, this study revisited a cohort of 101 CAKUT patients who initially remained genetically undiagnosed after whole-exome sequencing (WES).

Methods: Raw WES data from genetically unsolved CAKUT-patients were reanalyzed with our current bioinformatics pipeline prioritizing rare coding variants and copy-number variations. Near-coding variants possibly affecting splicing were analyzed using Squirls and SpliceAI. Digenic inheritance was predicted using ORVAL and DiGePred. To identify or verify structural variants, high molecular weight DNA was assessed by optical genome mapping (OGM). Co-segregation analysis and reverse phenotyping were done in selected cases.

Results: In eight patients, we identified rare variants in genes associated with kidney disorders undetected by previous WES analysis, e.g. heterozygous variants in HNF1B, SALL1, TBX6, WNT4, ZMYM2, or biallelic variants in BBS9 or GREB1L. A novel heterozygous splice-site variant in OFD1 associated with orofaciodigital syndrome including polycystic kidneys was found in a female patient with multicystic dysplastic kidneys and extrarenal features. Digenic combinations of variants of uncertain significance, including FRAS1_FREM2, FRAS1_GRIP1, CRKL_TBC1D1, ROBO1_DACT1, were predicted as disease-causing in 11 patients by one or two algorithms. By OGM, copy number aberrations were detected in eight syndromic patients, encompassing CAKUT-associated genes in 4/8 cases, including chr17q12 loss (HNF1B-locus), chr22q11.21 loss (CRKL-locus), and chr16p11.2 gain (TBX6-locus). A complex chromosomal rearrangement involving a locus previously described in patients with lower urinary tract abnormalities was found in a female patient with CAKUT and complex extrarenal features including urogenital sinus.

Conclusion: Using new technologies, improved bioinformatic tools, updated variant classification in databases, literature reports on disease gene identification and variant characterization, by genetically testing family members, and assessing patients' clinical phenotype, 13% and 15% of previously unsolved patients clinically diagnosed with CAKUT received a definitive or putative genetic diagnosis, respectively.

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TGFB SIGNALLING PROMOTES MURINE RENAL PATTERNING AND NEPHROGENESIS VIA CADM1

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Aims/Purpose: Impaired nephrogenesis affects kidney health, causing childhood CKD and increasing CKD risk in adults. Foxd1+ kidney stromal cells regulate nephron development by interacting with Six2+ nephrogenic precursors. Previously, we (Rowan CJ et al, Development, 2018) demonstrated that Hedgehog-GLI signaling in Foxd1+ stromal cells is required to promote murine nephrogenesis through TGF signaling, specifically via promoting the transformation of mesenchymal cells into epithelial cells (MET) in the Six2+ nephrogenic zone. However, the underlying molecular mechanisms that guide MET are incompletely defined. Here we aim to define molecular mechanisms by which TGF signaling regulates nephrogenesis.

Methods: Whole-kidney RNA seq and single-cell RNA seq to examine Tgfr2 deficiency in Foxd1+ stromal and Six2+ nephrogenic kidneys. Compound mutant mice were generated to investigate the deficiency of Cadm1 alone or both Tgfr2 and Cadm1, followed by histological analysis, immunostaining, and nephron quantitation.

Results: Whole-kidney RNA seq(n = 4) and scRNA seq in Foxd1+ stromal and Six2+ nephrogenic Tgfr2-deficient kidneys identified Cadm1 in Foxd1+ stromal cells as a downstream target of TGF signaling. Kidneys deficient in Cadm1 in stromal or nephrogenic cells exhibited normal nephrogenesis (n = 2-3, $p < 0.01$). Kidneys with deficiency in both Tgfr2 and Cadm1 in Foxd1+ stroma showed renal hypodysplasia, with a 32% and a 35% reduction in kidney: body weight (n = 6, $p < 0.0001$) and nephron number (n = 3, $P < 0.05$), respectively, along with an increased SIX2+ cell number and irregular stromal patterns (n = 3). Similarly, deficiency in both Tgfr2 and Cadm1 in Six2+ nephrogenic cells led to renal hypodysplasia, showing a 27% reduced kidney: body weight (n = 3, $p < 0.01$) and a 48% decline in nephron number (n = 2, $P < 0.05$), with an expanded SIX2+ cell number (n = 3, $p < 0.01$). Deficiency in both Tgfr2 and Cadm1 in Foxd1+ and Six2+ cells resulted in severe renal hypoplasia with detached renal capsule and reduced nascent nephron structures. Additionally, In HEK-T293 cells, TGF1 treatment increased CADM1 expression in a dose-dependent manner (n = 3). Co-immunoprecipitation demonstrated a potential interaction between TGFR2 and CADM1, and wound healing assays in Cadm1 deficient HEK-T293 cells showed a 24% reduction in cell migration compared to control.

Conclusion: Cadm1 is essential for normal nephrogenesis in mice and regulates nephrogenic precursor epithelialization under the influence of TGF signaling.

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A WHOLE-GENOME SEQUENCING GENOME-WIDE ASSOCIATION STUDY META-ANALYSIS TO UNCOVER THE GENETIC AETIOLOGY OF POSTERIOR URETHRAL VALVES

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Aims/Purpose: Posterior urethral valves (PUV) are the predominant underlying cause for dialysis and kidney transplantation in boys. Despite a suspected contribution of genetic factors, the precise molecular causes of PUV remain largely unknown. To better understand this aetiology, we performed a genome-wide association study using whole-genome sequencing data (seqGWAS) and combined our results with a published seqGWAS in a meta-analysis.

Methods: The new cohort of PUV patients was derived from the AGORA Data- and Biobank, containing 77 cases and 232 controls of European ancestry, all of whom were male and had undergone whole-genome sequencing. Quality control included a minor allele frequency threshold (MAF) of ≥ 0.1%, missingness of < 1% and Hardy Weinberg equilibrium of < 1 x 10-6 for controls. 11,372,461 variants remained for analysis. Samples with a calculated kinship coefficient > 0.0885 (i.e. first and second degree relatives) were excluded. A genome-wide logistic regression analysis was performed to detect genotype-phenotype associations, with the use of five covariates (principal components 1-5). All analyses were performed in PLINK. The results were meta-analyzed with a mixed ancestry cohort from Genomics England, consisting of 132 cases and 10,425 male ancestry-matched controls using the inverse-variance approach in METAL. A total of 9,175,971 common variants were analyzed; variants with a minimum and maximum allele frequencies difference > 0.1 and a heterogeneity P value < 0.01 were excluded. Next to the genome-wide significance threshold, we used a suggestive threshold of P < 1 x 10-5.

Results: The seqGWAS in the AGORA cohort did not reveal any genome-wide significant associations (= 0.93). In the meta-analysis (= 0.92), genome-wide significance of the TBX5 locus on Chromosome 12 (Figure 1) was retained, with the common lead intergenic variant rs10774740_T having a protective effect (odds ratio (OR) 0.48; 95% confidence interval (CI) 0.38-0.60; MAF 0.37; P =1.03 x 10-10; P =0.11 in the AGORA cohort). The previously identified genome-wide significant variant rs144171242 on Chromosome 6 did not reach genome-wide significance in the AGORA cohort (P =0.31), however suggestive association was seen at this locus in the meta-analysis (rs142976101; OR 9.3; 95% CI 3.51-24.62; P =7.20 x 10-6; MAF 0.01; EUR R2 0.4 with rs144171242). Ten additional loci had suggestive association with PUV. Post-GWAS analyses, including statistical fine-mapping and gene-based and gene-set analyses, are pending for these loci.

Conclusions: We present the first meta-analysis of seqGWAS data from boys with PUV, confirming

one genome-wide significant locus on Chromosome 12 and suggesting evidence of association at 11 other loci. Larger studies are needed to determine if these represent genuine additional causal loci.

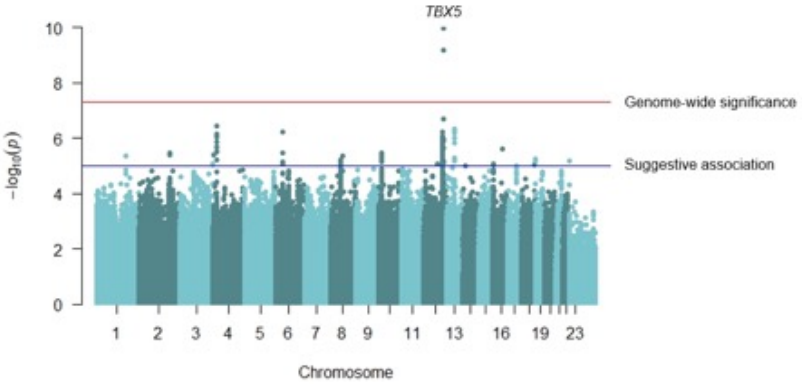

Figure 1: Manhattan plot of seqGWAS meta-analysis.

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PREVALENCE AND DETERMINANTS OF FAILURE TO THRIVE IN CHILDREN WITH VESICO-URETERAL REFLUX

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Aims/Purpose: Failure to thrive (FTT) is considered indicator of urinary tract infection (UTI), leading to routine inclusion of urinalysis and urine cultures in the evaluation of children with FTT. Consequently, it might be anticipated that patients experiencing recurrent UTIs have an elevated risk of FTT. However, we observed no clear correlation between FTT and recurrent UTIs and we formulated the hypothesis that the FTT in these patients is likely linked to urinary solute losses (sodium and bicarbonates) due to tubular losses associated with the most severe forms of vesico-ureteral reflux (VUR), rather than to the UTIs themselves. To test our hypothesis, we designed a retrospective study that included patients with VUR, who typically have an increased risk of UTIs. We aimed assessing prevalence and determinants of FTT among patients with VUR and evaluating the effects of tubular losses supplementation on growth in patients with urinary solute losses.

Methods: We retrospectively enrolled 1277 patients with VUR (mean age at diagnosis: 6.5months) from 2009 to 2023. Patients with FTT were screened for renal tubular impairment. If fractional excretion of sodium (FENa) > 2% or blood bicarbonate < 20mmol/L, supplementation was provided.

Results: Among 1277 patients, 56 (4.4%) had FTT. Out of the 56 patients, 42 (75%) presented extrarenal causes of FTT, 3 (5.4%) had chronic kidney disease (CKD), 9 (16.1%) had tubular function impairment and 2 (3.5%) had CKD and tubular function impairment. FTT occurred in 8/208 patients (3.8%) with and in 48/1069 patients (4.5%) without (p =0.68) recurrent urinary tract infections (UTIs). Multiple logistic regression revealed associations between FTT and birth weight < 10th percentile, preterm birth, tubular function impairment, identified or suspected syndromes and miscellaneous causes comprehending congenital cardiopathies, endocrinopathies, and food allergies. Eleven (19.6%) patients with FTT presented tubular function impairment, 5 with increased FENa and/or acidosis. These 5 patients were supplemented obtaining a catch-up growth. The remaining 6 patients showed spontaneous catch-up growth.

Conclusion: FTT was found in < 5% of children with VUR. It was not determined by recurrent UTIs and was mainly associated to extrarenal causes. Regarding renal causes, tubular function impairment played a significant role. Supplementation with sodium and bicarbonates in patients with elevated FENa and/or acidosis was followed by catch-up growth.

SESSION 9

GLOBAL PEDIATRIC NEPHROLOGY SESSION

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THE ROLE OF THE INTERACTION BETWEEN ARTERIAL HYPERTENSION AND PROTEINURIA IN THE PROGRESSION OF PEDIATRIC CHRONIC KIDNEY DISEASE: DATA FROM A COHORT IN A DEVELOPING COUNTRY

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Aims/Purpose: Pediatric data on Chronic Kidney Disease (CKD) and Arterial hypertension (AH) are scarce in countries in the southern hemisphere. The objective of this study is to investigate the role of AH and proteinuria in the progression of pediatric CKD, whether treatment with renin-angiotensin-aldosterone system inhibitors (RAASi) attenuates the impact of these factors, and if there is a statistical interaction between AH and proteinuria.

Methods: A prospective cohort in seven pediatric nephrology centers, with children and adolescents, CKD stages 3 and 4. The inclusion criteria were age between 1 and 17 years, eGFR: 60-15 mL/min/1.73m^2. Transplanted patients, those with malignancies, and HIV-positive individuals were excluded. Outcomes: initiation of renal replacement therapy and > 50% reduction in eGFR. Multivariate Cox regression models were used.

Results: A total of 296 children were included in the analysis, with a median follow-up of 3.1 years (interquartile range [IQR]: 1.60–3.7). Among them, 178 (60.14%) were males. The predominant etiology of chronic kidney disease (CKD) was congenital anomalies of the kidney and urinary tract (CAKUT), accounting for 71.6% of cases. The median age of the participants was 9 years (IQR: 5-13), and the median baseline eGFR was 33 ml/min/1.73m^2 (IQR: 25-41). AH was present in 199 children (67.2%), with 160 (52%) receiving anti-hypertensive medications and 64 (21.6%) using renin-angiotensin-aldosterone system (RAAS) inhibitors. Proteinuria was observed in 160 children (54%). The primary outcome occurred in 114 of the 296 individuals (38.5%). Hypertensive patients had a 1.6 times higher risk of reaching the primary outcome (95% CI 1.11–2.50, p =0.015). Among hypertensive patients, those not using RAAS inhibitors had a relative risk (RR) of 1.8 (95% CI 1.2-2.8, p =0.07). Baseline proteinuria was associated with a worse prognosis (RR: 2.31, [95% CI 1.54-3.48], p < 0.001), and individuals not using RAAS inhibitors had a poorer prognosis (RR 1.88, [95% CI 1.2-2.6], p < 0.001). Concurrent presence of both hypertension and proteinuria was associated with a more severe progression (RR 2.7, [95% CI 1.5-4.8], p < 0.001). However, statistical evaluation regarding the interaction between hypertension and proteinuria did not show a significant result (hazard ratio [HR] 1.4, [95% CI 0.6-3.3], p =0.44).

Conclusion: The impact of AH and proteinuria on worsening CKD progression is evident and appears to be dependent on each factor individually, which adds up but does not potentiate each other. The low use of RAAS inhibitors suggests the need for pediatric protocols and reinforces the importance of referral to specialized centers. Data from developing countries are essential to identify specific risks and patterns, aiding in the effectiveness of interventions and the efficient allocation of resources for public health measures.

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ROLE OF URINARY POTASSIUM INDEX IN ASSESSING THE VOLUME STATUS IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME PRESENTING WITH EDEMA

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Aims/ Purpose: The assessment of intravascular volume status is difficult in children with nephrotic syndrome (NS) with moderate to severe oedema because of confounding factors like pain or discomfort due to oedema, which gives rise to fallacious clinical findings of blood pressure or pulse rate. The vasoactive hormones like renin and aldosterone are costly and not readily available. Urinary potassium index is a simple and non-invasive investigation to assess hypovolemia in NS children with oedema. This study aimed to evaluate the diagnostic performance of the urinary potassium index (UKI) [urine potassium/(urine potassium + urine sodium)] for the assessment of hypovolemia (as defined by a combination of clinical, biochemical, and radiological parameters) in children with idiopathic NS (INS) with oedema.

Methods: This was a prospective observational study of 80 children aged 1 to 12 years with INS from July 2022 to June 2023. All the hospitalized children with oedema were assessed for hypovolemia state using clinical criteria (pulse rate, capillary filling time, blood pressure), biochemical criteria (blood urea/serum creatinine ratio, haematocrit, serum aldosterone) and radiological criteria, i.e. inferior vena cava collapsibility index (IVCCI) after obtaining consent. The assessed volume status was then compared with the status expected from the UKI value obtained. Patient data were compared with 59 controls (31 children with known nephrotic syndrome but in remission with no active nephrosis & 28 healthy children with no renal disease). Data were analysed using SPSS software version 28.0.

Results: Out of 80 patients, 50 (62%) were males. The median age of children in the active nephrosis group was 49.5 months (36 – 84 months). Hypovolemia was seen in 30 (38%). Higher values of blood urea/serum creatinine ratio, serum aldosterone, IVCCI and lower values of fractional excretion of sodium (FENa) were seen in cases, as compared to controls. These values were statistically significant and had a significant correlation with the values of UKI. The sensitivity and specificity of UKI were 64.5% & 65.3%, respectively (using a value of > 0.6 from existing literature). A value of 0.54 or above for UKI was calculated as having a sensitivity of 77% and a specificity of 50% for predicting hypovolemia.

Conclusion: UKI relates to the clinical and laboratory indices of hypovolemia in assessing intravascular volume status in children with INS with oedema. UKI did not emerge as a promising standalone marker for deciding hypovolemia in this subset of patients. FENa emerged as a good indicator of hypovolemia in this group of patients, but further studies are required to decide a definite cut-off.

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URINARY EXCRETION OF PROTEIN, ALBUMIN AND BETA2-MICROGLOBULIN-TO-CREATININE RATIOS IN HEALTHY INFANTS AND CHILDREN

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Aims/Purpose: Proteinuria is one of the main urinary markers of kidney disease. Measurements of high molecular proteins, such as albumin and low molecular proteins as beta2- microglobulin (B2 mg) provide valuable information concerning glomerular and tubular function. Normal values for these urinary proteins remain unclear. The present study aimed to establish the reference values for urinary protein, albumin and B2 mg-to-creatinine ratios in healthy infants and children.

Methods: A total of 894 spot urine samples were obtained from 526 healthy children of Caucasian origin, aged 6 days to < 15 years, born at term and normal prenatal ultrasound. Exclusion criteria: background of kidney disease, active infection or children on medication except vitamin D prophylaxis. The children were recruited from a primary health center at the time of their scheduled visits (6-17 days, 1, 2, 4, 6, 9, 12, 15 and 18 months and between 2.5-4 years old), and a group of schoolchildren > 5 to < 15 years old. Urine was collected no fasting in infants < 18 months by special plastic bags and first morning fasting in children aged 2.5-14 years. A dipstick was made and if it was normal (no hematuria-proteinuria), density was measured (refractometer), and creatinine (Cr), protein, albumin and B2 mg were determined in the hospital laboratory. Values are expressed as proteins-to-Cr ratios and were analyzed with descriptive and analytical statistics (SPSS v. 28.0)

Results: Urinary values were grouped according to the child´s age (Table). Protein/Cr, albumin/Cr and B2 mg/Cr median showed an age-related statistically significant decrease.

Table Urinary protein, albumin and B2 mg-to-Cr ratios in the population studied

Parameter	G1 6-17 days n = 51	G2 1-5 months n = 184	G3 6-12 months n = 151	G4 13-18 months n = 70	G5 2.5-4 years n = 88	G6 5-10 years n = 140	G7 11-14 years n = 210
Protein/Cr (mg/mg)	0.58* (0.4-1.0)	0.35* (0.2-0.8)	0.21* (0.1-0.4)	0.18*(0.1-0.3)	0.12* (0.1-0.2)	0.10¶ (0.1-0.2)	0.07¶ (0.0-40.1)
Albumin/Cr (mg/g	56.41 & (22.0-184.1)	62.50 & (22.7- 166.6)	31.25* (12.0- 82.8)	17.88* (8.35-8.2)	12.05* (5.92-6.2)	7.92* (4.42-0.4	6.15* (3.9-17.6)
B2MG/Cr (mg/g)	10.48* (0.73-5.3)	1.04* (0.1-9.8)	0.43* (0.1-1.6)	0.34* (0.04-0.8)	0.22* (0.1-0.5)	0.14¶ (0.1-0.5)	0.11¶ (0.1-0.3)

Data presented median (5th, 95th percentiles). Significant differences ($p < 0.05$) between groups: * vs all other groups; ¶ vs groups 1-5; & vs group 3-7.

Conclusions: Changes of urinary protein excretion were verified in the first 18 months of life, as an expression of glomerular-tubular maturation. Reference values for urinary protein/Cr, albumin/Cr and B2 mg/Cr in infants and children < 15 years were updated. We proposed new cutoff values for the diagnosis of proteinuria in infants < 6 months.

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CAN WE PREDICT WHICH CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME WILL BE STEROID DEPENDENT

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Aims/Purpose: Around half of children with idiopathic nephrotic syndrome will develop steroid dependent or frequent relapsing disease. Guidelines recommend switching these patients to immunosuppressive therapy to minimize side effects of corticosteroids and achieve remission. Clinicians often wait to diagnose steroid dependence until the patient relapses more than once while on steroids. Finding an early, reliable predictor of steroid dependent nephrotic syndrome can help clinicians to confidently initiate immunosuppressive therapy earlier in these patients, thus avoiding additional steroid courses. We hypothesize that a single relapse on a steroid dose of at least 0.5 mg/kg every other day predicts future relapses on this dose or higher.

Methods: Children diagnosed with nephrotic syndrome in a single center were enrolled prospectively. We performed a post hoc analysis comparing the outcomes of patients with relapses on prednisone doses of 0.5 mg/kg/every other day or higher to those that relapsed while on lower doses or no steroids.

Results: Of the 122 enrolled patients with nephrotic syndrome, 51/122 (42%) relapsed on doses of at least 0.5 mg/kg/every other day with 29/51 (57%) of these patients relapsing for the first time during induction. Fourteen of these patients were switched to alternative therapy before they experienced another relapse. The other 36 patients that relapsed on doses beyond this threshold were not switched immediately to steroid alternatives. The vast majority, 33/36 (92%) went on to have at least one more relapse above this threshold and were then switched to alternate therapy.

Conclusions: Patients that relapsed once on steroid doses equal to or higher than 0.5 mg/kg/alternate days are very likely to continue to relapse on similar or higher doses of steroids. It might thus be reasonable to consider initiation of immunosuppression following the first relapse on steroid doses beyond this cut-off.

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UROLITHIASIS AND MEDULLARY NEPHROCALCINOSIS ARE LESS FREQUENT AND EASIER TO TREAT IN PH1CHILDREN TREATED WITH RNAI THERAPY

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Aim: Children and infants diagnosed with primary hyperoxaluria type 1 (PH1) experience early-onset nephrolithiasis and nephrocalcinosis. In the infantile form of PH1, these conditions can rapidly progress to Chronic Kidney Disease (CKD) within the first months of life. Stones may be the first clinical manifestation, resulting in hematuria and flank pain, often requiring multiple medical interventions. In recent years, RNA interference (RNAi) therapies have emerged as a promising treatment option for PH1 patients. Our study aims to investigate the incidence of nephrolithiasis and compare interventional treatment strategies before and three years after the emergence of RNAi therapy.

Methods: This study included seventeen patients diagnosed with PH1, aged 3 to 18 years old (7 males and 10 females). They were stratified into two groups based on their kidney function: the first group with Creatinine Clearance (CrCl) > 30ml/min/1,73 m2 and the second group with CrCl < 30ml/min/1,73 m2. We compared in both groups the progression of medullary nephrocalcinosis before and after treatment over a six-year period (three years before and three years after initiating RNAi therapies targeting PH1, specifically (Lumasiran or Nedosiran). We used renal ultrasound to categorize the progression of medullary nephrocalcinosis (MN) into four stages: A) stable (no change in either kidney), B) improving (either one or both kidneys), C) worsening (either one or both kidneys), and D) indeterminate (one kidney improving while the other one worsening). We then analyzed the incidence of spontaneous stone elimination and new stone formation before and after the introduction of RNAi therapy.

Results: Sequential renal ultrasounds conducted every six months showed that MN was stable in 35% of our patients, improved in 11%, worsened in 17% and indeterminate in 35%. We observed a significant reduction in the annual rate of kidney stone events during the treatment period compared to the pre-treatment period: 2,9 events per year per patient (95% CI: 2,36 - 3,81) versus 0,9 events per year per patient (95% CI: 0,59 - 1,05) ($p < 0.05$). Additionally, the incidence of spontaneous stone passage was higher, even for stones up to 10 mm in size. Moreover, double stent placement was easier with reduced incrustation and peri-stent stone formation. Endoscopic procedures were also simplified due to decreased stones incrustation, stone burden, bleeding, and inflammation of the urothelium in the urinary tract.

Conclusion: Our study demonstrated that medullary nephrocalcinosis improved or remained stable in 46% of cases during the last three years of RNAi therapy. The incidence of new kidney stones events decreased, with a higher incidence of spontaneous stone passage, accompanied by a reduction in the need for surgical endoscopic interventions and associated complications compared to the pre-treatment era.

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OXALOSIS AROUND THE WORLD: GLOBAL DISPARITIES IN THE MANAGEMENT OF PRIMARY HYPEROXALURIA

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Aims/Purpose: Primary hyperoxaluria (PH) is a rare metabolic disorder with significant morbidity and mortality if left untreated. Given the rarity and specific needs of these patients, global inequities in diagnostics and treatment are expected. Recent therapeutic advances (e.g. RNA interfering therapy) have dramatically modified the management of PH, possibly disproportionately affecting low-resource regions. Understanding these disparities is crucial for developing targeted interventions and ensuring equitable healthcare access for PH patients worldwide. This study aims to evaluate the global health situation for patients with PH, highlighting pervasive global inequities in access to diagnostics and treatment.

Methods: An international cross-sectional questionnaire study was conducted among healthcare professionals involved in PH management. Responses were gathered between March 2023 and January 2024 and distributed by email via the ESPN, OxalEurope network and international PedNeph email server. Meta-analysis (mixed random effects model with inverse-variance weighing) was used to analyze data and adjust for subgroup differences.

Results: In total, 107 responses were gathered from 56 countries, representing all World Bank regions. Overall access to diagnostics was high, with 83% (CI, 75-92%) having access to genetic analysis and 96% (91-100%) to urinary oxalate measurement. Although significant differences ($p < 0.05$) between low- and high-income countries were found for most diagnostics (i.e. genetic testing, plasma oxalate, plasma and urinary glycolate), for pyridoxine and potassium citrate, a high overall access of 98% (93-100%) and 90% (83-97%) was reported. Large differences in access to peritoneal dialysis, kidney and liver transplantation (solo or combined) were reported between high- and middle- or low-income countries ($p < 0.05$). Access to lumasiran was limited to high- and middle-income countries, with 53% (40-66%) of all countries having access (78% of high-income versus 56% of middle-income).

Conclusion: This study highlights the global landscape of PH, emphasizing disparities in diagnostic and therapeutic access, especially in low-income countries. These results may provide support for global initiatives to improve management of PH patients worldwide.

SESSION 10

UPDATE ON PEDIATRIC VASCULITIS

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DIGITAL SPATIAL PROFILING TO STUDY IGA NEPHROPATHY AND IGA VASCULITIS NEPHRITIS ACROSS PAEDIATRIC AND ADULT PATIENTS

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Aims: The aim of this study was to determine the feasibility of performing digital spatial profiling (DSP) in kidney biopsies from paediatric and adult cases of IgA nephropathy (IgAN) and IgA vasculitis nephritis (IgAV-N).

Methods: A GeoMx® Digital Spatial Profiler protocol was optimised to profile formalin fixed paraffin embedded (FFPE) kidney biopsy specimens. Three paediatric and four adult IgAN, and two paediatric and two adult IgAV-N biopsies were included. Disease severities were matched for IgAN (adult vs child) and IgAV-N (adult vs child) using the histology report. Five-micron thick kidney sections were taken from each specimen, deparaffinised, and subjected to antigen retrieval prior to the of addition nucleotide barcoded probes designed to evaluate the expression of > 18,000 unique transcripts (GeoMx® Human Whole Transcriptome Atlas). Each probe is coupled to a photocleavable oligonucleotide that is released into solution following exposure to ultraviolet (UV) light and aspirated into a collection plate well for downstream processing. Fluorophore-conjugated antibodies against CD31 and CD10 were used to stain for endothelial cells, and podocytes and proximal tubular epithelial cells respectively. Regions of interest (ROIs) were drawn around glomeruli and interstitial tissue. A custom JavaScript function was used to separately mask over endothelial cells, podocytes and proximal tubular epithelial cells (segmentation), which were selected as areas of illumination (AOIs). The photocleaved nucleotide barcodes were PCR amplified, pooled, purified and sequenced using an Illumina sequencer. Ethical approval of the study was received from the University of Leicester (adult patients) and as part of the IgA vasculitis study (paediatric patients).

Results: Eleven kidney biopsies were included, and ROIs drawn around each complete glomerulus and 4-6 interstitial regions per section. ROI segmentation enabled collection of oligonucleotide barcodes from glomerular endothelial cells, podocytes, the mesangium, proximal tubular epithelial cells, interstitial endothelial cells and remaining interstitium separately [Figure 1]. Overall, 535 AOIs from 182 ROIs across the 11 biopsies were selected. Sequencing data are awaited: once obtained, single cell deconvolution will be conducted to assess performance at enriching for transcript signals from each cell type before exploring differential gene expression.

Conclusions: To our knowledge, this is the first time DSP has been used to analyse the transcriptomic profiles across multiple kidney cell types in IgA-mediated glomerular diseases, in both adult and paediatric patients. These insights hope to offer a unique understanding of dysregulated pathways in IgAN and IgAV, providing a platform to design larger comparative studies.

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EARLY RISK STRATIFICATION IN PEDIATRIC LUPUS NEPHRITIS USING RENAL BIOPSY HISTOPATHOLOGY: DEVELOPMENT AND VALIDATION OF A DEEP LEARNING BASED MODEL

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Aims/Purpose: Lupus nephritis (LN) is a heterogeneous disease with outcomes differ by ages and races, up to 20% of pediatric patients will ultimately progress to end-stage kidney stage disease (ESKD) within a decade. Early prediction of disease progression can assist in optimising patient management, thus improve long-term prognosis of LN. This study aimed to develop and validate a weakly-supervised deep learning (DL) based prediction model for long-term prognosis in childhood-onset LN using whole slide images (WSIs) of renal biopsy specimens at initial diagnosis.

Methods: This retrospective study included 121 pediatric LN patients who were diagnosed and treated at the First Affiliated Hospital of Sun Yat-sen University as a development cohort. The development cohort was randomly divided into training and internal validation datasets at a split ratio of 7:3. DL model based on renal biopsy WSIs at initial diagnosis was developed using the training set to predict whether the patient would have poor prognosis and its predictive performance was evaluated in the internal validation set. Poor prognosis was defined as a composite event of all-cause death or ESKD or decline in estimated glomerular filtration rate (eGFR) ≥30% from baseline. Feature extraction of normalized WSIs was achieved based on several pretrained DL algorithms for hematoxylin-eosin (HE) stained renal biopsy slides with each magnification scale (10×, 20×, 40×) and further integrated to build a multi-scale model. Area under the receiver operating characteristic curve (AUC) was used to evaluate the performance of the model.

Results: The median follow-up time of the development cohort was 57.0 (44.7, 89.2) months, and 19.0% of patients enrolled reached the composite event. Among five DL algorithms (ResNet18, ResNet50, Inception_v3, AlexNet, Densenet121) used to extract features of patches cropped from WSIs, AlexNet achieved overall good performance at three magnification scales (mean AUC = 0.9118, 0.9444, 0.8659 at 10×, 20× and 40×, respectively). An integrated multi-scale model of AlexNet had an AUC of 0.9567 (95%CI: 0.9248-0.9885) and showed significant risk stratification (mean survival time: 58.7 and 148.3 months for predicted high- and low- score groups, HR: 19.83, 95%CI 3.43-114.60, P < 0.0001) in Kaplan-Meier analysis. Multivariate Cox regression analysis indicated that the multi-scale model could predict prognosis in pediatric LN (HR: 14.02, 95%CI 2.54-77.50, P < 0.01) independently of chronicity indices, renal response to therapy at 6 months and eGFR slope. Model visualisation based on GradCAM highlighted tubulointerstitium as the key predictive region for poor prognosis.

Conclusion: This study showed that DL-based model of renal biopsy WSIs at initial diagnosis could predict prognosis in childhood-onset LN. External test cohorts and prospective studies are needed to validate its clinical utility.

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THE X-LUPUS STUDY: UNVEILING THE ROLE OF THE X-CHROMOSOME IN THE PATHOGENESIS OF SYSTEMIC LUPUS ERYTHEMATOSUS AND LUPUS NEPHRITIS

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Aims / Purpose: There is an association between the number of X chromosomes and the risk of developing systemic lupus erythematosus (SLE). SLE prevalence is 9 times higher in women (XX) than men (XY), and it increases in triple X syndrome (XXX) and Klinefelter syndrome (XXY), while it decreases in Turner syndrome (X0). In each female cell, one of the X chromosomes is randomly silenced by XIST, a long noncoding RNA, with no preferential inactivation of the maternal or paternal chromosomes. We hypothesize that an aberrant X chromosome inactivation (XCI) may participate in SLE pathogenesis and explain the higher prevalence of this disease in women. This study aims to evaluate if there is an aberrant XIST expression or preferential inactivation of one of the X chromosomes in SLE.

Methods: We studied children and adults with SLE (n = 37), who fulfilled the 2019 ACR/EULAR SLE criteria, 54% with lupus nephritis (20/37), and healthy controls (n = 29). Monocytes, B, CD4+ and CD8+ T lymphocytes were isolated by cell sorting. The XIST was quantified by RT-qPCR. The HUMARA assay was used to evaluate the preferential inactivation of one of the two X chromosomes.

Results: 1) XIST was over-expressed in SLE patients compared to healthy controls in all cells studied. This difference was statistically significant for B lymphocytes (p =0.008) and CD4+ T lymphocytes (p =0.0442). 2) XIST expression was 4 times higher in monocytes of patients with lupus nephritis than in SLE patients without renal involvement. Moreover, XIST expression was significantly increased in monocytes of patients with active lupus nephritis comparing with patients with inactive lupus nephritis (p =0.02). 3) Nonrandom X-chromosome inactivation was more common in SLE. In CD4+ T lymphocytes, 38% of SLE patients and 15% of controls showed preferential inactivation of one of the X chromosomes (70%). In B lymphocytes, 29% of SLE patients and 11% of controls had a preferential inactivation.

Conclusions: These results highlight the potential involvement of X-chromosome inactivation in the pathogenesis of SLE and lupus nephritis, suggesting an over-expression of XIST and a bias in the inactivation of maternal and paternal X chromosomes, which may contribute to the female bias seen in this disease.

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PREDICTION OF RENAL RECURRENCES OF IGA VASCULITIS NEPHRITIS IN CHILDREN USING KIDNEY BIOPSIES AND IMMUNOLOGICAL MARKERS

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Aims/Purpose: Immunoglobulin A vasculitis (IgAV), formerly Henoch-Schonlein purpura, is the most common vasculitis in children. Amongst its multisystemic manifestations, IgAV nephritis (IgAVN) is prevalent, with highly variable kidney outcome. A subgroup of patients with a relapsing disease course has a clinical evolution mirroring IgA nephropathy (IgAN). The four hit hypothesis is now accepted as the main pathophysiological pathway for both these diseases. Novel studies suggest the role of A Proliferation Inducing Ligand (APRIL) in the inflammation cascade causing glomerular injury in IgAN, but this has yet to be studied in IgAVN. Pediatric IgAVN presents with heterogeneous disease courses and unpredictable long-term renal outcomes. Currently, we lack the ability to predict which cases of IgAVN will progress towards a relapsing disease resembling IgAN. This study seeks to identify clinical, biochemical, and immunopathological patterns to better predict prognosis and outcome in IgAVN. Amongst immunological predictors, it explores the role of APRIL in this specific patient population.

Methods: We conducted a multicentric retrospective cohort study of pediatric patients from Canada and France. Seventy-two children with biopsy-proven IgAVN were divided in three clinical groups: monophasic renal disease, renal relapsing disease, and renal and cutaneous relapsing disease. Record reviews were conducted to collect clinical, biochemical, and pathological data. Biopsy specimens were classified according to the Oxford score (MEST-C score). Banked serum samples from prospective institutional biobanks were used to quantify circulating immune complexes including IgA-APRIL complexes and circulating APRIL levels using ELISA techniques.

Results: Baseline characteristics were similar in the three clinical subgroups. On the initial kidney biopsies, relapsing patients presented more segmental glomerulosclerosis (S1) ($p = 0.021$) and crescents (C1/C2) ($p = 0.049$) on the Oxford score. Relapsing patients with endocapillary hypercellularity (E1) on the Oxford score also presented with significantly higher APRIL-IgA circulating complex levels, suggesting APRIL is involved in IgAVN disease activity.

Conclusion: Segmental glomerulosclerosis and crescents on the initial kidney biopsy seem to suggest a more severe evolution in patients with IgAVN. APRIL-IgA immune complex levels in IgAVN are higher in relapsing patients and might suggest more severe glomerular involvement. APRIL-IgA immune complex could represent an interesting biomarker to identify patients who will present with relapses. Further research is necessary to assess the implication of APRIL in the kidney, and to better correlate these findings with clinical course from a prognostication perspective.

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COMPARING REAL-WORLD KIDNEY OUTCOMES VERSUS PREDICTED OUTCOMES AT THE TIME OF DIAGNOSIS IN A COHORT OF CHILDREN WITH IGA NEPHROPATHY

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Aims/Purpose: IgA nephropathy (IgAN) is the most common form of primary glomerulonephritis, with a highly variable clinical presentation and prognosis. We aimed to compare real-world kidney outcomes in a cohort of children with IgAN with the predicted kidney outcomes at the time of kidney biopsy based on the International IgAN Prediction Tool adapted for children (IIgAN-PT).

Methods: Single-centre longitudinal retrospective study of patients aged between 0 and 18 years who had a biopsy-proven IgAN diagnosis between 2010 and 2022. IgA vasculitis and secondary IgAN cases were excluded. Demographic, clinical, laboratory, and histological variables were analysed. The IIgAN-PT score was calculated for each patient according to the follow-up time in the study. The primary outcome was a composite of ≥30% decrease in eGFR or progression to CKD stage 5. Secondary outcomes were a new onset of albuminuria/proteinuria and any reduction in eGFR from baseline.

Results: In our cohort of 23 patients, 13 (57%) were male, and the median age at biopsy was 13.8 years (interquartile range (IQR) 9.6-16.3). The MEST-C score was M1 in 20 (87%), E1 in 5 (22%), S1 in 9 (39%), T1/2 in 3 (13%), and C1 in 6 (26%). Based on the IIgAN-PT score at the biopsy, the median predicted risk of ≥30% decline in eGFR or progression to CKD 5 accounting for each individual's follow-up time was 6.5% (IQR 4.5-8.6). After a median follow-up of 3.1 years (IQR 1.7-7.3), six (26.1%) patients met the primary outcome, including one (4.3%) patient who had received a kidney transplant. Two (9%) patients developed de novo albuminuria/proteinuria, and the eGFR decreased in 13 (57%) patients. The median annual decline in eGFR was 5.6 ml/min/1.73m2 (IQR 1.98-17.4).

Conclusions: In our cohort, a decrease in eGFR ≥30% or progression to CKD 5 occurred four times more frequently than expected at the time of biopsy. This disparity could be at least partially attributed to different duration of symptoms/signs of IgAN before biopsy. Despite our small sample size and relatively short follow-up, small-scale reproducibility studies such as ours may provide insights to improve the study design of larger studies conducted to improve the prediction ability of this tool across different clinical settings.

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THE IGA VASCULITIS STUDY: CAPTURING THE DISEASE ACTIVITY AND OUTCOMES IN CHILDREN

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Aims/Purpose: This study aims to describe the disease course and outcomes of a UK cohort of children with IgA vasculitis (IgAV).

Methods: Any child with a clinical diagnosis of IgAV was eligible for inclusion to the IgA Vasculitis Study (REC 17/NE/0390) at Alder Hey Children's Hospital (Liverpool, UK). Data were collected prospectively and longitudinally, and were enriched using medical notes and study file case reports. This included patient sociodemographics; baseline and follow-up clinical, urinary, and biochemical data; histology; use of immunosuppression; number of hospital visits; and overall clinical outcomes. IgAV nephritis (IgAV-N) was defined as a urine albumin:creatinine ratio (UACR) > 30 mg/mmol.

Results: 100 children were included. Most were Caucasian (n = 84) with a mean age of 7.3 ± 3.7 years and a male:female ratio of 1.5:1. All children presented with a lower limb-predominant rash, and some had a rash extending to their upper limb (n = 26), trunk (n = 17), and face (n = 5). Seventy-six children had musculoskeletal involvement and 43 had gastrointestinal (GI) involvement at presentation. Eleven were hypertensive and two presented with IgAV-N, of whom one had reduced kidney function. Seventy-six children initially presented to our centre and were commenced on the monitoring pathway. Most children (n = 41) were discharged after six months, with 22 lost to follow-up, and 13 referred to paediatric nephrology. Overall, 23 children developed IgAV-N. Mean timing of onset was 48.1 ± 108.2 days post first presentation (range 0.0–522 days). Mean worst UACR for this subgroup was 543.2 ± 509.4 mg/mmol (range 79.0-2357.7 mg/mmol). Older age at onset (OR 1.24, 95% CI [1.09;1.42]) and higher index of multiple deprivation (OR 1.27, 95% CI [1.09;1.49]) were significantly associated with development of IgAV-N, as well as GI involvement and positive urine dipstick (for proteinuria and/or haematuria) at baseline (OR 3.43, 95% CI [1.16;10.45]; OR 20.03, 95% CI [2.66;483.6] respectively). A negative urinary dipstick at baseline had a positive predictive value of 98.2% for not developing IgAV-N. Six children did not require any treatment, ten received ACE inhibitors, 14 received corticosteroids (oral n = 14; intravenous n = 4), and six received other disease modifying drugs (cyclophosphamide n = 1; azathioprine n = 4; mycophenolate mofetil n = 3). Mean follow-up for children with IgAV-N was 28.70 ± 21.97 months (range 2.40-79.90) and overall had a significantly higher number of hospital visits compared to children without IgAV-N (mean 13.4 vs 6.2 respectively, $p < 0.0001$).

Conclusions: Nephritis remains a serious consequence of IgAV, and further work is needed to improve the early risk stratification of children to identify those who would benefit from intervention.

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CHILDHOOD TAKAYASU ARTERITIS: A MULTICENTRE RETROSPECTIVE STUDY

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Aims/Purpose: Takayasu arteritis (TA) is a rare, large vessel vasculitis affecting mainly the aorta and its major branches. Data on paediatric TA (pTA) is very scarce. The aim of this study was to characterize clinical presentation, therapy and outcome of pTA in a global study population.

Methods: We conducted an international multicentre retrospective observational study of children diagnosed with pTA. Inclusion criteria were an age of less than 18 years at initial presentation in the year 2000 or more recently. Clinical data were collected from patients' charts by the treating paediatric rheumatologist or nephrologist; data were fully anonymised for analysis purposes. Follow-up data was collected up to 2 years after diagnosis.

Results: 198 patients from 20 countries were included (76% female). The median age at disease onset was 12 years. Arterial hypertension (67%), a difference in pulses between limbs (65%) and fatigue (66%) were the most common symptoms at presentation. The gastrointestinal system was the second most affected organ system. The median eGFR (estimated glomerular filtration rate) at baseline was 105 ml/min/1.73m2. Renal artery stenosis was documented in 58% of all patients and in 37% there was need for an invasive renovascular procedure. In 25 of 32 (78%) patients who had either a positron emission tomography–magnetic resonance imaging (PET-MRI) or PET-computed tomography (CT) there was evidence of active inflammation mainly of the aorta. 67% of all patients showed thickened wall abnormalities and 31% had arterial dilatations in a major vessel on any one or more anatomical imaging modality such as ultrasound, CT or MRI. Immunosuppressive treatment was primarily steroids, cyclophosphamide and methotrexate, 37% of all patients were treated with monoclonal antibodies of which 65% received an anti-tumor necrosis factor (TNF) antibody, 31% an anti-Interleukin 6 (IL-6) antibody and 4% an anti-B-cell antibody. Dialysis was necessary in 7% and one patient underwent kidney transplantation. Seven patient deaths (4%) were documented at the most recent follow-up. The renal function after two years was median eGFR 102 ml/min/1.73m2, with 67% showing normal function, 31% presenting with chronic kidney disease (CKD) stage 1, 1% with stage 2, 1% with stage 3 and no patients showed stages 4 and 5. A quarter of the patients (27%) were still symptomatic at the 2-year follow-up. The median systolic blood pressure was 117 (interquartile range 107 – 125) mmHg. 64% of all patients still had antihypertensive treatment, and 87% were still on immunosuppressive therapy.

Conclusion: Our study represents the largest paediatric cohort of children diagnosed with Takayasu arteritis. Several organ systems were involved at onset and the clinical spectrum was highly variable. We will in our further analyses in more detail describe the outcome in relation to presenting symptoms and treatment.

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PLASMAPHERESIS IN CHILDREN WITH BIOPSY PROVEN IGA VASCULITIS NEPHRITIS - SUBANALYSIS OF A LARGE RETROSPECTIVE STUDY

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Aim/Purpose: Plasmapheresis (PEX) is described in several case series as a treatment option for refractory IgA vasculitis nephritis (IgAVN). The aim of our study was to analyse clinical features and outcome of children treated with PEX.

Methods: We analysed data at baseline and outcome of children with biopsy proven IgAVN treated with PEX in our previously published retrospective international cohort of 1148 children. Children treated with at least two different immunosuppressing agents in the same cohort served as a comparator group.

Results: Thirteen patients (median age at biopsy 9.6 years (IQR 6-12.2)) from 9 international centers were treated with at least four sessions of PEX. Median estimated glomerular filtration rate (eGFR) at biopsy was 80.0 ml/min/1.73m2 (IQR 46.7-116.6) and 10 had nephrotic range proteinuria (urinary protein/creatinine ratio (UPUC) > 200 mg/mmol). Biopsy ISKDC stage III was detected in 4 patients, IV in 2, V in 4, and VI in 1. All but one had immunosuppressive treatment in addition to steroids. Seven patients received more than 7 sessions of PEX. Compared to the patients treated with two or more immunosuppressive drugs from the total IgAVN cohort (n = 479), there was no statistically significant difference in eGFR and proteinuria at onset. Relatively more patients in the plasmapheresis group had biopsy grading ISKCD IV, V and VI and positive C in the MEST C score. Other baseline parameters such as gender, ethnicity, nephrotic syndrome, hypertension and the use of other treatments were not different. The group of children who had PEX showed a greater, but not statistically significant improvement of their eGFR and proteinuria compared to the children treated with two immunosuppressive drugs (Figure). At last follow up (median duration 3.1 years (IQR 2-4.8)) 9 patients (69%) had normal eGFR > 90ml/min/1.73m2. Complications of PEX were not recorded in this study.

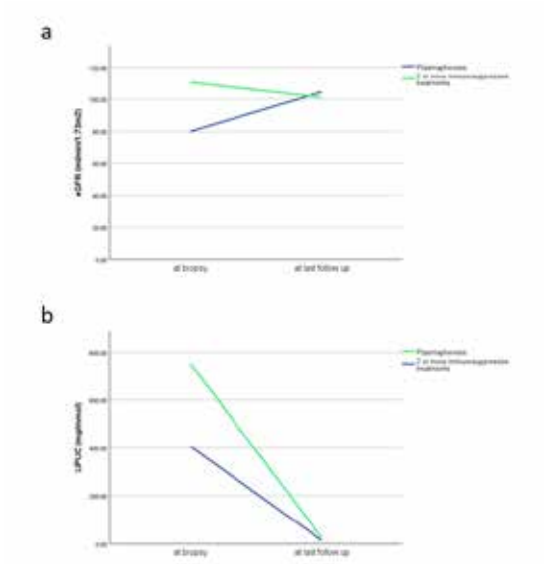

Figure: Median of a) eGFR and b) UPUC at biopsy and last follow up

Conclusion: Our data suggests that PEX in patients with severe IgAVN could be beneficial in the small number of children who had had at least four sessions. This is in concordance with other small case series but prospective studies are needed to with any certainty define the effect of PEX in severe IgAVN. The available data suggest that such a study is warranted.

SESSION 11

UPDATE ON CYSTIC KIDNEY DISEASE

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BIALLELIC MUTATION IN PDIA6 GENE ASSOCIATED WITH POLYCYSTIC KIDNEY DISEASE AND EARLY-ONSET DIABETES

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Aims/Purpose: Autosomal recessive polycystic kidney disease (ARPD) is an entity with variable phenotype usually caused by mutations in PKHD1 and PKHD2 genes, which encode proteins involved in the functioning of the cilium. Since 2021, 2 patients have been described with polycystic kidney phenotype, liver fibrosis, deafness, early-onset diabetes and microcephaly with biallelic mutation in PDIA6 gene (loss of function). The objective is to present and make know a patient with this mutation and phenotype.

Methods: Retrospective review of medical record, nephrectomy samples and genetic study.

Results: Preterm patient with consanguineous Arabic parents, prenatal diagnosis of suspected ARPD due to nephromegaly and oligohydramnios, who associated hepatomegaly, hepatic fibrosis, hypersplenism, intrahepatic biliary dilation with normal hepatocellular function, microcephaly, blepharophimosis and juxtapapillary coloboma. He required respiratory support for 48 hours and was diagnosed neonatal hypertension treated with triple therapy. At 3 months of age he had hypertensive emergency with left ventricular hypertrophy, hypertensive retinopathy and bilateral nephromegaly (right:+10SD, left:+9SD), unstructured, hyperechogenic parenchyma and cortical cysts. Psychomotor development delay, bilateral sensorineural hearing loss, onset of diabetes at 8 months and severe delayed height growth (-4SD) were evident. He maintained creatinine at around 0.4 mg/dl but at 6 months of age he required left nephrectomy to reduce abdominal volume, nutritional and respiratory improvement, after which glomerular filtration rate worsened starting hemodialysis at 9 months. Subsequently, when he was 3 years old, right nephrectomy was performed as pre-transplant preparation, with histology compatible with ARPD: tubular dilation in a radial pattern replacing renal parenchyma. Since he started hemodialysis, blood pressure control improved, currently without drugs. A genetic study (performed in 2020, before the PDIA6 phenotype was described) showed no evidence of mutation in the genes most frequently associated with ARPD. Nevertheless, he had heterozygous mutation of the WFS gene and two mutations (homozygous) in PDIA6, being his parents heterozygous. A recent review of the genetic study led to confirmation of the diagnosis.

Conclusion: This patient is consistent with the phenotype described in the literature in other patients with this mutation, who died at 4 and 18 months. This makes our patient, to the best of our knowledge, the oldest alive. Given the suspicion of ARPD, other mutations such as PDIA6 should be considered, especially if childhood-onset diabetes, hearing loss and microcephaly are associated.

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MACROSCOPIC HEMATURIA IN CHILDREN WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE - REPORT FROM 4 CENTRAL EUROPEAN TERTIARY CENTERS

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Aims/Purpose: In adults with autosomal dominant polycystic kidney disease (ADPKD) episodes of gross hematuria are relatively common and are an independent predictor of arterial hypertension (Martinez et al. 2023). In children there is little information on the prevalence, risk factors and sequelae of macroscopic hematuria. Therefore, we aimed to study the prevalence and risk factors associated with gross hematuria in a large cohort of children with ADPKD.

Methods: Altogether 292 children (median age 10.3 years, range 0.2-18.0) with ADPKD followed-up in four Central European tertiary nephrology centers were retrospectively investigated. A presence of ≥1 episode(s) of macroscopic hematuria defined a group of MaHu+ patients and the absence a group of MaHu- patients. Hypertension was defined as use of antihypertensive drugs at the last investigation. The glomerular filtration rate was estimated using the Schwartz formula (eGFR) and proteinuria as protein/creatinine ratio.

Results: At least one episode of macroscopic hematuria occurred in 7.2 % of children (n = 21). It was the first symptom of ADPKD leading to the diagnosis in 11 children (3.8%) and was the second most frequent presenting symptom of ADPKD (11 out of 51 children) after abdominal pain. The age at the first episode of gross hematuria was between 4-17 years in 6 children and unknown in 15 children. The etiology of gross hematuria was ruptured cyst, urinary tract infection, urolithiasis (two each) and unknown in 15 children. The prevalence of hypertension at the last follow-up in MaHu+ children was significantly higher than in MaHu- children (19% vs. 2.9%, p =0.006). Children from the MaHu+ group has significantly higher number of cysts in both kidneys than from the MaHu- group (18 vs. 13 cysts, p =0.04). There were no significant differences between MaHu+ vs. MaHu- groups in kidney length (1.1 vs. 1.0 SDS), percentage of severe cystic involvement defined as ≥10 cysts (62% vs. 49%), eGFR (112 vs. 119 ml/min/1.73m2) or proteinuria (29% vs. 37%). Only two children had microscopic hematuria at the current investigation (one child in each group).

Conclusions: In children, similarly to adults, ADPKD patients with a history of macroscopic hematuria are at increased risk of developing hypertension and higher number of kidney cysts.

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WHOLE GENOME SEQUENCING IN CYSTIC RENAL DISEASE - AN NHS ENGLAND SERVICE EVALUATION

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Aims/Purpose: NHS England offers comprehensive genomic testing for patients with cystic renal disease and is the first national health system in the world to provide whole genome sequencing (WGS) to patients as part of routine clinical care. Testing for genetic causes of cystic renal disease has been through a WGS platform since April 2021, provided by the South West and North Thames Genomic Lab Hubs. The virtual panel (R193 test code) covers 111 'green' genes, where strong evidence exists for a disease–gene association. We present data on all cases tested through R193 (WGS) in England since this time.

Methods: Our dataset was extracted from the Genomics England database to include all patients in England tested through R193 (WGS) between April 2021 and December 2023. Patients were eligible for testing if they fulfilled criteria specified in the National Genomic Test Directory for 'R193 cystic renal disease'. The dataset captured demographic data alongside molecular variant data. Children were defined as individuals below 18 years of age on 1st December 2023.

Results: 1783 individuals were tested through WGS using the R193 test code between April 2021 and December 2023. Of these, 262 individuals (14.7%) were below 18 years of age and defined as children. The median age of the cohort was 42 years (range 0 to 91 years). 1154 patients (65%) were of White, 126 (7%) Asian, 91 (5%) Black ethnicity with 344 (19%) unrecorded. 923 (52%) were female, 858 (48%) were male and 2 had unrecorded sex. 47 individuals had more than 1 variant that was pathogenic, likely pathogenic or variant of unknown significance (VUS). 795 pathogenic or likely pathogenic variants (43.4%) and 120 VUS (6.7%) were reported in a total of 20 'green' genes. The majority of these variants were in the PKD1 (32.1%), followed by PKD2 (9.0%), PKHD1 (2.3%), IFT140 (1.5%) and HNF1B (1.0%) genes. In children, 99 (35.5%) pathogenic or likely pathogenic variants and 20 (7.2%) VUS were reported. PKD1 variants were the most common (19.7%), followed by PKHD1 (8.9%), PKD2 (3.5%) and HNF1B (3.9%). There was only one IFT140 variant reported in children. The majority of IFT140 cases were identified through a post-hoc analysis following addition of the gene to the R193 panel in November 2022.

Conclusion: The overall diagnostic yield for patients undergoing genetic testing for cystic renal disease is excellent. WGS technology has clear benefits in renal genomics, including the ability to capture intronic variants, improved capture of pseudogene-impacted exons (for example in PKD1), and in providing a platform for re-analysis where required (as with the IFT140 variants identified). WGS has an enhanced diagnostic yield with significant impacts on patient diagnosis, treatment, prognostication and genetic counselling. Our data thus outlines the crucial and expanding role of WGS technology in the diagnosis and management of rare disease.

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NEONATAL RISK FACTORS ASSOCIATED WITH SURVIVAL AND END-STAGE RENAL DISEASE IN AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE

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Aims/Purpose: To evaluate patient survival and the incidence of end-stage renal disease (ESRD) in children affected by autosomal recessive polycystic kidney disease (ARPKD) and associated risk factors in the neonatal period.

Methods: Retrospective study of medical records of patients with clinical and/or genetic diagnosis of ARPKD followed in outpatient nephrology consult from 1990-2023.

Results: Seventy-five patients (47 with genetic confirmation) were included with a median follow-up of 12.11 years (interquartile range 13.19 years). 45 patients were diagnosed prenatally, 7 neonatally, 9 before one year of life, 10 before 10 years of age and 4 with more than 10 years. Ten patients died (13%), 80% in the neonatal period due to respiratory failure, the rest died on due to abdominal sepsis and the other due to leukaemia secondary to post-transplant immunosuppression. Analysing the 67 patients who survived the neonatal period, 24 patients (36%) developed ESRD. Renal actuarial survival at 3, 10 and 15 years was 97, 80 and 63.5% respectively. The risk factors studied were prenatal diagnosis (38/67 patients), oligohydramnios (30/67), pulmonary hypoplasia (PH) (20/67), prematurity (19/67), neonatal arterial hypertension (NAH) (32/67) and neonatal chronic kidney disease (NCKD) (19/67). Actuarial survival at 3 and 10 years in each of the groups was 100 and 96.6% in non-prenatal Vs 94.6 and 67.2% in the prenatal group, 100 and 94.2% without oligohydramnios Vs 93.1 and 60.6% with oligohydramnios, 100 and 90. 2% without HP Vs 90 and 57.6% with HP, 97.9 and 90.2% not preterm Vs 94.7 and 56.2 % in preterm, 100 and 97.1% without NAH Vs 93.5 and 59.2% with NAH and 100 and 94.9% without NCKD Vs 89.5 and 45.2 % with NCKD. The differences observed were statistically significant (p-value < 0.05) (Figure 1).

Conclusion: ARPKD is a genetic disease with variable clinical expressivity. It presents higher mortality in the first year of life and a good prognosis afterwards. The incidence of ESRD is 36%. Prenatal diagnosis, the presence of oligohydramnios, PH, NAH, NCKD and prematurity carry a higher risk of requiring early renal replacement therapy.

Table 1. Actuarial survival at 3 and 10 years according to the presence of risk factors

Risk Factors	Actuarial survival without risk factor		Actuarial survival with risk factor		P-value
	3 years s.	10 years s.	3 years s.	10 years s.	
Prenatal Diagnosis	100%	96.6%	94.6%	67.2%	0.019
Oligohydramnios	100%	94.2%	93.1%	60.6%	0.014
Pulmonary Hypoplasia	100%	90.2%	90.0%	57.6%	0.000
Preterm	97.9%	90.2%	94.7%	56.2%	0.044
NAH	100%	97.1%	93.5%	59.2%	0.000
NCKD	100%	94.9%	89.5%	45.2%	0.000

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VARIABLE PHENOTYPE AND GENOTYPE OF PEDIATRIC PATIENTS WITH HNF1B NEPHROPATHY

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Aims: Hepatocyte nuclear factor 1 (HNF1B) mutations are the most common monogenic cause of congenital anomalies of kidney and urinary tract (CAKUT) (1). We aimed to investigate clinical and genetic characteristics of patients with HNF1B nephropathy to expand its phenotypic and genetic spectrum.

Methods: This retrospective cohort study included 16 unrelated pediatric patients (6 females, 10 males) from 13 families with genetically confirmed HNF1B-related nephropathy. The HNF1B score suggested by Faguer et al. (1) was calculated for each patient.

Results: The study included 16 patients (6 females, 10 males) from 13 different families. Abnormal prenatal kidney abnormalities were present in 13 patients (81.3%). The most common antenatal kidney abnormality was kidney cysts, which were observed in 8 patients (61.5%). Vesicoureteral reflux (VUR) and ureteropelvic junction obstruction (UPJO)) were present in two patients, respectively. HNF1B analysis uncovered missense variants in 4 families (30.8%) as the most common genetic abnormality which was followed by frameshift variants (3 families (23%)), whole gene deletion (2 families (15.4%)), nonsense variants (2 families (15.4%)) and splice site variations (2 families (15.4%)) (Figure 1). Besides, four novel pathological variations have been defined. During follow-up, hypomagnesemia and hyperuricemia were observed in seven (43.8%) and five patients (31.3%), respectively. None of the patients with a missense variant had hypomagnesemia. However, 7 out of 12 patients (58.3%) with a non-missense variant had hypomagnesemia (p =0.09). Diabetes mellitus was observed in five patients (31.3%). Increased liver transaminases were observed in three patients (18.8%). None of the patients had a HNF1B score below 8 and the mean score was 15.3 ± 4.4. The mean follow-up period was 7.4 ± 5.0 years. While 100% of patients (n = 4) with missense variants were on various stages of CKD (CKD2; 2 patients, CKD3; 2 patients), 25% of those with non-missense variants had CKD (CKD 2, 3, and 5; 1 patient, respectively) (p =0.026). Patients with missense variants and those with non-missense variants did not have any difference in weight, length and body mass index z scores at last visit (p =0.10, p =0.10 and p =039, respectively).

Conclusions: Patients with HNF1B associated disease have concomitant urinary system abnormalities such as VUR or UPJO. Missense variants seem to be the most common pathological variations in HNF1B gene and has higher risk of CKD.

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ENHANCING DETECTION OF GENETIC KIDNEY DISEASE THROUGH DIGITAL SOLUTIONS - A PROOF-OF-CONCEPT STUDY

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Aims/Purpose: Microscopic haematuria (MH) is frequently encountered in childhood, often resolving spontaneously but potentially indicative of underlying genetic kidney disease. Despite guidelines recommending follow-up testing for persistent MH, a lack of clear pathways often leads to missed opportunities for diagnosis. This proof-of-concept study sought to address this gap by implementing a digital solution to facilitate repeat testing and early identification of genetic kidney disease, focusing on Alport Syndrome. We focussed on how this digital approach could streamline the identification and management of these diseases, ultimately supporting a value-based healthcare approach by improving outcomes and reducing costs.

Methods: A retrospective clinical audit of the electronic medical record (EMR) system at the Royal Children's Hospital Melbourne was performed to identify children with MH, without evidence of a subsequent normal result. An EMR-based automated report was developed, using a defined digital phenotype, to stratify and select at-risk children for repeat testing. Children with persistent MH were referred for genetic counselling and genomic testing. Feedback led to refinements including the creation of patient resources and process improvements. Data were collected on patient responses and outcomes.

Results: Contact via the automated report was attempted with 1335 children, resulting in 261 repeat urinalysis samples within the reference range and 16 with persistent MH. Twelve of the children with persistent MH were female. Three children had incidental findings and were linked to appropriate services. Genomic testing was completed for 15 patients. Four children were diagnosed with COL4A3/COL4A4 Alport syndrome, and a fifth diagnosis identified in a sibling. Families were very accepting of this proactive form of healthcare.

Conclusion: Our study highlights the potential of digital solutions to enhance proactive healthcare delivery, particularly in early detection of genetic kidney disease. Low response rates overall are a limitation of the study. Challenges remain with the need for true interoperability between health systems and the reliance on postal communication with patients. Further research and collaborative efforts are needed to address the existing limitations and realise the full benefits of digital health stratgies.

1174

PATHOGENIC OLIGOMERS OF R229Q PODOCIN FAIL TO DECREASE THE DISTANCE BETWEEN THE NEPHRIN MOLECULES IN CIS

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Aims/Purpose: NPHS2 is the most frequently mutated gene in podocytopathies. The encoded podocin homooligomerizes through its C-terminal and binds nephrin in the slit diaphragm. We formerly showed that its R229Q variant is only pathogenic when associated to specific 3' variants in trans. We explained its interallelic interactions by an altered trafficking of the pathogenic R229Q oligomers. However, it contrasts the mild course of the associated renal failure. We recently showed that podocin decreases the distance between the nephrin molecules. Unexpectedly, we also found that in the presence of nephrin, pathogenic R229Q podocin oligomers become membrane-associated, refuting our former pathogenicity explanation. Here, we aimed to assess the effect of R229Q oligomers on the nephrin-nephrin distance.

Methods: HEK293 cells were transfected with two pEGFP-N1 vectors encoding nephrin constructs with either YPet or mCherry replacing the extracellular fibronectin domain, and either a pLEX-MCS vector encoding a single podocin variant or a pKK-BI16 plasmid encoding two different ones. FRET efficiency was measured between YPet and mCherry in living HEK293 cells, 48h after transfection. Measurements were repeated nine times in three experiments. Furthermore, the distance between podocin monomers in different oligomers was assessed by FRET measurement between differently stained (AF-488 C5-donor, AF-555 C2-acceptor maleimid) podocin variants obtained by transient expression in HEK293 cells and peptide elution/HPLC purification and fluorescent maleimide staining.

Results: While all benign podocin variants/associations (wt, R229Q, R229Q-wt, R229Q-R138Q, R229Q-V290M) increased the FRET efficiency between the nephrin molecules, none of the pathogenic variants/associations (R138Q, A284V, R286Tfs, V290M, R229Q-A248V, R229Q-A297V, R229Q-F344Lfs, R229Q-R291W) exerted such an effect. Not only was there a highly significant difference in the FRET efficiency between the benign and the pathogenic variants/associations ($p = 1.19 \times 10^{-33}$), but a cut-off value could distinguish them in 97% of the measurements. We found a strong negative correlation between the distance of the podocin monomers and the associated nephrin-nephrin distance ($p = 7.3 \times 10^{-5}$).

Conclusion: Pathogenic R229Q podocin oligomers are unable to decrease the distance between the nephrin molecules: the shortest dimension of the glomerular pore. This mechanism explains the molecular basis of the first clinically relevant interallelic interactions in human genetics, as well as the mild disease course. This method is specific enough to help the distinction of pathogenic and benign R229Q associations.

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EXPRESSION PATTERN OF KALLIKREIN 6 DURING NORMAL HUMAN KIDNEY DEVELOPMENT AND IN CONGENITAL NEPHROTIC SYNDROME OF THE FINNISH TYPE

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Aims/Purpose: Kallikrein 6 (KLK6) is a serine protease highly expressed in the brain, which can degrade components of the extracellular matrix. It can also participate in processes of inflammation, inhibition of apoptosis, calcium signaling, and maintenance of epithelial cell fate. Congenital nephrotic syndrome of the Finnish type (CNF) is caused by recessive mutations in the NPHS1 gene and presents as massive proteinuria at birth, with irregular microcystic dilatations of proximal tubules. KLK6 expression has been previously described in both proximal and distal tubules of the human kidney. We aimed to analyze the distribution of KLK6 in developing, postnatal, and CNF human kidney samples.

Methods: Double immunofluorescence staining for KLK6, the proximal tubule marker aquaporin 1 (AQP1), and the collecting tubule marker aquaporin 2 (AQP2) was performed in 6 human conceptuses aged 10 to 38 weeks, in 3 postnatal and 3 CNF kidneys. Images were captured using an Olympus BX51 microscope with a mounted Nikon DS-Ri2 camera.

Results: In the 10-week kidney, moderate KLK6 expression characterized apical regions of some tubules adjacent to glomeruli, while AQPs were not expressed at this developmental stage. At 16 and 27 weeks, KLK6 expression characterized the apical regions of tubules expressing AQP1. Some AQP1-positive tubules were KLK6-negative. At 38 developmental weeks, KLK6 co-expressed with AQP1 in all proximal tubules, while all other tubules were KLK6-negative (Figure 1). In healthy postnatal kidneys, KLK6 was expressed only in AQP1-positive tubules, while AQP2-positive collecting tubules were devoid of KLK6. The kidneys of patients with CNF showed a dysregulation of KLK6 and AQP1 expression: non-dilated AQP1-positive tubules were often KLK6-negative; most dilated proximal tubules had strong KLK6 expression and weak-to-none AQP1 expression, while some dilated tubules had no KLK6 or AQP1 expression. Interestingly, KLK6 expression could be found in some tubules with apical AQP2 expression, while AQP2 was observed in some regions of dilated tubules (Figure 2).

Conclusion: KLK6 appears early during human kidney development and is expressed in the apical regions of developing proximal tubules. Compared to healthy kidneys, loss of KLK6 and AQP1 expression is present in some proximal tubules of CNF patients, indicating that they may be involved in structural and/or functional changes of proximal tubules exposed to massive proteinuria.

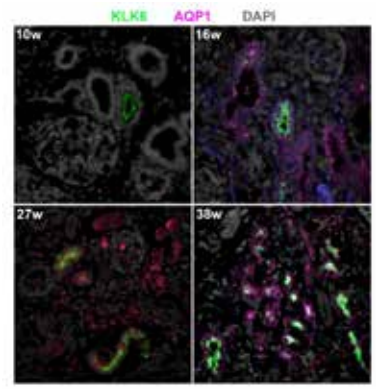

Figure 1

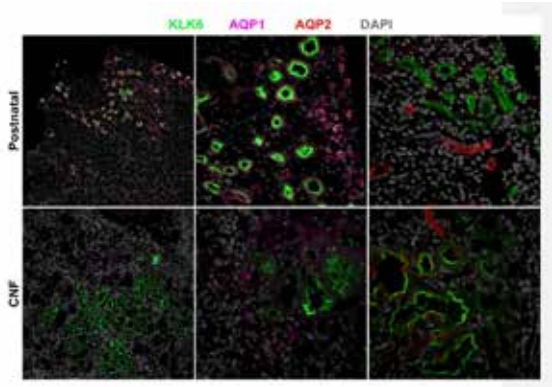

Figure 2

SESSION 13
GUT-KIDNEY CROSSTALK

1159

IMPACT OF CONTINUOUS ANTIBIOTIC PROPHYLAXIS ON GUT MICROBIOTA DEVELOPMENTAL TRAJECTORIES, RESISTOME AND FOCAL METABOLITES IN INFANTS WITH HIGH-GRADE VESCICO-URETERAL REFLUX ENROLLED IN THE PREDICT TRIAL

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Aims / Purpose: The gut microbiota (GM) is a complex and dynamic ecosystem, involved in different host-related physiological functions. The exposure to different environmental factors, such as antibiotics, has a major impact on the crucial GM development during the first years of life. We aimed at evaluating the effect of continuous antibiotic prophylaxis (CAP) on the GM of infants enrolled in the PREDICT trial.

Methods: The PREDICT trial evaluated the efficacy of CAP in infants with congenital high-grade vesicoureteral reflux (VUR). Children < 5 months of age and naïve from urinary tract infections (UTIs) were randomized to either CAP or no-treatment and followed for 2 years to evaluate the incidence of UTI and kidney function. For the purposes of this nested study, fecal samples were collected at 6 time points (0, 4, 8, 12, 18 and 24 months) for structural and functional GM characterization. The phylogenetic GM profile was characterized by next-generation sequencing of the bacterial 16S rRNA gene in all the samples (Illumina MiSeq platform). The pattern of antibiotic resistance genes was determined at 3 time points (0, 12, 24 months) by shotgun metagenomics (Illumina NovaSeq platform). At the same time points, GM metabolomics was performed by short chain fatty acids (SCFAs) analysis through a gas chromatography mass spectrometry approach.

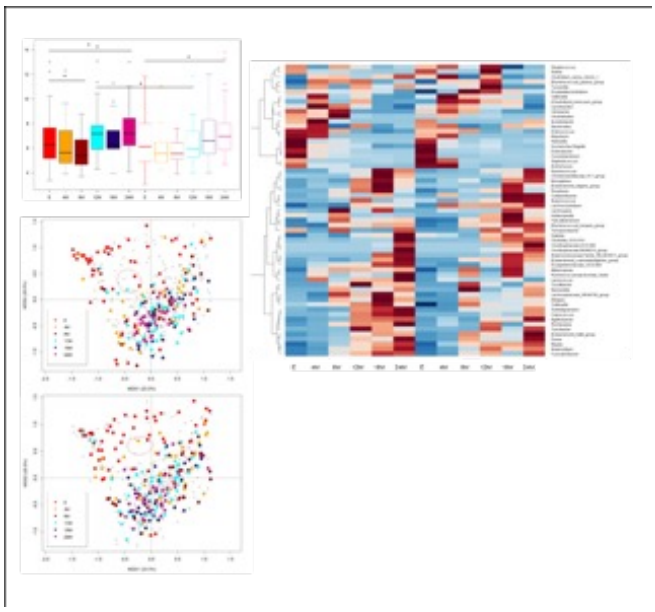

Figure 1

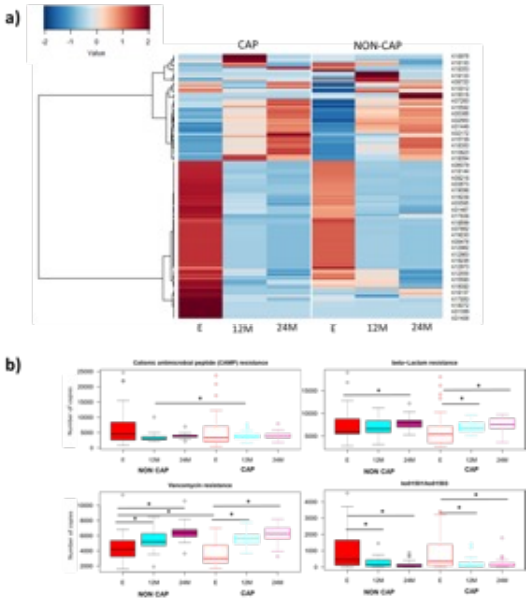

Figure 1

Results: Samples from 122 patients were analyzed (61 randomized for CAP and 61 untreated). For these subjects it was possible to evaluate the GM trajectories over time during the 24 months of the study. Comparative subgroup analysis revealed temporal changes in GM diversity in CAP-exposed infants compared to the no-treatments group. From the taxonomic standpoint, CAP-related GM was characterized by an initial dysbiosis, i.e., an increased relative abundance of opportunistic pathogens and decreased proportions of health-associated taxa (Figure 1). Furthermore, the CAP group showed a significant increase over time of genes grating resistance to beta-lactams and vancomycin, as well as an overrepresentation of genes granting antimicrobial cationic peptides resistance at 12 months compared to the untreated group (Figure 2). From the functional standpoint, a significant increase in propionic acid levels, a crucial GM-produced SCFA was observed at the 12-month time point in untreated patients compared to the CAP group.

Conclusions: Exposure to CAP in children with high-grade VUR can lead to long-term structural and functional GM alterations, with potential long-lasting health consequences.

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THE PRISMA TRIAL - EXPLORING THE ROLE OF THE GUT MICROBIOME IN PERSONALISED IMMUNOSUPPRESSIVE THERAPY IN KIDNEY TRANSPLANT RECIPIENTS

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Aims/Purpose: Potent immunosuppressive drugs, such as tacrolimus (Tac) have markedly improved clinical outcomes in kidney transplant recipients. However, due to its narrow therapeutic index and large interpatient variability, patients suffer from serious adverse events caused by over- or under-exposure. Known modulators of Tac exposure, such as pharmacogenetics, explain only a fraction of the interpatient variability. Increasing evidence suggests that the metabolism of Tac by gut bacteria contributes to this variability. The objective of this research project is to identify gut microbiome-based features to better predict tacrolimus exposure.

Methods: PRISMA is a multicenter, prospective, longitudinal clinical study of de novo kidney transplant recipients. Stool samples were collected at defined time points before and within the first six months after transplantation and analyzed by metagenomic sequencing. The results were correlated with the Tac concentration/dose ratio (C/D ratio), a surrogate marker of tacrolimus clearance. In addition, known factors influencing Tac pharmacokinetics, such as clinical, pharmacogenetic and demographic parameters were taken into account. Patients were recruited from the Department of Pediatrics I at the University Children's Hospital Heidelberg, the Department of Nephrology at the University Hospital Heidelberg and the Department of Nephrology at the University Hospital Münster.

Results: We report the results of an interim analysis of the PRISMA study including 30 patients with a longitudinal follow-up of 6 months after transplantation. Our results show that the integration of clinical and microbial characteristics improves the prediction of the Tac C/D ratio. In particular, it is possible to associate interpatient differences in the abundance of specific bacterial genera (namely Roseburia, Coprococcus) with interpatient variations in the Tac C/D ratio. In vitro validation of the identified genera suggests bacterial biotransformation of Tac to an inactive metabolite as a possible underlying mechanism.

Conclusion: Our preliminary results suggest a potential paradigm shift in our understanding of tacrolimus exposure. It highlights the gut microbiome as a novel and innovative tool for personalized tailoring of immunosuppressive therapy. Completion of patient enrollment and subsequent validation of our model are the next steps in the PRISMA study.

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ALTERATIONS IN GUT MICROBIOTA IN KIDNEY TRANSPLANT RECIPIENTS

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Aims/Purpose: Changes in the gut microbiota of individuals undergoing kidney transplantation have been proposed as a potential direct or indirect contributor to several complications in the host. The aim of this study was to investigate the changes in gut microbiota and bacterial diversity between children and adolescents with kidney transplants. The focus was to demonstrate how these changes were reflected in clinical outcomes and to what extent they contribute to the challenges observed during medical monitoring.

Methods: This cross-sectional, observational, case-control, and single-center study included 30 pediatric kidney transplant (KTx) recipients aged between 7 and 21 years (median age 15.6 years, 15 females) and 25 age- and gender-matched healthy controls. Patients with ongoing gastrointestinal infections at the time of stool collection or those taking antibiotics or probiotics for any reason were excluded from the study. The gut microbiota was assessed using 16S rRNA gene sequencing technique. The results were analyzed using the Illinois software data analysis program.

Results: There were no significant differences in age, gender and body mass index between the patient and control groups. When bacterial diversity and abundance were evaluated in terms of alpha and beta diversity, there were no significant differences between the two groups. However, more detailed comparisons revealed a significant increase in the abundance of the phyla Verrucomicrobiota and Proteobacteria in the KTx group. At the genus level, the KTx group showed an increase in some genera belonging to the phyla Firmicutes, Actinobacteria and Proteobacteria and a decrease in some genera belonging to the phyla Eubacteriales and Bacteroidetes (Figure 1). In addition, significant increases in Bacilli, Enterococcaceae, Corynebacteriaceae, Pasteurellaceae, Haemophilus and Clostridium species were found in individuals with a history of frequent urinary tract infections, diarrhea and a GFR < 60 mL/min/1.73m^2. KTx recipients with a history of rejection had particularly high rates of Clostridium and Acidaminococcus.

Conclusion: Our study is one of the few in the literature to examine changes in the gut microbiota of pediatric KTx recipients. Of particular note are the significant alterations in bacterial compositions, especially at the genus level. It is anticipated that such changes in the gut microbiota may be causative and/or consequential factors for urinary tract infections, recurrent diarrhea, decline in GFR and rejection commonly observed clinical issues following kidney transplantation. Comprehensive studies are needed to further elucidate the cause-effect relationship of the microbiota changes and their impact on long-term prognosis.

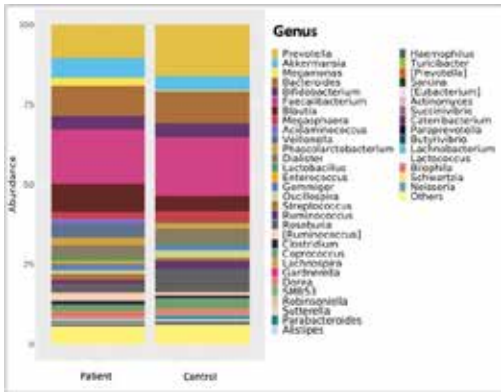

Figure 1. Taxonomic column plots show the comparison of gut microbiota at the genus level between KTx recipients and controls.

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FAECAL MICROBIOTA TRANSPLANTATION FOR RECURRENT CLOSTRIDIOIDES DIFFICILE IN PAEDIATRIC RENAL TRANSPLANTATION

Cansu Ceren Eryilmaz[1,2], Zainab Arslan[1], Garth Dixon[1], James Hatcher[1], Kelsey Jones[1], Nigel Klein[1], Delane Shingadia[1], Jelena Stojanovic[1], Stephen D. Marks[1]

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Purpose: Patients who have undergone renal transplantation (RTx) are immunosuppressed and more susceptible to developing Clostridioides difficile infection (CDI), which can increase the risk of life-threatening sepsis and organ rejection. Faecal microbiota transplantation (FMT) is a highly effective treatment for CDI. We present a 7-year-old boy with a history of posterior urethral valves (PUV) who underwent RTx followed by successful FMT.

Case Presentation: A two year old boy with chronic kidney disease secondary to congenital anomalies of the kidney and urinary tract due to bilateral renal dysplasia and PUV underwent pre-emptive living related renal transplantation. He experienced three recurrences of CDI over five months from six years of age and was hospitalised due to abdominal pain and watery stools, requiring hydration and oral vancomycin treatment. He had positive Clostridioides difficile (C. diff) PCR test and C. diff toxin A in three repeated analyses. Serologic tests for parasitic infections were negative. After an initial positive response to vancomycin treatment, the patient experienced repeated CDI and subsequently underwent a colonoscopy. The macroscopical and histopathological results were unremarkable, and inflammatory bowel disease and post-transplant lymphoproliferative disease were ruled out. After multiple treatment regimens, including reducing vancomycin and adding fidaxomicin, FMT was required five years after RTx to eliminate C. diff from the patient's gastrointestinal tract. Donor faeces were collected in accordance with the regulations of the Human Tissue Authority. A successful FMT via colonoscopy under general anaesthesia was performed. No complications, fevers, adverse effects, or UTIs were observed post-procedure. During a 12-month follow-up after FMT, he remains clinically stable with stable renal allograft function with an estimated glomerular filtration rate of 42mls/min/1.73m2.

Conclusion: Children who have undergone RTx need to be closely monitored for recurrent CDI due to the increased risk of dehydration and renal allograft function deterioration. Although there is limited data regarding the effectiveness of new therapies for CDI, recent case reports indicate that FMT is a promising option for patients who have undergone RTx and are experiencing recurrent symptomatic episodes of CDI.

SESSION 14
BEST CLINICAL CASES

A COMPLICATED NEPHROTIC SYNDROME RELAPSE

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Aims/Purpose: Nephrotic syndrome is characterized by severe proteinuria, hypoalbuminemia, edema, and hyperlipidemia. Common complications of nephrotic syndrome include infections and thromboembolic events, which should be promptly recognized and treated.

Methods: Case description.

Results: A 10-year-old Caucasian boy first presented with nephrotic syndrome at 2.5 years old. Due to steroid dependence, he had already received treatment with mycophenolate mofetil, cyclosporine, and tacrolimus. At 10 years old, he experienced a recurrence of nephrotic syndrome, for which he received corticosteroids, optimized tacrolimus dosing, and Rituximab. One week after Rituximab infusion, he was reevaluated because of anorexia, vomiting and dyspnea. Clinical examination revealed tachycardia, hypertension, and diminished breath sounds on the right side of the thorax. A chest X-ray showed extensive right-sided pleural effusion and possible atelectasis. Lab work revealed respiratory alkalosis with increased D-dimers. A chest CT with contrast revealed diffuse bilateral lung embolism, prompting transfer to our pediatric intensive care unit. He received treatment with antibiotics, alteplase, enoxaparin, and the placement of a thoracic drain. His course was complicated by the development of acute respiratory distress syndrome, for which he required intubation and ventilation. One week after extubation, he was transferred to the ward and discharged 4 days later. He was treated with oral Rivaroxaban for 6 months after discharge, with a good clinical outcome and no recurrence of thromboembolic complications to date.

Conclusion: Thromboembolic events are rare in pediatric patients with nephrotic syndrome but can have severe consequences. The diagnosis of pulmonary embolism is easily overlooked due to its low incidence and nonspecific signs and symptoms. However, it Is crucial to recognize and treat this rare complication as soon as possible to improve the outcome. Additionally, the treatment of lung embolism in pediatric nephrotic syndrome is challenging due to the lack of robust data on this rare complication. Our case highlights the importance of identifying an uncommon but severe complication in nephrotic syndrome and reveals the difficulties in treating such a rare complication.

INITIAL PRESENTATION AND CLINICAL MANAGEMENT OF ATYPICAL HEMOLYTIC UREMIC SYNDROME AND MENINGOCOCCAL INFECTION DURING C5 INHIBITOR THERAPY IN A PEDIATRIC PATIENT: A CASE REPORT

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Aims: Atypical hemolytic-uremic syndrome (aHUS) is a rare disease marked by acute kidney injury, thrombocytopenia, and microangiopathic hemolytic anemia. In 2011, Eculizumab, and in 2018, Ravulizumab, were approved for aHUS treatment, significantly improving patient outcomes. (1). However, C5 inhibitors pose risks, including up to a 2,000-fold increased risk of meningococcal disease compared to healthy individuals. (2). This case report aims to document the clinical presentation, diagnosis, and treatment outcomes of a 6-year-old patient with aHUS, acute kidney failure, and meningococcal infection.

Methods: A clinical case report methodology was used to document the patient's initial presentation, diagnostic process, and treatment. Data were collected from medical records, laboratory results, imaging studies, and treatment notes.

Results: 6-year old boy was admitted to the hospital due to fatigue, jaundice and dark urine. Laboratory findings showed elevated urea and creatinine, non-immune microangiopathic hemolytic anemia, and thrombocytopenia. Stool tests were negative for verotoxin. ADAMTS 13 activity was 88%, and ADAMTS 13 antibodies were negative. Complement system activation was confirmed, with C3 levels decreased and C5b-9 levels elevated, supporting the diagnosis of aHUS. Treatment with Eculizumab resulted in improved hemolysis and increased platelet count. The patient required hemodialysis for 20 days until renal function began to improve. While receiving Eculizumab, the patient received three doses of the MenB (Meningococcal group B) vaccine, a booster dose four years later, and one dose of the MenACWY (Meningococcal groups A, C, W, and Y) vaccine with a booster after four years. During the initial vaccine doses, he was on antibiotic prophylaxis for four months. After 4.5 years of regular Eculizumab therapy, the patient switched to Ravulizumab. He experienced an IgG-mediated reaction during the second administration, which was managed with a desensitization protocol. The patient had no aHUS relapses till now. After 5.5 years of receiving C5 inhibitors, the patient presented with fatigue, fever, vomiting, diarrhea, and a mild headache. The presence of a rash was ruled out. Laboratory tests showed elevated inflammatory parameters and leukocytosis. Proteins were present in the native urine, but urine culture was negative. Ultrasound showed reactive lymph nodes along the mesentery and a slightly enlarged, homogenous liver. Blood culture revealed Neisseria meningitidis type B. Parenteral antibiotic therapy was introduced. His overall condition improved, remaining stable with no new neurological symptoms. The patient received prophylactic antibiotics to prevent recurrent meningococcal infections, despite complete vaccination against meningococcal disease.

Conclusions: This case report highlights the complexities in managing a pediatric patient with an rare kidney disease. The importance lies in the rapid recognition of the initial presentation during acute kidney failure and the timely introduction of a biological drug. Although the underlying disease was stabilized, the side effects of C5 inhibitors persist. The successful management of Neisseria meningitidis infection supports the need for constant monitoring and aggressive treatment of bacterial infections in these patients.

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Keywords: Atypical hemolytic-uremic syndrome (aHUS), complement inhibitor, Neisseria meningitidis infection

PRIMARY, SECONDARY OR APPARENT: A DIAGNOSTIC CHALLENGE IN AN ADOLESCENT WITH CHRONIC KIDNEY DISEASE

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Introduction: The combination of hypokalaemia and metabolic alkalosis suggests aldosterone excess, which may be primary, secondary or apparent (pseudohyperaldosteronism), representing a diagnostic challenge. We present a case of an adolescent girl with failure to thrive associated with chronic kidney disease (CKD), hypokalaemic alkalosis, nephrocalcinosis and hypertension due to apparent mineralocorticoid excess (AME). AME is a rare and potentially lethal autosomal recessive disorder caused by mutations in HSD11B2, resulting in decreased or absent function of 11-hydroxysteroid dehydrogenase type 2 (11 -HSD2). Under normal conditions, this enzyme converts cortisol into inactive cortisone, thereby protecting the mineralocorticoid receptor (MR) from non-specific stimulation by cortisol.

Case Presentation: A 15-year-old Syrian refugee presented with short stature, several months after arriving to The Netherlands. She was born with a very low birth weight (700 g) at 32 weeks' gestation. The pregnancy was complicated with oligohydramnios. At 7 months of age, she developed polydipsia and polyuria. Lab tests revealed hypokalaemia. Oral potassium suppletion was started but discontinued when she was 7 years old when the family fled abroad. At age 11 she developed muscle cramps and episodes of paralysis. Potassium supplements were reintroduced but parents were told to stop them because they were thought to cause hypertension. Instead she had been advised to consume potassium-rich foods. At presentation in our centre, she was asymptomatic except for short stature (height: -3.5SD) and being underweight (weight: -3.0SD). Her blood pressure was 130/80 mmHg and initial lab investigations showed hypokalaemic metabolic alkalosis and CKD stage 3B. Aldosterone and renin levels were both low. Abdominal ultrasound showed the presence of small kidneys with bilateral nephrocalcinosis. Genetic testing revealed a homozygous missense variant in exon 3 of HSD11B2 (c.623G>A (p.Arg208His)), confirming the diagnosis of AME. She was started on a low-sodium diet, potassium supplements, and a MR antagonist, next to CKD-specific medication.

Conclusion: Evaluation of the blood pressure and the RAAS are pivotal to distinguish salt-wasting from salt-retaining disorders and those mimicking aldosterone activity. Evaluation of the blood pressure and renin/aldosterone are pivotal in diagnosing AME, since it has a variable presentation and shares clinical features with other rare diseases. Timely diagnosis and treatment could help prevent life-threatening symptoms and improve end organ damage. At the same time, our case illustrates the vulnerability and health challenges in a growing population of displaced children.

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TRANSIENT CAROTID ARTERY STENOSIS IN STEC+ HUS: A RARE BUT DRAMATIC EVENT

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Aims/Purpose: Hemolytic uremic syndrome (HUS) is the primary cause of acute renal failure in pediatric patients, with cerebral complications occurring in 20% of cases. Magnetic Resonance Imaging (MRI) typically detects diffusion abnormalities in the basal nuclei, thalami, and white matter.

Methods: We present the cases of two children with bilateral carotid siphon stenosis during the acute phase of STEC-HUS, with significant clinical correlation.

Results: Patient 1, a 4-year-old boy, initially presented with abdominal pain, progressing to hematuria, oliguria, hypertension, and fluid overload during hospitalization. Laboratory exams showed non-immune hemolytic anemia and thrombocytopenia confirming HUS. Stool analysis revealed STEC O26. Due to AKI stage III, CVVHD was initiated. On day 8, neurological deterioration ensued, with EEG showing slowed electrical activity. Brain MRI revealed multiple lesions consistent with HUS. Seizures emerged without treatment response, followed by a new brain MRI revealing extensive cortical changes and bilateral carotid siphon stenosis on MR Angiography (MRA). Treatment with Eculizumab, steroids, and plasma exchange (PEX) led to biochemical improvement and seizure resolution but with slow and hypovoltage EEG tracing. MRA at 1 month showed stenosis resolution. Patient 2, a 2-year-old girl, presented with fatigue, irritability, and watery stools. Hospitalization revealed thrombotic microangiopathy, declining renal function, and neurological symptoms. Stool testing confirmed STEC O26. Seizures occurred on day 5, prompting treatment with anticonvulsants, alongside CVVHDF, PEX, Eculizumab, and steroids. Initial brain MRI revealed basal nuclei involvement. Despite transient improvement, seizures recurred, leading to refractory status epilepticus. MRA revealed bilateral carotid siphon stenosis. Infliximab and Nimodipine were administered, resulting in stenosis resolution in 2 days. Unfortunately, both patients progressed to a vegetative state, with follow-up brain MRI revealing diffuse cerebral atrophy. Molecular analysis for genetic complement dysregulation yielded negative results in both cases.

Conclusion: To our knowledge, these are the first reported cases of bilateral carotid stenosis during the acute phase of STEC-HUS. In our setting, anti-inflammatory therapy was administered in analogy to great vessel vasculitis. Nimodipine, used for its anti-inflammatory and vasodilatory properties in preventing and treating vasospasm following subarachnoid hemorrhage, was employed in an attempt to reverse arterial spasm. Despite stenosis resolution, these therapies failed to halt the catastrophic progression of brain damage caused by stroke and inflammation. In severe STEC-HUS with neurological involvement, a broader use of MRA should be considered, to promptly reveal steno-occlusive lesions of cerebral arteries.

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REPURPOSING SGLT2 INHIBITORS: TREATMENT OF RENAL PROXIMAL TUBULOPATHY IN FANCONI-BICKEL SYNDROME WITH EMPAGLIFLOZIN

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Aims/Purpose: Renal proximal tubulopathy in Fanconi-Bickel syndrome is caused by impaired basolateral glucose transport via GLUT2 and consequently, intracellular accumulation of glucose and glycogen. SGLT2 inhibitors act on apical glucose reabsorption of renal proximal tubular cells. The purpose of this study was to retrospectively describe the first experiences with repurposing the SGLT2 inhibitor empagliflozin to treat the generalized tubulopathy in Fanconi-Bickel syndrome.

Methods: Case series of seven individuals from five families (five males, two females; including three children) with genetically confirmed Fanconi-Bickel syndrome, off-label treated with empagliflozin. Median (range) age at start of empagliflozin was 27 years (1y6m – 61y) and duration of follow-up under empagliflozin treatment was 169 days (57 – 344).

Results: Under empagliflozin (up to 25 mg/d), biochemical parameters of tubular cell integrity (urinary N-acetyl-glucosaminidase) and/or tubular functions (including urinary 1-microglobulin) improved in all individuals with Fanconi-Bickel syndrome, albeit to varying degrees. Clinically, supplementations (i.e. phosphate, alkali, carnitine, and alfacalcidol) could be completely discontinued in the three children, whereas results in the four adult patients were more variable and not as significant. Empagliflozin was well-tolerated and no symptomatic hypoglycemia was observed.

Conclusion: SGLT2 inhibitors such as empagliflozin shift the metabolic block in Fanconi-Bickel syndrome, i.e. they intervene specifically in the underlying pathophysiology and can thus attenuate renal proximal tubulopathy, especially when started in early childhood.

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HNF4A-ASSOCIATED FANCONI SYNDROME: EXPANDING THE PHENOTYPIC SPECTRUM OF A RARE ENTITY

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Aims/Purpose/Introduction: Mutations in HNF4A gene are known to cause congenital hyperinsulinism (CHI) and maturity-onset diabetes of the young (MODY1). Most recently, the phenotypic spectrum has been extended to include renal tubular dysfunction.

Results/Case Report: We present a case of a preterm male, weighing 3540g (P97), born to non-consanguineous parents at 36+6 weeks of gestation. His mother had gestational diabetes controlled with insulin therapy. Due to persistent hypoglycemia with hyperinsulinism (max 42.5uU/ml), the boy was transferred to neonatal intensive care unit within the first hours of life, needing high glucose infusion rate to maintain normoglycemia. Physical examination was unremarkable, and septic and newborn screening were negative. He also presented liver involvement with neonatal cholestasis treated with ursodeoxycholic acid, elevated transaminases and biliary cysts. With a poor response after three weeks, oral maltodextrin was added to each meal and nasogastric feeding was necessary. At 2.5 months, diazoxide therapy was initiated with better control of hypoglycemia. The abnormal serum transferrin isoelectric focusing prompted a panel of congenital disorders of glycosylation to be requested, which returned negative. From the age of 14 months, the patient exhibited electrolyte loss, aminoaciduria, glycosuria, tubular proteinuria, renal-origin hypophosphatemia (fractional tubular reabsorption of phosphate 48%) and hypercalciuria, with normal eGFR, features compatible with renal Fanconi syndrome. Enalapril and supplementation with bicarbonate and phosphorus were started. To improve his growth, control nocturnal hypoglycemia and alleviate maternal exhaustion, at 20 months he began overnight feeding by percutaneous endoscopic gastrostomy. At age 4, a genetic panel for congenital hyperinsulinism disclosed the pathogenic heterozygous variant c.187C > T (p.(Arg63Trp)) in HNF4A. Given that some phenotypic features were not described in the literature, whole-exome trio sequencing was performed, finding no other variants and establishing de novo occurrence.

Conclusion: Our case reaffirms the kidney phenotype of HNF4A deleterious variants. It also highlights the importance of considering de novo presentations in phenotypes typically associated with autosomal dominant inheritance but lacking an apparent family history. Close long-term follow-up and family counseling are crucial for the proper management of these patients.

SESSION 15
BREAK THROUGH CLINICAL TRIALS

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INITIAL TREATMENT OF IDIOPATHIC NEPHROTIC SYNDROME IN CHILDREN WITH MYCOPHENOLATE MOFETIL VS. PREDNISONE: A PROSPECTIVE, RANDOMIZED, CONTROLLED, MULTICENTER, OPEN, PHASE III, NON-INFERIORITY STUDY (INTENT-STUDY) - BASIS FOR AMENDING THE STANDARD?

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Aims/Purpose: Initial treatment of idiopathic nephrotic syndrome in children requires sufficient immunosuppressive therapy to induce and sustain remission and consists of a prolonged course with glucocorticoids. Even though being effective, this treatment is associated with pronounced glucocorticoid associated toxicity. Mycophenolate mofetil (MMF) is effective in sustaining remission in patients with frequently relapsing or glucocorticoid dependent nephrotic syndrome. The hypothesis of the INTENT-Study was that MMF is not inferior to standard therapy with glucocorticoids (GC) in the initial treatment of steroid-sensitive nephrotic syndrome (SSNS) in children with regard to maintenance of remission and subsequent recurrence rate.

Methods: 272 children (mean age at onset 4.1 ± 2.3 years; 64.3% males) with a first episode of SSNS were randomized to either standard treatment (12 weeks of GC) or experimental treatment (MMF only after induction of remission with GC for a total treatment period of 12 weeks). Primary end-point was occurrence of treated relapse within follow-up of 24 months after completion of initial treatment. Secondary end-points included i.a. course of the disease and drug toxicities.

Results: MMF was not inferior to GC treatment in terms of the primary end-point (imputed mITT set: relapse rate 79.1% (MMF group) vs. 74.8% (GC group), difference 4.3% [-4.2%;12.7%], p =0.019; imputed per protocol set: relapse rate 79.2% (MMF group) vs. 77.7% (GC group), difference 1.5% [-7.7%;10.8%], p =0.008). In the MMF arm, there were fewer glucocorticoid-related side effects, such as lower blood pressure and body mass index as well as less frequent psychological abnormalities and cushingoid appearance. Cytopenias were more frequent in the MMF group but overall rare and mild. The rate of frequently relapsing nephrotic syndrome in the follow-up was comparable between the groups (MMF: 47.2%, GC: 45.2%).

Conclusion: The presented results of the INTENT-Study show non-inferiority of the MMF arm to the standard GC arm with no safety concerns and fewer glucocorticoid-related side effects, providing an excellent extension of the evidence base for future patient-centered shared therapeutic decision-making.

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SINGLE (375 MG/SQM) VS DOUBLE DOSE OF RITUXIMAB ALONG WITH MYCOPHENOLATE MOFETIL FOR CHILDREN WITH STEROID DEPENDENT / FREQUENTLY RELAPSING NEPHROTIC SYNDROME - MULTICENTER OPEN LABELLED RANDOMIZED CONTROLLED TRIAL

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Aims/Purpose: Rituximab has evolved into an important armamentarium for difficult nephrotic syndrome (both frequently relapsing and steroid dependent). It is usually given at 375 mg/m2 per dose twice over an interval of 7 to 14 days. Benefit of continuing mycophenolate mofetil (MMF) post rituximab has been shown in recent randomized controlled trial (RCT) but the dose of rituximab has not been explored in any RCT. We undertook this non-inferiority RCT to assess our hypothesis that in the context of post rituximab continuation of MMF, single dose of rituximab is non-inferior to double dose of rituximab in children with difficult nephrotic syndrome (DNS) in respect to time to first relapse.

Methods: A multi-center open label randomized controlled non-inferiority trial was conducted in children (2-18 yrs) with difficult nephrotic syndrome (DNS), wherein they received either single dose or double dose of rituximab. Post rituximab follow up was for 18 months with continuation of MMF but steroid was tapered over next 3 months. Standard guidelines were used for defining and treating relapses. Complete blood count and liver function test was done every 2 months along with CD19, which was tested till CD 19 normalization (> 1%). Primary outcome was time to first relapse post rituximab. Secondary outcome assessed included time to CD19 normalization, post rituximab cumulative dose of steroid and incidence of serious adverse effect (SAE).

Results: A total of 94 children were randomized to receive either single dose [Group A: 51, 67% male; median age 9 (6.3 – 12.5) years] or double dose rituximab [Group B: n = 43, 79% male; median age 8 (6.6-10.2) years). Two children in Group A and 4 children in Group B were lost to follow up. No differences between the groups were noted in the baseline criteria (demographic, anthropometric, time to onset of nephrotic syndrome, steroid threshold, number of failed steroid sparing agent and cumulative dose of steroid in prior 6 months). Primary outcome was tested by intention to treat analysis and median time to first relapse in months was similar between single dose rituximab (11.5; IQR: 6 to 13) and double dose (10; IQR: 6 to 13.5), p =0.72, Fig 1. Comparison of rest of secondary outcome between Group A and Group B were also similar (time in months for CD19 normalization: 6 (6 to 7) vs 6 (6 to 7), p =0.5, post rituximab cumulative steroid dose mg/kg/day: 0.14; IQR: 0.0 to 0.23 vs 0.13; IQR: 0.05 to 0.23 and SAE: 3 (5%) vs 5 (13%), p =0.2).

Conclusion: The current RCT demonstrated that among children with difficult nephrotic syndrome treated with rituximab and continued on MMF, single dose rituximab is non-inferior to double dose rituximab. Future studies are required to assess the utility of double dose rituximab over single dose rituximab in presence of discontinuation of immunosuppressant post rituximab.

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EUROPEAN MULTI-CENTRE TRIAL WITH IMLIFIDASE PRIOR TO KIDNEY TRANSPLANT IN HIGHLY SENSITISED CHILDREN

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Aim: A single-arm, multi-centre trial to evaluate efficacy and safety of imlifidase in highly sensitised (HS) children (1-17 years) receiving a kidney transplant with positive crossmatch against a living (LD) or deceased donor (DD) converted to negative after imlifidase treatment.

Introduction: Imlifidase is an immunoglobulin G-degrading enzyme of Streptococcus pyogenes, a protease that specifically inactivates all four human subclasses of soluble and membrane bound immunoglobulin G (IgG). Imlifidase reduces the load of donor-specific antibodies (DSAs) to a level enabling kidney transplantation. In Europe, imlifidase is conditionally approved for this indication in adult patients. As in adults, the sensitisation of paediatric patients scheduled for transplantation is usually due to previous renal or other solid-organ transplants, although sensitisation can also occur as a result of blood or platelet transfusion, infections, or other immunisations. In paediatric patients receiving a first transplant, about 70% have no panel reactive antibodies (PRA), whereas 3% have a PRA of more than 80%. To date, high levels of DSAs are if present an insurmountable barrier to transplantation in both adults and children.

Methods: This European multi-centre trial (5-10 centres) will investigate the efficacy and safety of imlifidase administered to 10 paediatric patients 1-17 years old with end stage renal disease (ESRD) waiting for a kidney transplant. The trial will include HS paediatric patients who will receive and accept crossmatch positive kidney offers from DD or LD, where imlifidase will convert a positive crossmatch to a negative. The primary objective is to evaluate crossmatch conversion within 24 hours of imlifidase treatment. The duration of the interventional trial period after an organ has been tranplanted will be 6 months for each patient. The trial also includes collection of efficacy and safety data up to 5 years after the transplantation (ClinicalTrials.gov, NCT05753930).

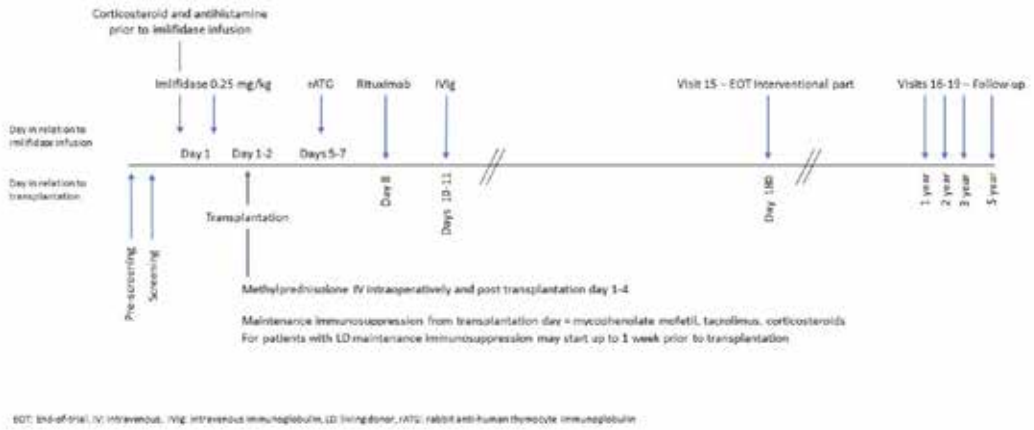

Figure 1. Trial design.

Conclusions: The successful completion of the trial is aimed at addressing an unmet medical need in highly sensitised kidney transplant paedriatic/child patients and will be presented.

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PEGCETACOPLAN FOR PAEDIATRIC PATIENTS WITH C3 GLOMERULOPATHY OR IMMUNE COMPLEX MEDIATED MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS: PHASE 3 VALIANT STUDY

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Aims/Purpose: C3 glomerulopathy (C3G) and primary immune complex-mediated membranoproliferative glomerulonephritis (IC-MPGN) are debilitating, fast-progressing kidney diseases caused by complement dysregulation and deposition of C3 breakdown products in the glomeruli, leading to nephritic syndrome (often with severe proteinuria/acute kidney injury) and the risk in some cases of progressive kidney failure. Currently, there are no approved, targeted treatments for these diseases. Pegcetacoplan, a C3 inhibitor, targets the primary pathogenic driver in C3G and IC-MPGN and has shown promising results in phase 2 trials DISCOVERY (NCT03453619) and NOBLE (NCT04572854).

Methods: This randomized, double-blind, placebo-controlled, pivotal Phase 3 study (VALIANT; NCT05067127) aims to evaluate the efficacy and safety of pegcetacoplan in patients with C3G or primary IC-MPGN. The study enrolled patients with a confirmed diagnosis of C3G or primary IC-MPGN, either in the native kidney or as post-transplant recurrence, with proteinuria ≥ 1 g/day and an estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73m^2. It included both adults (≥18 years) and adolescents (12-17 years). Patients were randomized 1:1 to receive either pegcetacoplan 1080 mg (or a weight-related dose) twice weekly, or placebo for 26 weeks (double-blind period), followed by open-label treatment with pegcetacoplan for another 26 weeks. The primary objective is to evaluate the efficacy of pegcetacoplan versus placebo in reducing proteinuria, measured as urine protein–creatinine ratio at 26 weeks. Key secondary endpoints include the assessment of kidney function measured by eGFR, the number of patients who achieve a proteinuria–eGFR composite renal endpoint, and for patients with available renal biopsy, the change from baseline in the activity score of the C3G histologic index and the change in intensity of C3c staining. Additionally, the study will evaluate the safety of pegcetacoplan. Patients who complete VALIANT may roll over into a long-term extension study, VALE (NCT05809531).

Results: The study is currently ongoing and a total of 124 patients were enrolled from North America, Europe, South America, the Middle East, and the Asia-Pacific. Of these, 55 patients (44.4%) were adolescents aged 12 to 17 years, while 69 patients (55.6%) were adults aged 18 years or older. The mean (SD) age at screening for the entire cohort was 26.0 (15.87) years. Gender distribution included 70 females (56.5%) and 54 males (43.5%).

Conclusion: The phase 3 VALIANT study will investigate the efficacy and safety of pegcetacoplan in adults and adolescents with C3G or primary IC-MPGN in either native kidney disease or as a post-transplant recurrence.

ORAL COMMUNICATIONS 1

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COMPARISON OF KIDNEY MICROVASCULAR ULTRASOUND WITH DYNAMIC RENAL SCAN IN CHILDREN WITH UNILATERAL HYDRONEPHROSIS

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Aims: Dynamic renal scintigraphy (DRS) is considered the gold standard technique to study the obstruction and the split renal function (SRF) between the two kidneys. In this study we aimed to evaluate the accuracy of the microvascular ultrasound (mUS) image mode in determining SRF in children with unilateral pyelo-ureteral junction obstruction, by comparing the measures with the dynamic renal scan (DRS)

Methods: In this prospective cross-sectional interventional study, we enrolled children with ultrasound diagnosis of unilateral isolated urinary tract dilation with an indication for DRS. In all patients, mUS was performed before DRS to have a blind assessment. Ultrasound scans using the mUS method were performed on the upper, middle and lower portions of both kidneys by sampling elliptical areas including both the medulla and the cortex. The perfusion index (PI), defined as the ratio of colored pixels to total pixels in the area, was determined for each of these scans; the mUS-based SRF (mUS-SRF) was calculated by relating the median PI of each of the two kidneys to the sum of the median PIs of the two kidneys, e.g., mUS-SRFright kidney = median PIright kidney / (median PIright kidney + median PIleft kidney). The difference between the mUS-SRF of the non-dilated kidney and the dilated kidney (delta-mUS-SRF) was compared to the same difference assessed using the DRS (delta-DRS-SRF). A delta-DRS-SRF of 20% was considered significant.

Results: We included 40 children with a mean age of 1 year (IQR 10 month- 4 years) (qui metterei tutti I valori di età in mesi), of whom 60% were male; 48% had severe renal calyx dilation (based on the urinary tract dilatation classification - UTD). In all ten patients with a significant delta-DRS-SRF, the delta-mUS-SRF was also significant. The remaining cases that presented balanced renal perfusion on scintigraphy, had the same result on mUS evaluation. The sensitivity and specificity of mUS in predicting a significant renal perfusion difference determined with DRS were both 100%. The Pearson correlation coefficient between delta-mUS-SRF and delta-DRS-SRF in the entire population was 0.8, and increased to 0.98 considering only patients with a significant perfusion difference.

Conclusions: mUS appears to be a reliable technique in determining the difference in SRF in children with unilateral hydronephrosis. Therefore, it could be integrated into the work-up of patients with intrarenal urinary tract dilation, potentially reducing radiation exposure resulting from DRS.

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FUNCTIONAL CHARACTERIZATION OF A NOVEL PBX1 MISSENSE VARIANT IDENTIFIED IN A PEDIATRIC PATIENT WITH CAKUT

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Aims/Purpose: The Pre-B cell Leukemia Factor 1 (PBX1) gene encodes for a protein belonging to the PBX homeobox family of transcriptional factors (TFs) whose alterations have been associated with CAKUT (OMIM: 617641). The aim of the study was to functionally characterize the impact of a novel missense variant [c.712C > T p.(Arg238Trp), NM_002585.3], classified as variant of unknown significance – C3-VUS, identified in a 4-year old patient presenting with a syndromic condition characterized by CAKUT, patent Botallo's duct that was surgically treated, hypotonia, slight growth retardation developmental delay, in the absence of a positive familial history.

Methods: The patient, referred to the Immunogenetics and Transplant Biology Service, University Hospital "Città della Salute e della Scienza di Torino" by the Pediatric Nephrology, underwent clinical exome sequencing followed by the analysis of an in-silico gene list associated with CAKUT. Variant validation and family segregation analyses were performed by Sanger sequencing. For its functional characterization, HEK293T cells were transfected with a plasmid encoding either PBX1WT or PBX1c.712C > T. Expression, localization, and molecular association of PBX1 were then evaluated.

Results: NGS analysis identified the novel [c.712C > T p.(Arg238Trp)] C3 variant, mapping in the first nuclear localization signal (NLS) of PBX1. Family segregation analysis indicated the de novo nature of the variant. When introduced in an ad hoc cellular model, PBX1c.712C > T did not affect protein expression, which was comparable to the WT counterpart. However, when investigating subcellular localization, the variant resulted in a significantly reduced translocation into the nucleus compared to PBX1WT, as shown both by biochemical and confocal analyses. To further corroborate these results, a second missense variant [c.863G > A (p.Arg288Gln)], localized in the second NLS of the protein and not previously functionally characterized, was modeled. Similarly to PBX1c.712C > T, also this variant resulted in an impaired localization of PBX1 into the nucleus. Being a TF, PBX1 exerts its function working in association with MEIS and PKNOX1/2 cofactors, whose expression was comparable in cells expressing either PBX1WT or PBX1c.712C > T/PBX1c.863G > A, suggesting that both variants did not impact on their expression.

Conclusion: We have identified a novel de novo heterozygous missense C3 variant in the PBX1 gene, which impairs nuclear localization of the protein, potentially affecting its role as a TF and possibly explaining the clinical phenotype of the patient.

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PREDICTORS FOR BACTEREMIA IN INFANTS UNDER THREE MONTHS WITH THEIR FIRST URINARY TRACT INFECTION: A MULTICENTER OBSERVATIONAL STUDY

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Aims/Purpose: Urinary tract infections (UTI) in infants under three months have historically been treated with initial intravenous antibiotics, which are burdensome and costly. We aimed to identify predictors of bacteremia in these infants, potentially enabling the use of initial oral antibiotics in low-risk cases.

Methods: Between January 2017 and December 2022, this multicenter observational study retrospectively included all infants under three months with their first UTI, including those with urological abnormalities. We collected demographic, clinical, and paraclinical variables and compared infants with and without bacteremia. Uni- and multivariate logistic regression analyses were conducted, with statistical significance set at p under 0.05.

Results: Of 329 infants presenting with their first UTI, 289 (87.8%) were included after excluding 40 (12.2%) without blood culture collection. Among them, 18 (6.2%) had bacteremia. Factors associated with bacteremia included younger age (mean difference (MD) 14.1 days, 95% confidence interval (CI) 1.15 to 27.1, P =0.035), male gender (odds ratio (OR) 3.35, 95% CI 0.92 to 18.5, P =0.049), higher temperature (MD 0.5 ˚C, 95% CI 0.04 to 0.95, P =0.034), and higher C-reactive protein (CRP) at treatment onset (MD 43.3, 95% CI 12.8 to 73.8, P =0.0079). Multivariate analysis demonstrated that younger age (OR 0.98, 95% CI 0.95 to 1.00, P =0.044) independently predicted bacteremia, while temperature (OR 2.01, 95% CI 0.99 to 4.11, P =0.054) and CRP at treatment onset (OR 1.01, 95% CI 1.00 to 1.02, P =0.08) showed non-significant trends.

Conclusion: In infants under three months with their first UTI, younger age, higher temperature, and higher CRP at treatment onset may predict concomitant bacteremia.

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CLINICAL AND MOLECULAR CHARACTERIZATION OF A COHORT OF PATIENTS WITH CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT

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Aims/Purpose: Clinical and molecular characterization of a cohort of patients (fetuses, children and adults) with congenital anomalies of the kidney and urinary tract (CAKUT), by targeted Next Generation Sequencing (tNGS) and Whole Exome Sequencing (WES).

Methods: A cohort of 103 patients underwent screening for pathogenic variants through tNGS, comprising:
- 6 fetuses from pregnancy terminations due to severe and bilateral renal malformations.
- 97 patients with CAKUT (children and adults) with one or more of the following characteristics: bilateral CAKUT, unilateral CAKUT with anomalies in other organs and/or familial association of nephrourological anomalies.

A targeted panel for CAKUT was designed, encompassing 117 genes involved in renal development, whose pathogenic variants have been associated with isolated or syndromic CAKUT. In those highly suggestive cases of CAKUT of genetic origin where a confirmatory genetic diagnosis was not achieved after tNGS, a WES study was carried out. Familial segregation study was performed by Sanger sequencing.

Results: Pathogenic or probably pathogenic variants were identified in nine patients (belonging to eight families) out of the 103 patients studied through tNGS, potentially explaining their clinical diagnosis. Additionally, WES revealed pathogenic variants in two out of the seven patients studied. Thus, an overall confirmatory genetic diagnosis of 10.7% was achieved, with pathogenic variants in the HNF1B, NPHP1, OFD1, PKD1, PKHD1, PMM2, SALL1, SEC6A1, SIX5 and TTC21B genes. Regarding the clinical manifestations of the patients with a confirmatory genetic diagnosis, all exhibited bilateral renal anomalies, with 60% also presenting extrarenal manifestations. Moreover, 44.4% of the patients had early-onset chronic kidney disease and 33.3% had a family history of nephrourological anomalies.

Conclusion: Patients with CAKUT of genetic origin typically display bilateral alterations and, in a high percentage, extrarenal manifestations and familial association of nephrourological anomalies. Additionally, this study shows that there is a high frequency of phenocopies in patients with apparent kidney dysplasia of genetic origin. Lastly, our results further highlight the importance and usefulness of strategies aiming to identify pathogenic variants based on a genotype-first approach, such as extended NGS panel or WES, in order to resolve and identify the molecular basis of rare hereditary disorders, facilitating family counseling.

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PATIENT SURVIVAL AND CLINICAL OUTCOME FOLLOWING SERIAL AMNIOINFUSIONS FOR EARLY-ONSET RENAL ANHYDRAMNIOS

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Introduction: Long-standing renal anhydramnios (RA) is fatal in almost all cases due to pulmonary hypoplasia. There is anecdotal evidence that outcome may be improved by intrauterine serial amnioinfusions (iAI). The purpose of our retrospective analysis is to report a series of 12 subsequent children (10 boys; 2 girls) who received standardized iAI and postpartum multidisciplinary care at our centres since 2016.

Results: iAI were started on average at gestational week 20 (range 13 to 29, in 9 children before 23) and the mean number of iAI administered was 4 (1 to 9). Underlying kidney diseases were bilateral kidney dysplasia with lower urinary tract obstruction (LUTO) (n = 7), bilateral kidney agenesis (n = 4) and bilateral kidney dysplasia without LUTO (n = 1). RA had developed despite placement of vesicoamniotic shunts in 6 of the 7 children with LUTO. Genetic disorders (PAX2 and HNF1beta) were identified in 2 cases. The children were born at a mean gestational age of 34 (30–37) weeks and a mean birth weight of 2,280 (1,530-3,350) g. Ten children were intubated on the first day of life and received mechanical ventilation for 12 (0-32) days. High frequency oscillation ventilation was temporarily required in 5 and pneumothorax occurred in 7 children. The mean duration of ventilatory support was 24 (0-49) days. All children remained anuric and peritoneal dialysis (PD) was started on average on day 4 (2-21). PD was complicated early on by inguinal hernia/hydrocele in 10 and dialysate leakage in 5 cases, all of which were corrected surgically and PD could be continued successfully. The mean length of hospital stay after birth was 10.7 (5 -17) weeks. The mean period of postnatal follow was 2.4 years (range 2.5 months to 7.8 years). At last observation, the mean BMI corresponded to the 43rd (8th-98th) percentile and mean body length to the 8th (1st-23rd) percentile. All children required transient or permanent enteral feeding support. Peritonitis occurred in 4 children, the first one at 2 months of age. One child died at home at 9 months of age from circulatory decompensation caused by peritonitis and one child was switched to haemodialysis due to fungal peritonitis at age 4 years. All other children continued PD successfully and the first child has undergone kidney transplantation at age 2.9 years. Recurrent respiratory tract infections occurred in three children. Five children showed mild to moderate cognitive and/or motor developmental delay. In addition, 3 children required surgical interventions due to anal atresia with retrovesical fistulae.

Conclusion: Our series shows that serial iAI in a standardized setting are highly effective in achieving lung-rescue and improving the chances of survival of children with RA. Nevertheless, the multidisciplinary postnatal treatment of this patient population remains challenging.

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SOLITARY KIDNEY: A NOT-SO-BENIGN CONDITION

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Aims/Purpose: The reduced nephron number, a consequence of a solitary kidney (SK), increases the risk of hypertension (HT), proteinuria and chronic renal failure. The aims of this study were to describe a cohort of children with SK, congenital (CSK) or acquired (ASK), and to know its evolution and risk of complications during its first 18 years.

Methods: Retrospective study of children with SK from 4 Spanish Pediatric Services, between 2000-2023. Variables: clinical (weight, height, blood pressure), ultrasound renal length (centiles, Spira 2009) and analytical data: estimated glomerular filtration rate (eGFR) by serum creatinine, proteinuria and albuminuria at diagnosis (E1) and at 6 months (E2), 1 year (E3), 2-3 years (E4), 5-6 years (E5), 10-11 years (E6), 14-15 years (E7) and 17-19 years (E8) from diagnosis. Statistical analysis: descriptive analysis and relative risk (RR) of kidney injury.

Results: The cohort includes 116 patients (75 males), 100 with CSK (59 renal agenesis, 41 multicystic dysplastic kidney) and 16 with ASK (11 uropathy, 5 Wilms tumors). CAKUT ipsilateral with SK was observed in 12% of patients and extrarenal anomalies in 13% of them; overweight and obesity was present in 22% and 18% at E6 and E8, respectively. The mean follow-up time was 8.7 ± 5.3 years for CSK and 11.7 ± 5.2 for ASK. At 10 years of follow-up (E6), the 66 patients studied presented adequate compensatory renal growth, proteinuria 3%, albuminuria 3.1% and 4.5% HT. At E7 (42 patients) and E8 (20 patients) HT was observed in 9% and 25% respectively. Only 1/42 patient showed lack of compensatory renal growth in E7. Decreased eGFR was found in 13% at 10-year follow-up and in 27% and 63% at 15 and 18 years, respectively (all of them > 70mL/min/1.73m2). The eGFR was lower in ASK compared to CSK in E6 and E7 ($p < 0.05$). CAKUT ipsilateral showed more risk of decreased eGFR (OR 4.5, 95% CI 1.4-14.7). At E6, proteinuria and/or albuminuria and/or HT increased the risk of decreased eGFR (OR 6.2, 95% CI 2.1-18.7; $p < 0.05$). HT also increased this risk at E7 (OR 3.4, CI 1.5-7.8; $p < 0.05$). No correlation was found between decreased eGFR and absence of compensatory renal growth.

Conclusion: Children with CKS show an increased risk of decreased eGFR after the age of 10 years. The presence of proteinuria and/or albuminuria and/or HT make eGFR measurement advisable. No correlation has been found between compensatory renal growth assessed by renal length (Spira) and decreased eGFR. The high percentage of overweight/obesity is a cause for concern.

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LONG-TERM OUTCOME OF CHILDREN (4-10 YEARS) WITH PRESERVED RENAL FUNCTION AFTER VESICO-AMNIOTIC SHUNT INSERTION FOR FETAL URINARY TRACT OBSTRUCTION

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Aims/Purpose: The purpose of this study was to assess the long-term outcome and development of renal function of children (4-10 years) who showed normal kidney function in the neonatal period after being treated with vesico-amniotic shunt insertion (VAS) as a treatment for LUTO.

Methods: From initially 63 prenatally treated fetuses 47 survived the pregnancy and neonatal period. 24 survivors were born with normal kidney function – 15 of them were treated before 16+0 weeks of gestation, 8 between 16+0 and 24+0 and 1 after 24+0 weeks of gestation. We were able to contact 20/24 former patients successfully (83,3%). All of them agreed to participate in our study. The former patients transmitted the medical records of their children to our center. We subsequently analysed the pediatric, pediatric surgical, pediatric urological and radiological medical records from their first 4-10 years of life.

Results: All children of the cohort are still alive. None of the investigated children need renal replacement therapy. Only one child shows significantly elevated laboratory values for creatinine and urea. However, as a urological comorbidity she was born with a solitary kidney. Except for that case, no child shows the tendency for deterioration of renal function.

Conclusion: If kidney function is normal in the neonatal period, it can be assumed that it is possible to preserve that function at least for a decade. Even after up to ten years the children do not seem to deteriorate in renal function.

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IDENTIFICATION AND DEEP PHENOTYPING OF PAX2 LOSS-OF-FUNCTION VARIANT CARRIERS IN PEDIATRIC PATIENTS WITH CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT

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Aims/Purpose: PAX2 loss-of-function (LOF) variants are a common cause of renal coloboma syndrome associated with congenital anomalies of the kidney and urinary tract (CAKUT). Pediatric CAKUT patients with PAX2 LOF variants may develop kidney failure. This study aimed to identify and deeply phenotype patients with PAX2 LOF variants in a pediatric CAKUT cohort, and to review the literature.

Methods: Whole-exome sequencing was performed on 307 pediatric unrelated CAKUT patients. Patients carrying PAX2 LOF variants underwent deep phenotyping. Twelve previous studies reporting pediatric CAKUT patients with PAX2 LOF variants and kidney failure were reviewed.

Results: In our cohort, 2.3% (7/307) of CAKUT patients carried heterozygous pathogenic or likely pathogenic PAX2 LOF variants. All patients with PAX2 LOF variants presented with bilateral kidney dysplasia, accounting for 6.7% (7/105) of patients with this phenotype but no posterior urethral valves. Due to kidney failure, 57% (4/7) of patients with PAX2 LOF variants received kidney transplantation between 4 and 15 years of age. Severe albuminuria of stage A3 (68-505 g/mol) was observed in 4/7 patients, with three and one patient with kidney failure and CKD stage G3, respectively. Phenotypic variability was evident from (i) two patients carrying the same PAX2 variant presenting either with CKD stage G3b and marked albuminuria or CKD stage G2 and no A3 albuminuria at four years of age, and (ii) two parents carrying PAX2 LOF variants were not affected by CAKUT but had adult-onset kidney failure due to focal segmental glomerulosclerosis or A3 albuminuria. In 56 pediatric patients with PAX2 LOF variants and kidney failure reported here and in 12 previous studies, kidney hypodysplasia was the predominant CAKUT phenotype in 93% (52/56) of cases, and mean age of onset of kidney failure was 9.3 years. Albuminuria was significantly higher in eight CAKUT patients with PAX2 LOF variants and kidney failure reported here and previously versus 41 patients with wildtype PAX2 and kidney failure from our cohort ($p < 0.05$).

Conclusion: As CAKUT patients carrying a PAX2 LOF variant are prone to early-onset kidney failure and severe albuminuria, close monitoring and antiproteinuric measures should be considered. However, kidneys of PAX2 LOF variant carriers may appear sonographically normal in early adulthood. Therefore, screening for PAX2 variants is suggested in related living donor evaluation from CAKUT patients with PAX2 LOF variants.

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RECOVERY PREDICTORS FOR ANTENATAL HYDRONEPHROSIS

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Aim: Antenatally-diagnosed hydronephrosis (ANH), also known as urinary tract dilatation or renal pylectasis, refers to dilatation of the renal pelvis. It is one of the most detected anomalies on foetal and postnatal ultrasounds, occurring in 1-5% of all pregnancies. Despite its high prevalence, there is a lack of defined predictors for recovery. We investigated correlations between spontaneous resolution of ANH and confounding factors.

Methods: A retrospective outpatient review study was conducted from 2012 to 2017. The inclusion criterium was ANH of any severity, exclusion criteria were lost to follow-up, no prenatal diagnosis or surgical intervention < 12 months. Recovery was defined as an anteroposterior diameter ≤10mm. Data were analysed using Pearson Chi-square or Fisher's exact test and correlations between recovery and confounders were analysed using Spearman correlation coefficients.

Results: In our study, 237 newborns had hydronephrosis (4.6% of the outpatients, n = 5117), 38 newborns were excluded (n = 29 failed prenatal diagnosis, n = 5 lost to follow-up, n = 4 surgical intervention < 12 months). The final study group comprised of 199 patients. Among the 199 cases of prenatal ANH, 186 (93.5%) of the patients showed a spontaneous resolution of APD≤10mm within 12 months, while 13 (6.5%) had persistent moderate to severe ANH. Most neonates (n = 186, 93.5%) showed a spontaneous resolution within 1 year, with 94.1% < 2 months. Males were more prevalent (n = 156 (78.4%) vs. n = 43 (21.6%)), but sex did not correlate with recovery (p =0.738). There were significantly more cases of right-sided unilateral ANH than left-sided and bilateral cases which had similar numbers (n = 37 right vs. n = 78 left vs. n = 75 bilateral, p =0.057). However, laterality did not correlate with outcome (rs = -0.042, p =0.806). In the cohort, 40 (20.1%) had a relevant comorbidity and this group was less likely to recover spontaneously (congenital anomaly rs = -0.273, p =0.001; infection rs = -0.283, p =0.002).

Conclusions: ANH is common, but most infants had a spontaneous recovery. Neonates with comorbidities including infection were less likely to recover spontaneously. These findings could guide clinicians in their follow up plans and reassurance of parents. Validation of these findings should be confirmed in future studies.

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UROFACIAL SYNDROME: CASE SERIES, UROLOGICAL MANAGEMENT, AND RENAL EVOLUTION

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Aims/Purpose: Urofacial syndrome (UFS) is a rare autosomal recessive disease caused by mutations in HPSE2 and LRIG2. It is characterized by vesical dysynergy and a distinctive facial expression upon laughing, due to abnormal contraction of the mouth and eye corners. There are no standardized clinical criteria for its diagnosis. We present a case series followed at a tertiary hospital to analyze its characteristics, evolution, and urological management.

Methods: Retrospective study of patients diagnosed with UFS treated between January 2015 and December 2023. Epidemiological data, radiological and functional studies, and renal function assessment were collected.

Results: We analyzed 5 patients (3/5 HPSE2 mutation; 2/5 LRIG2 mutation) with a mean age of diagnosis of 8.4 years (SD 4.6) and an average follow-up of 31.4 months, all born to consanguineous parents. Only 1/5 had prenatal diagnosis of pelvic dilatation. Initial follow-up reasons included: recurrent urinary tract infections (3/5), voiding dysfunction with renal insufficiency (1/5), and family study (1/5). All presented the characteristic facial expression. On ultrasound, 2/5 had bilateral pelvicalyceal dilatation, 1/5 unilateral dilatation, 1/5 thickened bladder walls, and 1/5 normal ultrasound. On cystography, 4/5 cases showed trabeculated bladder and 2/5 bilateral vesicoureteral reflux. Functionally, all but the asymptomatic patient detected by family study had high-risk hypertonic bladder with reduced capacity and severe emptying disturbance, requiring anticholinergic treatment. Initial urinary diversion was performed in four patients (1/4 suprapubic cystostomy; 3/4 vesicostomy), followed by laparoscopic Mitrofanoff catheterizable conduit, with one patient additionally requiring bladder augmentation (late diagnosis, 9 years). Urinary diversion resulted in cessation of urinary tract infections and improvement in glomerular filtration rate in the patient with renal insufficiency (onset: creatinine 2.6 mg/dl - Schwartz 2009 eGFR 22 ml/min/1.73m^2; current/lowest value: creatinine 0.96 mg/dl - Schwartz 2009 eGFR 45 ml/min/1.73m^2). Other patients had normal eGFR, none had proteinuria, arterial hypertension, or intestinal motility disorders.

Conclusion: Although rare, UFS should be considered in the differential diagnosis of patients with bladder dysfunction, especially in consanguineous families. Early diagnosis facilitates optimal urological management in initial stages, crucial for preventing renal disease progression. Most will require early urinary diversion to avoid future need for bladder augmentation.

ORAL COMMUNICATIONS 2

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CLINICAL PRACTICE OF COMPLEMENT INHIBITOR USE IN HEMOLYTIC UREMIC SYNDROME: FINDINGS FROM THE EUROPEAN RARE KIDNEY DISEASE REGISTRY

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Aims/Purpose: Over the last decade, significant advancements have emerged in the field of rare kidney diseases, notably the introduction of C5 inhibitor therapy. The C5 inhibition has transformed the prognosis for atypical Hemolytic Uremic Syndrome (aHUS), offering improved clinical outcomes. However, despite these advancements, the utilization of C5 inhibitor therapy varies significantly, with disparities in treatment duration, reasons for discontinuation, and consideration of extending treatment to patients with infectious HUS (iHUS). This variability is further compounded by the considerable cost associated with C5 inhibitor treatment.

Methods: This retrospective cohort study utilized data from the ERKNet Registry. The study cohort comprised 726 HUS patients enrolled in the ERKNet Registry between November 2018 and January 2024. The dataset encompassed patient demographics, disease and diagnostic records, medication profiles, dialysis or transplantation requirements, kidney function monitoring at the last visit, and clinical outcomes.

Results: Among 261 aHUS patients, 27 underwent kidney transplantation. 11 received C5 inhibitor therapy before kidney failure. The majority of these patients had genetic aHUS with various mutations (2 CFH, 2 CFI, 2 CFH, 1 C3, 1 CFHR3/CFHR1, 1 COL4A3 and 1 CD46). The only death in the study was from this group of patients, unresponsive to C5 Inhibition. Out of 185 aHUS patients treated with Eculizumab, 22 (12%) transitioned to Ravulizumab. Among 108 patients who discontinued C5 inhibitors, 14 (13%) had to resume treatment, half of them with genetic aHUS, with three cases of each C3 and CD46 mutations, as well as one each involving mutations in CFHR5 and C3. Only two patients required dialysis. Among 465 iHUS patients, 87 (19%) received C5 Inhibitor treatment.

Conclusion: In the context of aHUS, we found that discontinuing C5 inhibitors is generally safe, with a slightly higher relapse rate in patients with complement gene variants, though most relapses were mild, requiring dialysis in only a few cases. Long-term follow-up revealed a return to normal kidney function following TMA relapses. Transitioning from Eculizumab to Ravulizumab exhibited promising outcomes, with no relapses or kidney failures in 22 patients. Our analysis of C5 inhibitor use in iHUS emphasized its association with more severe disease progression. While some studies question C5 inhibitors' acute-phase efficacy, others report remarkable improvements in patients unresponsive to other treatments. Overall, our findings underscore the safety of discontinuation practices, the potential benefits of Ravulizumab, and the ongoing need for further research on C5 inhibitor treatment in iHUS.

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EVALUATION OF SERUM COMPLEMENT C4 LEVEL IN CHILDREN WITH IGA NEPHROPATHY

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Introduction: IgA nephropathy (IgAN) is the most common chronic glomerulonephritis worldwide, in Europe, diagnosed in 20% of kidney biopsies performed in childhood.

Objectives: The aim of the study was to evaluate the serum C4 level on the clinical course and outcomes of IgAN in children.

Material and Methods: The study included 175 children (110 boys, 65 girls) from the Polish Pediatric IgAN Registry, diagnosed based on kidney biopsy. Patients without complete clinical and histopatological data were excluded from the study. Proteinuria (mg/kg/d), erytrocyturia, serum: creatinine, albumin, IgA, C3 and C4 level were evaluated twice in the study group, at baseline and the end of follow-up. Kidney biopsy was categorized using the Oxford classification, with a calculation of the MEST-C score. Depending on the serum C4 level patients were analyzed in two groups: A - C4 < norm, B -C4 within the norm.

Results: The mean age of diagnosis of IgAN in children was 11.68 ± 4.09 years. No significant differences between groups A and B were found in regard to the severity of proteinuria, creatinine, GFR level and the intensity of IgA deposits in renal biopsy at baseline and at the end of follow-up. In group B, GFR at the end of follow-up was significantly higher than at baseline, in group A no such relationship was observed (t-student test). The Wilcoxon test showed a significant decrease in proteinuria and hematuria at the end of follow-up in both groups. Survival curve analysis using the Cox proportional hazard model showed no difference in renal survival with normal GFR between groups A and B.

Conclusions: A reduced serum C4 level has not been a prognostic factor in children but perhaps this finding should be confirmed in a larger group of children.

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ANTIMICROBIAL PROTECTION IN PATIENTS TREATED WITH COMPLEMENT INHIBITORS

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Aims/Purpose: C5 inhibitors stand as potent medication, profoundly altering the trajectory of certain rare diseases. However, their use presents significant risks, an up to 2,000-fold increase in susceptibility to meningococcal disease compared to healthy individuals. It is therefore recomended that all recipents of C5 inhibitors are vaccinated against meningococcal infections before starting the treatment. Recent evidence suggests that meningococcal vaccines offer only partial protection. Consequently, antibiotic prophylaxis alongside vaccination may further diminish the risk of meningococcal infection in individuals treated with C5 inhibitors. This study aims to identify the optimal strategy for preventing meningococcal infections in patients treated with C5 inhibitors.

Methods: This retrospective study analysed ERKNet Registry data on 136 patients treated with C5 inhibitors. The cohort was divided into solely vaccinated individuals, those who in addition to vaccination received antibiotics, and a subset of patients with solely antibiotic prophylaxis. Vaccinations included doses of meningococcal B vaccine (MenB) and/or meningococcal conjugate vaccine (MenACWY). The study spanned from November 2018 to January 2024.

Results: Out of 136 patients, 22 (16.2%) were solely vaccinated, 101 (74.3%) received antibiotic prophylaxis in addition to vaccination and 13 patients (9.5%) were protected solely with antibiotics. We recorded 12 cases (12/136, 8.8%) of meningococcal infections, of whom seven (7/101, 6.9%) were from the group with both antibiotic prophylaxis and vaccination; three (3/22, 13.6%) from the group with solely vaccination and two (2/13, 15.4%) who were solely on antibiotics. Half of the infections were attributed to serogroup B meningococcus. Recovery without permanent sequelae was reported in ten patients (10/12, 83.3%). The study reported one fatality in a patient who was vaccinated and on antibiotic prophylaxis. This patient, undergoing extensive immunosuppressive treatment, had Neuromyelitis Optica Spectrum Disorder (NMOSD), Systemic Lupus Erythematosus (SLE), and nephrotic syndrome. Another patient, who received antibiotics in addition to vaccination, was reported to have mild disability following a meningococcal infection.

Conclusion: This study indicates a lower incidence of meningococcal infection among patients who received both vaccination and antibiotic prophylaxis compared to those who were either solely vaccinated or solely on antibiotics. Serogroup B was the most common causative agent. The post-infection outcomes were predominantly favourable, with only one reported fatality associated with multiple immunosuppressive conditions.

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SWITCHING FROM ECULIZUMAB TO RAVULIZUMAB IN PEDIATRIC PATIENTS WITH ATYPICAL HEMOLITIC UREMIC SYNDROME: A SINGLE- CENTRE PROSPECTIVE ANALYSIS

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Aims/Purpose: Ravulizumab is a novel complement inhibitor developed from Eculizumab via the targeted substitution of four aminoacids, resulting in enhanced recycling and a mean half-life more than 4 times longer than that of Eculizumab. Ravulizumab exerts a more stable complement inhibition and appeared non-inferior to Eculizumab. By reducing dose frequency, it improves quality of life. To date, few studies exist on the use of Ravulizumab in children with atypical hemolytic uremic syndrome (aHUS).

Methods: A single center prospective analysis of children with aHUS who were switched from Eculizumab to Ravulizumab at our tertiary pediatric nephrology hub. At every infusion, clinical and laboratory parameters and side effects were recorded. Pre-dose CH50 levels and serum-induced C5b9 deposits on activated and unstimulated endothelium were analyzed at specific time-points to monitor complement inhibition. Ravulizumab was administrated according to the European Medicines Agency dosing schedule.

Results: From November 2023, 3 out of 6 patients treated with Eculizumab for aHUS were switched to Ravulizumab. The other patients were not switched due to the possibility of therapy withdrawal for clinical or genetic reasons. Patient 1, a 5-year-old male with a heterozygous MCP mutation and heterozygous CFHR3-CFHR1 region deletions, was treated with Eculizuamb for 4 years. Patient 2, a 13-year-old female with a CFH mutation, was treated with Eculizuamb for 6 years. Patient 3, a 7-year-old male with neonatal onset aHUS due to a heterozygous CFH gene mutation, has been in therapy with Eculizumab since three months of age. No adverse events were noted during Eculizumab therapy. To date, Patients 1 and 2 have received 4 doses of Ravulizumab each with no adverse events. Patient 3 had an anaphylactic reaction during their second infusion that necessitated infusion discontinuation and adrenaline administration. Therefore, we applied a 12-step desensitization protocol, consisting in slowly increasing infusion rates. It was well tolerated and the patient has received 2 additional doses of Ravulizumab until now, with methylprednisolone and clorphenamine premedication. To date, all 3 patients are in stable remission, with pre-dose CH50 levels and C5b9 deposits within normal ranges.

Conclusion: In children with aHUS, the decision to switch from Eculizumab to Ravulizumab requires careful evaluation of the potential benefits, costs, and adverse reactions. In our experience, all the patients who switched to Ravulizumab are, to date, in stable remission. One patient experienced an anaphylactic event but had no subsequent complications. Further data are needed to better evaluate the safety profile of Ravulizumab in children. Considering the rarity of childhood aHUS, multicenter studies to further assess the efficacy and safety of switching therapy are needed.

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USEFULNESS OF ECULIZUMAB IN THE TREATMENT OF NEUROLOGICAL COMPLICATIONS OF TYPICAL HEMOLYTIC UREMIC SYNDROME IN CHILDREN

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Aims/Purpose: To study the usefulness of treatment with eculizumab in pediatric patients affected by neurological complications within the typical hemolytic uremic syndrome. To know the severity score of neurological complications to identify patients who are candidates for treatment with eculizumab and who may benefit from it.

Methods: To analyze the clinical, epidemiological, therapeutic and evolutionary characteristics of children under 15 years of age diagnosed with typical hemolytic uremic syndrome in a tertiary hospital in the last 10 years, focusing on patients with severe neurological complications treated with eculizumab. Review of medical records.

Results: 15 patients with hemolytic uremic syndrome (HUS) were registered, of which 10 (66.7%) were typical forms with a positive microbiological diagnosis for Shiga toxin-producing Escherichia coli (STEC), being diagnosed with STEC-HUS. Of those 10 children, 3 (30%) presented severe symptoms, with a median age of 18 months (15-24), two of them were women. These patients were admitted to a Pediatric Intensive Care Unit and presented with acute renal failure upon diagnosis with a median plasma creatinine of 3.2 mg/dl (2.5-3.9), median plasma hemoglobin of 5.8 g/dl (5.3-6.3) and median platelet count of 68,500/mm3 (55,750-73,275). They required transfusion of blood products and extrarenal purification techniques through continuous veno-venous hemodiafiltration for a median of 7 days (5-9). Two of them developed severe neurological symptoms in the first 24-48 hours of admission, in the form of altered level of consciousness and seizures, presenting status epilepticus with pathological EEG. All the patients showed serological signs of complement activation (low C3 levels and high C3d levels). Central nervous system (CNS) examination with MRI showed local acute lesions at the basal ganglia and at white matter. Both patients were treated with two doses of IV eculizumab. After eculizumab treatment, a regression of CNS MRI lesions and the disappearance of neurological signs and symptoms were observed. Subsequent favorable clinical evolution of these patients and the rest of the series.

Conclusions: Although systematic reviews of the benefit of treatment with eculizumab in patients with severe neurological involvement in typical hemolytic uremic syndrome are inconclusive, there are more and more publications of pediatric clinical cases that support its use in this context. There is a neurological symptom severity score that could be applied to identify the cohort of patients who could benefit from it, based on neurological symptoms, EEG alteration and CNS MRI. Knowing and applying this score could help us in making decisions in these critically ill patients, improving their prognosis.

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THERAPEUTIC DRUG MONITORING IMPROVES THE EFFICACY OF MYCOPHENOLATE MOFETIL IN CHILDREN WITH STEROID DEPENDENT AND FREQUENTLY RELAPSING NEPHROTIC SYNDROME

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Aims/Purpose: The aim of this retrospective and observational study was to assess if mycophenolic acid (MPA) therapeutic drug monitoring (TDM), performed by trough levels, improves the efficacy of Mycophenolate Mofetil (MMF) in maintaining remission at 6 months in children with frequently relapsing or steroid-dependent nephrotic syndrome (FRNS/SDNS).

Methods: We included FRNS or SDNS patients, aged between 1-18 years, and treated with MMF as the first steroid-sparing agent with a follow-up > 6 months. Patients were enrolled in the Pediatric Nephrology Units of Ospedale Maggiore Policlinico of Milan (Italy) and Necker-Enfants Malades Hospital in Paris (France) from January 2013 to December 2022. Children were divided in two groups: TDM, if MPA trough levels were monitored and NO-TDM, if trough levels were not performed. In the TDM group, MPA levels were monitored 1 month after the introduction and on a 3-months basis thereafter. MMF doses were modified to maintain MPA trough levels > 3 mcg/ml, unless toxicity occurred.

Results: 167 patients were included, 90 in the TDM and 77 in the NO-TDM group. Relapse-free survival was significantly different in the 2 groups (TDM 73.3% vs no-TDM 55.5%; p =0.018) (Figure 1). After correcting for confounders (numbers of relapses 1 year before MMF, age at MMF introduction, ethnicity and mean daily dose of prednisone [PDN] before MMF), the relationship between TDM and relapse-free survival remained statistically significant (p =0.002). Accordingly, TDM patients received lower doses of PDN after the introduction of MMF (median PDN/year, TDM 463 mg/sqm vs NO-TDM 814 mg/sqm; p =0.02). In the TDM group, 72.2% of patients increased the initial MMF doses according to trough levels, while only 11.7 % of children in the NO-TDM group increased the initial dose (p < 0.00001). Reported side effects were similar in both groups (20% of patients in group TDM, 22% in group NO TDM). Finally, in the TDM group, children who did not relapse within the first six months of treatment had higher mean MPA trough levels (Figure 2) and higher maximum trough levels than those who relapsed (p =0.002).

Conclusion: MPA trough levels improved by around 20% the efficacy of MMF in maintaining remission at 6 months in children with FRNS or SDNS. It is safe and effective to use personalized and increased doses of MMF, even when exceeding 1200 mg/sqm/day in order to maintain MPA levels above 3 mcg/ml. We suggest starting with an initial dose of MMF of 1200 mg/sqm/day and then using MPA trough levels to adjust the dosage. If TDM by trough levels is not available, MMF doses > 1200 mg/sqm/day should be tried, when relapses occur. Future studies comparing MMF with other steroid-sparing agents in SDNS/FRNS should include MPA trough levels.

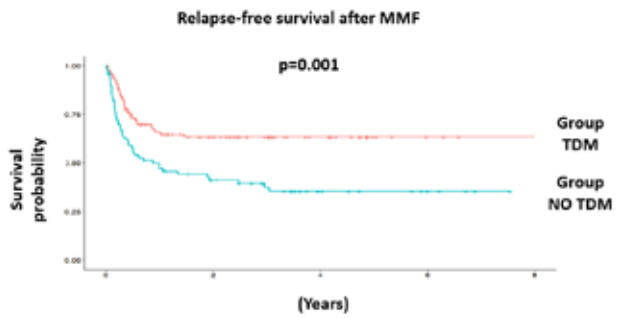

Figure 1

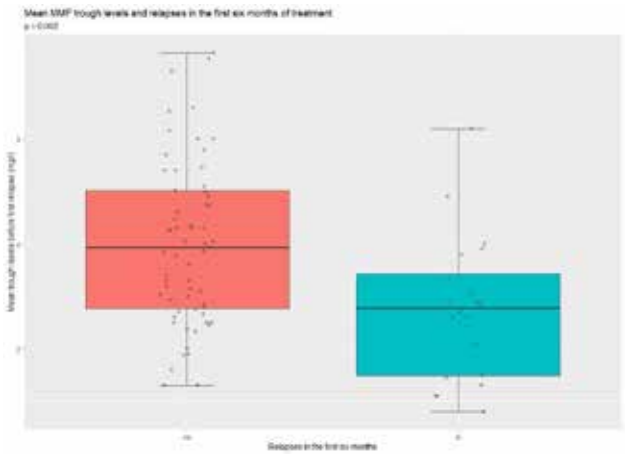

Figure 2

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INTRAVENOUS RITUXIMAB VERSUS ORAL MYCOPHENOLATE MOFETIL IN SUSTAINING REMISSION OF CALCINEURIN INHIBITOR DEPENDENT STEROID RESISTANT NEPHROTIC SYNDROME: AN OPEN LABEL RANDOMIZED CONTROLLED TRIAL

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Aims/Purpose: Retrospective unicenter studies in patients with steroid-resistant nephrotic syndrome (NS) show that switching of calcineurin inhibitors (CNI) to oral mycophenolate mofetil (MMF) or IV rituximab enables remission and is corticosteroid and CNI-sparing, while avoiding therapy-associated adverse effects (AE). However, prospective controlled studies are lacking.

Methods: This open-label multicenter RCT will examine the superiority of IV rituximab versus oral MMF in maintaining satisfactory remission in patients with steroid-resistant NS who were in complete or partial remission while on therapy with tacrolimus or cyclosporine for over 2-yrs, but continued to show steroid-sensitive relapses. Eligible consenting patients with steroid-resistant NS, 1-18 yr-old, with complete or partial remission and steroid sensitive relapses while on ≥2-yr therapy with CNI, will be randomized to switch therapy to either oral MMF for 1-yr or IV rituximab (2 doses a week apart; 1 dose 6-months later). The primary outcome, on intention-to-treat analysis, will be the proportion of patients with satisfactory remission (sustained remission or infrequent relapses) at 1-yr (Fig. 1). Secondary outcomes are the proportions of patients with frequent relapses, steroid resistance & serious AE, incidence of relapses, prednisolone exposure, and changes in anthropometry & biochemistry (CTRI/2022/10/046890).

Results: The study began enrolment in October 2022 and is expected to close enrolment in September 2025.

Conclusion: Findings from the study shall have important implications for guiding the choice of non-nephrotoxic therapies following induction and maintenance of remission with CNI for childhood idiopathic steroid-resistant NS.

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SHIGA-TOXIN ASSOCIATED HEMOLYTIC UREMIC SYNDROME WITH NEUROLOGICAL INVOLVEMENT: IDENTIFICATION OF PROGNOSTIC FACTORS AND DEVELOPMENT OF A MACHINE LEARNING MODEL TO PREDICT OUTCOME

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Aims: Hemolytic uremic syndrome (HUS) is the leading cause of acute kidney injury in children and Shiga toxin E. coli (STEC+) associated HUS accounts for the majority of cases. Morbidity and mortality are elevated, especially in children with neurological involvement. Treatment remains supportive, but the risk stratification could allow to identify those patients potentially requiring a higher level of therapy (i.e. steroids, eculizumab, PEX).

Methods: 30 patients with STEC+ HUS and neurological involvement were treated at the Pediatric department of the University Hospital of Padova, Italy, from January 2009 to December 2023. Of these, clinical, laboratory, and instrumental data were collected at HUS diagnosis, including brain MRI and EEG. Patients were stratified based on neurological outcome at the last available follow-up as defined by the Pediatric Cerebral Performance Category (PCPC) Scale and on the severity of cerebral outcomes at the last available MRI, scored (0,1, 2 points) by a blinded and experienced neuroradiologist. Clinical and neuroradiological scores at follow-up were then combined in a composite neurological outcome (CNO) of clinical-neuroradiological damage. Characteristics of patients with mild-moderate vs. severe CNO were compared to identify potential risk factors for outcome. Prediction of severe CNO based on acute characteristics at HUS presentation was then derived using a machine learning algorithm.

Results: CNO was calculated for all the patients, with a median follow-up time of 73 months (IQR 89 months). Patients with severe CNO exhibited older age at diagnosis (p =0.048), more severe neurological signs at HUS onset (p =0.004), and longer dialysis duration (p =0.006). They also had more severe leukocytosis (p =0.004) and higher C-reactive protein levels (p =0.03) at onset, along with elevated D-Dimer levels during hospitalization (p =0.009). Neurological outcome was not associated with any STEC serotype.

EEG abnormalities at HUS onset correlated significantly with worse CNO (p =0.006) and increased risk of disability (p =0.009), whereas acute MRI lesions only predicted neuroradiological (p =0.007), but not clinical outcomes. EEG at HUS onset resulted the best predictor of severe CNO in the machine learning predictive model.

Conclusion: In children with STEC+ HUS with neurological involvement, the combination of biochemical profile and EEG findings at disease onset allows to identify patients at risk of severe neurological outcomes. This could potentially influence the choice of using specific therapeutic measures in selected patients.

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IMMUNOMODULATORY EFFECTS OF LEVAMISOLE IN IDIOPATHIC NEPHROTIC SYNDROME IN CHILDREN

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Aims/Purpose: This study aimed to systematically investigate the effects of Levamisole (LMS) on the human immune system, including its impact on isolated human immune cells in vitro. The objectives were to elucidate the immunological mechanisms underlying idiopathic nephrotic syndrome (INS) in children, assess the immunomodulatory effects of LMS, and investigate its potential therapeutic implications in INS management.

Methods: Blood samples were collected from INS pediatric patients and age-matched healthy controls (HC) for flow cytometry and immunoplexing analysis. Additionally, whole blood samples from pediatric INS patients treated with LMS or placebo were stimulated with lipopolysaccharide (LPS) or anti-CD3/anti-CD28, and cytokine production was measured.

Results: Compared to HC, INS patients exhibited elevated levels of circulating T-cells, particularly CD8+ T-cells, and an increased presence of plasmablasts. Moreover, INS patients demonstrated heightened IgM production and reduced IgG levels at diagnosis, suggesting early activation of the humoral immune response. LMS-treated patients showed decreased B-cell counts and altered cytokine profiles, with enhanced production of TNF-, IFN-, and IL-2 upon stimulation, and reduced levels of IL-13 compared to placebo-treated patients. Earlier work from our group has shown that LMS suppresses the proliferation and activation of both CD4+ and CD8+ T-cells by modulating gene expression associated with cell cycle progression and p53 activation [1]. Additionally, LMS treatment decreases B-cell proliferation, Ig production, and metabolism, while inducing upregulation of genes involved in plasmablast differentiation.

Conclusion: These findings highlight the immunomodulatory effects of LMS on the human immune response, shedding light on its potential therapeutic role in INS management in children. LMS appears to suppress immune cell proliferation, alter gene expression profiles, and induce DNA damage, suggesting its capacity as an immunosuppressive agent. Further research is needed to fully elucidate the therapeutic implications of LMS in immune-mediated disorders and its underlying mechanisms of action.

References

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EFFECT OF THYMIC STROMAL LYMPHOPOIETIN (TSLP) ON RNA-SEQ-BASED TRANSCRIPTOMIC PROFILING OF HUMAN PODOCYTES: A PATHOGENIC ROLE IN PROTEINURIA

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Aims/Purpose: Thymic stromal lymphopoietin (TSLP) is a major cytokine that promotes TH2 responses and polyclonal B cell activation in various auto-inflammatory diseases and allergy. Previous researches showed that TSLP overexpression in mice results in the development of cryoglobulinemic membranoproliferative glomerulonephritis and TSLP promotes renal fibrosis by activating STAT3 in renal fibroblasts. However, there has been no report on the effect of TSLP on changes in podocytes which is related to proteinuria. The aim of our study was to show this effect by RNA-Seq-Based bioinformatics analysis.

Methods: Podocytes were incubated with TSLP during the indicated time periods (6, 12, and 24 h) and whole-transcriptome RNA and microRNA (miRNA) sequencing was erformed. Differentially expressed genes (DEGs) were analyzed.

Results: There were distinct changes between control and TSLP condition. DEGs at 6 h were 113 genes, DEGs at 12 h were 19 genes, and DEGs at 24 h were 33 genes. Protein-protein interaction network was analyzed by STRING and PodNet which is a protein-protein interaction network of the podocyte and covers 315 genes and 223 interactions. Through the PPI interactions between DEGs, hub genes were identified such as POLE, SMAD4, HDAC9, SIRT1, and APOB by STRING. By comparison with PodNet, 38 genes are overlapped including Nck1, Vhl, Arhgap24, Map1lc3a, Cdk5, Cdkn2A, and Tln1 (p-value <0.01). Four genes (Robo1, Foxc2, Vav2, Ddr1) were overlapped (adjusted p-value <0.05). In addition, differentially expressed 23 microRNAs were identified (p-value <0.05), and their target DEG mRNAs were found using the microRNA Target Databases.

Conclusion: We identified meaningful DEGs in TSLP-induced podocytes and made an mRNA-miRNA gene network. This could be used in understanding the pathogenesis of proteinuria in various primary and secondary kidney diseases.

ORAL COMMUNICATIONS 3

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ACUTE RENAL REPLACEMENT THERAPY IN PEDIATRIC PATIENTS: A NATIONAL SURVEY ASSESSING PROGRAMMATIC DELIVERY OF CARE

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Aims/Purpose: Acute kidney injury occurs commonly in critically ill children and is associated with significant morbidity and mortality. Advances in pediatric renal replacement therapy (RRT) technology, along with the challenges of providing multidisciplinary care for medically complex patients, have led to an increased need for critical care nephrology expertise and support across pediatric, neonatal, and cardiac intensive care units (ICUs). In response to these growing needs, individual children's hospitals have implemented Acute Care Nephrology (ACN) programs to improve the delivery of safe, timely, and effective evidence-based care for children with AKI and other non-renal conditions that can benefit from RRT. Given inherent variations in practices, resources, and RRT modalities from physician, nursing, and infrastructure perspectives, we aimed to evaluate current practices of ACN programs across the USA (US).

Methods: An electronic survey was distributed to the top 50 pediatric nephrology programs from the US News & World Report Best Children's Hospitals 2023 ranking. Questions included details of programmatic structure, therapies provided, volume of procedures, quality improvement (QI), and educational practices.

Results: 47 centers (94%) completed the survey, with Table 1 showing selected results by center volume. Overall, 79% of respondents have a dedicated ACN program, with 53% jointly managed within their chronic dialysis program. 68% have a medical director with a median (IQR) full time equivalent (FTE) of 10% (5, 20%), though 13% (6 programs) report 0 FTE. Only 45% have an ACN nursing director. Other available personnel include nurse educator (53%), program administrator (17%), advanced practice provider (13%), and QI specialist (21%). ACN focused QI programs are present in only 40%, with an additional 34% of centers collecting some metrics related to patients, circuits, and access, while 36% do not track any data. The most common barriers for implementing QI programs include lack of protected time, resources, and support from leadership. Despite variability in program size, structure, and modalities offered, 81% of responding centers identified a need for increased medical director FTE, and 90% identified a need for increased nursing director FTE.

Conclusions: This data provides a first-of-its-kind description of the current structure/delivery of care in pediatric ACN practices from hospitals across the US and identifies potential areas for systematic improvement in the delivery, monitoring, and comprehensive approach to pediatric acute RRT.

Table 1. Survey responses from hospitals across the US by patient volume (i.e., estimated CRRT patient days per year).

Estimated patient volume [avg. CRRT patient days per year]	< 250	250-499	500-749	750-999	>1000
Number of survey respondents by volume [%, (number of programs)]	19% (9)	30% (14)	21% (10)	9% (4)	17% (8)
Have an established ACN program	66% (6)	64% (9)	100% (10)	100% (4)	75% (6)
ACN is part of chronic dialysis	55% (5)	64% (9)	50% (5)	25% (1)	37.5% (3)
Have a medical director	33% (3)	71% (10)	70% (7)	100% (4)	88% (7)
Current % FTE for medical director [Median; (IQR)]	20% (12.5; 22.5)	6% (0; 13.75)	10% (7.5; 10)	12.5% (7.5; 17.5)	15% (10; 20)
Needed % FTE requested for medical director [Median; (IQR)]	21% (10; 25)	20% (15; 25)	22.5% (16.3; 32.3)	17.5% (13.8; 21.3)	20% (17.5; 26.3)
Have a nursing director	22% (2)	35% (5)	40% (4)	100% (4)	63% (5)
Current % FTE for nursing director [Median; (IQR)]	10% (5; 15)	50% (5; 100)	45% (36.3; 60)	28.5% (25.3; 47.5)	40% (20; 40)
Needed % FTE for nursing director [Median; (IQR)]	20% (20; 25)	50% (20; 50)	27.5% (25; 50)	50% (43.7; 62.5)	50% (23.8; 62.3)
Have a dedicated APP	0	14% (2)	0	25% (1)	37.5% (3)
Have a nurse educator	33% (3)	42% (6)	90% (9)	75% (3)	37.5% (3)
Have a program administrator	0	21% (3)	10% (1)	25% (1)	25% (2)
Have a dedicated pharmacist	33% (3)	21% (3)	20% (2)	50% (2)	75% (6)
Have a QI leader	0	29% (4)	30% (3)	25% (1)	25% (2)
Have a QI program	22% (2)	29% (4)	50% (5)	75% (3)	62.5% (5)
Have dedicated ACN nurse(s)	11% (1)	7% (1)	10% (1)	75% (3)	62.5% (5)
Perform CRRT in the NICU	22% (2)	71% (10)	90% (9)	75% (3)	75% (6)
Perform CRRT in the CICU	66% (6)	100% (14)	100% (10)	100% (4)	100% (8)
Perform CRRT via Carpediem	55% (5)	35% (5)	40% (4)	50% (2)	62.5% (5)
Perform ultrafiltration via Aquadex	33% (3)	35% (5)	10% (1)	75% (3)	50% (4)
Perform CRRT via Aquadex with mCVVH	0	29% (4)	10% (1)	75% (3)	50% (4)
Perform MARS	11% (1)	7% (1)	0	25% (1)	12.5% (1)
Plasmapheresis is managed by nephrology	0	35% (5)	30% (3)	25% (1)	88% (7)
LDL apheresis is managed by nephrology	11% (1)	7% (1)	10% (1)	25% (1)	25% (2)

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ACUTE KIDNEY INJURY IN PEDIATRIC ONCOLOGY PATIENTS IN A NATIONAL 6 YEARS COHORT STUDY; EPIDEMIOLOGY, RISK MEDICATION AND THE CONSEQUENCE OF KIDNEY INJURY USING A MULTI-STATE MODEL

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Aims/purpose: Acute kidney injury (AKI) is one of the serious complications during pediatric cancer treatment, being multifactorial in etiology. AKI can lead to amending regular cancer treatment (dose adjustment or treatment delay). It is unknown whether AKI is a risk factor for CKD. We investigated the incidence of AKI, the effect of individual medications on the evolution of AKI and we aimed to assess the association between AKI and the occurrence of CKD in a Dutch national cohort.

Methods: We included all pediatric cancer patients treated in the Princess Máxima Center from 2015-2022. A multi-state Cox Hazard model was estimated to study the impact of nephrotoxic medication on the time to different AKI episodes during cancer treatment. A logistic regression model was estimated to study the association between co-variates and the occurrence of CKD.

Results: A total of 1525 patients were included. Treatment-related AKI occurred in 37%. Medication associated with the occurrence of first episode of AKI were Cisplatin (HR 1.68; 95%CI 1.32-2.15), Methotrexate (MTX) (HR 1.84; 95% CI 1.42-2.38), Rituximab (HR 1.55; 95% CI 1.00-2.42), Amfotericin B (HR 2.04; 95% CI 1.30-3.21), Enalapril (HR 1.61; 95% CI 1.10-2.37), Fluconazol (HR 1.77; 95% CI 1.19-2.64) and Spironolactone (HR 1.45; 95% CI 1.01-2.08). Medication associated with a second period of AKI were Vancomycine (HR 1.82; 95% CI 1.19-2.81) and Voriconazol (HR 1.85; 95% CI 1.07-3.19). In patients who experienced three episodes of AKI, only Amfotericine B (HR 3.22; 95% CI 1.51-6.85) was significant. One year after stop treatment, CKD occurred in 13.6%. According to the multivariate logistic regression model, variables associated with CKD included age (OR 1.07 (95% CI 1.03-1.11), nephrectomy (OR 4.64 (95% CI 2.33-9.24), Ifosfamide (OR 2.30 (95% CI 1.44-3.68), the occurrence of more than one AKI episode during treatment (OR 4.00 (95% CI 2.54-6.31) and duration of the AKI episode of more than 7 days (OR 10.6 (95% CI 6.66-17.0).

Conclusion: AKI is very common in children and is associated with CKD. Awareness for patients at risk is important. Patients who had > 1 AKI episode and patients who underwent nephrectomy or treated with ifosfamide must be monitored. Monitoring at diagnosis, during and after treatment is recommended in order to apply interventions and to prevent AKI and CKD as much as possible.

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ACUTE KIDNEY INJURY AFTER CARDIAC SURGERY IN INFANTS, CHILDREN, AND ADOLESCENTS: INCIDENCE, STAGING, AND RISK FACTROS

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Background: Acute kidney injury is a common complication of cardiac surgery, particularly in pediatric patients. The development and progression of acute kidney injury are associated with a higher mortality rate, more complex hospital course, and higher risk of infection.

Methods: We conducted a retrospective study of all patients admitted to the post-cardiac pediatric intensive care unit in one of the largest tertiary hospitals in Saudi Arabia over seven years (2014–2021). The Kidney Disease-Improving Global Outcome criteria were used to define the different stages of acute kidney injury.

Results: The study cohort comprised 628 children who underwent cardiac surgery, 186 of whom (29.6%) developed acute kidney injury. Younger children were more likely to develop acute kidney injury than younger children. Higher risk adjustment for congenital heart surgery scores (3, 4, and 5) were associated with acute kidney injury in 43.3% (vs. 35.1% without acute kidney injury), 14% (vs. 5.8%), and 6.7% (vs. 2.8%) of patients, respectively ($p < 0.01$). Preoperative hypoalbuminemia and exposure to contrast medium were associated with a higher risk of acute kidney injury (26.3% vs. 15.4%, $p < 0.01$ and 9.1% vs. 2.5%, $p < 0.01$, respectively). Patients who required an interventional cardiac catheter either pre- or post-operatively had a higher risk of acute kidney injury (9.1% vs. 2.5%; $p < 0.01$).

Conclusions: This study provides valuable insights into the risk factors for acute kidney injury in children undergoing cardiac surgery. Age, surgical complexity, preoperative hypoalbuminemia, comorbidities, and perioperative procedures were identified as significant contributors to increased acute kidney injury risk.

Table 1: Baseline characteristics of pediatric patients who underwent cardiac surgery.

	Total	No AKI	AKI	P-value
Number (%)	628	442 (70.4)	186 (29.6)	
Demographics				
Age, months (median [IQR])	36 (24–60)	36 (24–60)	36 (12–48)	0.01
Sex, male (n [%])	303 (48.3)	220 (49.8)	83 (44.6)	0.24
Weight, kg (median [IQR])	13.5 (10–17)	14 (10–17)	13 (10–16)	0.35
Height, cm (median [IQR])	94 (77–106)	95 (80–108)	91.5 (75–103)	0.17
Congenital heart disease category				
Acyanotic CHD (n [%])	363 (57.8)	266 (60.2)	97 (52.7)	0.053
Cyanotic CHD (n [%])	254 (40.5)	171 (38.7)	83 (44.6)	
Complex CHD (n [%])	11 (1.8)	5 (1.1)	6 (3.2)	

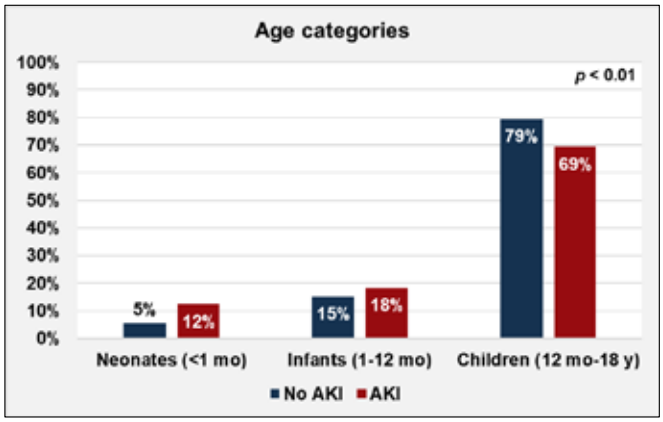

Figure 1 Risk of acute kidney injury (AKI) development after cardiac surgery by age

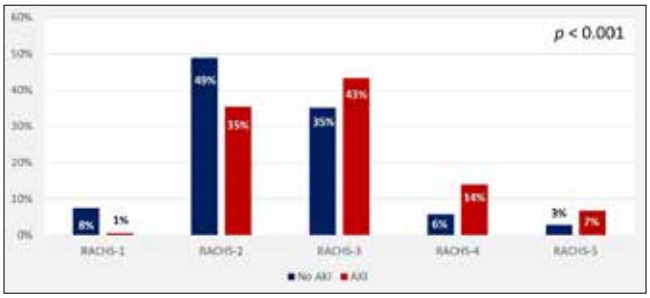

Figure 2 The association between RACHS-1 score and the development of acute kidney injury (AKI) following cardiac surgery

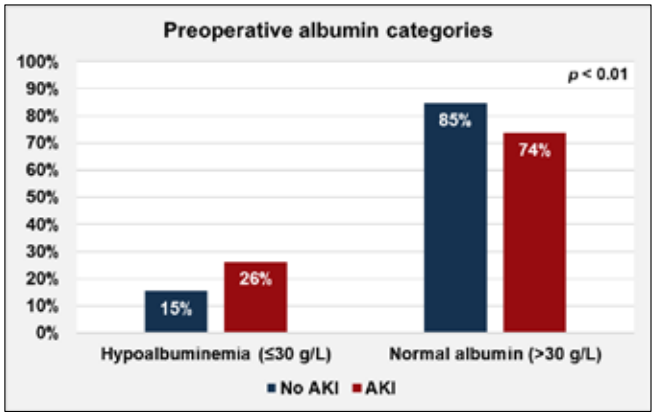

Figure 3 Risk of acute kidney injury (AKI) development following cardiac surgery according to preoperative albumin category

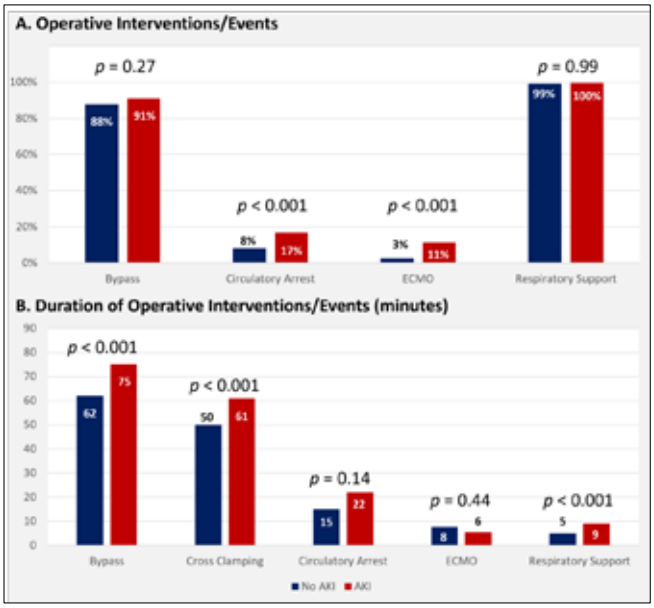

Figure 4 Operative factors and their association with acute kidney injury (AKI) development following cardiac surgery

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CHRONIC KIDNEY DISEASE AMONG PEDIATRIC SURVIVORS OF EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) THERAPY

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Aims/Purpose: Extracorporeal membrane oxygenation (ECMO) is a medical technology of in vitro oxygenation using artificial equipment, which has been operating for approximately 30 years. High rates of mortality have been seen in children receiving ECMO and among those who survive there have been reports of multiorgan complications. Acute kidney injury has been reported at high rates among these children but the rate of long-term chronic kidney disease (CKD) among the surviving children is less known specifically in the pediatric population. This study aimed to assess the rate of CKD following ECMO therapy at Schneider Children's Medical Center and identify the associated risk factors.

Methods: A retrospective cohort study that included patients treated with ECMO at Schneider Children's Medical Center between the years 2010 and 2020. Demographic data, ECMO duration, need for dialysis, type and dosage of medications, and laboratory test results were collected from patients' electronic medical records. CKD was defined as a GFR (glomerular filtration rate) below 90 ml/min/1.73 m2. (CKID formula).

Results: The study population included 229 patients, 52% (120) were neonates, 54.6% (125) Male. The average time on ECMO was 10.4 days with the most common cause being cardiac at 48.5% (n = 111) followed by respiratory failure at 44.5% (n = 102). 85.2% (n = 195) of patients developed AKI (based on KDIGO creatinine criteria). For CKD analysis we excluded all patients who died on ECMO (n = 96) and patients with no available long-term data beyond hospitalization(n = 38). Ninety-five patients (41.5%) were included in the analysis; 25 (26.3%) of surviving patients developed CKD. GFR at hospital discharge was found to be the stronger predictor for the development of CKD ($p < 0.01$).

Conclusions: This study found that estimated GFR at hospital discharge is an important predictive factor for CKD. It is important to establish long-term nephrology follow-up for children following ECMO therapy who have abnormal estimated GFR at hospital discharge for appropriate monitoring of renal function proteinuria and hypertension.

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ADOLESCENCE MILD TO MODERATE KIDNEY INJURY AND ADVANCED KIDNEY DISEASE IN YOUNG ADULTHOOD - AN HISTORICAL COHORT STUDY

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Aims: Renal injury in adolescence is associated with end stage renal disease in later life, but data regarding the association between mild kidney injury at this age and renal morbidity in early adulthood is scarce. We aimed to evaluate this association.

Methods: This is a longitudinal historical cohort utilizing Clalit Health Services' (CHS) database, the largest of four integrated health care organizations in Israel, which insures 4.7 million patients. The cohort included all patients born between 1986 and 1995 who were followed at CHS from childhood and had at least one recorded serum creatinine result at age 14-18 years, or a recoded diagnosis of a congenital anomaly of the kidney or urinary tract (CAKUT). They were followed since the establishment of CHS' database (2000) until 2022, move to another health network, or death. The cohort was divided into a study group - including adolescents with CAKUT and/or mild-moderately increased serum creatinine (1.2-1.7 mg/dl in males, 0.95-1.35 in females) and controls. Our outcomes were defined as CKD3, CKD 4-5 (based on serum creatinine level at last follow up) or ESRD (based on EMR diagnoses) at last follow up.

Results: The cohort included 304,574 patients, 299,752 (98.5%) in the control group, and 4,603 (1.5%) in the study group. At baseline, study group patients were more likely to be diagnosed with CKD (2% vs 0.1%, $p < 0.01$), proteinuria (2.1% vs. 0.1% $p < 0.01$), and hypertension (1.1% vs. 0.8%, $p = 0.02$). At last follow up, 244 patients (0.08%) had CKD3, 115 (0.04%) had CKD4-5, and 240 (0.08%) had ESRD. On a multivariate analysis, study group patients were more likely to have CKD3 (OR 10.9, 95% CI 7.4-15.9), CKD3-5 (OR 7.7, 95% CI 4.2-14.1), and ESRD (OR 5.7, 95% CI 3.2-10.0) at last follow up, independent of diagnoses commonly associated with CKD (hypertension, proteinuria, acute kidney injury, glomerular disease, cystic kidney disease, etc.)

Conclusion: Mild to moderate kidney injury in adolescence is associated with more severe kidney disease, including ESRD, in early adulthood, and requires close monitoring and steps to prevent such progression.

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HAEMOLYTIC URAEMIC SYNDROME: A 26 YEAR RETROSPECTIVE REVIEW OF CASES AT A UK REGIONAL NEPHROLOGY SERVICE

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Aims/Purpose: Haemolytic uraemic syndrome (HUS) is a common cause of AKI in young childhood. Although the majority of childhood cases are associated with Shiga-toxin producing Escherichia coli (STEC) infection, atypical HUS represents ~20%. There is limited literature reporting the longer-term outcomes of HUS, particularly atypical STEC-HUS. The aim of the retrospective study is to describe the aetiologies and outcomes of patients presenting in childhood, and explore the differences in outcomes depending upon aetiology, and other factors.

Methods: A retrospective, single-centre case notes review of paediatric HUS over a 26-year period collected clinical, demographic, and outcome data. Following descriptive statistics, associations and correlations were explored, and both individual and composite outcomes of chronic kidney disease were assessed.

Results: Of the 109 cases reviewed, 74% were STEC-HUS. Cerebral HUS was the most commonly reported extrarenal manifestation (17%). Children with pneumococcal HUS had a longer time of dialysis. Age at presentation of atypical HUS with confirmed pathogenic genetic variants ranged from 4 months to 16 years old. Mortality was 0.9% (1/109 due to pneumococcal meningitis). After a median follow-up of 42 months, 49% had physician-coded CKD outcomes (GFR < 90 ml/min/1.73m2BSA, hypertension, and/or proteinuria). There was a higher incidence of CKD outcomes in the pneumococcal subgroup (60%). CKD was more likely the longer the follow-up period. There was a tendency for those with higher pre-morbid BMI to have lower GFR at follow-up. Poorer GFR was associated with shorter stature. Those that had an adverse renal outcome (low GFR/HTN/proteinuria) at follow up spent longer on dialysis during the acute phase.

Conclusion: Data suggested an improving mortality pattern compared to previous reports, and that mortality is associated with non-HUS pathology rather than the HUS itself. Atypical HUS due to genetic variants may present at any age, not just infants. Non-cerebral HUS extrarenal manifestations are rare. With increasing length of follow-up observation, CKD outcomes become more likely to be present, and highlights the importance of long-term follow-up following apparent renal recovery.

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NEPHRODREPA STUDY: RENAL COMPLICATIONS SCREENING IN CHILDREN WITH SICKLE CELL DISEASE

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Aims/Purpose: Sickle cell anemia induces various glomerular and tubular renal disorders, often beginning with hyperfiltration in childhood. Despite its occasional manifestation during childhood, it can lead to end-stage kidney failure in adulthood and is challenging to diagnose through conventional methods. Adequate screening poses a significant challenge for optimal care of these patients. This study aims to evaluate renal function in children and young adults with sickle cell disease through a select number of examinations, conducted during the annual check-up.

Methods: The NEPHRODREPA study, a prospective study involving 12 patients aged between 4 and 17 years of age, enrolled between November 2022 and March 2024, undergoing treatment for major sickle cell syndrome at The university hospital of Nice. In addition to the annual check-up recommended by the French health authority (HAS), cystatin C assays and 99m technetium-DTPA clearance were conducted to assess glomerular filtration rate (GFR). GFR was calculated using three methods: the 2009 Schwartz formula (based on creatinine), CKiDU25Cyst (based on cystatin C) and CKiDU25 (based on both creatinine and cystatin C). Data are presented as median [25th-75th quartile].

Results: The median age was 11.3 [IQ 8.0-15.6] years, the median GFR measured by 99mTc-DTPA clearance was 111 [103-122] mL/min/1.73m^2. The 2009 Schwartz formula yielded a median GFR of 141 [133-169] mL/min/1.73m^2, CKiDU25Cyst a median of 108[98-133] mL/min/1.73m^2, and CKiDU25 a median of 127 [117-132] mL/min/1.73m^2. GFR was significantly overestimated with the 2009 Schwartz formula and the CKiDU25 formula compared to GFR measurement by 99mTc-DTPA clearance after paired t-test ($p < 0.0001$; $p = 0.0001$ respectively). No difference was observed between 99mTc-DTPA clearance and GFR estimated by the cystatin C formula ($p = 0.95$).

Conclusion: These preliminary results highlight an overestimation of GFR when using formulas that include creatinine. Isotopic methods, such as 99mTc-DTPA clearance, provide a reliable measurement of the GFR in this cohort. Similarly, formulas incorporating cystatin C yield accurate assessments of renal function, suggesting their potential utility in routine evaluations for these patients.

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GOING GREEN IN PEADIATRIC NEPHROLOGY

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Aim: Incorporating environmentally sustainable practices in our daily dialysis practice is paramount as it mitigates ecological harm, optimizes resource utilization, and contributes to the overall well-being of patients and communities. This study aims to investigate the awareness and practices related to environmental sustainability among pediatric nephrology units and assesses their potential impact on waste management and energy consumption.

Materials and Methods: The "Going Green in Paediatric Nephrology" survey was distributed to members via the ESPN mailing list, eliciting responses from 72 paediatric nephrology units representing 32 countries, including 23 paediatric dialysis units in Europe. The survey focused on facilities, awareness of Green Nephrology concepts, current sustainability practices, waste management strategies, energy consumption, and water usage monitoring. Data analysis aimed to identify trends and gaps in environmental practices.

Results: Of the participating units, 56.9% were familiar with the concept of Green Nephrology, yet only 28.2% had practices in place to promote sustainability. A significant proportion (59.7%) of countries did not provide education on sustainable health services. While many centers recognized the need for improvements in waste management practices (77.8%), only a small fraction (11.1%) claimed their practices were well-established. Furthermore, a considerable percentage of centers lacked programs for material reuse or recycling (72.2%) and did not utilize renewable energy sources (80.6%). Water consumption monitoring was not available in most haemodialysis units (72.3%), and water recycling systems were absent in the majority (87.5%). Plastic waste minimisation practices in peritoneal dialysis treatment were lacking in 61.1% of the centers. Although 97.2% of pediatric nephrologists have made changes in their personal lifestyles to improve environmental health and have knowledge on the subject, the overwhelming majority of participants (94.4%) expressed the need for additional environmental education.

Conclusion: Paediatric nephrology units show varying levels of awareness and implementation of environmental sustainability practices. While some centers have recognized the importance of sustainability, there is a clear need for standardised education, improved waste management strategies, and greater integration of green initiatives to minimise environmental impact and enhance long-term sustainability in paediatric nephrology care. Collaboration with environmental organisations, pharmaceutical companies and initiatives such as the ESPN Green Nephrology Taskforce could facilitate the adoption of more environmentally friendly practices in paediatric nephrology units worldwide.

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CONTINUOUS KIDNEY THERAPY REPLACEMENT WITH CARPEDIEM (CARDIO.RENAL. REPLACEMENT.PEDIATRIC.EMERGENCY.DIALYSIS.MACHINE) OF PREMATURE AND LOW-BIRTH-WEIGHT NEONATES : A REPORT OF FRENCH EXPERIENCE

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Aims/Purpose: Acute Kidney Injury (AKI) is a common complication with a prevalence of 30% among hospitalized pediatric patients. Associated mortality rates are particularly high in neonates. The Cardio-Renal Pediatric Dialysis Emergency Machine® is a novel continuous kidney replacement therapy (CKRT) device specifically designed for neonates and small infants weighing between 2.0 to 9.9kg. Two recent studies in France and Italy reported the use of CARPEDIEM® with effective results on feasibility and efficiency. The application in neonates below 2 kilograms is uncertain. Premature and low birth (LBW) neonates are at high risk of renal failure secondary to imcomplete nephrogenesis, low kidney reserve and postnatal comorbidities. This study assessed the performance, complications and outcome of the use of CARPEDIEM® system with miniuature blood pump and extracorporeal volume in theses small and fragile patients.

Methods: We retrospectively analyzed the use of CARPEDIEM® in LBW below 2 kilograms and premature neonates with AKI treated in six French pediatric and neonatal intensive care units. Continuous veno-venous hemofiltration (CVVH) was performed in all children. Data are presented as median [25th-75th quartile].

Results: Ten neonates with a median gestational age of 30 [29-32] weeks and a birth weight of 1.1 [1.0-1.7] kilograms received CVVH during 22 sessions. CKRT was initiated at a median age of 6 [2-12] days and a body weight of 1.9[1.5-2.4] kilograms,with a range of 1.3 - 2.8 kilograms. CVVH was performed using a 4.5 French double-lumen central venous catheter in six preterms, a 5.5, 6 and 6.5 Fr catheter was used in four preterms. Two different hemofilters were used (0.15 or 0.25m2). . Blood flow rate was 8[7-12] ml/kg/min, ultrafiltration (UF) flow rate 80 [60-94] ml/kg/h and net UF 6 [2-9] ml/kg/h. Circuits were primed with NaCl 0.9% in all patients except for one, in whom the system was primed with packed erythrocytes. Anticoagulation consisted of heparin at 6 to 13 IU/kg/h. All CVVH sessions achieved efficient blood purification and improved fluid balance control. Thrombocytopenia, requiring platelets transfusion, was the main complication observed in 15 sessions, but was not associated with bleeding episodes. Hemodynamic instability requiring volume replacement developed in 13 sessions and clotting of the circuit in three sessions. All premature and LBW neonates survived until treatment discontinuation, but all children died 6 [1-9] days later, mainly due to multi-organ failure or ethical considerations linked to severe brain injury.

Conclusion: Our observations suggest that CVVH using CARPEDIEM® is technically feasible and effective in neonates weighing less than 2 kilograms at birth weight with AKI and multi-organ dysfunction, with the potential to improve clinical management. The impact on patient outcomes requires further study.

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PRESCRIPTION OF THE FIRST HAEMODIALYSIS IN A 2-YEAR-OLD PATIENT WITH END-STAGE KIDNEY DISEASE: APPLICATION OF A CALCULATOR CAPABLE OF PREDICTING THE ADEQUATE DELIVERED Dose

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Aims/Purpose: The delivery of an adequate haemodialysis (HD) dose in paediatric patients is often challenging, mainly because of their small urea distribution volume (V) and the consequent higher risk of disequilibrium syndrome, which is caused by an excessive or overly rapid correction of urea levels, particularly during the first HD session. The availability of a tool capable of predicting the delivered HD dose based on renowned urea kinetic equations may be of great usefulness.

Methods: We report the case of a 2-year-old girl with a monogenic form of nephrotic syndrome, whose rapid decline of renal function required the initiation of HD in March 2024 (pre-HD urea = 262 mg/dL). At that time the patient was 87 cm high and weighted 14 kg (V assessed using the Morgenstern formula = 8.31 L); her haematocrit was 23% and her plasma proteins were 4.2 g/dL. To ensure an adequate HD dose, not exceeding the recommended urea removal ratio (URR) for the first treatment (i.e., 40% over 2 hours), we designed her first HD prescription with the assistance of a purposely structured informatic worksheet that provides the expected urea clearance (K) after considering all adjustable parameters, namely:

- the filter mass transfer-area coefficient (KoA) "in vivo", derived as suggested by Daugirdas from the KoA "in vitro" (the latter is calculated from K values reported on product data sheets, using the Michaels equation)
- ultrafiltration volume (UF) and duration of the session (t)
- blood flow (Qb), dialysate flow (Qd), and their reciprocal direction (co-current or counter-current)
- effective inlet blood flow (Qe), corresponding to the blood water flow, derived from Qb considering patient's haematocrit and plasma protein levels
- estimated recirculation.

The derived parameter K was used to calculate the expected single pool Kt/V (spKt/V). The latter was finally compared to the real-life spKt/V, computed from URR and UF values obtained at the end of the HD session.

Results: We applied the following prescription, based on results provided by our calculator, aiming at an expected spKt/V of 0.57, corresponding to a URR of 39.5%:

- Qb = 70 mL/min, Qd = 100 mL/min, co-current flows, estimated recirculation 0%
- filter KoA "in vitro" = 494 mL/min
- t = 120 minutes, UF = 0.3 L.

The post-HD urea resulted 154 mg/dL, meaning that the obtained URR and spKt/V were comparable to the theoretical ones computed by our informatic worksheet: URR = 41% (vs expected URR = 39.5%), spKt/V = 0.59 (vs expected spKt/V = 0.57). The little girl well tolerated the HD session, and no treatment-related complication was observed.

Conclusion: The use of this calculator proved to be accurate in predicting the delivered HD dose, guaranteeing an adequate and complication-free treatment. The availability of tools like this could be of considerable use, particularly in paediatric patients, who are at increased risk of treatment-related complications.

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AN APPROACH TO THE PREVENTION AND MANAGEMENT OF NEONATAL ACUTE KIDNEY INJURY

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Aims/Purpose: Acute Kidney Injury (AKI), is characterised by a sudden decline in kidney function resulting in derangements in fluid balance, electrolytes and waste products. Neonatal AKI is common (30% of hospitalized neonates), can occur without symptoms and is associated with reduced or occasionally normal urine output (non oliguric AKI). Neonatal AKI is difficult to diagnose due to "physiological" fluctuations in creatinine levels and lack of a clear baseline, during the first days of life. Studies showed that the average age of diagnosis was 5 +/- 2 days and was associated with fluid overload and dysnatraemia - both associated with worse outcomes. Neonates born preterm are more prone to AKI due to impaired nephrogenesis. Neonatal AKI is associated with an increased risk of death, bronchopulmonary dysplasia, intraventricular haemorrhage, chronic kidney disease (CKD), non optimal neurodevelopmental outcomes and cost to the NHS. Early detection and appropriate management of neonatal AKI can minimise further injury and improve outcomes.

Methods: Reviewed existing AKI national standards, including NICE guidelines and the clinical practice guidelines published by KDIGO group in 2012 (updated 2023).

Literature review to identify relevant articles in:

- Medline (Ovid),
- Embase (Ovid),
- Pubmed

The guideline was shared with the staff of the tertiary NICU, including neonatal consultants, junior doctors, and ANNPs, as well as the Paediatric Nephrology team and was amended and refined through an iterative feedback process.

Results: The guideline was formulated and implemented after ratification in the integrated governance meeting of the regional tertiary NICU, in October 2023. The implementation strategy included presentation to the clinical team, as part of the weekly guideline teaching, and uploading to the online resource that contains all existing guidelines in the neonatal network. Following implementation, there is a departmental plan to audit the guideline during 2024.

Conclusion: We present our approach to the development of a regional tertiary NICU guideline for the prevention and management of neonatal AKI. This guideline introduces the definition and classification of AKI based on the KDIGO classification It aims to identify and highlight the risk factors (such as nephrotoxic drugs) and high risk states (such as hypotension) for neonatal AKI. The flowcharts (see figures) focus on prevention (3 M model: daily monitoring, maintaining circulation and minimizing kidney insult) and management (4 M model: as per prevention & manage). It suggests follow-up in an AKI clinic to capture longer term complications. With this guideline, we have enhanced collaboration across the region and aim to standardize the approach to the complex entity of neonatal AKI.

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X-LINKED RECESSIVE VARIANTS IN X-PROLYL AMINOPEPTIDASE 2 (XPNPEP2) AS A POTENTIAL NEW CAUSE OF NEPHROTIC SYNDROME

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Aims/Purpose: Steroid-resistant nephrotic syndrome (SRNS) is the second most frequent cause of chronic kidney disease in children. Major insights into its pathogenesis came from discovery of 68 monogenic causes that contribute to ~12-30% of SRNS with onset at < 25 years of age. We hypothesized that additional monogenic causes of nephrotic syndrome (NS) exist, which may be identified by exome sequencing.

Methods: To identify novel potential monogenic causes of SRNS, we performed exome sequencing in a worldwide cohort of 1,283 different families with NS. We evaluated potential pathogenicity of bi-allelic hemizygous genetic variants with minor allele frequency < 1% by predefined criteria: in-silico deleteriousness prediction scores, evolutionary conservation, and allele frequency in gnomAD database.

Results: We discovered 3 X-linked recessive hemizygous, likely deleterious variants in gene XPNPEP2 in 3 unrelated males with childhood onset of SRNS: nonsense variant c.670C > T, p.(Arg224*), splice variant c.1107+1G > A, and missense c.346C > T, p.(Arg116Cys) with the arginine part of a highly evolutionary conserved DXRY motif deemed as likely disease-causing by prediction programs. All variants are absent hemizygously from gnomAD database. Utilizing PyMol software, we generated a 3-dimentional protein structure illustrating the position of the arginine residue converted to cysteine in individual from family A4966, highlighting its proximity to the enzymatic center and its protential deleterious impact on protein function, if mutated. To localize XPNPEP2 within the kidney, we conducted co-staining with specific kidney cell markers on frozen kidney sections from healthy adult rats revealing co-localization of XPNPEP2 with podocin and synaptopodin in podocytes. For further functional genomic investigations to test the deleterious effects and causality of the identified 3 variants in association with nephrotic syndrome, we performed enzymatic activity assay and showed reduced or absent activity of XPNPEP2 in overexpressed human podocytes and HEK293T cells transfected with XPNPEP2 cDNA constructs bearing patient variants compared to normal activity in wild-type (WT), ($P < 0.0001$). Moreover, overexpression with cDNA constructs bearing patient variants transfected in human podocytes and imaged hourly using the IncuCyte ZOOM System showed reduced podocyte migration rate and reduced filopodia formation compared to WT ($P < 0.001$).

Conclusion: We demonstrated that recessive variants in XPNPEP2 are potential novel monogenic causes of SRNS in humans using a combination of functional genomic approaches including (i) exome sequencing analysis and protein structures, (ii) IF and high-resolution confocal microscopy imaging and live cell imaging of two-dimensional podocyte culture (migration and filopodia assays), (iii) in-vitro enzymatic (protein) activity assay.

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INCOMPLETELY PENETRANT CYSTIC KIDNEY PHENOTYPE ASSOCIATED TO THE NON-CILIARY TMEM260 VARIANTS: ROLE OF THE ENVIRONMENT

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Aims/Purpose: Biallelic TMEM260 variants were initially described in children with truncus arteriosus with a variable neurological and renal involvement. We identified compound heterozygous variants (c. 592_593delTT p.Leu198Valfs44* and c.1854C > A p.Tyr618*) in a five-year-old boy with polycystic kidneys (+ 9 SD in length), severe cerebral atrophy and truncus arteriosus. Out of the two TMEM260 isoforms, the long is defected in all patients, and the short remains intact in the majority, suggesting a difference in their function. Despite the similarly preserved function of the short, the renal phenotype is highly variable between the patients ranging from lack of involvement to the severe polycystic kidney disease, found in the index patient. We aimed to understand the difference in the function of the two isoforms and the reason for the variable renal phenotype.

Methods: Ciliary localization of the two isoforms was studied in transiently transfected mIMCD3 cells with anti-acetylated-tubulin or anti-ARL13B staining. A tmem260 deficient zebrafish line was generated by CRISPR/Cas9. The effect of heat shock on the endogenous expression level, as well as the nuclear membrane localization was studied in HEK293 cells, the latter with anti-lamin B1 staining. Stress granular localization was investigated in HK2 cells stained with anti-eIF3 or anti-G3BP1 antibodies.

Results: None of the two isoforms was localized to the primary cilium. The long isoform is localized to the cytoplasm and the nuclear membrane, the short only to the cytoplasm. The tmem260 deficient zebrafish line does not show any major ciliary defects, nor any diseased phenotype. Intriguingly, we found the knockout larvae to be heat shock sensitive: they developed severe muscular defect upon increased ambient temperature. Nevertheless, we found no difference in the expression level or in the localization of any of the two isoforms upon heat shock. Furthermore, none of them was localized to the stress granules after heat shock.

Conclusion: TMEM260 is not a ciliary protein. The two isoforms have different localization, the long is localized to nuclear membrane. The phenotype of tmem260 -/- larvae is strongly influenced by the environment. This may explain the variable renal phenotype of patients with a similar degree of function loss.

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LONG-TERM OUTCOME OF NPHS2-RELATED GLOMERULOPATHY

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Aims/Purpose: NPHS2-related glomerulopathy is the most common hereditary cause of steroid-resistant nephrotic syndrome in children and young adults among Western populations. The aim of the study was to evaluate the long-term renal outcome with respect to demographic and genotypic features.

Methods: We obtained longitudinal clinical information for 433 patients with confirmed biallelic variants in NPHS2 from the PodoNet Registry, the European Rare Kidney Disease Registry (ERKReg), the National Registry of Rare Renal Diseases UK (RADAR), and regional registries run by Necker-Enfants Malades Hospital, Fundació Puigvert and Semmelweis University. Kidney survival was assessed using KM analysis and risk factors for kidney replacement therapy (KRT) using multivariate Cox regression models.

Results: The most frequent pathogenic variant was the missense p.R138Q mutation present in 102/433 subjects, residing mainly in Western and Central Europe. Compound heterozygosity for the p.R229Q non-neutral polymorphism was prevalent in Eastern Europe and Latin America. At age 10 years, KRT-free survival was 48%, 48%, 96% and 73% in children with biallelic-truncating variants, p.R138Q homo- or heterozygotes, p.R229Q compound heterozygotes and other mutation types, respectively. 65% of patients carrying the heterozygous p.R229Q variant retained kidney function beyond age 18 years, as compared to 37% of all other patients. Kidney failure rates were independent of the age at diagnosis, with roughly 60% necessitating RRT 10 years after diagnosis. Patients with Hispanic or Middle Eastern ethnicity showed a 4.3-fold (95%CI: 2.1-8.8) and 2.6-fold (1.6-4.3) increased KRT risk as compared to Caucasians. KRT risk appeared increased in patients born in 2000-2009 compared to those born before 1990 (OR 1.76 (1.17; 2.65)).

Conclusion: In NPHS2 glomerulopathy, biallelic truncating variants but also p.R138Q mutations are associated with early progression to end-stage kidney disease. The age at diagnosis does not impact kidney survival. Outcomes have not improved over the past four decades.

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HIGH INCIDENCE OF POST TRANSPLANT LYMPHOPROLIFERATIVE DISEASE IN DENYS DRASH SYNDROME RECEIVING KIDNEY TRANSPLANTATION: MORE THAN A COINCIDENCE?

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Background and Aims: Denys-Drash syndrome (DDS) is a rare disease associating early-onset nephrotic syndrome, gonadal dysgenesis, and predisposition to Wilms tumor (WT). It is caused by mutations in exons 8 or 9 of the WT1 gene. EBV-associated post-transplantation lymphoproliferative disease (PTLD) is recognized as one of the most devastating complications of organ transplantation. Its incidence depends on the type of organ transplanted and kidney transplant recipients are at relatively low risk (1-2%). This study aimed to describe children with DDS who developed EBV-associated PTLD.

Methods: We performed a nationwide retrospective analysis of children diagnosed with DDS between 2000-2022. We analyze the occurrence of PTLD in those who receive a kidney transplant and compare it to a cohort of children kidney transplanted from database APHP cohort360.

Results: Among 58 patients with DDS, 36 had received kidney transplantation. 7/36 (20%) developed an EBV-associated PTLD at a median age of 8 years (6-15). This proportion is significantly higher than the one observed in the cohort of 471 children without DDS (20% vs 4%, p =0.0012). The median delay of PTLD after transplantation was three years (1.7-10.0) in DDS. The median age at transplantation was similar in children with or without PTLD (3.4 vs 3.9, p =0.9). The proportion of patients treated for WT was similar in DDS patients with or without PTLD (43%vs 39%, p =0.9)

Conclusions: Overall, children with DDS appear to have a higher incidence of PTLD than other kidney-transplanted children. This incidence does not seem to be related to previous chemotherapy for WT. This higher risk should be confirmed in a larger-scale study and may lead to an adaptation of post-transplant immunosuppression in children with DDS.

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SULFATE HOMEOSTASIS IN PROXIMAL TUBULAR DYSFUNCTION

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Aims/Purpose: Sulfate is the 4th most abundant anion in humans, with serum concentrations of around 300 µmol/l. It is required for sulfonation of proteoglycans, cholesterol and cholesterol derivatives, such as steroid hormones and bile acids, proteins and exogenous compounds. Sulfonation changes the function, structure and solubility of these compounds. Genetic defects causing decreased sulfonation cause skeletal dysplasias, chondropathy, neurologic developmental disorders and endocrinopathies. Sulfate is filtrated in the glomerulus and re-absorbed in the proximal tubule via the NaS1 channel on the apical and the Sat1 channel on the basolateral membrane. Defects in the genes encoding these channels are associated with low serum sulfate, (mild) skeletal dysplasia, chondropathy and neurological developmental disorders. As renal sulfate handling takes place in the proximal tubule, our study aims to assess sulfate homeostasis in children with generalized proximal tubular dysfunction.

Methods: In pediatric patients with cystinosis or Dent disease type 1, paired blood and urine samples were collected. Sulfate was measured using liquid chromatography-tandem mass spectrometry in the negative ion mode in deproteinized plasma and in urine. All patients were treated with electrolyte and citrate suppletion as needed, the cystinosis patients also received cysteamine. Results were compared to normal values from the literature and to 13 samples from healthy adults measured in our laboratory.

Results: Six patients were included, four with cystinosis and two with Dent disease. Ages ranged from 5.5 to 19 years. Serum sulfate ranged from 126 to 393 µmol/l, while this was 231 to 432 µmol/l in healthy controls. Fractional sulfate excretion (FES) exceeded the normal values of 17-34% in five patients, three with cystinosis (38, 51, 91%) and two with Dent disease (36, 62%). The three cystinosis patients also had the highest serum levels, while the Dent disease patient with FEs of 62% had the lowest serum level (126 µmol/l).

Conclusion: All but two patients had normal serum sulfate levels, albeit at the lower end of the normal range. Five patients had increased FES suggesting tubular dysfunction. However, in the cystinosis patients cysteamine treatment might be a confounding factor as it is a potential source of sulfate. This would explain the relatively high serum levels with exceedingly high FES. The Dent disease patient with high FEs and low serum level is highly suspect for renal sulfate loss. Future research should compare patients with different etiologies of generalized proximal tubular dysfunction.

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CTNS -/- OSTEOBLAST TRANSCRIPTOMIC RESPONSE TO 1,25OH-VITAMIN D REVEALS A TRANSITIONAL SHIFT TOWARDS AN OSTEOCYTE PHENOTYPE

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Introduction: Nephropathic cystinosis is a rare autosomal recessive lysosomal storage disorder caused by the lysosomal accumulation of cystine crystals in various organs. The use of cysteamine, a cystine depleting drug, has dramatically improved patient survival, but also revealed late onset complications, notably bone disease described as a "novel" complication of cystinosis, named "cystinosis metabolic bone disease" (CMBD). In vitro and in vivo cell biology studies showed an increase number of osteoclasts but also an inhibition of their resorption activity. So cysteamine does not prevent the onset of bone disease and there is an initrinsic defect in osteoclasts in cystinosis.

Methods: Knock-out Ctns (KO) osteoblats display an altered response to 1,25 vitamin D3 (1,25VD) treatment compared to wild-type (WT) leading to a pro-osteoclastic osteoblast/osteoclast cross-talk. To investigate this response RNAseq experiments were performed. Five biological replicates of osteoblasts derived from MSCs of individual animal from each genotype were amplified and cultured in osteogenic media supplemented with 1,25VD. The differentially expressed genes were analyzed through Gene Ontology enrichment process and Ingenuity Pathways to delineate transcriptional networks involved in CMBD.

Results: Using the RNASeq experiment, we found 786 DEG. With a p-value adjusted ≤ 0.05, we reduced the list to 34 genes: 20 up- and 14 down-regulated expressed genes. Three main axes were identified, i.e., inflammation, autophagy and osteogenesis. We decided to focus first on the osteogenesis axis, which showed 4 upregulated genes involved in osteo-formation (namely Bglap, Bmp2, Dmp1 and Phex) and 4 upregulated genes involved in osteo-inhibition (namely Sost, Bmp3, Ppar1 and Ccl3). We validated all these genes of interest by qRT-PCR, except Ppar1. Strikingly Sost, Phex and Dmp1 are not osteoblastic but osteocyte markers and important bone regulatory factors. KO osteoblasts also show upregulation of podoplanin. Thus, the osteogenic pathway found in KO osteoblasts showed a transcriptomic profile of osteoblast/osteocyte in transitional. These results prompted us to examine the expression of these genes also in mature osteocytes. To this end we collected RNA from WT and KO cortical bone (the bone compartment enriched in osteocytes, 90% of the cells). KO cortical cells expressed higher levels of all the osteogenic markers except Phex and Bmp3 in the absence of 1,25VD treatment, showing a more advanced osteocytic phenotype versus WT explants.

Conclusion: We validate the transcriptomic results for the osteoformation pathway, and highlight a potential pre-osteocyte phenotype of cystinotic osteoblasts. This is confirmed in KO cortical explants. Our data strongly suggest that the epigenetic landscape of Ctns osteogenic cell lineage is altered compared to WT, and highlighted by 1,25VD treatment.

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CLINICAL COURSE AND LONG TERM OUTCOMES IN AN EXTENDED FAMILY WITH AUTOSOMAL RECESSIVE NEPHROGENIC DIABETES INSIPIDUS

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Aim: To assess the clinical course, complications and long term outcomes of patients from an extended consanguineous family with autosomal recessive (AR) Nephrohgenic Diabetes insipidus (NDI).Methods: We conducted a single-center retrospective medical record review of patients with AR congenital NDI followed between 1983 and 2023. We collected available data on their neonatal course, clinical and laboratory presentation, growth, calculated glomerular filtration rate (GFR), electrolytes, renal & urological complications and comorbidities.

Results: We identified 33 patients of whom 21 were males (63.6%), with ages ranging from 10 months to 40 years old (mean age 11.8 ± 10.3 years). Fifteen (45.5%) individuals underwent confirmed genetic analysis revealing the AQP2 mutation c.83T > C. Given the high rate of consanguinity, similar mutations are expected among clinically diagnosed siblings and relatives. All patients were born full-term except one who was born late preterm. Birth weight and head circumference were appropriate for gestational age (AGA) in all patients. Patients presented in the first weeks of life and commenced routine medical management upon diagnosis. The most common presenting symptoms were hypernatremia 27 (81.8%), fever 20 (60.6%) and weight loss 12 (36.4%). Ten neonates (30.3%) underwent sepsis work up to rule out infectious cause for their fever. Growth was compromised during the first two years of life. Two children died during their second year, one of them due to severe hypernatremia and dehydration and the other due to infectious complications.Abnormalities in kidneys and urinary tract ultrasound were observed in 13/32 (40.6%) starting at the age of 2 years, including: hydroureteronephrosis and/or large capacity bladder and/or trabeculated bladder. Five males with bilateral hydroureteronephrosis and large capacity bladder required clean intermittent catheterizations (CIC) due to atonic bladder. The median estimated glomerular filtration rate (GFR) was 110 ml/min/1.73m2 in patients above 18 years old according to CKD-EPI and 174 ml/min/1.73m2 in patients below 18 years old. Dialysis was initiated in 3 patients aged 19, 27 and 30 years old. Urodynamic study performed in the latter showed a transition from atonic bladder to hostile bladder with low compliance end filling pressure above 50 cmH20.

Conclusions: Growth improves after the second year in AQP2 mutation NDI patients, but renal function may decline with age. Complications stemming from polyuria are common, underscoring the need for vigilant monitoring to detect and address low compliance bladder and renal insufficiency.

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BUROSUMAB: A NEW STRATEDY IN THE TREATMENT OF X-LINKED HYPOPHOSPHATAEMIA

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Introduction: Hypophosphatemic rickets (R-XLH) is a Ca-P metabolism disorder caused by the inactivating mutation of the PHEX gene, regulator of FGF23 (fibroblast growth factor 23) activity, whose increased expression results in reduced renal phosphate reabsorption and reduced renal 1alpha-hydroxylase activity with consequent hyperphosphaturia and hypophosphatemia. This causes repercussions on bone mineralization. The typical phenotype is characterized by short stature and bone deformities (valgus or varus, "rachitic rosary", prominent frontal bumps, craniotabe, delayed tooth eruption).

Objectives: Burosumab, an anti-FGF23 monoclonal antibody, has innovatively modified the treatment and prognosis of R-XLH. Until 2019, "conventional" therapy aimed to correct serum phosphate and Vitamin D levels, through the administration of an oral solution containing phosphorus ("Joulie potion") and alpha-calcidol or calcitriol. Currently Burosumab with its inactivating action on FGF23, leads to a reduction in phosphaturia and an increase in active VitaminD level.

Methods: In our UOSD we follow 10 patients affected by XLH (8F and 2M), with genetic confirmation. The clinical presentation was characterized by short stature with varus n 8/10 and orthopedic hypercorrection valgus in 2/10. Osteosonography was pathologic in 3/10; 2/10 had painful symptoms. One patient had spontaneous bone lesions. Hemiepiphysiodesis was necessary in 7/10 and osteotomy in 2/10. We detected dental abnormalities (spontaneous dental and periodontal abscesses, cariogenic processes) in 7/10. "Conventional" treatment based on a mixture of phosphates and active vitamin D was carried out in 7/10. 3 presented nephrocalcinosis, none hyperPTH. 4/7 switched to innovative therapy with Burosumab: in two the prescription met the criteria of the NHS; one patient, with severe nephrocalcinosis, benefited from Law 326/2003 (AIFA 5% Fund for orphan drugs) while the last patient, > 18 yo, benefited from "compassionate use" as she was outside the prescribability criteria. Another 3/10 are on "naïve" treatment with Burosumab according to the NHS criteria.

Results: In patients treated with Burosumab, plasma phosphorus level is higher than the one achieved with conventional treatment, with progressive normalization of ALP and 1-25OHvitD. In addition, clinical and radiographic improvement is recognizable since the 40th week of therapy. Compliance has been significantly improved: repeated daily oral administrations are replaced by a fortnightly subcutaneous administration of Burosumab.

Conclusions: Our experience demonstrates that Burosumab is a safe drug, more effective than conventional therapy in the treatment of pediatric XLH patients. Further longitudinal, long-term, multicenter studies are needed to evaluate its safety and to verify the effect on statural prognosis and to reduce the use of orthopaedic treatments.

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HDR SYNDROME DUE TO GATA3 HAPLOINSUFFICIENCY: CLINICAL CHARACTERISTICS AND GENOTYPE-PHENOTYPE CORRELATION IN A NATIONWIDE COHORT

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Aims/Purpose: Hypoparathyroidism-deafness-renal dysplasia (HDR) syndrome is a rare autosomal dominant disorder characterized by hypoparathyroidism, sensorineural deafness, and renal dysplasia caused by GATA3 variants. In order to better understand the relationship between genotype and phenotype in HDR syndrome, we describe a new French cohort of individuals with GATA3 variants. We aim to gain insights into the molecular mechanisms underlying this complex disorder and improve diagnosis and management strategies for affected individuals.

Methods: Laboratories that analyse the GATA3 gene in France were contacted. GATA3 is analysed in a hypoparathyroidism gene panel at Limoges University Hospital, in a deafness gene panel at Lille University Hospital and in a calcium-phosphate metabolism gene panel at Caen University Hospital. We included all patients with GATA3 mutations diagnosed in these three laboratories and contacted the physicians who had requested the genetic analyses to obtain further clinical and laboratory data.

Results: 48 individuals from 33 families were included. Median age at last available follow-up was 17 years. 29 (60.6%) presented with kidney diseases, 43 (89.6%) had deafness, and 26 (54.2%) had hypoparathyroidism. Of note, 8 (16.7%) had genital tract anomalies which was not a feature previously described. Chronic kidney disease (CKD stage 3 or higher) was reported in 25% of patients including 2 patients who reached kidney failure and received a kidney transplant. HDR syndrome was complete in 19 patients (39.6%), the syndromic association was HR in 19 (39.6%) and DR in 8 (16.7%). Genetic analyses revealed deletions in 7 cases (including 4/8 genital malformations and earlier diagnosis), 21 frameshift variants, 9 missense variants and 5 intronic variations without evidence for a clear genotype-phenotype association.

Conclusion: This French cohort of HDR syndrome showed a wide clinical heterogeneity, a significant proportion of CKD, an unexpected high frequency of genital anomalies, and no clear genotype-phenotype association except a trend for an earlier diagnosis in patients with deletions.

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RARE REPEATS, RAPID RESPONSES: DISSECTING LOW RECURRENCE AND HIGH EMERGENCY INTERVENTIONS IN PAEDIATRIC UROLITHIASIS

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Aims: We aimed to examine the incidence of paediatric urolithiasis in our paediatric population and describe the characteristics of our patients, with a focus on recurrence and emergency intervention.

Methods: We conducted a retrospective observational cohort study involving paediatric patients aged 0 to 16 years old, diagnosed with urolithiasis between January 2015 and September 2023 at the Royal Manchester Children's Hospital, United Kingdom. Comprehensive data analysis was performed using electronic medical records to assess demographic and clinical parameters including age, gender, ethnicity, genetic diagnoses, stone analysis, body mass index and intervention strategies. Descriptive statistics and frequency distributions were utilised to summarise the data.

Results: 112 patients were included, with a predominant male prevalence (F:M ratio 7:9). Median age at presentation was 8 years (range: 0.2-16) and mean follow-up was 33 months (range 0-103). The majority, 59%, were White British followed by 24% of Asian origin. The mean incidence was 2 per 100,000 children; this doubled from 1.4 between 2015-2019 to 2.6 between 2019-2023. Emergency stent insertion was required in 46% (n = 51). 20% (n = 22) had a genetic diagnosis, with 59%, having cystinuria (n = 13) and 23% primary hyperoxaluria (n = 5). 55% of those with a genetic diagnosis identified as Asian (n = 12). The most common aetiology was metabolic (n = 45), followed by infective/structural (n = 33) then idiopathic (n = 24). Stone analysis was performed in 46% (n = 52): 54% (n = 28) calcium oxalate, 35% (n = 18) calcium phosphate, 48% (n = 25) apatite, 12% (n = 6) cystine and 4% (n = 2) uric acid. Recurrent stones were identified in seven patients, including 2 children each, with cystinuria and spina bifida.

Conclusions: We demonstrate a rising incidence of paediatric urolithiasis, with almost half requiring emergency intervention. Recurrent stones are rare except in children with cystinuria and spina bifida. Our recurrence rate was significantly lower than expected (6% compared to an anticipated 50%)1. A genetic diagnosis was common and was more prevalent in children of Asian ethnicity.

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ORAL COMMUNICATIONS 5

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PREDICTIVITY OF ESTIMATED HEART RATE VARIATION IN PEDIATRIC DEHYDRATION AND ACUTE KIDNEY INJURY: A PROSPECTIVE VALIDATION STUDY

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Aims/Purpose: Dehydration poses significant challenges in children. Timely identification of dehydration symptoms and precise evaluation of its severity are paramount to optimizing patient care and reducing hospitalizations. Our study sought to assess the estimated percentage of heart rate variation (EHRV) as a potential marker for both dehydration and acute kidney injury (AKI) among pediatric patients presenting to the Emergency Department. Specifically, our objective was to prospectively validate the efficacy of the previously identified EHRV cutoff of 24.5%, which emerged as a predictor for ≥5% dehydration and/or AKI in an our previous study, in accurately identifying and stratifying dehydration severity in pediatric patients attending the Pediatric Emergency Department.

Methods: Prospective enrollment of pediatric patients requiring blood sample collection was conducted at the Pediatric Emergency Department of Sant'Anna e San Sebastiano Hospital, Caserta, Italy, from July 2022 to August 2023. Inclusion criteria comprised pediatric patients (aged 0–18 years) necessitating blood sample collection as per clinical assessment. EHRV was calculated based on heart rate (HR) measurements at admission and percentile charts for age and sex as follows: [(HR at admission – 50th percentile of HR for age and sex)/HR at admission]*100. Patients with fever at the time of HR measurement were excluded. Dehydration was classified as < 5% or ≥5% fluid deficit, while AKI was defined using KDIGO serum creatinine criterium by back-calculating basal serum creatinine. Statistical analyses included receiver-operating characteristic (ROC) curve analysis and logistic regression.

Results: We enrolled 256 patients with a mean age of 60.2 ± 48.6 months. As per inclusion criteria, none of them presented with fever or pain at the time of the HR measurement. Out of the 256 enrolled patients, 52 showed ≥5% dehydration and 50 showed AKI. Sixteen patients presented with both ≥5% dehydration and AKI. The ERHV showed a significant ROC curve either for ≥5% dehydration (AUROC = 0.71; 95%CI: 0.63-0.78; p < 0.001) or AKI (AUROC = 0.78; 95%CI: 0.71-0.84; p < 0.001). The logistic regression analysis showed that patients with EHRV > 24.5% showed an OR to present with ≥5% dehydration of 2.6 (95%CI: 1.3-5.2;p < 0.001) and an OR to present with AKI of 2.9 (95%CI: 1.5-5.9; p < 0.001).

Conclusion: This study validates EHRV as a promising predictor for identifying ≥5% dehydration and AKI in pediatric patients. The identified EHRV cutoff of 24.5% exhibits significant prognostic accuracy, suggesting its potential utility in clinical practice for timely intervention and patient management. The integration of EHRV assessment into clinical practice could potentially lead to earlier interventions, improved patient management and decreased mortality rates associated with dehydration and AKI in pediatric populations.

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INTRODUCING NIKI-TAG (NEPHROTOXIC INJURY IN KIDS-TAG): A QUALITY INITIATIVE FOR REDUCING ACUTE KIDNEY INJURY IN PEDIATRIC HOSPITALIZED PATIENTS EXPOSED TO NEPHROTOXIC MEDICATIONS

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Aims: In hospitalized children, exposure to nephrotoxic medication is the first cause of acute kidney injury (AKI) and is associated with increased morbidity, cost and length of stay. Aiming to reduce this risk, we developed a quality improvement program comprising computer alerts on nephrotoxic prescribed medications and a multimodal educational program.

Methods: This quality program was implemented between September 2020 and July 2023 in the Pediatric Department of the University Children's Hospital in Geneva, Switzerland. The computer alert prospectively detected the prescription of ≥2 concomitant or > 72 hours nephrotoxic medications from health records in paediatric hospitalized patients (0-18 years). A pharmacist or pediatric nephrologist assesses the relevance of the alert. Non-interventional (NI) period was conducted during 14 months, was followed by a 2-month washout period and an interventional (I) phase lasting 11 months. During the washout period, the multimodal educational program was implemented, comprising a micro-learning course, a pocket card, and 20-minute interactive training workshops for all medical and nursing staff in the pediatric department. Throughout the intervention phase, direct contact between the physician analyzing the alert and the prescribing physician, based on defined algorithms, allowed recommendations on nephrotoxicity and AKI detection or management.

Results: Alerts were identified in 5.2% (555/10,698) of hospitalized pediatric patients, with 5.2% (285/5,473) occurring during the NI period and 5.2% (270/5,225) during the I phase (NS). The implicated drugs were predominantly antibiotics (35%) followed by nonsteroidal anti-inflammatory drug (21%). The alerts occurred more frequently in the pediatric intensive care unit (25%) followed by a surgical unit which includes the post-transplant care of hepatic transplant recipients (21.2 %) and the oncologic department (19.3%). AKI occurred in 22.5% (64/285) of alerts during the NI period and in 11.9% (32/270) of alerts during the I phase (p =0.001). After adjusting for patient age, hospital ward, type of alert, the presence of risk factors for CKD, and the presence of CKD, a significant 40% reduction in the AKI rate was observed in cases of alert during the I phase (adjusted odds ratio, 0.54; 95% confidence interval, 0.33 to 0.87, p =0.011). We observed a significant improvement in diuresis monitoring (48.1% (137/285) vs 65.9% (178/270), P =< 0.001) and a trend towards clinicians' increased ability to recognize AKI during the I phase (68% (43/63) vs 84% (27/32), p =0.09).

Conclusions: Implementing a quality project with informatics alerts on nephrotoxic prescribed medications, direct recommendations to the prescribing physician and a multimodal educational program results in a noteworthy 40% reduction in AKI incidence among pediatric hospitalized children exposed to nephrotoxic medications.

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DECIPHERING COMPLEMENT ACTIVATION MECHANISMS IN CHILDHOOD IGA NEPHROPATHY

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Aims/Purpose: The complement pathway plays a crucial role in developing IgA nephropathy (IgAN), as evidenced by the association of complement C3 with IgA deposits. However, the precise mechanisms underlying complement pathway activation remain unclear. Recent research has highlighted the importance of the soluble myeloid receptor CD89 (sCD89) as a critical initiator of glomerular inflammation in childhood IgAN (cIgAN). Thus, this study aims to investigate how sCD89 and collectin-11 (C-11), an initiator of the lectin complement pathway could lead to the formation of the terminal complement complex C5b-9 in cIgAN.

Methods: An international prospective cohort study involving children diagnosed with IgA nephropathy (cIgAN) was conducted (n = 52). We assessed the concentration of C-11 and soluble C5b-9 (sC5b-9) in both urine and plasma samples using ELISA. These measurements were then correlated with the clinical, biological, and histological data of these patients. To identify the presence of C-11 within circulating immune complexes (CICs), we performed immunoprecipitation using CD89. Additionally, in vitro experiments involved stimulating human mesangial cells (HMCs) with cIgAN plasma or recombinant sCD89 (rsCD89). We evaluated the production and secretion of C-11 using RT-PCR and ELISA, respectively.

Results: Overall sC5b9 was correlated to glomerular damage. Urinary sC5b-9 correlates with lower eGFR ($r = -0.642$, $p < 0.001$) and increased proteinuria ($r = 0.789$, $p < 0.001$). Elevated urinary and plasma sC5b-9 levels are linked to glomerular inflammation ($p = 0.047$ and $p = 0.012$, respectively), and fibrotic crescents ($p = 0.0098$ and 0.050 respectively). Plasma sC5b-9 is associated with increased endocapillary cell proliferation ($p = 0.045$) and glomerulosclerosis ($p = 0.029$). Strikingly, plasma sC5b-9 was found to be linked to the endocapillary deposition of C5b-9 in kidney glomeruli ($r = 0.443$, $p = 0.023$). Furthermore, C-11 levels were elevated in cIgAN patients compared to healthy controls ($p = 0.0043$) and associated with increased glomerular inflammation ($p = 0.0038$). C-11 levels were also significantly correlated with sC5b-9 levels in the plasma ($r = 0.5881$, $p = 0.0040$). Intriguingly, we found the presence of C-11 within the CICs in conjugation with sCD89. Most of all we found that C-11 is expressed ($p = 0.006$) and secreted by the HMCs, with its upregulation upon stimulation with rsCD89 or cIgAN plasma.

Conclusion: Our prospective study demonstrates a significant correlation of sC5b-9 and C-11 with disease severity in cIgAN, thus opening new avenues for biomarkers discovery. Specifically, plasma sC5b-9 levels > 250 ng/ml serve as an indicator of proliferative cIgAN. Furthermore, our investigation suggests that C-11, in conjunction with sCD89, may lead to the activation of the lectin complement pathway, thus providing a mechanistic insight into the disease.

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PREDICTORS OF SHORT-TERM RENAL FUNCTION IN PATIENTS WITH STEC-INDUCED HAEMOLYTIC UREMIC SYNDROME

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Aims/Purpose: Predicting short-term outcome in patients with Haemolytic Uremic Syndrome (HUS) caused by Shiga toxin-producing E. coli (STEC) can be crucial for patient management during hospitalization. Blood parameters such as lactate dehydrogenase (LDH) and C3 complement protein concentration, which are easily measurable in the hospital setting, can provide valuable information.

Methods: In this retrospective study, we analyzed the case files of 62 patients who were diagnosed with STEC-associated HUS at the Paediatric Nephrology Unit of S. Orsola University Hospital in Bologna, Italy, between 2009 and 2022. In particular, we analyzed the blood and urine test results obtained during hospitalization, paying special attention to values at admission and those obtained immediately before discharge; both sets of values were analyzed using multiple linear regression models to highlight possible correlations between the parameters at onset of the overt disease and nephrological outcomes in terms of eGFR and proteinuria.

Results: According to our findings, low eGFR values (< 90 ml/min/1.73m^2) together with low C3 levels (< 90 mg/dL) at admission were predictive of low eGFR at discharge (PLR = 3.71, p value = 0.003). This model had a sensitivity of 69% (95% CI = 41%-89%) and a specificity of 81% (95% CI = 62%-94%). Furthermore, LDH levels measured at patient admission were found to be highly correlated with simultaneous levels of proteinuria (adjusted R^2 = 0.73, p value = 6.27e^-11).

Conclusion: Based on these results, we can conclude that the recovery of adequate renal function in STEC-associated HUS patients presenting with acute renal failure at onset can be predicted by eGFR and C3 levels measured at admission to the ward. The obvious collinearity between LDH values and proteinuria suggests that LDH could be considered an early indicator of acute renal damage.

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CHANGES IN HEALTHCARE DELIVERY TO CHILDREN AND YOUNG PEOPLE WITH SLE AFTER THE COVID-19 PANDEMIC

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Aims/Purpose: To evaluate the impact of the COVID-19 pandemic on the care of children and young people (CYP) with systemic lupus erythematosus (SLE).

Methods: We conducted a monocentric retrospective analysis involving 115 CYP diagnosed with SLE, all under 21 years old (86.1% females), spanning January 2019 to December 2021. Our study aimed to evaluate two main objectives: 1) the influence of the government policy on healthcare delivery and accessibility, and 2) the effects of service restrictions on physical health. Comparative analyses were performed across three one-year intervals: January to December 2019 (pre-pandemic), January to December 2020 (lockdown phase), and January to December 2021 (post-lockdown phase).

Results: While the average number of total in-person visits remained stable at 5.2 ± 3.0 episodes per person annually across the periods (Fig 1a), a significant increase in appointment rescheduling was noted post-pandemic ($p < 0.001$). For unscheduled visits, more patients resorted to emergency room care post-pandemic (Fig 1a, inset). Post-pandemic, telemedicine utilization surged and persisted even after lockdown measures were lifted ($p < 0.001$, Fig 1b). Rates of newly-diagnosed patients, lost to follow-up cases, transferred cases, and kidney biopsies did not significantly differ between the periods (Fig 1c). Similarly, there were no significant changes in overall hospitalization rates or proportions of elective and emergency admissions (Fig 2b). Although SLE flare rates peaked during the lockdown phase, statistical significance was not reached (Fig 2a). Notably, COVID-19 infections occurred in 31 patients (26.7%), all post-lockdown.

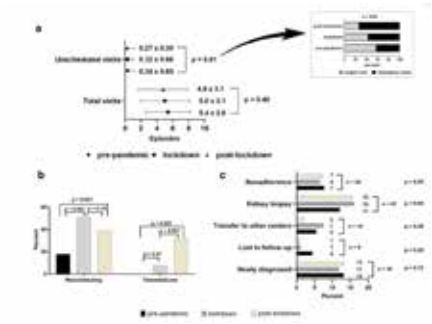

Figure 1 Comparative assessment within the first objective

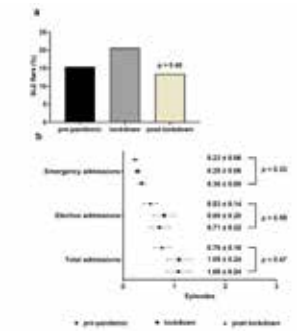

Figure 2 Comparative assessment within the second objective

Conclusion: Our study highlights the pronounced impact on scheduled appointments, with a notable increase in rescheduled visits during lockdown and post-lockdown phases. The observed shifts towards emergency room visits and increased telemedicine utilization post-pandemic underscore the need for adaptive healthcare strategies. Further investigation is needed to evaluate the effectiveness of healthcare adaptations for CYP with other chronic conditions.

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ASSESSMENT OF ADHERENCE TO ANTIHYPERTENSIVE MEDICATIONS AFTER PEDIATRIC KIDNEY TRANSPLANTATION BY LIQUID CHROMATOGRAPHY-TANDEM MASS SPECTROMETRY OF SPOT URINE

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Aims/Purpose: Non-adherence to oral medication is common in children and adolescents. Patients after kidney transplantation during childhood frequently suffer from arterial hypertension. The required antihypertensive medication increases their already high pill burden even further. The present study evaluates adherence to prescribed oral antihypertensive therapy by measuring drugs in single spot urine using liquid chromatography-tandem mass spectrometry (LC-MS/MS).

Methods: We analyzed spot urine samples of 114 children and adolescents from a prospective multicenter observational study. Mean age was 14.0 years, mean time since transplantation was 7.1 years and 39% of patients were female. LC-MS/MS was used to determine presence or absence of 19 commonly used antihypertensive drugs and/or their metabolites, including ACE inhibitors angiotensin receptor blockers, beta blockers, calcium antagonists and diuretics. We assumed non-adherence if at least one of the prescribed medications was not detected able.

Results: The LC-MS/MS method was capable of detecting all drugs prescribed in our patient cohort. In 53% (60/114) of the analyzed urine samples non-adherence to prescribed medication was found. This was independent of the number of antihypertensive drugs prescribed (Figure). Comparison of patients, in whom all prescribed drugs were detectable did not differ from those, in whom drugs were missing with regard to age, sex, and office blood pressure z-score. In a sub cohort (n = 83) ambulatory blood pressure monitoring (ABPM) data was available. ABPM parameter did not differ between adherent and non-adherent individuals. We observed a positive relationship between the number of antihypertensive drugs and 24h mean systolic z-score (Pearson's r = 0.248 p =0.024).

Conclusion: Antihypertensive medication and their metabolites can be reliably detected in spot urine samples of patients after pediatric kidney transplantation. Non-adherence to at least one prescribed medication was frequent, but did not seem to affect blood pressure levels in our medium-sized cohort. We plan to validate our preliminary results by analyzing more samples and including multiple timepoints allowing for longitudinal assessment.

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IMPACT OF ANTI-ANGIOTENSIN II TYPE 1 RECEPTOR AND ANTI-ENDOTHELIN TYPE A RECEPTOR ANTIBODIES ON PEDIATRIC RENAL TRANSPLANTATION

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Aims/Purpose: Non-HLA antibodies targeting allogeneic molecules have emerged as possible contributors to graft dysfunction. The harmful effects of anti-Angiotensin-II Type 1 Receptor (AT1R) and anti-Endothelin-1 type A Receptor (ERTA) antibodies have been reported in both paediatric and adult renal transplant recipients, but the evidence supporting a significant detrimental role of these antibodies remains scanty. Aim of this study was to evaluate the incidence and impact of anti-AT1R and anti-ETAR antibodies in paediatric kidney transpant recipients.

Methods: Anti-AT1R and anti-ETAR antibodies were measured pre- and post-transplant for at least 2 years in a cohort of pediatric renal transplant recipients. The influence of anti-AT1R and ETAR antibodies on chemotaxis of immune cells was also studied. Histological and immunohistochemical analyses were performed on protocol biopsies at 6, 12, and 24 months post-transplantation. The relationship between non-HLA antibodies, biopsy-proven antibody-mediated rejection and clinical outcomes was evaluated.

Results: 169 paediatric kidney transplant recipients were enrolled in the study and more than 500 sera were evaluated. Pre-formed anti-AT1R and anti-ETAR antibodies were detected in 49% and in 48,4% of patients, respectively. At all timepoints, 39,1% and 42,2% of children were negative for anti-AT1R and anti-ETAR antibodies, respectively. Anti-AT1R and anti-ETAR antibodies were significantly associated. De novo appearance of AT1R or anti-ETAR antibodies was detected in 11,7% and 9,4% of patients, respectively. In vitro data suggested a positive correlation between natural killer (NK)/T cell migration and non-HLA antibodies levels.

Conclusion: Anti-AT1R and anti-ETAR antibodies are detectable in half of the paediatric renal transplant recipients and are highly associated. Preliminary data suggest a possible role of these antibodies on T cell and NK recruitment. The studies underway are expected to increase the knowledge on the role of non-HLA antibodies on the survival of pediatric renal allografts.

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AGE-RELATED EFFICACY AND SAFETY OF TACROLIMUS-BASED IMMUNOSUPPRESSION IN PEDIATRIC KIDNEY TRANSPLANTATION - A BENCHMARK STUDY OF THE CERTAIN REGISTRY

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Aims/Purpose: This study investigates age-related differences in rejection rates, infectious episodes and tacrolimus exposure in a large European cohort of pediatric kidney transplant recipients (pKTR).

Methods: We performed a retrospective analysis of 802 pKTR from the CERTAIN registry from 53 centers in 14 countries. Inclusion criteria were a tacrolimus-based immunosuppressive regimen and at least two years of follow-up. The patient population was divided into three age groups (infants < 6 years, school-age children 6-12 years, and adolescents > 12 years) to assess age-related differences of outcome. Data analyzed included demographics, immunosuppressive regimen, tacrolimus exposure, allograft function, biopsy-proven acute rejection episodes (BPAR), and prevalence and type of infections.

Results: The mean age at transplantation was 11.2 ± 5.1 years, with 31.2% of patients receiving a living donor transplant. Besides tacrolimus, the most common immunosuppressive drugs at 1 year post-transplant were MMF (77.8%) and glucocorticoids (82.8%). During the first 2 years post-transplant, infants had a significantly higher incidence of infections ($P < 0.001$), with gastrointestinal infections being the most common, and a significantly higher number of cumulative hospital days ($P < 0.001$). Cox regression analysis showed a significantly lower risk of infection in adolescents, with a hazard ratio (HR) of 0.54 (95% CI 0.43-0.66, $P < 0.001$). On the other hand, adolescents had significantly higher rejection rates ($P = 0.032$). Multivariable Cox regression analysis revealed an increased risk of rejection in patients > 12 years, with an HR of 1.53 (95% CI 1.10-2.13, $P = 0.01$). Infants had significantly lower tacrolimus trough levels, lower body surface area-corrected concentration-to-dose (C/D) ratios, and increased intrapatient variability ($P < 0.002$).

Conclusion: This so far largest study on efficacy and safety of a tacrolimus-based immunosuppressive regimen in pediatric kidney transplant recipients highlights important age-related differences in rejection rates, infection episodes and tacrolimus exposure. Based on these findings immunosuppressive therapy in pKTR should be tailored according to the age-specific risk profiles of this vulnerable, but heterogenous patient population.

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INCREASED BLOOD PRESSURE VARIABILITY IS ASSOCIATED WITH CARDIOVASCULAR DAMAGE IN CHILDREN AFTER KIDNEY TRANSPLANTATION

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Aims/Purpose: Children after kidney transplantation (KTx) have a high burden of cardiovascular disease with arterial hypertension being the most important risk factor. The gold standard for diagnosing arterial hypertension is ambulatory blood pressure monitoring (ABPM). Evidence in adults demonstrates blood pressure variability (BPV) in ABPM as an independent risk factor for cardiovascular disease and mortality. The present study analyses short term blood pressure (BP) variability in children after KTx and its association to left ventricular mass index (LVMI) and aortic pulse wave velocity (PWV) as markers of cardiovascular end organ damage.

Methods: We analyzed 371 ABPM profiles from 159 children after KTx from the prospective international multicenter observational 4C-T study. Mean age at inclusion was 14.6 years and 43% were female. Variability was assessed by calculation of Standard Deviation (SD) for the 24-hour (24h) recording period and for day- and nighttime, separately. Additionally, we computed average real variability (ARV). ARV averages the absolute difference between consecutive BP measurements, thereby accounting for speed and order of BP changes. Linear mixed models adjusted for BMI, eGFR, age, sex and mean BP were constructed using directed acyclic graphs.

Results: Increased systolic BP SD during daytime was associated with faster PWV (ß = 0.038, p =0.01; Fig. 1); a similar tendency was seen for systolic BP SD during 24h. For diastolic BP, increased diastolic BP SD during 24h and daytime were associated with a faster PWV (ß = 0.049 p =0.006 and ß = 0.051 p =0.002, respectively). In contrast, higher diastolic BP SD during nighttime was associated with slower PWV (ß = -0.034 p =0.01). A similar association was seen for higher systolic BP SD with slower PWV, but this association did not reach significance. No significant associations were detected between ARV and PWV. For LVMI, an increase in diastolic ARV (ß = 1.26 p =0.01; Fig. 2), but not systolic ARV, was associated with higher LVMI. 24h, day- or nighttime BP SD showed no correlation with LVMI.

Conclusion: In children after KTx increased short term BP variability was associated with cardiovascular damage, assessed by PWV and LVMI. Elevated arterial stiffness might augment pulse pressure and thereby increase BP variability. Interestingly, the most prominent effects were seen for diastolic BPV, while in adults systolic BPV was more influential. Some ABPM software already provides BPV measures, making it easy to integrate our findings into clinical practice. A closer look at the variability in ABPMs could improve cardiovascular risk stratification and preventive treatment in children after KTx.

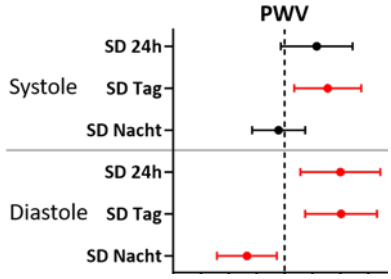

Fig. 1

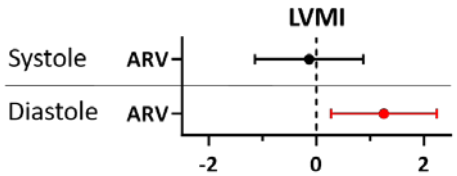

Fig. 2

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TRANSPLANTATION STRATEGY IN PATIENTS WITH PRIMARY HYPEROXALURIA TYPE 1 AND RNAI MEDICATIONS

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Aims/Purpose: Primary hyperoxaluria (PH) is a family of three ultra-rare autosomal recessive inherited disorders of hepatic glyoxylate metabolism characterized by oxalate overproduction. Nedosiran and lumasiran are RNA interference (RNAi) agents that inhibit the endogenous oxalate production in the liver. Both agents are approved for treatment of PH1. In patients with PH1 and end stage kidney failure, isolated kidney transplantation (iKTx) is supposed to be sufficient under treatment with either RNAi medication, as it is in patients with proven vitamin B6 (VB6) sensitivity.

Methods: We report clinical follow up of 10 patients with PH1 and on maintenance hemodialysis (HD), who either received lumasiran (patients #1-6, age 35-68 yrs, 3 females), or nedosiran (#7-9, age 11-44 yrs, 1 female). One patient with infantile oxalosis (#10) and combination of HD and PD received lumasiran first as monotherapy (7 dosages), but was then treated with both RNAi agents to ameliorate the clinical situation. Plasma oxalate (Pox) pre-HD was measured before (pre) and at each new RNAi injection. Systemic oxalate grading (SOG) was evaluated by bone MRI (when applicable), or speckle echocardiography before start and repeatedly during treatment. Medications were administered according to guidelines.

Results:

Pat No	AGXT Mutation	SOG Pre RNAi	VB6	Poxµmo/l Pre RNAi	Poxµmo/l 6 m	Pox µmo/l 9 m	Poxµmo/l 12 m	Poxµmo/l last visit (months)	SOG Current	Tx performed or Strategy
1	c.454T > A c.454T > A	0-1	yes	57.7				48.3 (m 3 pre iKTx)	0-1	iKTx with PKF
2	c.508G > A c.508G > A	0-1	yes	33.5	29.1	32.2	16.4	20.7 (m 15, pre iKTx)	0-1	iKTx with RKF
3	c.994_995.del p, c.508G > A	1	yes	139.9	45.3	78.7	57.5	151.7 (m 27)	1	iKTx planned
4	c.33-34insC c.508G > A	2	Yes	57.3	50.1	104.6	44.1	161.9 (m 36)	3	Double RNAi / LKTx
5	c.245G > A c.245G > A	3	No	98.9				68.3 (m 4)	3	LKTx planned
6	c.508G > A c.508G > A	2	yes	45.1	39.9	32.7	37.7	49.1 (m 21)	2	RNAi stoppediKTx planned
7	c.508G > A c.508G > A	3	yes	84.9	51.3	113	80.8	151.4 (m 41)	3	LKTx planned
8	c.508G > A c.508G > A	0	Yes	71.6	23.2	26.98	37.92	85.5 (m 42)	1	iKTx planned
9	c.997A > T; c.997A > T	2	No	101.28	150.5			116.2 (m 7)	2	To be evaluated
10	c.33dupC c.33dupC	1	No	47.6	136.5 (start double RNAi)	71.6		93.23 (m 12)	to be dermined	LKTx discussed

SOG: nothing = 0, minor = 1, medium = 2, severe = 3; AGXT = alanine glyoxylate aminotransferase gene; PKF = preserved kidney function; RKF = reduced kidney function; LKTx = liver-kidney transplantation; months = m.

Conclusion: In patients with minor oxalate deposition sensitive to vitamin B6 or under RNAi treatment (with or w/o VB6) iKTx can be considered. However, in patients with severe systemic oxalate deposits the high levels of plasma oxalate and no change in systemic oxalate deposits over time of RNAi treatment and maximum dialysis makes us reconsider a combined or sequential LKTx rather than iKTx. Our data clearly shows that the original idea of avoiding liver Tx under RNAi medication is not an option in all patients.

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RANDOM FOREST CLASSIFIER FOR THE PREDICTION OF ACUTE KIDNEY INJURY IN CHILDREN UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Aims/Purpose: Acute kidney injury (AKI) is one of the most common complications in children undergoing hematopoietic stem cell transplantation (HSCT), affecting up to 84% of patients. Matched unrelated donor, cord blood transplantation, and sinusoidal obstruction syndrome are among established risk factors of AKI development. Recent studies suggest additional influence of drug nephrotoxicity and malignant disease, as an indication for HSCT, on AKI incidence. However, efficient prophylaxis or early diagnostics of AKI still remain a challenge. Therefore, our aim was to test the potential of artificial intelligence (AI) methods in building a model identifying significant clinical risk factors of AKI development in HSCT patients.

Methods: The retrospective analysis covered clinical data of 135 children, aged 2-18 years, followed up for 6 months after HSCT. Type of donor, medicines constituting conditioning protocol, complications like infections or graft versus host disease, were implemented into the model. Kidney function was assessed before conditioning therapy, 24 hours after HSCT, 1, 2, 3, 4, and 8 weeks after transplantation, then 3 and 6 months post-transplant. Complete timely observations from 93 children served as input data. The ratio of training and testing sets was 80:20. The model was built with the brute force method and all combinations of input parameters were tested. Random forest classifier (RFC) turned out the most suitable model due to the simplicity of data preparation and transparency of analysis.

Results: AKI according to pRIFLE criteria was diagnosed at least once in 54% of patients. Random forest classifier (RFC) model has labelled 93 patients according to presence or absence of AKI. The positive predictive power of AKI during the follow-up period was 0.92, sensitivity 0.85 and F1 score 0.88. The positive predictive value of absence of AKI was 0.71, sensitivity 0.83, F1 score 0.77. The RFC correctly classified 84.21% of the records from the test set. It showed precision of 0.85 and sensitivity of 0.84, respectively. The value of the area under the ROC curve was also significant (0.84). RFC model revealed that the major determinants of AKI incidence within the 6-month post-transplant observation period were: values of estimated glomerular filtration rate (eGFR) before and just after HSCT, methotrexate use, viral infections, and acute graft versus host disease (aGVHD).

Conclusion: Random forest classifier model turned out a promising tool in the prediction of AKI development among children after HSCT, allowing identification of patients at risk even already before HSCT or just after the procedure. Current renal function remains the major determinant of prospective kidney damage, in concert with complications like chemotherapy, viral infections, or aGVHD.

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MEASLES IMMUNITY IN PAEDIATRIC KIDNEY TRANSPLANT PATIENTS

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Aims/Purpose: Measles is reported to be one of the most contagious diseases in the world. In 2023 the World Health Organisation recently declared a 45-fold increase in measles cases across Europe. By January 2024, the West Midlands was the epicentre of an outbreak of Measles, putting immunocompromised children at risk of developing complications such as pneumonia and encephalitis. The aim of the study was to determine the current immunity status of paediatric kidney transplant patients, inform decisions regarding future Measles IgG antibody testing and to advise patients in contact with this highly transmissible disease.

Methods: This prospective study looked at the Measles Immunoglobulin (Ig)G status of paediatric recipient kidney transplant outpatients seen at Birmingham Children's Hospital between January and March 2024. Information regarding the patient demographics, transplant details, complications and immunosuppression regimen were collected.

Results: We reviewed 61 paediatric transplant patients aged between 4-18 years who had Measles IgG antibody testing. The average age was 12 years at the time of testing and the majority of children were male (39/61, 64%). 38/61(62%) were Caucasian, 17/61 (28%) Asian, 4/61 (7%) African and 2/61 (3%) Mixed ethnicity. 8/61 (13%) were negative for measles antibodies at the time of testing having been positive pre-transplantation. The average time of testing in these negative patient was 5 years post- transplant, whereby 50% received a living related donor and 50% received a deceased donor. Of the 8 patients with negative measles antibodies, 3/8 (38%) were treated for rejection with IV Methylprednisolone and 1 had regular IgG for hypogammaglobulinaemia. There were no patient factors pertaining to a negative IgG Measles Antibody result.

Conclusion: In conclusion, 1 in 10 (13%) paediatric transplant patients had negative Measles IgG antibodies and would therefore require Immunoglobulin treatment if they were exposed to measles (despite having positive antibodies pre-transplantation). We advocate for early Measles IgG testing in transplant patients at the time of clinical outbreaks and communicating these risks to patients and families in order to ensure prompt assessment and initiation of treatment.

	Positive IgG Measles (n = 53)	Negative IgG Measles (n = 8)
Immunosuppression:		
Tacrolimus, MMF & short course Prednisolone	31/53 (58%)	3/8 (37.5%)
Tacrolimus, MMF & long course Prednisolone	9/53 (17%)	1/8 (12.5%)
Tacrolimus +/- Prednisolone	2/53 (4%)	2/8 (25%)
Prednisolone, Azathioprine & Tacrolimus	3/53 (6%)	1/8 (12.5%)
Sirolimus & MMF +/-Prednisolone	8/53 (15%)	1/8 (12.5%)
Rejection treated with IV Methylprednisolone	10/53 (19%)	3/8 (37.5%)
Other	1/53 IgG (2%) 1/53 Eculizumab (2%) 3/53 (6%) Rituximab (and T cells in 1/53) 1/53 Plasmapheresis (2%)	1/8 (12.5%) IgG

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HAEMODYNAMIC EFFECT OF DEXMEDETOMIDINE DURING PEDIATRIC KIDNEY TRANSPLANTATION

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Aims/Purpose: Dexmedetomidine, a highly selective alpha-2 agonist, is increasingly used in anesthesia as part of opioid free-anesthesia (OFA) protocols. Numerous studies have also highlighted its hemodynamic stability property during general anesthesia, however, there is no data on pediatric kidney transplant recipients. Our study investigates the hemodynamic effect of perioperatively administered dexmedetomidine in pediatric kidney transplant recipients.

Methods: Between January 2019 and June 2023, all pediatric kidney transplant recipients below 18 years were studied retrospectively at Nantes University Hospital. Intraoperative hemodynamic status was compared between patients who had received dexmedetomidine during kidney transplantation (DEX group) and patients who had not (no-DEX group). Repeated measurements of mean arterial pressure and heart rate were recorded between the two groups throughout the duration of anesthesia and compared by applying linear mixed models adjusted for age and duration of anaesthesia. Graft function was assessed by creatinine levels and glomerular filtration rate at specific time points, as per protocol. The use of fluid and vasoactive drugs peri-operatively and within 24 hours after surgery was also studied.

Results: Thirty-eight patients were included, ten in the DEX group et twenty-eight in the no-DEX group. Intraoperative heart rate was similar between the two groups, however, mean arterial pressure was significantly higher (mean difference 8, standard deviation [SD: 2-14] mmHg, p =0,034) in the DEX group. No differences were found regarding the use of fluid and vasoactive drug therapy between groups. Glomerular filtration rate at one month was significantly higher in DEX group (p =0,009).

Conclusion: Children receiving intraoperative dexmedetomidine during a kidney transplantation presented higher perioperative mean arterial pressure compare to children receiving other sedative agents. DEX group also showed better graft function at one month. The direct impact of dexmedetomidine on immediate post-operative graft function in pediatric kidney transplant recipients should be studied in a prospective multicenter randomized study.

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LONG-TERMS OUTCOMES IN KIDNEY TRANSPLANTATION AFTER REJECTION: ADULT-CHILD COMPARISON

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Aims/Purpose: Renal transplantation is the best treatment for end-stage kidney failure. In recent decades, transplant survival has increased,both among adults and children. However,several risk factors are associated with reduced graft function;among these, rejection is still a major cause of graft loss.The aim of our study was to identify risk factors for reduced graft function and to analyze long-term outcomes,in adult and pediatric patients with rejection.

Methods: We retrospectively analyzed data of 509 adult and 279 pediatric kidney recipients, transplanted between 2011 to 2022 selecting those of patients with histological diagnosis of rejection. In particular,demographic characteristic of the patients, comorbidities, living versus cadaveric donors, mismatches, ischemia time, compliance to treatment,immunosuppressive treatment, presence of donor specific antibodies, glomerular filtration rate (GFR) at the time of rejection and at 6 and 12 months, histological characteristics of rejection, treatment of rejection, infections and graft loss were analyzed.

Results: 49(9.6%) adults and 88(32%) children presented rejection.The median time from transplant to rejection was seven months for both populations.Therapeutic non-compliance was 20% among adults and 26% in children (p =ns); graft-loss 20% in adults and 17% in children (p =ns). GFR at discharge from transplantation, at the time of rejection and at 6 and 12 months after its treatment remained stable in children. In adults, GFR decreased at the time of rejection, with subsequent improvement 6 months and one year after its treatment. Treatment adherence emerged as associated with recovery from rejection. In adults, infections were associated with reduced graft survival. In children, cadaveric donor, proteinuria at the time of rejection, GFR at discharge and at the time of rejection were associated with reduced graft survival whereas living donor and protocol biopsies were related to less progression of chronic kidney disease (tab1). Finally, pediatric transplantation is characterized by better graft survival than in adults.

Conclusion: Our study demonstrates several risk factors for reduced transplant survival among patients with rejection. Compared to adults, children presented higher rate of rejection but better graft survival.Protocol biopsies in the first year post-transplantation and treatment adherence could improve long-term graft survival.

Table 1

Risk factors for reduced graft survivalChildren				
	Overall	eGFR <30 last follow-up	eGFR>30 last follow-up	p-value
Cadaveric donor	60/88(68%)	17/19(89%)	43/69(62%)	0.03
eGFR post tx	72.5(59;90)	64.8(46;80.8)	73.3(54.9;92.4)	0.005
eGFR rejection	56.2(36.7;75.5)	35.5(22.8;52.9)	65.2(47.1;84.6)	0.003
Protocol biopsy	37/88(42%)	4/19(21%)	33/69(48%)	0.04
ProtU rejection	30/88(34%)	11/19(58%)	19/69(28%)	0.03

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EVALUATION OF THE ALTERNATIVE COMPLEMENT PATHWAY IN PEDIATRIC PATIENTS WITH TYPICAL HEMOLYTIC UREMIC SYNDROME

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Background: Atypical hemolytic uremic syndrome (aHUS) is a disorder of the complement alternative pathway regulation. Occasionally, the presence of pathogenic variants in genes encoding for complement factors, has also been detected in Shiga-toxin of E. Coli (STEC)-HUS patients. The aim of our study was to evaluate the dysregulation of the alternative complement pathway in patients with STEC-HUS.

Methods: 15 patients with STEC-HUS admitted to Bambino Gesù Children's Hospital in Rome, were evaluated in collaboration with the Mario Negri Institute in Bergamo, Italy. In these patients were analyzed: detailed complement gene analysis, including factor H, factor B, factor I, membrane cofactor protein, C3, complement factor H related 5, and thrombomodulin; an ex-vivo assay based on serum-induced complement deposits on cultured human microvascular endothelial cells (HMEC-1).

Results: Table 1 details the demographic and clinical features of the patients. Genetic analysis showed mainly single nucleotide polymorphisms and genetic susceptibility variants for HUS. Only 1 patient had a heterozygous variant ([c.1771G > A p.Ala591Thr] [=]) in the C3 gene, for which the available data suggests clinical relevance. The HMEC test was available in 8 patients in the acute phase and was positive in both resting and activated conditions. All patients had rapid clinical improvement, and did not present relapses after an average follow-up of 30 months.

Conclusions: Complement gene abnormalities can be observed in patients with STEC-HUS. Results of the ex-vivo HMEC test suggest that complement activation might play a role in some forms of typical HUS. In these patients, activation of the terminal pathway of complement and C5b9 endothelial depositions can be observed during the acute phase of the disease. When present, abnormal alternative complement pathway findings may represent a risk factor for relapse. The value of the HMEC test in clinical practice however, remains uncertain when applied to patients with STEC- HUS, and requires further validation studies.

Table 1. Demographic and clinical features of the patients

Age, y(median)	1.88 (0.71-12.25)
Male, n(%)	10/15 (66,6)
VTEC positive, n(%)	15/15 (100)
Hypertension n(%)	12/15 (80)
Neurological events n(%)	6/15 (40)
Bloody diarrhea n(%)	10/15 (66,6)
Anuria n(%)	11/15 (73,3)
Proteinuria n(%)	10/15 (66,6)
Hematuria n(%)	15/15 (100)
Anemia n(%)	12/15 (80)
Thrombocytopenia n(%)	13/15 (86,6)

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PATIENT-REPORTED SYMPTOMS AND BIOCHEMICAL CHARACTERISTICS OF BUROSUMAB-TREATED ADOLESCENTS WITH XLH AT THE END OF SKELETAL GROWTH - FINDINGS FROM THE 'MYXLH STUDY'

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Aims/ Purpose: X-linked hypophosphataemia (XLH) is a rare, genetic, renal phosphate-wasting disorder characterised by elevated serum FGF23 levels as a result of loss-of-function mutations in the PHEX gene. As a result of chronic hypophosphataemia and suppression of 1-alpha hydroxylation of vitamin D by FGF23, clinical manifestations including skeletal abnormalities begin in infancy and extend to additional morbidities in adulthood. This study aims to describe the lived experience of XLH for adolescents at the end of skeletal growth (EOSG) treated with burosumab for at least 1 year. Here we describe patient reported symptoms and biochemical characteristics of this cohort of adolescents at the EOSG.

Methods: This observational, prospective, multicentre study with 14 sites across the UK, France, Netherlands, Germany and Spain, collected data from medical records as well as directly from adolescents with XLH via a smartphone app, wearable device and 1:1 interviews for a duration of 4 weeks within a 26-week period prior to EOSG. Patients rated their symptom intensity (pain, stiffness and fatigue) on a scale of 0 (none) to 10 (worst imaginable).

Results: 24 adolescents with XLH were enrolled between November 2021 and January 2023. The majority were female (15 [63%]) and all diagnosed in childhood (median [interquartile range (IQR)] age 2.0 [2.3] years). They had been treated with burosumab for median (IQR) 4.1 (1.6) years prior to reaching EOSG. Median (IQR) age at EOSG was 15.0 (1.5) years for females and 17.0 (2.0) years for males. Serum phosphate concentrations measured within 6 months prior to EOSG for 17 (71%) patients were collected from patients' medical records. Median (IQR) serum phosphate concentration for the cohort was 0.92 (0.24) mmol/L with 9 patients (53%) within normal range (per local lab reference ranges). Median (IQR) patient-reported fatigue, pain and stiffness scores during the 4 week period prior to EOSG were 1.85 (1.97), 1.02 (2.00) and 0.65 (1.12) respectively. A total of 87 adverse events were reported within the 26-week period prior to EOSG, primarily reported via the 1:1 interviews. 42 (48%) were related to musculoskeletal and connective tissue disorders. None of the adverse events were serious; only 5 were deemed related to burosumab following causality assessment conducted by the company. Events were consistent with those observed in clinical trials in paediatric patients.

Conclusions: Our findings on this European cohort of 24 adolescents with XLH treated with burosumab prior to reaching EOSG showed that patients reported low symptom intensity scores. Of those with recorded laboratory data, approximately half had serum phosphate concentrations within normal range within 6 months prior to EOSG. There were no new safety concerns identified during the study period.

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USING NEAR INFRARED SPECTROSCOPY TO ASSESS RENAL ANTIBIOTIC TOXICITY IN NEWBORNS

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Aims/Purpose: Infections and sepsis are significant causes of hospital admissions among newborns. Vancomycin, an antibiotic commonly used in the treatment of late-onset neonatal sepsis, has been shown to induce oxidative stress in animal experiments. Near Infrared Spectroscopy (NIRS), a promising non-invasive technology, shows potential for detecting antibiotic-associated kidney damage.

Methods: This is a single-center, prospective, observational study in which patients diagnosed with late-onset neonatal sepsis and initiated on antibiotic treatment were evaluated with renal NIRS on days 0, 3 and 7 of their treatment. These data were compared with antibiotic doses and combinations, daily weight and blood pressure monitoring, intake-output records, hemoglobin (hgb) levels, serum cystatin-C levels and serum Vancomycin levels. Patients with critical congenital heart disease, those with renal anomalies, individuals undergoing hypothermia therapy, patients requiring surgical intervention during monitoring, individuals receiving treatment for PDA and patients requiring inotropic support during follow-up were excluded from the study.

Results: 26 patients enrolled (12 male) with the median gestational age at birth for infants was 39 weeks (range: 30-40), with a median birth weight of 2530 grams (range: 610-3455). The median post-conceptional age at the time of study enrollment was 39.9 weeks (range: 30.9-41.4). All patients received treatment with vancomycin. Additionally, 23 of these patients were treated with amikacin, and 6 received meropenem therapy. A statistically significant decrease in renal oxygenation was observed in patients on days 0 and 7 of treatment (p =0,002). Additionally, anemia significantly affected renal oxygenation. When patients were divided into two groups based on Vancomycin levels above and below 15 mg/L, the group with levels above 15 mg/L showed a noticeable lower mean rSO2; however, no significant statistical difference was detected.

Conclusion: Since neonates have not yet completed their development, commonly used antibiotic treatments may cause harm. Detecting statistically significant differences in NIRS measurements between days 0-7 may serve as a guiding factor in understanding the cumulative effect of antibiotic treatment. NIRS proves to be a promising method for monitoring antibiotic toxicity. Based on studies in the literature, it will shed light on prospective studies with a larger number of patients regarding AKI as well.

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INCREASED FLUID INTAKE CAN LOWER BLOOD PRESSURE IN HEALTHY CHILDREN. THE SPAII PROJECT

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Aims/Purpose: Sodium (Na) intake is known to contribute to the development of hypertension, thus the reduction of its intake is a cornerstone in the prevention and management of hypertension. The increase in renal Na excretion might represent a further potential preventive and/or therapeutic opportunity. The present study was aimed at exploring the working hypothesis that an increased fluid intake can decrease blood pressure (BP) in healthy children by increasing Na excretion.

Methods: The SPA Project is a multicenter, prospective, controlled, randomized study investigating if an increased fluid intake for 1 year can lower BP in healthy children. At baseline and again after 1 year, BP was determined by means of multiple office blood pressure measurements (mOBPM) and fluid intake was estimated by measuring urine dilution (mean urinary creatinine of different days). Subjects were randomized in 2 groups: one was actively motivated to drink more water than usual, particularly during school hours, while the other group served as control. Urinary Na and K were also measured.

Results: One hundred and seventy-five healthy children (89 females, 54.9%) with a median age of 8.6 years (IQR: 8.4-8.9) were enrolled but only 152 successfully completed the study (baseline and final mOBPM and coefficient of variation of BP less than 15%). Compared with controls, children addressed to introduce more fluids showed a lower systolic BP (-0.87 and -0.69 SDS; p: 0.07) and diastolic BP (+0.12 and +0.31 SDS; p: 0.02) at 12 mos. The recorded difference in SDS is equivalent to 1.7 and 2.4 mmHg on systolic and diastolic BP, respectively.

Conclusion: An increased fluid intake can lower BP. It is speculated that this is due to an increased efficiency in sodium handling (excretion) by kidneys. This simple, highly acceptable, inexpensive, and harmless measure might have a role in preventing and/or minimizing the epidemics of hypertension and of its related morbidities both in children and in adults.

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MASKED HYPERTENSION IN CHILDREN WITH CHRONIC KIDNEY DISEASE AND ASSOCIATION WITH LEFT VENTRICULAR HYPERTROPHY

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Aims: Masked hypertension (MH) is seen especially in children with chronic kidney disease (CKD) and is characterized by normal office blood pressure but high ambulatory blood pressure (ABPM) and is associated with serious target organ damage. Our study aimed to evaluate the incidence and cardiovascular complications of MH in pediatric CKD patients.

Methods: In this study, 50 children with CKD and 33 healthy children were included. ABPM was performed in all children with CKD. Echocardiographic examination and office blood pressure measurement was performed in both groups.

Results: Our data showed that 27 (%54) patients had normal blood pressure, 3 (%6) patients had white coat hypertension, 13 (26%) patients had ambulatory systolic+diastolic hypertension, 4 (8%) patients had ambulatory diastolic hypertension, and 3 (6%) patients had ambulatory systolic hypertension. There were 11 (22%) children with MH. Three children with masked hypertension had moderate hypertensive load (25-50%) and 7 had severe hypertensive load (> 50%). The incidence of left ventricular hypertrophy (LVHT) in the CKD group was 38%. LVHT was found to be higher in the CKD group with severe hypertensive load compared to the normal blood pressure and moderate hypertensive load (p =0.043). The left ventricular mass index (LVMI) of the MH group was found to be statistically higher than that of CKD patients with white coat hypertension and healthy children (p =0.038 and < 0.001). Diastolic functions which were evaluated with E/E', LV Mass Z Score and LVMI parameters were found to be statistically significantly worse in the MH group compared to the controls (Table 1) (p < 0.05).

Conclusions: In our study, we demonstrated that the incidence of Masked Hypertension in pediatric CKD patients was 22%, and the frequency of LVHT in patients with MH was 54%. We showed that diastolic dysfunction was more common in the MH group compared to the controls. The deteriorating effect of the MH on the cardiovascular system was similar to ambulatory hypertension with CKD. To evaluate the cardiovascular complications of children with CKD; LVHT and systolic and diastolic functions should be evaluated together with the echocardiographic examination and routine ABPM must be performed.

Table 1: Comparison of Diastolic Functions in controls and CKD patients with masked hypertension

	Study Groups		
Variable	**Control Group (n = 33)**	**Masked HT (n = 11)**	**P-value**
EF	69 (66-70)	70 (66-70)	0,936µ
KF	38 (36-39)	38 (36-39)	0,852µ
E/A	1,4 (1,28-1,6)	1,36 (1,16-1,5)	0,555µ
E/E'	0,65 (0,53-0,8)	0,88 (0,75-1,15)	0,010µ
LV Mass Z score	-0,27 (-0,78-0,28)	0,72 (-0,37-2,48)	0,041µ
LVMI (g/m2)	31 (28-33)	44 (35-75)	< 0,001µ
LVHT			< 0,001
Absent	33 (100)	5 (45,5)	
Present	0 (0)	6 (54,5)	

µMann Whitney U test, Med (IQR)*Pearson ki kare test, Fisher Exact Test, n (%).

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APPARENT MINERALOCORTICOID EXCESS IN ISRAEL- A CASE SERIES AND LITERATURE REVIEW

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Aim: Apparent mineralocorticoid excess (AME) syndrome is an ultra-rare autosomal-recessive tubulopathy caused by HSD11B2 mutations, leading to excessive activation of the kidney mineralocorticoid receptor, and characterized by early-onset low-renin hypertension, hypokalemia, and risk of chronic kidney disease (CKD). To date, most reports included few patients, and none described patients from Israel. We aimed to describe AME patients from Israel and to review the relevant literature.

Methods: We retrospectively describe the clinical and genetic characteristics of seven patients from two families diagnosed with AME in Israel.

Results: Both mutations found in the HSD11B2 gene are novel. Five patients presented at age < 4 years, and had low birth weight, failure to thrive, and normal creatinine, while two (who had three siblings with same manifestations that died before diagnosis), presented later with CKD. All patients had severe hypertension (mean 169/100mmHg), hypokalemia (mean potassium 2.5mmol/L), and metabolic alkalosis. All patients developed nephrocalcinosis on kidney ultrasound although only one had hypercalciuria. All patients received mineralocorticoid receptor antagonists, other antihypertensive medications, and potassium supplements. Remarkably, one patient had cardiac arrest due to severe hyperkalemia but underwent successful resuscitation and fully recovered after intensive treatment. At last follow-up, patients 3-7 (mean current age 11.2 years, mean follow-up time 9.8 years) have normal kidney function and low-normal potassium, but all remain hypertensive despite treatment with spironolactone and amlodipine. One has left ventricular hypertrophy and two have hypertensive retinopathy. Patients 6 and 7 progressed to end-stage kidney disease and underwent dialysis and subsequently kidney transplantation, 1 has normal graft function while the other succumbed.

Conclusions: In this 11-year follow-up report of two Israeli families with AME, patients who presented early maintained long-term normal kidney function, while those who presented late progressed to end-stage kidney disease. Nevertheless, albeit early diagnosis and management, AME is commonly associated with serious complications of the disease or its treatment. More reports are needed for better understanding of the long-term outcomes and best management of this rare disease.

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ESTIMATING THE GLOMERULAR FILTRATION RATE IN THE PEDIATRIC INTENSIVE CARE UNIT: USING THE KINETIC EQUATION

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Aims/Purpose: Commonly used measures for the estimation of glomerular filtration rate (eGFR) are based on spot serum creatinine (Cr) determinations. The efficacy of these methods is generally good as long as GFR remains stable. But it becomes a big challenge when it is rapidly changing, which is frequent in patients admitted in the Paediatric Intensive Care Unit (PICU). The Kinetic Estimated Glomerular Filtration Rate (KeGFR) formula by S. Chen estimates the GFR by factoring the time interval between changing Cr values. It has been applied in studies involving adult patients, but pediatric data is missing. The aim of this study is to compare the most common equation used in pediatric population, the Schwartz modified 2009, with the KeGFR, in the PICU environment. Our purpose is to show the accuracy between both equations in this setting.

Methods: Retrospective, descriptive and analytical study by reviewing the medical records of pediatric patients admitted in the PICU of a tertiary hospital in Barcelona the last 10 years. Demographic, anthropometric and analytical variables were collected. Patients aged between 1 and 18 years who had more than one Cr measurements within a 48h period were included. Patients who had a change of serum creatinine < 4,3% (biological variation) during time of admission were excluded. GFR was estimated using the modified Schwartz 2009 equation and the KeGFR. A Pearson correlation coefficient was computed to assess the relationship between both equations.

Results: From a total of 1787 patients, a preliminary analysis was conducted on 100 patients. The median eGFR values obtained for the first creatinine measurement using the Schwartz 2009 equation and the KeGFR formula were 83 and 76 mL/min/1,73m2, respectively. For the second measurement, they were 91 and 99. For the third measurement, they were 95 and 97. And for the fourth measurement, they were 83 and 85. The difference in mL/min/1,73m2 between the Schwartz and the KeGFR equations for each creatinine measurement was -7, 8, 3 and 2, with 1 mL/min/1,73m2 being the median difference. The Pearson correlation coefficient for each creatinine measurement showed a correlation of 0.98, 0.89, 0.98 and 0.99, respectively, indicating a strong and stable correlation between the estimates. These results are provisional and subject to change as further data is analyzed.

Conclusion: In the PICU environment, the Schwartz 2009 and the KeGFR equations demonstrated a high correlation in estimating the GFR. The mean difference between the two eGFR values was higher at admission, of -8 mL/min/1,73m2 in the first creatinine measurement, showing worse results of eGFR with the Kinetic formula. This difference was lower in the following creatinine measurements.

While these preliminary findings provide valuable insights into the estimation of eGFR using different equations in the PICU setting, additional data is needed to validate these results.

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VOLUME EXPANSION MITIGATES THE COURSE AND OUTCOME OF SHIGA TOXIN-PRODUCING E. COLI ASSOCIATED HEMOLYTIC UREMIC SYNDROME

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Aims/Purpose: Previous studies have shown that the course and outcome of Shiga toxin- producing *E. coli* induced hemolytic uremic syndrome (STEC-HUS) might be improved through therapy with targeted volume expansion. The aim of this study was to evaluate the effect of volume expansion in our cohort of patients with HUS.

Methods: The clinical data of all pediatric patients with STEC-HUS in our center were analyzed retrospectively. Course and outcome of patients from 2019 – 2022 treated with volume expansion (VE) (n = 38) were compared with historical controls (HC) from the years 2009 – 2018 (n = 111).

Results: Patients in the VE group had a significant relative weight gain compared to the HC group (7.8% (3.4 – 11.3) vs. 1.2% (–0.7 – 3.9), $p < 0.0001$) 48 hours after admission. A difference in the proportion of patients with dialysis therapy was not observed between the groups (VE 21/38 (55.3%) vs. HC 64/111 (57.7%), $p = 0.8$). However, neurological involvement (reduced consciousness, seizures, focal neurological deficit and/or Visual impairment) was reduced in the VE group (VE 6/38 (15.8%) vs. HK 38/111 (34.2%), $p = 0.039$). None of patients in the VE group died or had CKD stage 5 at latest follow-up. In the HC group 3 patients died and 3 pa-tients had CKD stage 5.

Conclusion: Volume expansion is associated with an improved course and out-come of STEC-HUS, especially regarding the neurological involvement.

1209

PROMPT AND FIRST-LINE INITIATION OF RAVULIZUMAB IN CHILDREN WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME RESULTS IN EARLY DIALYSIS INDEPENDENCE: REAL-WORLD EVIDENCE

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Aims/Purpose: In clinical trial settings, ravulizumab has proven effective in complement inhibitor-naive children with atypical hemolytic uremic syndrome (aHUS). Here, we present the first, to our knowledge, real-world data of two pediatric patients with aHUS receiving first-line treatment with ravulizumab.

Methods: Our case series consists of two children with genetically and/or serologically proven aHUS and acute kidney injury, who were admitted to our clinic during the preceding 9 months and received first-line treatment with ravulizumab. Both patients initiated peritoneal dialysis (PD) during their admission and before the first dose of ravulizumab, whereas plasma infusion was allowed up to 24 hours after the first dose of ravulizumab.

Results: Patient characteristics are shown in Table 1.

Table 1: Characteristics, genetic findings and baseline (before ravulizumab administration) laboratory values of the two patients with aHUS

Patient	Sex	Age (years)	Etiology of aHUS	Genetic findings	Anti-CFH antibodies	Platelets (K/μL)	LDH (U/L)	Serum Creatinine (mg/dl)
1	Male	6	C3 mutation	C3 p.Ile1157Thr (Heterozygous)	Negative	79	5034	4.36 (eGFR=11)
2	Female	12	DEAP-HUS	Deletion of CFHR1 and CFHR3 (Homozygous)	Positi-ve(>2000 AU/mL)	54	2656	3.67 (eGFR=16)

DEAP-HUS: deficiency of CFHR plasma proteins and autoantibody-positive form of HUS; CFH: complement factor H

Both patients presented with active thrombotic microangiopathy (TMA) and acute kidney injury, and initiated PD on day 4 after admission. Both patients demonstrated undetectable haptoglobin levels (< 0.07 g/L) and elevated sC5b-9 levels at baseline. The first dose of ravulizumab was administered to both patients on day 7 after disease onset (day 6 after admission). Both patients became dialysis-independent in < 10 days. On day 14 after the first dose of ravulizumab, the improvement in serum creatinine was 81.9% and 77.6%, respectively, whereas the decrease in LDH was -4543 U/L and -2193 U/L, respectively. Complete and sustained TMA response was achieved on days 21 and 24, respectively. Currently, the patients have completed 26 weeks (5 doses) and 18 weeks (4 doses) of follow-up after ravulizumab initiation, demonstrating an eGFR of 94 and 87 ml/min/1.73m2, respectively. To date, no unexpected adverse events or meningococcal infections have occurred. Due to high titers of anti-CFH and sustained subclinical hemolysis (based on undetectable haptoglobin) despite complete TMA response after 2 doses of ravulizumab, therapy with rituximab was added in patient 2.

Conclusion: Initiation of ravulizumab in ≤7 days after disease onset, as first-line treatment, in children with aHUS leads to improved renal recovery, early dialysis independence, and sustained eGFR increase. Our data support that ravulizumab is effective and feasible as first-line treatment of aHUS in real-life settings.

1071

FROM GENOTYPE TO PHENOTYPE: THE COMMON DUTCH C3 VARIANT IN CHILDREN AND ADULTS WITH COMPLEMENT-MEDIATED ATYPICAL HEMOLYTIC UREMIC SYNDROME

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Aims/Purpose: A gain-of-function mutation in C3 (c.481C > T, p.Arg161Trp) is the most frequent rare variant found in patients with complement-mediated atypical hemolytic uremic syndrome (CaHUS). In fact, this variant is found in a quarter of Dutch CaHUS patients. This study entails an in-depth characterization of a large cohort of CaHUS patients carrying an identical pathogenic variant.

Methods: This is a retrospective, observational Dutch study includinging CaHUS patients with the C3 p.Arg161Trp variant identified between 2010 and 2023. A comprehensive genetic and clinico-epidemiological analysis was performed.

Results: In total, 37 CaHUS patients (11 children and 26 adults) were included. Genetic analysis showed MCPggaac risk haplotype homozygosity in 61% of patients. Median (range) age of CaHUS onset was 32 (0.5-62) years, and median (range) follow-up time was 12 (0.3-55) years. Compared to adults, children presented more often with high levels of LDH (1167 vs. 2644 U/L, P =.045), jaundice (11% vs. 50%, P =.063), and red-colored urine (28% vs. 90%, P =.004), indicative of hemolysis as no erythrocyturia was detected. Of the 37 patients, 17 patients had CaHUS onset after introduction of eculizumab in 2012 in the Netherlands. Their first episodes were treated with eculizumab (n = 9), supportive treatment (n = 5), or plasmapheresis (n = 3). Patients were not treated with eculizumab, despite its availability, due to several reasons: delayed recognition of CaHUS until after initial presentation, swift recovery following onset of plasmapheresis, or spontaneous recovery within initial days of presentation. All patients presenting before 2012 were either treated with plasmapheresis (n = 9) or supportive treatment (n = 11). Patients treated only with plasmapheresis, at onset, showed full recovery (n = 5), partial recovery (n = 3), or end-stage kidney disease (ESKD) (n = 4). Only one patient after eculizumab treatment developed ESKD. Adults who received supportive treamtent mainly developed ESKD (n = 6/7), whereas children showed mainly full recovery (n = 8/9). In total, 70% of patients experienced one or more relapses. Median (range) time between first episode and first relapse was 2.5 (0.3-17.6) years. Relapses did not seem to negatively influence long-term kidney function in patients treated adequately with eculizumab.

Conclusion: Patients with CaHUS carrying the C3 p.Arg161Trp variant, the common Dutch C3 variant, exhibit a diverse spectrum of phenotypes, underscoring the heterogeneity within this cohort. Distinctive clinical features of C3 p.Arg161Trp include a high rate of recurrence. This does not appear to negatively influence long-term kidney function. Remarkably, pediatric patients presented with more pronounced signs of hemolysis and showed far better outcomes than adult patients.

1144

A NOVEL, DOMINANT DISEASE MECHANISM OF DISTAL RENAL TUBULAR ACIDOSIS WITH SPECIFIC VARIANTS IN ATP6V1B1

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Aims/Purpose: Distal renal tubular acidosis (dRTA) is a rare disorder characterized by impaired acid secretion, leading to metabolic acidosis and other clinical manifestations, including hypokalaemia, hypercalciuria and nephrocalcinosis. Mutations in ATP6V1B1, encoding the B1 subunit of the vacuolar H+-ATPase in alpha-intercalated cells are associated with autosomal recessive dRTA with sensorineural hearing loss. Heterozygous variants predicted to affect a specific aminoacid, Arg394, have been recurrently reported in sporadic cases of dRTA, but their significance has been unclear. We aimed to review the pathogenicity of such heterozygous variants by collecting clinical and genetic evidence from available cases.

Methods: Retrospective analysis of cases identified in our genetic laboratories. In addition, a survey was sent through the working groups inherited kidney diseases and tubulopathies from ESPN, ERA and ERKnet. Clinicians were asked to provide data regarding demographics, clinical presentation, laboratory findings, imaging studies of kidneys and hearing studies. Genetic information on the index patient and, if available, other family members was also collected. Allele frequency in the general population was assessed in gnomAD. The potential disease mechanism was investigated through structural modelling.

Results: Eighteen index patients in total were included, of which 17 carried the variant c.1181G > A; p.(Arg394Gln) and one c.1180C > G; p.(Arg394Gly). In addition, there were 5 affected family members of 4 index patients and the variant segregated with the disease in all. In no patient was a second causative variant in trans identified. In all index patients tested (N = 7), the variant was confirmed to be de novo. No unaffected variant carriers were seen and both variants are absent in gnomAD. Sensorineural hearing loss was reported in 5 of the 23 patients. Structural modelling identifies a crucial role for Arg394 in nucleotide binding.

Conclusion: Our study provides strong evidence for the pathogenicity of heterozygous variants affecting Arg394 and thus a novel inheritance modus for ATP6V1B1-associated dRTA. Clinically, this form differs from the recessive one by the low prevalence of hearing loss. The prominent position of Arg394 in the nucleotide binding fold of the H+-ATPase structure suggests a dominant negative mechanism. Our findings inform the diagnosis and management of patients with dRTA.

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REAL WORLD EXPERIENCE WITH POTASSIUM CITRATE AND POTASSIUM HYDROGEN CARBONATE PROLONGED RELEASE GRANULES (SIBNAYAL) IN PAEDIATRIC RENAL TUBULAR ACIDOSIS

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Aims/Purpose: Renal tubular acidosis (RTA) is a rare condition characterized by dysfunction of proximal bicarbonate reabsorption (pRTA) and/or impaired distal urinary acidification (dRTA). Treatment consists of alkali supplementation and most products need to be taken multiple times a day with perceived poor palatability. Retrospective data in dRTA suggest that "adequate metabolic control" (normalization of blood bicarbonate level and urinary calcium excretion) is associated with improved outcome but achieved in only half of patients. We describe our experience with a new prolonged-release formulation (Sibnayal) that consists of tasteless granules taken twice daily.

Method: Retrospective, single-centre study of all patients who were prescribed Sibnayal. The median of plasma bicarbonate, potassium and urinary calcium/creatinine ratios were obtained for 1 year before (standard treatment) and 1 year after commencement of Sibnayal. Additionally, plasma bicarbonate at presentation to our centre, prescribed alkali dose and growth SDS score at the end of the respective treatment periods were assessed.

Results: There were a total of 20 patients who were prescribed Sibnayal, of whom 13 had dRTA. Six patients (30%) preferred standard treatment and returned to it. Almost all (5/6) of these were either below 4y or had developmental delay. Pertinent data from the remaining 14 patients are summarized in table 1. Median age at presentation was 4.2months (range 2.3-16.4). All patients had genetically confirmed diagnosis. Median age at start of Sibnayal was 9.6y (range 5.7-13.7) and 57% were male. The median prescribed daily alkali dose was similar with 2.17 vs 2.63 mEq/kg/d for standard and Sibnayal treatment, respectively.

Table 1. Summary of data. HCO3-: median plasma bicarbonate concentration [mmol/l]; K+: median plasma potassium concentration [mmol/l]; nCa/Crea: median urinary calcium/creatinine ratio normalized to the age-specific upper limit of normal (value > 1 indicates hypercalciuria); Height SDS: End of treatment standard deviation score; N: number of patients; Std: standard treatment; Sib: Sibnayal treatment; AMC: adequate metabolic control [%]; p: p-value (paired t-test); *: comparisons not made as hypercalciuria does not normalise with correction of acidosis in renal fanconi syndrome

Diagnosis (N)	HCO3-		p	K+		p	nCa/Crea		p	Height SDS		p	AMC		p
	Std	Sib		Std	Sib		Std	Sib		Std	Sib		Std	Sib	
dRTA (10)	25.5	25	0.9	3.7	3.8	0.1	0.5	0.62	0.5	-0.27	-0.15	0.4	77.8	88.9	0.5
All (14)	25	25	0.7	3.7	3.8	0.4	*	*	*	-0.49	-0.25	0.4	*	*	*

Conclusion: In this cohort of paediatric RTA patients, 78% of patients achieved adequate metabolic control with standard treatment. Sibnayal was equally effective and 70% of patients preferred this formulation. Those who preferred standard treatment were mostly younger or developmentally delayed, suggesting that the granule formulation may be better suited for school-aged children.

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GENETIC RENAL WASTING OF PHOSPHATE

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Aim/Purpose: To evaluate clinical presentation, biochemical profiles and treatment response in children with tubular phosphate transporter defects.

Methods: This retrospective, single-center observational study analyzed pediatric patients diagnosed with pathogenic variants in SLC34A1 or SLC34A3.

Results: The study included 10 patients (3 girls): 3 patients with SLC34A1 variants (all heterozygous) and 7 patients with (homozygous (n = 3) and heterozygous (n = 4)) SLC34A3 variants. Median (range) age at presentation was 6.6 years (0-13.1). One patient was diagnosed due to prenatal hyperechoic kidneys, 6 presented with symptoms of urinary stone disease, 2 because of hypercalciuria and one had a urinary tract infection. Seven patients were found to have nephrocalcinosis; among these, 4 also had kidney stones. One patient had kidney stones only. Two patients, both with heterozygous SLC34A3 variants, did not exhibit any abnormalities on ultrasound. Serum calcium (Ca) and phosphate (P) levels at time of diagnosis were known for 9 cases. Serum P levels were normal in 7 and elevated in 2 patients. Similarly, 2 cases exhibited hypercalcemia while the remainder had normal Ca levels. For 7 cases, parathyroid hormone (PTH) levels were available; 4 had suppressed PTH levels (median (range) 1.2 pmol/l (0.5-1.5), reference value 1.6-6.9)) and 3 cases had normal levels. Serum 1,25(OH)2-vitamin D levels prior to initiation of phosphate supplementation were known for 8 cases. In all but one, levels were elevated (median (range) 238 pmol/L (162-451), ref. 59-159 pmol/L). Urinary studies obtained prior to commencing phosphate supplementation revealed normal TmP/GFR-values in all but one case, where it was slightly decreased (1.01 mmol/l at the age of 1 year, Ref. 1.13-1.92). Of the 7 cases where Ca excretion was known, 6 showed hypercalciuria (median (range) 5.5 mg/kg/day (4.32 – 10.77)). In all but one patient phosphate supplementation (median (range) dose 1.0 mmol/kg/day (0.1-1.0)) was initiated. Among the 9 patients on phosphate supplementation, PTH increased to normal values in 7 and remained depressed in 2. Normalization of 1,25(OH)2-vitamin D levels following phosphate supplementation was seen in 3 cases. Levels remained elevated in the remaining 6 patients. In 4 patients, Ca excretion post-supplementation was measured by means of 24-hour urine collections. In all, hypercalciuria persisted (median (range) 10.36 mg/kg/day (7.46 – 16.44)).

Conclusion: In this study of 10 patient with SLC34A1 or SLC34A3 variants, elevated levels 1,25(OH)2-vitamin D levels and hypercalciuria were prevalent findings on presentation whereas no patient had hypophosphatemia. Phosphate supplementation resulted in normalisation of PTH levels in most patients, but 1,25(OH)2-vitamin D levels and calcium excretion remained abnormal in most.

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CHARACTERIZATION OF CARDIOLOGICAL MANIFESTATIONS IN PATIENTS WITH SALT-WASTING TUBULOPATHIES

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Aims/Purpose: Bartter (BS) and Gitelman (GS) syndromes are rare tubulopathies caused by mutations affecting renal NaCl transporters, resulting in similar symptoms like muscle weakness, cramps, and electrolyte imbalances, with GS also presenting with hypomagnesemia. Treatment focuses on electrolyte and fluid balance, using supplements and drugs to inhibit prostaglandin production and RAAS activation. Electrolyte deficits in these conditions can extend the QT interval and increase the risk of potentially fatal cardiac arrhythmias. This study aims to profile BS and GS patients followed at our hospital, focusing on cardiological phenotyping. We assessed diagnostic, clinical, and lab data, particularly examining the link between electrolyte imbalances (like hypokalemia or hypomagnesemia) and electrocardiographic changes or cardiac symptoms during follow-up.

Methods: We screened all BS and GS patients for study inclusion, requiring a genetic diagnosis with disease-causing mutations and comprehensive clinical and electrocardiographic data. We excluded cases lacking sufficient data. We gathered demographic and health information retrospectively, categorizing patients based on electrocardiographic results into groups: 1) persistent long QT interval, 2) transient long QT interval, and 3) no long QT interval. Data were summarized with medians, interquartile ranges, and frequencies.

Results: A total of 27 patients were enrolled in the study, 16 with Bartter Syndrome (BS) and 11 with Gitelman Syndrome (GS); median lenght of follow-up was 6 years (range 3- 19). Only one patient was classified in group 1, with a constant QTc prolongation (446.3 ms); 8 patients (34.8%) fell into group 2 with median QTc values of 420 ms, all exhibiting hypokalemia and hypomagnesemia. The majority (14/23, 61%) were in group 3, with a median QTc of 399.2 ms and 79% displaying hypokalemia and hypomagnesemia. All 9 patients who experienced cardiac-related symptoms were adults, with 8 presenting these symptoms during intercurrent episodes. The study also compared clinical differences between BS and GS patients, noting a higher frequency of hypokalemia and hypomagnesemia in GS, whereas BS patients had more electrocardiographic alterations, although not statistically significant. No echocardiographic abnormalities were detected from the available data, and there were no recorded incidents of malignant arrhythmias or sudden death.

Conclusion: Electrocardiographic abnormalities in BS and GS patients fluctuate, often related to episodic events, with QT prolongation in one-third of cases but no severe cardiac complications, indicating a generally positive prognosis.

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MONITORING LEVAMISOLE IN PLASMA AND SALIVA FROM CHILDREN WITH FIRST ONSET STEROID-SENSITIVE NEPHROTIC SYNDROME

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Aim: Levamisole is a perfect candidate drug to be added to initial corticosteroid treatment of steroid-sensitive nephrotic syndrome (SSNS) to prevent relapses. To demonstrate feasibility of saliva monitoring of levamisole, we aimed to describe the pharmacokinetics (PK) of levamisole in plasma and saliva.

Methods: Children (age 2-16 years) with first onset SSNS participating in a randomised, placebo-controlled trial were treated with levamisole 2.5 mg/kg on alternate days (intervention group) for 24 weeks. Five serial samples were collected at 8 (plasma + saliva) and 20 (plasma) after first onset. A non-linear mixed effect model was used to describe the PK of unbound levamisole in plasma and saliva. Monte Carlo simulations were performed to assess the predictive performance of saliva monitoring.

Results: From 19 children, 124 plasma and 89 saliva samples were available. Based on a two-compartment model, estimates (RSE) of unbound levamisole plasma clearance (CL) and central volume of distribution were 85 (16%) L/h/70 kg and 365 (13%) L/70 kg, respectively. CL was positively correlated to the haemoglobin level. The saliva-to-plasma ratio < 12 hours after administration was 3.8 (15%), with an inter-individual variability of 57%. Monte Carlo simulation showed that four saliva and two plasma samples can reliably predict plasma exposure with < 20% imprecision in 73% of the patients.

Conclusions: Saliva is a reliable and non-invasive option to determine levamisole exposure in children with SSNS. Yet, two plasma samples are needed to obtain sufficient precision. Ultimately, saliva sampling can contribute to more patient-friendly monitoring of exposure.

POSTE SESSION 1

621 - P1.001

GENETIC STUDY OF CONGENITAL ANOMALIES OF THE UPPER URINARY TRACT IN CHILDREN

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Aims/Purpose: Congenital Anomalies of the Urinary Tract (CAKUT) are multifactorial disorders and constitute the leading cause of chronic kidney disease in children. Their etiology involves genetic, epigenetic mechanisms as well as environmental factors. Despite being the most common prenatal abnormality, their genetic basis has not been fully understood. The purpose of our study is to investigate the genetic etiology in children with CAKUT especially with unilateral renal agenesis, multicystic dysplastic kidney (MCDK), renal hypodysplasia, horseshoe kidney, and children with ectopic kidney monitored at the Pediatric Outpatient Nephrology Clinic of our hospital.

Methods: 47 individuals were included in our study. Peripheral blood samples were collected, DNA was extracted, and analysis of the coding regions of the genome (Whole Exome Sequencing-WES) was performed using Next Generation Sequencing (NGS). Exome capture was carried out using xGen Exome Research Panel v2 (Integrated DNA Technologies, Coralville, Iowa, USA,) followed by sequencing on the NovaSeq 6000 platform (Illumina, San Diego, CA, USA) performed by the company 3 billion.

Results: Pathogenic/Likely pathogenic variants were identified in 6 out of 47 patients with CAKUT. In a female patient with horseshoe kidney, Turner syndrome was detected, which was confirmed by karyotype analysis. The genes in which nucleotide variants were identified are shown in the table below.

Gender	CAKUT	Gene	Variation	Associated syndromes/ diseases or CAKUT according to the literature
Female	MCKD	BBS1	Heterozygosity	Bardet-Biedl Syndrome (autosomal recessive inheritance) Renal agenesis, Horseshoe kidney
Male	MCDK	PKHD1	Heterozygosity	Autosomal recessive polycystic kidney disease
Male	Renal hypodysplasia	XPNPEP3	Heterozygosity	Nephronophthisis (autosomal recessive disease)
Male	Solitary kidney	GREB1L	Heterozygosity	Renal agenesis, renal hypoplasia
Female	MCDK	KCTD1	Heterozygosity	Scalp-ear-nipple Syndrome (autosomal dominant inheritance) Renal hypoplasia

Conclusions: In our study, no variants were found in the most common genes associated with CAKUT. Further studies are required to confirm whether the variants found in heterozygosity in our patients are related to them, taking into account that according to the literature, these variants in homozygosity are associated with syndromic conditions.

646 - P1.002

KIDNEY FUNCTION AND APPEARANCE OF URINARY TRACK IN ULTRASOUND AND VCUG IN CHILDREN WITH MMC AT INITIAL EVALUATION

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Aims/Purpose: It is believed that children with MMC are born without kidney abnormalities which appears later on in course of neurogenic bladder. Recent studies shows that up to 60% of children with neurogenic bladder develops some degree of chronic kidney disease at the time of transition to adult care. Baseline evaluation of kidney function and appearance in ultrasoud and VCUG may reveal children at risk.

Methods: Among 101 children born in our centre between 2004 and 2022 with MMC 60 had available data of kidney function, ultrasound examination and VCUG within first 3 months of life. Kidney function were evaluation according to creatinine level. During ultrasound examination significant hydronephrosis and bladder wall appearance were evaluated. Evaluation of VUR was done during VCUG study.

Results: Among 60 children MMC was diagnosed prenatally in 30 cases and 6 of them had performed prenatal closure of the congenital malformation. All of children have introduced CIC since birth. Only one child have increased level of creatinine comparing to normal ranges for the age. 16 (26%) children have significant hydronephrosis at least of one kidney, and bladder wall thickness was observed in 17 (28%). VUR was diagnosed in 14 (23%) cases.

Conclusion: Approximately 25% of children with neurogenic bladder due to MMC have significant abnormalities in ultrasound and/or VCUG at the initial evaluation during the first 3 months of life. This children may have increased risk of chronic kidney disease development and need to be treated proactively.

77 - P1.003

THE COMPARISON OF CLINICAL OUTCOMES OF UNILATERAL ATROPHIC / HYPOPLASTIC / NEPHRECTOMIZED AND SOLITARY KIDNEY

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Aim: The congenital anomalies of the kidney and urinary tract (CAKUT) are the most common findings in the pediatric age group with congenital malformations. The aim of this study is to evaluate clinical characteristics and follow-up results of children with unilateral solitary kidney (SK) / hypoplasia/ atrophy and nephrectomized kidney.

Methods: We retrospectively reviewed the medical records regarding the demographic data, laboratory findings, imaging results and clinical course of patients with unilateral atrophic/hypoplastic/SK and nephrectomized kidney who presented to pediatric nephrology clinic between January 2010 and January 2023

Results: Eighty-nine patients were included in the study (M/F = 52/37). Forty-two (47.2%) patients had SK, 29 (32.6%) patients had atrophy, 6 (6.7%) patients had hypoplasia, and 12 (13.5%) patients had undergone nephrectomy. At the last examination, hypertension was present in a total of 8 patients (9%). While 16.7% of nephrectomized patients had hypertension, 11.9% of the SK patients had hypertension. Proteinuria was detected in 15 (16.9%) patients at the last follow-up visit. The patient group with the most frequent proteinuria was the nephrectomized patients (33.3%). The 4 groups exhibited notable variations in terms of serum creatinine and phosphorus levels. This difference was due to a higher creatinine level (p =0.004) and a lower phosphorus level (p =0.027) in the nephrectomized patient group compared to the SK group.

Conclusions: Since there are relatively high rates of proteinuria, hypertension and increased creatinin in nephrectomy patients, they should be closely monitored. The follow-up of children with a single kidney requires long-term and vigilant monitoring, actively investigating conditions such as proteinuria and hypertension. Besides an echocardiographic examination should be done especially in patients with unilateral kidney agenesis .

233 - P1.004

CHANGES IN ETIOLOGIC AGENTS AND ESCHERICHIA COLI SENSITIVITY TO ANTIBACTERIAL TREATMENT IN ACUTE PYELONEPHRITIS: 2010-2011 VS 2020-2021 AT LITHUANIAN UNIVERSITY OF HEALTH SCIENCES KAUNAS CLINICS DEPARTMENT OF CHILDREN DISEASES

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Aim: To evaluate the etiologic agents of acute pyelonephritis, their sensitivity to antibacterial treatment, and to assess changes in E. coli sensitivity to antibiotics.

Methods: This retrospective study involved collecting medical history data from children diagnosed with acute pyelonephritis and treated at the LUHS Kaunas Clinics Department of Children's Diseases in 2020–2021 (n = 270). The collected data were compared with those from 2010 – 2011, as published in the study by Atkočiūnas and co-authors titled "Acute pyelonephritis in children: etiology and antibiotic susceptibility". Statistical analysis was conducted using the "IBM SPSS Statistics" program, employing the 2 criterion, Mann-Whitney test, and Score test. Results were deemed statistically significant if $p < 0.05$.

Results: In 2020–2021, 270 patients were diagnosed with acute pyelonephritis at LUHS Kaunas Clinics Department of Children diseases. Urine cultures were collected from 266 subjects, with significant positive results in 204 cases. Among these, E. coli was detected in 83.3 % and E. faecalis in 6.9 % of cases. The sensitivity of E. coli to antibiotics varied: ampicillin (50.3 %), cefuroxime (95.2 %), ciprofloxacin (94.6 %), gentamicin (95.8 %), nitrofurantoin (98.2 %), trimethoprim (79.6 %). E. faecalis showed 100 % sensitivity to ampicillin and nitrofurantoin. Additionally, in 2020–2021, E. faecalis was significantly more prevalent than in 2010–2011 ($p < 0.001$). In 2020–2021, the sensitivity of E. coli to cefuroxime in urine cultures significantly decreased compared to 2010–2011 ($p < 0.001$).

Conclusion: Most cases of acute pyelonephritis were caused by E. coli, which exhibited high sensitivity to nitrofurantoin, gentamicin, and cefuroxime. Over the decade, the incidence of acute pyelonephritis caused by E. faecalis increased, and the sensitivity of E. coli to cefuroxime decreased.

274 - P1.005

CLINICAL UTILITY OF VOIDING CYSTEOURETHROGRAM FOLLOWING KIDNEY ABCESS IN CHILDREN

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Aims/Purpose: This study investigates the clinical utility of voiding cystourethrogram (VCUG) in diagnosing vesicoureteral reflux (VUR) following a first presentation of kidney abscess in children.

Methods: A single-center retrospective analysis of 17 children (< 18 years) with a first kidney abscess diagnosed between 2011 and 2022 underwent VCUG, as standard of care. Demographic, clinical and laboratory information was collected, alongside imaging (including DMSA scan) and follow-up data. VUR grading followed European Association of Urology guidelines.

Results: VUR was identified in 29% (5/17) of children, similar to reported rates in first febrile UTI cases. High-grade VUR (grades IV-V) was present in 2 children. VCUG did not significantly influence surgical decisions, primarily based on recurrent pyelonephritis and kidney scarring. However, VCUG findings guided antibiotic prophylaxis according to current recommendations. All abscesses resolved with conservative treatment (intravenous and oral antibiotics), and no percutaneous drainage was needed. All children had normal kidney function at 36 months of follow-up.

Conclusion: Following a kidney abcess, VCUG identified VUR at similar rates to uncomplicated UTIs. Even if VCUG outcomes did not impact surgical decisions, nonetheless, they informed antibiotic prophylaxis duration. Further research is needed to validate these findings at a large scale and inform future VCUG recommendations for children with kidney abscess.

289 - P1.006

IMPLICATIONS OF PRIMARY "OCCULT" VESICO-URETERAL REFLUX IN MALE CHILDREN

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Aims/Purpose: The gold standard for diagnosing vesico-ureteral reflux (VUR) is voiding cystourethrography (VCUG). This imaging technique allows an accurate VUR grading and detection of urethral abnormalities in male patients. However, VCUG exposes children to a significant radiation dose, and in up to 50% of the cases, VUR can be missed on VCUG ("occult" VUR) while detected by isotopic cystography (IC). Taking advantage of an approach that is no longer suitable, as it exposes to an increased radiation load, we retrospectively analysed the data deriving from a period when, in male patients, we first performed VCUG and –if negative– IC in the same session and exploiting the same catheter. We hypothesized that patients with occult VUR exhibit similar outcomes compared to those with VCUG-detected VUR. Thus, our aim was to compare the clinical characteristics and outcomes of VUR detected solely on IC ("occult" VUR) with VCUG-detected VUR.

Methods: Between 2015–2020, we retrospectively enrolled all male children firstly undergoing VCUG and, if negative, IC in the same session. Kidney injury (KI) was defined by abnormal estimated glomerular filtration rate and/or blood pressure and/or proteinuria.

Results: We enrolled 421males with median age = 3months and follow-up =5.3years. None exhibited KI initially, but 10% of those with VUR developed KI during follow-up. 222patients (52.7%) didn't show VUR, 152(36.1%) had VCUG-diagnosed VUR, and 47(11.2%) occult VUR. Therefore, 47/199patients (23.6%) with VUR had occult VUR. Among these, 34/47(72.3%) had dilated VUR and 22/47(46.8%) exhibited split renal function < 45% and/or scar (scintigraphic damage). Compared to patients with occult VUR, those with VCUG-diagnosed VUR showed similar prevalence of febrile urinary tract infection(fUTI) before and after VUR diagnostics and KI at last follow-up, but a higher prevalence of dilated VUR, of scintigraphic damage, and underwent surgery more frequently. At multiple logistic regression analysis, patients with VCUG-diagnosed VUR presented increased risk of fUTI either before or after VUR diagnosis and of KI while patients with occult VUR presented increased risk of fUTI before (and among patients with dilated VUR also after) VUR diagnosis and of KI.

Conclusion: Occult VUR affects 23.6% of male children with VUR with a non-negligible risk of VUR-associated KI and fUTI. IC could select, among males with recurrent fUTIs and negative VCUG, those requiring surgery for a possible dilated occult VUR.

329 - P1.007

AN UNEXPECTED CAUSE OF KIDNEY FAILURE AFTER HEMOLYTIC UREMIC SYNDROME

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Aims/Purpose: Typical hemolytic uremic syndrome (HUS) is characterized by non-immune microangiopathic hemolytic anemia, thrombocytopenia and acute kidney injury. Depending on the disease itself and the intensive treatment process, some complications may occur. Among the iatrogenic complications, urethral injuries and associated urethral strictures may be seen.

Methods: Here, we report a child who was successfully discharged after treatment of typical HUS but developed urethral stricture and kidney failure as a result of possible urethral catheterization.

Results: A 9-year-old boy who was diagnosed and treated with typical HUS upon the growth of Shiga-toxin-producing E.coli (STEC) in bloody diarrhea in another center 6 years ago was admitted to our hospital due to serum creatinine elevation. His serum creatinine and proteinuria levels gradually increased during 6 years of follow-up with normal complement levels (Figure 1). It was learned that the patient urinated with straining after HUS treatment and could not urinate by squirting. He was evaluated by the pediatric urology department with this complaint 1.5 years ago when his serum creatinine was 2.09 mg/dL. Urinary USG revealed dilatation in the bilateral collecting system, increased bladder wall thickness and excessive residual urine of 285 ml. Cystoscopy was planned but the patient was lost to follow-up. Current USG showed thinning of renal parenchyma thickness and increased echogenicity, and dilatation of the collecting systems. The bladder had a globular appearance. There was 450 mL of urine in the full bladder and its wall was thick and trabecular. The prostatic urethra appeared dilated. After micturition, the bladder wall thickness was 8 mm and 270 mL of residual urine remained. The patient voided 201 ml with a maximum voiding rate of 6 ml/sec in a plateau. Anterior urethral stricture (AUS) was considered due to increased bladder capacity, significant residual urine and voiding consistent with infravesical obstruction. Cystoscopy showed bird's eye stenosis and type 3 valvular structure in the bulbous urethra. The valve was resected and internal urethrotomy was performed. However, despite supportive treatment, the patient's kidney functions continued to deteriorate, and the estimated glomerular filtration rate decreased to 18.8 ml/min/1.73m2 in approximately 3 months. The patient was informed about kidney replacement therapy.

Conclusion: The only cause of increased serum creatinine in a patient with a history of HUS that may progress to end-stage kidney disease may not be due to the previous disease and that a simple anamnesis such as questioning the voiding pattern may reveal that the cause of kidney injury may be due to a cause other than HUS.

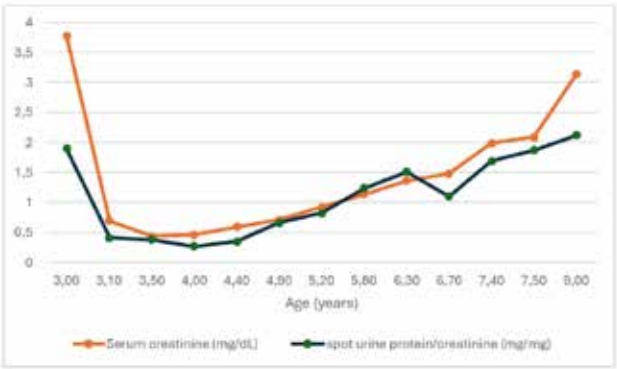

Figure 1. Serum creatinine and proteinuria levels of the patient during 6 years of follow-up

334 - P1.008

ANALYSIS OF THE INCIDENCE OF VESICOURETERAL REFLUX IN INFANTS REFERRED FOR VOIDING URETEROCYSTOGRAPHY WITH AN ASSESSMENT OF THE USEFULNESS OF CLINICAL DATA AND SELECTED PROTEIN MARKERS IN PREDICTION OF THE MALFORMATION

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Aims/Purpose:B Voiding ureterocystography (VUCG) is a test recommended for diagnosing vesicoureteral reflux (VUR). Due to the invasive nature of the test, the decision to perform it should be based on good data. The aim of the study was to analyse the incidence of VUR in infants referred to VCUG and to assess the usefulness of clinical data and selected protein markers in predicting the defect.

Methods: The study included 98 infants referred to VCUG (M = 58) after an episode of UTI. History data, ultrasound examination results and urine concentrations of albumin (albumin/creatinine ratio, ACR), NGAL (lipocalin associated with neutrophil gelatinase), TIMP1 (tissue inhibitor of protease 1) were analyzed. A multivariate logistic regression model with 10-fold cross-validation was used to create the VUR prediction model.

Results: VCUG was performed in 53% of children after the first episode of UTI. In 80% of cases, the course of UTI was febrile, in 84% the infections had a typical aetiology, and in 14% they were septic. VUR was diagnosed in 29 (30%) patients. The risk of VUR was higher in children with recurrent UTIs (OR 2.7, p =0.03), repeatedly hospitalized due to UTIs (OR 4.1, p =0.001), and with febrile UTIs (OR 3.0, p =0.0006). Detection of dilatations on ultrasound alone (in 50% of patients) had low sensitivity (64%) and specificity (45%) for confirming the defect. Only dilatation of the ureters increased the risk of VUR (OR 4.6, p =0.04). Of the biochemical markers, only ACR was associated with the presence of VUR (OR 1.5, p =0.01). The presence of ultrasound dilatation, other congenital anomalies, number of hospitalizations, number of febrile UTIs, and albuminuria testing were included in a multivariable model adjusted for sex and age. After 10-fold cross-validation, the model had high sensitivity (81%) and specificity (76%) (AUC 0.82, 95%CI: 0.721 - 0.922).

Conclusion: Confirmation of VUR in less than 1/3 of cases indicates the need to develop more effective defect prediction tools. The results of the study suggest that the prediction of VUR can be based on the history of recurrent febrile infections, the presence of ureteral dilatation on ultrasound and the ACR result in urine.

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394 - P1.009

THE FREQUENCY AND RISK FACTORS OF URINARY TRACT INFECTIONS IN THE NEONATAL PERIOD

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Aims/Purpose: The studies on neonatal urinary tract infection (UTI) are insufficient in the literature.In this study,we planned to retrospectively investigate the frequency,demographic characteristics,comorbid conditions,risk factors,laboratory and imaging findings of UTIs in neonatal intensive care unit (NICU). In addition, as a secondary aim,we aimed to determine the bacteriological profile and antibiotic susceptibilities of bacteria isolated from urine culture.

Methods: In this study, 4117 patients hospitalised in Marmara University NICU between 1 January 2014 and 12 September 2023 were screened and 183 neonates who were followed up and treated for UTI were retrospectively studied.Term and preterm infants were included in the study.Patients whose urine culture was obtained with a sterile urinary catheter were included.

Results: The incidence of neonatal UTI was 4.44%. 66.1% of the patients were male. 67.2% of the patients were born by caesarean section. 47.5% of the patients were preterm and 87.9% had nosocomial UTI. Hyperbilirubinaemia was present in 74.3% of the patients. The mothers of 35.5% of the patients had a history of UTI during pregnancy. The most common symptom/finding at the time of diagnosis was jaundice (47.2%). Sepsis clinic was present in 15.8% of the patients at the time of diagnosis. Pyuria was present in less than 1/3 of the patients and nitrite positivity was present in approximately 1/10 of the patients. Urinary anomaly was found in only 15.8% of the patients by urinary ultrasonography (USG). The most common anomaly was pelvicaliectasis. Of the pathogens isolated from urine, 76.5% were gram (-), 20.8% were gram (+) and 2.7% were fungi. The most frequently isolated pathogens were Klebsiella pneumoniae (28.5%), Escherichia coli (21.9%) and Enterococcus faecalis (17%). In the whole cohort, ampicillin resistance was 69.3% and gentamicin resistance was 24.8%. Among 168 patients whose susceptibility to ampicillin and/or gentamicin was studied, the rate of those who were not susceptible to at least one of ampicillin and gentamicin was 22%. Cefixime resistance was 74.6% and resistance rates to other cephalosporins were similar. Nitrofurantoin resistance was 28% and trimethoprim-sulfamethoxazole (TMP-SMX) resistance was 16.5%. The resistance rates of Escherichia coli to ampicillin, nitrofurantoin and piperacillin-tazobactam were statistically lower than those of Klebsiella pneumoniae.

Conclusion: UTI should be kept in mind in the etiology of neonatal jaundice. In the prenatal history, UTI in the mother during pregnancy should be questioned. Urinary USG should be performed in neonatal UTI in terms of underlying urinary pathologies. Each centre should determine antibiotic resistance rates at certain intervals and identify new combinations in empirical treatment in the light of these results.

431 - P1.010

DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING IN THE IDENTIFICATION OF RENAL PARENCHYMAL INVOLVEMENT DURING A FIRST EPISODE OF FEBRILE URINARY TRACT INFECTION IN CHILDREN AGED 0-5 YEARS

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Aims: To describe the diagnostic performance of diffusion-weighted Magnetic Resonance (DW-MRI) and the inter-reader agreement between two expert radiologists in identifying pyelonephritic foci during a first episode of febrile urinary tract infection (fUTI) in children between 0 and 5 years of age. To establish the correlation between clinical data and the results of DW-MRI examination.

Methods: Children in the age group between 0 and 5 years with a first episode of fUTI were enrolled and underwent a DW-MRI and Ultrasound (US) within 72 hours of admission. Inter-observer agreement between two expert radiologists in the evaluation of DW-MRI was assessed using Cohen's kappa. Clinical and laboratory data were statistically correlated with DW-MRI results.

Results: 84 children were enrolled (40 male, 44 female), mean age of 7.3 + 6.2 months. In 13.1% of patients vesicoureteral reflux was found. DW-MRI revealed pyelonephritis in 78/84 cases (92.9%), with multiple foci in 73/78 (93.6%). We found a "substantial" concordance between two expert radiologists (k 0.725; observed agreement 95.2%). Kidney US was positive for pyelonephritis in 36/78 (46.2%). The only clinical and laboratory parameters significantly higher in patients with positive DW-MRI were white blood cell (WBC)(p =0.04) and lymphocyte (p =0.01) count. Mean values of C-Reactive-Protein, Procalcitonin and neutrophil WBC count were higher in patients with positive DWI even if the difference was not statistical significant (7.72 mg/dL, 4.25 ng/dL and 9271/µL, respectively).

Conclusions: DW-MRI showed a very high diagnostic performance in identifying pyelonephritic foci. The inter-reader agreement among expert radiologists was substantial, supporting the reliability of the technique. A poor correlation was found between laboratory parameters and the MRI results; these findings could be due to the low negative DW-MRI rate.

461 - P1.011

SPONTANEOUS RENAL PELVIS PERFORATION IN A SINGLE KIDNEY PATIENT

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Introduction: Spontaneous perforation of the renal pelvis and extravasation of urine into the perinephric space is an extremely rare condition in childhood. It is mostly related to underlying congenital urinary tract abnormality and caused by urolithiasis or infection in the setting of urinary obstruction. Here, we report a 14-year-old case with acute kidney injury (AKI) due to spontaneous renal pelvis perforation of a solitary kidney.

Case: A 14-year-old girl was admitted to a local hospital with the complaints of abdominal pain and vomiting for 3 days and anuria for 1 day. Her past medical history was unremarkable. She was referred to our hospital due to acute kidney injury (creatinine: 8 mg/dl and K: 7 mEq/L). Physical examination revealed weak and pale appearence, abdominal tenderness and growth retardation. Laboratory tests showed Hb: 9.3 g/dl, MCV: 75fl, leukocyte count: 2070 x106/L, BUN: 195 mg/dl, creatinine: 8.5 mg/dl, K: 7mmol/L, CRP: > 350 mg/L. Hemodialysis was commenced. Imaging studies revealed grade 4 hydronephrosis and parenchymal thinning in the right solitary kidney, and perforation in the anteromedial renal pelvis. A dense (seems to be purulent) collection in the perirenal area, extending to the pelvis along the retroperitoeal region, was detected. Appropriate antibiotic therapy was started. The patient was consulted to pediatric urology, a DJ stent was inserted and retrograde pyelography showed no stenosis in the ureteropelvic junction. After the procedure, the patient started to urinate and urinalysis showed pyuria, but the urine culture was negative. Her kidney functions gradually improved and hemodialysis was terminated. Due to persistent fever retroperitoneal abscess drainage was performed, cultures for tuberculosis and possible factors were found to be negative. After antibiotic revision and abscess drainage, her fever returned to normal, general condition improved, and she started to feed. Patient's creatinine gradually decreased to 1.6 mg/dl within a month. AKI was considered on the basis of chronic kidney disease (CKD) due to elevated PTH levels and growth retardation. A percutaneous nephrostomy was placed due to recurrent double J stent occlusion and urine leakage from the perforated pelvis. After successful nephrostomy procedure, hydronephrosis improved and she was discharged from the hospital. In the 3rd month of follow-up, the nephrostomy catheter became dislodged spontaneously, perforated area was not seen on urinary US, and there was no urine extravasation into the retroperitoneal area. The patient is currently being followed up in our clinic with a diagnosis of stage 4 CKD.

Discussion: Spontaneous renal pelvis perforation is a very rare and serious clinical condition during childhood period. Spontaneous recovery can occur during follow-up.

510 - P1.012

PHENOTYPIC AND GENOTYPIC SPECTRUM OF FAMILIAL CASES WITH CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT (CAKUT)

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Aims/Purpose: Evidence suggests that many cases of CAKUT have a monogenetic origin. However, in only approximately 16% of affected individuals, a monogenic cause can be identified so far. To further identify monogenic causes and to delineate the phenotypic spectrum, a European registry for familial CAKUT cases was created (EURECA; https://www.eurecakut.org). This study aims to evaluate phenotypes and genotypes found in this cohort to expand the phenotypic and genetic spectrum.

Methods: 111 individuals with CAKUT, as well as affected family members, were collected according to their medical history. Information was gathered, including origin, family, pregnancy and prenatal abnormalities, laboratory values, renal and extrarenal manifestations, therapies, and genetic test results.

Results: Among the affected individuals n = 111, frequent shared phenotypic features were hydronephrosis n = 33, vesicoureteral reflux n = 22, kidney dysplasia n = 21, multicystic dysplastic kidney n = 20, hydroureter n = 16, kidney hypoplasia n = 7, bifid ureter n = 7, uteropelvic junction obstruction n = 7, unilateral kidney agenesis n = 6, and bilateral renal agenesis n = 1. Out of 38 genetically tested individuals in 23 (61%) disease-causing (pathogenic and likely pathogenic) variants could be identified, but most frequently, disease-causing variants in SALL1 n = 3, HNF1B n = 3, FREM3 n = 2, and PAX2 n = 2 were reported. For individuals with a SALL1 variant, shared anomalies were kidney dysplasia, hearing loss, dysplastic ears, and increased renal echogenicity compatible with Townes-Brocks syndrome. Individuals with an HNF1B variant showed MODY diabetes and kidney dysplasia as shared features. FREM3 variant-affected individuals had renal insufficiency and epilepsy. Individuals with a disease-causing variant in PAX2 showed bilateral kidney dysplasia as a shared renal phenotype.

Conclusion: Compared to the literature in the entire CAKUT cohort, a monogenic cause seems significantly more common in familial cases. This suggests that familial CAKUT cases should be investigated using molecular genetics. There is clear genetic heterogeneity within the familial cases, but HNF1B does not seem to play the major role compared to single cases.

518 - P1.013

PEDIATRIC URINARY TRACT INFECTION PATHOGENS AND ANTIBIOTIC RESISTANCE RATES

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[1]Marmara University, Pediatrics, Istanbul, Turkey, [2]Marmara University, Pediatric Nephrology, Istanbul, Turkey

Aims/Purpose: This study aims to determine the demographic, clinical, laboratory, and imaging findings of children presenting to our clinic due to urinary tract infections (UTI), identify the most common uropathogens, determine current antibiotic resistance rates, and identify antimicrobials that can be used in prophylaxis and treatment based on these data.

Methods: A total of 520 patients diagnosed with UTI aged 0-18 years who presented to the pediatric nephrology outpatient clinic of Marmara University Pendik Training and Research Hospital between January 01, 2015 and December 31, 2023 were evaluated in this study.

Results: A total of 692 UTI attacks and 713 microorganism growths were included in the study of 520 patients diagnosed with UTI. 72.3% of the patients were female. The median age at presentation was 72 months. The most common accompanying comorbidity was spina bifida (19.2%). The most commonly detected urogenital anomalies were vesicoureteral reflux (30.8%), neurogenic bladder (24%), and voiding dysfunction (13.1%), respectively. 82.5% of the patients had cystitis, 17.5% had pyelonephritis; 81.9% of the attacks were recurrent UTI. The most commonly encountered gram-negative pathogens were E.coli (61.9%), K.pneumoniae (17.7%) and P.mirabilis (4.5%); the most common gram-positive pathogen was Enterococcus faecalis (6.6%). In our study, ampicillin resistance was 77.2%, amoxicillin-clavulanate 57.5%. Resistance rates of frequently used cephalosporins were cefixime 43.2%, cefuroxime axetil 51.7%, ceftriaxone 40.4%, and cefepime 7.5%. TMP-SMX resistance rate was 51%, nitrofurantoin 23.2%, ciprofloxacin 33.9%, amikacin 17%, gentamicin 21.8%. The lowest resistance rate was shown in the carbapenem group (meropenem 1.5%, ertapenem 1.7%). 45.1% of gram-negative uropathogens (297/658) had multidrug resistance (producing bacteria with ESBL, AmpC, carbapenemases). VUR was detected in 37.8% of patients by VCUG; renal parenchymal scarring was detected in 47.9% of patients by DMSA scintigraphy. At the last follow-up, proteinuria was found in 5% of patients, hypertension in 5%. Only 0.8% of patients had an glomerular filtration rate below 90mL/min/1.73m^2 at the last follow-up.

Conclusion: In recent years, antibiotic resistance is increasing worldwide due to unnecessary and inappropriate antibiotic use, becoming a significant public health issue. Similarly, in our study, it is observed that pathogens with multidrug resistance are rapidly increasing, and there is a frightening rise in antibiotic resistance rates. Each country, city, and even each unit should review its resistance profile at certain intervals due to varying antibiotic resistance rates, determine current resistance rates, and minimize possible treatment failures by reviewing empiric treatment options.

592 - P1.014

SINGLE CENTRE EXPERIENCE: RETROSPECTIVE EVALUATION OF PATIENTS WITH MULTICYSTIC DISPLASTIC KIDNEY ANOMALY

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Objective: Multicystic dysplastic kidney is the most common cystic renal anomaly with an incidence of 1/4300 live births. The aim of this study was to evaluate the clinical, demographic, laboratory and radiologic characteristics of patients with multicystic dysplastic kidney anomaly.

Method: The data of the patients who were followed up in the Pediatric Nephrology Outpatient Clinic with the diagnosis of multicystic dysplastic renal anomaly were retrospectively analyzed.

Results: Our study included 120 patients. Of the patients, 51.7% were male. Follow-up period was 53.45 ± 44.9 months, median 38 months. Multicystic dysplastic kidney was found equally on the right and left sides. Antenatal diagnosis was made in 84.3% (n = 86) of the patients. Voiding cystogram was performed in 37 patients (30.8%), vesicoureteral reflux was detected in only three patients (2.5%) and was low grade. Five patients (4.1%) had additional congenital urinary anomalies. Extrarenal malformation was detected in 14 (11.6%) patients. Compensatrix hypertrophy was 75.5%. Five of the patients (4.1%) had undergone nephrectomy. Chronic kidney disease (stage 2), hypertension and proteinuria were found in 8.3%, 1.6% and 0.83%, respectively.

Conclusion: Multicystic dysplastic kidney usually has a good prognosis; renal function depends on the function of the contralateral kidney. It should be monitored for compensatory hypertrophy, hypertension and proteinuria in the long term.

669 - P1.015

PHENOTYPIC DESCRIPTION OF NEPHROUROLOGICAL INVOLVEMENT IN GENETIC COPY NUMBER VARIATION (CNV) ANOMALIES

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Aims: Congenital nephrouropathies affect approximately 6 out of every 1000 pregnancies, constituting the most common cause of pediatric chronic kidney disease (CKD). 20% of cases are attributable to genetic variants, one-third of which are Copy Number Variations (CNVs), with microdeletions at 22q11.2 and 17q12 being the most prevalent. This study aims to describe the nephrourological phenotype in CNVs.

Methods: A multicenter descriptive observational cross-sectional study was conducted. Clinical records of pediatric patients diagnosed with CNVs enrolled in the Rare Diseases Registry of our Autonomous Community were reviewed. Anthropometric and clinical variables related to nephrourological and extrarenal involvement, as well as data on genetic studies, were collected.

Results: A total of 175 patients aged 0-16 years, with a mean age of 9 years (± 4.3 SD), were included, comprising 55% males and 45% females. Seventy percent (123) had at least one renal ultrasound performed, with 70.7% (87) showing normal results and 29% (36) exhibiting some form of nephrouropathy. Renal dysplasia/hypoplasia (16/36, 44%) and urinary tract dilatations (12/36, 33%) were the most common findings. Thirty-six percent of those with nephrouropathy were diagnosed prenatally, 11% in the neonatal period, and 47% subsequently. The mean age at diagnosis for those diagnosed after one month was 2.5 years (± 3.5 SD). Sixty-five percent of those with nephrouropathy presented some degree of CKD (34% stage 1 with eGFR 90-120 ml/min/1.73m2, 14% stage 2, 11% stage 3-4, and 5.7% underwent kidney transplantation). Only 5% had hypertension. The most frequent chromosomal location was the long arm of chromosome 22, followed by the long arm of chromosome 17 and the short arm of chromosome 4. Of the total (175), 78% had neurological involvement (mostly some degree of developmental delay or intellectual disability), and 60% had dysmorphic facial features. These prevalences remained consistent when analyzing those with nephrourological involvement separately.

Conclusions: Nephrouropathies are a common clinical manifestation in genetic CNVs, with renal dysplasia/hypoplasia being the most frequent. A significant percentage presents some degree of CKD in pediatric age, highlighting the importance of early screening for nephrouropathies in CNV patients to implement measures that slow CKD progression.

685 - P1.016

EFFECTS OF PRE-18-WEEK VESCICOAMNIOTIC SHUNT PLACEMENT IN FETUSES WITH MEGACYSTIS > 15 MM ON POSTNATAL MORBIDITY INCLUDING LUNG/KIDNEY FUNCTION

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Aims/Purpose: At the Center for Perinatal Medicine Cologne, early vesicoamniotic shunting using the Somatex® shunt before the 18th week of gestation (eVAS) is considered in pregnant women with fetal megacystis > 15mm, as these fetuses have a very high risk of both acute postnatal respiratory problems and chronic kidney disease. Initial experiences with eVAS in our center have shown improved prognosis for mortality, kidney, and lung function, but also relevant pediatric surgical complications. In this study, the Cologne cohort of children with eVAS is characterized and compared to an in-house historic, more heterogeneous group of non-shunted children (noVAS).

Methods: We identified children born and managed at our center due to a prenatal diagnosis of megacystis/LUTO. The data collection period for eVAS was 6 years, and 18 years for noVAS. Clinical data were extracted from electronic health records and analyzed using SPSS. Parameters considered included neonatal complications and therapy, kidney disease and specifically the nadir creatinine level in the first year of life. 'General morbidity' was assessed based on hospital admissions, cumulative days of hospitalization, and the number of surgeries performed.

Results: Out of 65 children with LUTO in our center, we were able to include 39 with at least a minimum dataset for this analysis. Of these, 38 were male and 1 was female. 26 had noVAS (66.6%), and 13 had eVAS (33.3%). The median gestational age at shunt placement was 14+4 weeks of gestation. The median gestational age at birth was 36+3 weeks for noVAS and 38+2 weeks for eVAS. The nadir creatinine level was 0.66 mg/dl (IQR 0.33-2.31) for noVAS and 0.42 mg/dl (IQR 0.23-0.59) for eVAS. In the first year of life, the eVAS cohort had a median of 2 hospitalizations (IQR 1 – 5) with cumulative 25 days of hospitalization (IQR 9.5 – 44) and 2 surgeries (IQR 1 – 4.8), half of them being cystoscopies. One child required peritoneal dialysis in the first year of life despite eVAS. The underlying pathologies in our eVAS cohort were PUV (n = 4, 31%), urethral hypoplasia (n = 5, 38.5%), and complex conditions (n = 7, 54%).

Conclusions: Our data indicate that eVAS improves kidney function; however, these infants still require respiratory support and frequent surgeries. We observed that the underlying causes for fetal megacystis in our eVAS cohort are more diverse LUTOs than in our historic noVAS cohort, which predominantly consists of PUV cases. Predicting the prognosis of fetuses with megacystis > 15mm within the "window of opportunity" in the first trimester is challenging, as concomitant malformations may not be detectable at that early stage of gestation. Children with successful eVAS have a good chance to avoid kidney replacement therapy, but they remain at risk for chronic kidney disease and urological conditions.

690 - P1.017

RENOVASCULAR HYPERTENSION: A SIGNIFICANT CAUSE OF ARTERIAL HYPERTENSION IN CHILDREN

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Aims/Purpose: The aim of this text is to highlight the significance of renovascular hypertension as a rare but crucial cause of arterial hypertension in children.

Methods: The abstract presents a detailed case study of an 11-year-old boy with AH, describing his symptoms, initial evaluations, diagnostic process, and treatment. This case study serves to illustrate real-world applications of the information discussed and provides a practical example of managing pediatric arterial hypertension.

Results: An 11-year-old boy, of average musculoskeletal build, presented with episodes of headache and dizziness accompanied by tachycardia. Initial evaluations revealed elevated blood pressure values, and continuous monitoring of arterial blood pressure confirmed severe ambulatory hypertension. Renal ultrasound ruled out renal parenchymal diseases. Further evaluations excluded endocrinological causes of AH. Elevated aldosterone levels alongside increased renin were observed. Left ventricular hypertrophy was noted as a consequence of hypertension. Doppler examination of the right renal arteries showed restricted blood flow patterns with normal resistance indices, while CT angiography revealed a critical stenosis of the right renal artery, with a double left renal artery. Normal findings on brain MR angiography and immunological tests did not indicate vasculitis or changes suggestive of aneurysmal dilations or stenoses of cerebral blood vessels. Symptomatic treatment began with the initiation of antihypertensive therapy. Causative treatment was performed with percutaneous transluminal angioplasty, where balloon dilation of the main trunk of the right renal artery was conducted. Following the procedure, follow-up ABPM showed excellent control of arterial pressure with normal parameters of renal function.

Conclusion: Renovascular hypertension is a rare but important cause of AH in children that can be treated. It is estimated that approximately 1-5% of the adult population has renal artery stenosis, but this number may be higher in individuals with other risk factors for this disorder. In children, renal artery stenosis is much less common but accounts for 10% of secondary hypertension cases and less than 1% of all cases of arterial hypertension in children. Causes of renal artery stenosis in children include fibromuscular dysplasia, neurofibromatosis type 1, Williams syndrome, and Takayasu arteritis. Digital subtraction angiography is the gold standard for diagnosis, with an endovascular approach being the first choice for treatment, while a smaller number of patients require surgical intervention. Diagnosis, treatment, and monitoring of patients with this rare cause of arterial hypertension in children require a multidisciplinary approach involving pediatric nephrologists, cardiologists, neurologists, interventional radiologists, and vascular surgeons.

704 - P1.018

ANTIBIOTIC THERAPY FOR URINARY TRACT INFECTION IN CHILDREN: A FIVE-YEAR SINGLE-CENTER RETROSPECTIVE ANALYSIS OF MICROBIAL ETIOLOGY AND ANTIBIOTC RESISTANCE

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Aims/Purpose: Urinary tract infections (UTIs) are among the most common bacterial infections in children. The study aimed to analyze the etiology of UTIs in children and antimicrobial resistance of identified uropathogens, particularly in patients with congenital anomalies of kidney and urinary tract (CAKUT) and neurogenic bladder.

Methods: Medical records of 242 patients diagnosed with UTI and hospitalized in the Clinical Department of Pediatric Nephrology of Wroclaw Medical University Hospital from 2018 to 2022 were analyzed. To the final analysis, 140 patients were included (89 girls and 51 boys, mean age 5.2 years). The study group was divided into three subgroups: children with normal urinary tract (43.6%), CAKUT (44.3%), and neurogenic bladder (12.1%).

Results: The most common bacteria causing UTI were Escherichia coli (E.coli) in 64.3%, Klebsiella spp. (16.4%), Pseudomonas spp. (5.7%), and Enterobacter spp. (4.3%). The etiology significantly differed between patient's subgroups: E.coli was identified in urine cultures of 88.5% children with normal urinary tract, 45.2% children with CAKUT, and 47.1% with neurogenic bladder. In the analyzed period, the prevalence of E. coli resistant to amoxicillin/clavulanic acid varied from 16.7% in 2019 to 41.2% in 2021, while the resistance to cefuroxime increased four times (from 4.0% in 2018 to 16.7% in 2022). The analysis between patients' groups showed differences in the prevalence of E.coli strains resistant to antimicrobial agents. E.coli resistant to amoxicillin/clavulanic acid was identified in 43% of children with CAKUT, 38% with neurogenic bladder, and 26% in the group with normal urinary tract. Similarly, the rate of E.coli resistant or susceptible to increased exposure to cefuroxime was higher in patients with CAKUT and neurogenic bladder. The prevalence of E.coli resistant to trimethoprim/sulfamethoxazol was 32-38% in children with CAKUT or neurogenic bladder, and 17% in those with normal urinary tract. E.coli resistance to ciprofloxacin and nitrofurantoin was the highest among patients with neurogenic bladder.

Conclusion: A five-year observation (2018-2022) showed increasing rates of antibiotic-resistant bacteria. The empiric antibiotic therapy for UTI should be chosen according to regional antimicrobial resistance data together with individual assessment of each patient's risk factors. Our results might be of help in that scope in everyday clinical practice.

707 - P1.019

CHARACTERISTICS AND TREATMENT OF A PEADIATRIC COHORT OF PATIENTS WITH RENAL FUNGUS BALLS

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Aims/Purpose: Renal fungus balls are a rare complication of urinary tract infections with Candida albicans. The characteristics of such patients are poorly documented and the therapeutic management is not standardized. Local treatment by direct antifungal instillation via ureterostomy is a proposed strategy. The aim of this study was to describe the risk factors associated with occurrence renal fungus balls and their management.

Methods: Retrospective descriptive analysis of pediatric patients in three French pediatric hospitals, diagnosed between April 2016 and September 2023.

Results: Twelve patients with fungus balls were included, presenting with positive urinary mycology, associated with an ultrasound image compatible with the diagnosis of fungus balls. The median age at diagnosis was 58 days. All patients presented with a dilated upper urinary tract and 10/12 had urological malformations. All patients had a record of acute pyelonephritis with broad-spectrum antibiotic therapy. Four patients had bilateral infections. Candida albicans was found in all patients. A concomitant bacterial infection was found in three of them. Eight patients were treated by intrarenal instillation of caspofungin and a urine drainage by ureterostomy, combined with intravenous amphotericin B. Four patients were treated with intravenous and oral antifungal agents alone. One patient treated by instillation, required nephrectomy for persistence of the fungal infection and one developed a chronic form with renal failure. The other 10 patients recovered completely. The median time to fungus ball disappearance on ultrasound was 74 days. Two of these patients had sequelae on renal DMSA scan and altered function of the affected kidney.

Conclusion: Fungus balls are mainly diagnosed in children with obstructive urological malformations, who previously had an acute pyelonephritis and broad-spectrum antibiotics. Therapeutic management consists of urinary drainage and antifungal treatment by intra-renal instillation, and/or by general administration, resulting in a complete recovery in 80% of patients.

716 - P1.020

CLINICAL IMPLICATIONS OF MICROBIAL DIVERSITY IN URINARY TRACT INFECTIONS AMONG PEDIATRIC PACIENTS WITH RENO-URINAL ANORMALIES

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Introduction: Medical practice frequently encounters congenital anomalies, including renal-urinary malformations. Certain factors increase the risk of contracting infections caused by ESBL-producing microorganisms. These include a history of recurrent urinary tract infections, vesicoureteral reflux, young age, prior antibiotic use, particularly for long-term prevention, and the presence of Klebsiella spp.

Materials and Methods: The study aimed to identify the specific uropathogens causing the occurrence of urinary infections and compare the etiology of urinary infections in two distinct groups of patients: those with renal-urinary malformations (on the one hand) and those with an intact renal-urinary system (on the other hand). Furthermore, the study aimed to detect the presence of ESBL-producing bacteria and determine their frequency in these two groups of patients. A total of 212 urinary tract infections were diagnosed in 178 patients included in the study. The primary uropathogens responsible for causing UTIs, listed in order of occurrence, were Escherichia coli, followed by Klebsiella and Proteus. Escherichia coli ESBL was detected in 23 out of the 146 urine cultures that included E. coli, representing a prevalence of 15.75%. Imaging assessments identified a urogenital tract deformity or abnormality in 14 out of the total patients, accounting for 61% of the cases. Out of the 47 cases of positive urine cultures for Klebsiella spp., Klebsiella ESBL was found in 14 cases (29.78%), a higher incidence compared to E. coli ESBL. Renal-urinary anomalies have been identified in 9 out of the total individuals, accounting for 64.28% of the sample. A higher incidence of extended-spectrum beta-lactamase-producing strains is observed in those with renal-urinary malformative substrates.

Results/Conclusions: Multidrug-resistant uropathogens for first-line antibiotic treatment are increasing dynamically. Recurrent UTIs with ESBL or MDR bacteria were more common in patients with renal-urinary abnormalities. The prevalence of ESBL-producing E. coli and Klebsiella spp. infections is steadily rising in the population.

Key words: urinary malformations, urinary infection, antibiotic resistance, BLSE.

735 - P1.021

RENAL ABSCESS: A CASE REPORT

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Introduction: Renal abscess is a rare condition in children. Patients may present with non-specific symptoms such as fever, abdominal pain or vomiting. The most common pathogens are gram-negative bacterias. Risk factors include diabetes mellitus, vesicoureteral reflux and nephrolithiasis (1). In abscesses smaller than 4 cm, antibiotic treatment should be administered primarily, whereas surgical intervention may be required if it is resistant to appropriate treatment (2).

Case: A 3-year-old girl presented with fever dysuria, frequent urination, abdominal pain and vomiting. She had a history of recurrent febrile convulsions. Family history was unremarkable. Physical examination was normal except the tenderness in the right costavertabral region. Blood pressure was 100/60 mmHg. Laboratory results revealed normal serum creatinine levels (0,5 mg/dL) and slightly elevated acute phase response (CRP: 7 mg/L, ESR: 24 mg/h, leucocyte 10700/mm3). Urine and blood cultures were obtained from the patient as leucocyte esterase and nitrite reactions were found to be positive in urinalysis. Intravenous ceftriaxone was then started. Abdominal ultrasonography (USG) revealed grade 2 hydronephrosis in the right kidney. Escherichia Coli producing broad-spectrum beta lactamase was detected in the urine culture; although blood culture remained steril. Hence; the patient's antibiotic treatment was changed to ertapenem. Contrast-enhanced computed tomography performed due to resistant fever revealed a 3x2.5 cm, centrally hypodense, heterogeneous lesion (compatible with renal abscess) in the upper zone of the right kidney (Figure 1-2). On the 7th day of ertapenem treatment, the patient was evaluated by department of interventional radiology for drainage but it was stated that the size of abscess was clearly decreased. Therefore; ertapenem treatment was continued for 21 days and she was discharged with a complete clinical remission. After 1 month, no abscess was observed on USG.

Conclusion: Renal abscess is a rare and serious clinical entity. It is important to design the management with a multidisciplinary approach including interventional radiology, pediatric surgery, nephrology and infection diseases. Although surgical procedure still remains the first line therapy for visceral abscesses, complete resolution of renal abscess in children could be provided without any intervention by appropriate medical treatment with susceptible antibiotics.

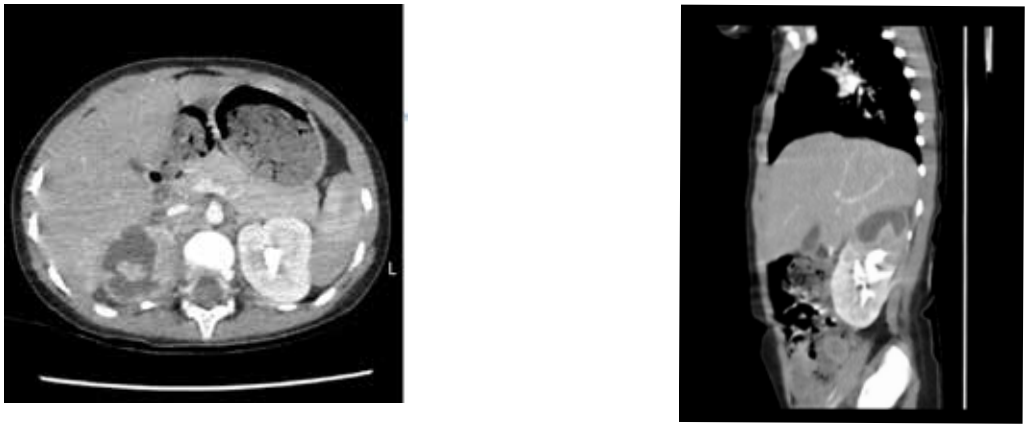

Figure1-2 Abscess image on contrast-enhanced computed tomography

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744 - P1.022

LONG TERM FOLLOW-UP OF CHILDREN WITH NEPHROCALCINOSIS: A TERTIARY CENTER EXPERIENCE

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Aims: Nephrocalcinosis (NC) is defined as calcium accumulation in kidneys and may cause important complications like chronic kidney disease. In the literature the data about long term follow-up of NC in pediatric patients is scarce. Our study aimed to investigate risk factors and analyze long term kidney functions.

Methods: This study included patients between years January 2013-January 2023 in whom nephrocalcinosis were proved in two different ultrasonograpy (USG) evaluation. The data were collected from medical records of the patients.

Results: A total of 106 patients (53 female, 53 male) were included. All patients had medullary NC (101 patients bilateral, 5 patients unilateral). None of the patients had cortical nephrocalcinosis. The median age at diagnosis was 2.4 (IQR; 0.5-5.8) years. A total of 12 patients (11.3%) had history of prematurity. NC was diagnosed mostly incidentally (60 patients, 56.6%). Following incidental diagnosis, the most patients were diagnosed after investigation of urinary tract infection (24 patients, 22.6%). The most common underlying cause was tubular diseases (28 patients, 26.4%) which was followed by inborn errors of metabolism (17 patients, 16%) and endocrinological diseases (15 patients, 14.1%). The most common risk factor was isolated hypercalciuria (27 patients, 25.5%) followed by isolated hypocitraturia (26 patients, 24.5%) and isolated hyperoxaluria (19 patients, 17.9%). The history of diuretic and D vitamin D usage was present in 9 (8.5%) and 7 (6.6%) patients, respectively. After a mean follow-up period of 5.3 ± 3,1 years, 14 patients (13.2%) had normal USG evaluation. First year after NC diagnosis, 4 patients had USG without NC and after first year, 1-2 patients had normal USG each year. Seven patients (6.6%) progressed to chronic kidney disease. And the most common underlying disease of this CKD group was familial hypomagnesemia with hypercalciuria and NC (2 patients, 28.6%). At last visit, 66 patients (62.2%) were under citrate replacement therapy. Patients without NC at last visit had lower urinary calcium and higher citrate excretion at diagnosis compared to the patients with NC at last visit.

Conclusion: Patients with NC had a very heterogenous underlying disease range and urinary calcium and citrate levels at diagnosis may predict resolution during follow-up.

764 - P1.023

RISK FACTORS EFFECTIVE IN REGRESSION OF CONGENITAL VESICOURETERAL REFLUX

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Aims/Purpose: Vesicoureteral reflux (VUR) is the most common congenital urinary system anomaly of childhood. In this study, it was aimed to determine the factors affecting reflux stage regression in patients diagnosed with congenital VUR.

Methods: This single-center, retrospective study was conducted between January 2016 and December 2021. Demographic information, age at admission, USG (ultrasonography) and VSUG (Voiding Cystourethrography) findings, number of febrile UTIs, presence of renal scarring, and prophylactic antibiotic use of 70 patients diagnosed with VUR before the age of one were evaluated.

Results: 60% of the patients were male. 51.4% had antenatal hydronephrosis and 77.7% of these patients were male, 55.7% had high-grade reflux. The history of febrile UTI was higher in girls (p =0.01). 32.9% had a unilateral scar. Spontaneous regression in the reflux phase was observed in 24.1%. 41.2% of these patients had a history of antenatal hydronephrosis. Low-grade reflux was higher in the group with spontaneous regression, and high-grade reflux was higher in the group without spontaneous regression (p =0.000). Renal scar was present in 11.8% of the group with spontaneous regression and in 39.6% of the group without regression (p =0.04). Right-sided reflux was higher in the group with spontaneous regression, and bilateral reflux was higher in the group without regression (p =0.02).

Conclusion: In conclusion; Patients with a diagnosis of VUR, to predict spontaneous regression; should be evaluated in terms of gender, reflux degree, reflux direction, presence of antenatal hydronephrosis, history of febrile UTI, presence of renal scarring.

786 - P1.024

NEONATE WITH RENAL TUBULAR DYSGENESIS AND 1Q DUPLICATION

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Aims/Purpose/Introduction: Renal tubular dysgenesis (RTD) is a rare and severe kidney disorder affecting the development of kidney tubules. It can be acquired or inherited as an autosomal recessive disorder, impacting the renin-angiotensin-aldosterone system. It's characterized by oligohydramnios in the antenatal period, leading to Potter sequence, and by postnatal kidney failure, hypotension, and respiratory insufficiency. Thus, it's associated with a poor prognosis. Herein, we present a case of neonatal RTD.

Results/Case Report: The patient was a late preterm female, the first child of non-consanguineous Brazilian parents, with no family history of kidney or cardiovascular disease and no maternal history of drug exposure. The pregnancy was complicated by oligohydramnios and fetal growth restriction noted at 31 weeks' gestation, leading to an elective caesarean section at 35 3/7 weeks. Apgar scores were 9 at 1st, 5th, and 10th minutes, and the infant somatometry was appropriate for gestational age. She presented with hypotonia and features consistent with Potter sequence. Within the first 24 hours of life, she required non-invasive ventilation due to pneumothorax and developed fluid-responsive hypotension without the need for aminergic support. She remained anuric, with no response to furosemide and intravenous fluids. Laboratory markers indicated kidney failure, with serum creatinine steadily increasing to 5.5 mg/dL, serum urea of 123 mg/dL, and refractory metabolic acidosis, and hyperkalemia. Kidney ultrasound showed increased cortical echogenicity, leading to a presumptive diagnosis of RTD. On day 2, peritoneal dialysis (PD) was initiated but was complicated by recurrent leakage, peritonitis, and bleeding. The patient developed kidney failure unresponsive to PD, with anasarca, and died on the 20th day. Karyotype analysis revealed 46,XX,dup(1)(q24.1q25.1), confirmed by array-CGH, with a duplication extending 9297Kb on the long arm of chromosome 1. Whole exome sequencing did not detect any other alterations. Kidney pathology confirmed the diagnosis of RTD.

Conclusion: We highlight this case for its rarity and the importance of including RTD in the differential diagnosis of anuria with structurally normal kidneys on ultrasound, particularly when associated with oligohydramnios. Moreover, the identification of a genetic anomaly, previously undocumented in RTD cases, raises the possibility that novel genetic alterations may contribute to the pathophysiology of this disease.

877 - P1.025

DURATION OF INTRAVENOUS ANTIOBIOTIC THÉRAPY IN NEONATES WITH UTI

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Aims: There are no precise clinical and biological data concerning the duration of IV antibiotics for urinary tract infections (UTI) in neonates less than 28 days of age. The aim of our work was to demonstrate that there is no difference in the early recurrence rate of UTI (until 30 days after the end of treatment), between newborns under 28 days of age treated with short (< 72 hours) and long (> 72 hours) IV antibiotics followed by an oral treatment of 10 days.

Methods: Retrospective study between 2019 and 2023. We included neonates less than 28 days old who had been hospitalized for UTI, with leukocytes ≥ 10,000 /mL in urine culture and ≥ 10,000 CFUs/mL of one pathogen in urine culture.

Results: 140 patients were included, 81.5% of patients were male, median age was 15.5 days, 77 patients (55%) were treated with IV antibiotics for less than 72h, vs. 63/140 (45%) more than 72h. Treatment duration was 3 days [2.7; 3] for the first group and 5 [4.1; 7] days for the second. There were no significant clinical differences at diagnosis between these two groups: presence of fever (69 vs. 69.9%), hypotonia (3.12 vs. 4.8%), heart rate > 180 bpm (9.3 vs. 17.4%), and blood PCT levels were similar at diagnosis (0.28 µg/L [0.12; 1.73] vs. 0.87 µg/L [0.19; 7.84]). All patients with bacteremia (4/140, 2.8%) were treated with long-acting IV antibiotics. Only one patient, initially treated with short IV antibiotics, was hospitalized for an early recurrence of UTI before 30 days.

Conclusion: In infants under one month of age, a 72-hour course of intravenous antibiotics followed by a 10-day course of oral antibiotics for the treatment of UTI does not appear to be associated with an increased risk of early recurrence.

908 - P1.026

AORTOMESENTERIC COMPRESSION SYNDROME ULTRASOUND BASED DIAGNOSTIC CRITERIA IN OUR UNIT

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Aims/Purpose: Nutcracker syndrome involves the entrapment of the left renal vein (LRV) between the superior mesenteric artery (SMA) and the aorta due to a decrease in the angle they form (anterior nutcracker) or due to a retroaortic or circumaortic course of the LRV, becoming compressed between the aorta and the vertebral column (posterior nutcracker). It can be asymptomatic (nutcracker phenomenon) or symptomatic, presenting with symptoms such as hematuria, proteinuria, lumbar or abdominal pain, and even periureteral or gonadal varicose veins or varicocele, indicative of nutcracker syndrome. The objective is to review the case series in our unit and its correlation with diagnostic ultrasound criteria: aortomesenteric angle, hilum diameter/SMA diameter ratio, aorta/SMA flow velocity ratio, aortomesenteric distance, and maximum velocity at the constriction.

Methods: Retrospective and descriptive study of cases diagnosed using Doppler ultrasound between January 2015 and February 2024.

Results: Thirteen patients with suggestive symptoms were studied, 7 females and 6 males, with a mean age at diagnosis of 11.92 years and a mean BMI of 19.95%. All had normal glomerular filtration and blood pressure. Hematuria was present in 38.46% at diagnosis, proteinuria in 38.46%, and lumbar or abdominal pain in 7.69%. Symptoms resolved in 53.54% of cases. Hypercalciuria or hypocitraturia was present in 15.38% of cases, potentially causing diagnostic uncertainty. All were diagnosed by Doppler ultrasound, and one underwent MRI to rule out other complications. At least three of the following ultrasound criteria were required: 30% had a pathological ratio between hilum diameter and SMA diameter, 80% had a pathological velocity flow ratio between them, 81.81% had an angle between SMA and hilum less than 25˚, 90.90% had a distance between the aorta and SMA less than 8 mm, and 60% had a maximum velocity at the constriction greater than 100 cm/s, all considered pathological values.

Conclusions: Persistent hematuria and proteinuria should raise suspicion of nutcracker syndrome. Doppler ultrasound provides a diagnosis without needing additional tests. Treatment is usually conservative in most cases.

937 - P1.027

THE USEFULNESS OF CALPROTECTIN AND YKL-40 IN URINARY TRACT INFECTIONS DIAGNOSIS IN CHILDREN UP TO 2 YEARS OF AGE

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Bacground: Urinary tract infection (UTI) is one of the most common causes of fever in children. The current diagnostic standard recommend a midstream or catheter urine sample for urinalysis and culture. Long wait for the culture result and difficulties with proper sample acquisition extend the time to diagnosis and are significant limitations of this method.

Aim: The aim of the study was to assess the usefulness of urinary calprotectin and YKL-40 in the diagnosis of febrile urinary tract infections in children up to 24 months of age.

Material and Methods: The study involved 67 children. They were divided into three groups: 1. The control group of healthy children (n = 11), 2. The group of children with diagnosed UTI (n = 20) and 3. The group of children with fever and excluded UTI (n = 36). The material for analysis consisted of the urine samples collected before starting the treatment. The calprotectin and YKL-40 concentrations in urine samples were determined using the ELISA enzyme-linked immunosorbent method.

Results: Calprotectin concentration in the group of children with UTI was 1273,35 ng/ml and was significantly higher than in the group of children with fever due to other causes - 35,42 ng/ml ($p < 0,001$), and also significantly higher than in the control group - 7,99 ng/ml ($p < 0,001$). YKL-40 concentration in the group of children with UTI was average 15542,11 pg/ml and was significantly higher than in the group of children with fever due to other causes - 138,14 pg/ml ($p < 0,0001$) and significantly higher in the group of healthy children 162 pg/ml ($p < 0,01$).

Conclusions: Both tested proteins: YKL-40 and calprotectin seem to meet the criteria of markers useful in the differential diagnosis of febrile UTIs in the youngest children.

942 - P1.028

KIDNEY ABNORMALITY AND OUTCOME OF RENAL FUNCTION IN PATIENTS WITH KABUKI SYNDROME

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Background: KABUKI syndrome (KS) is a rare autosomal dominant or X-linked syndromic genetic disease secondary to a mutation in the KMTD2 or KDM6A genes. The phenotype is heterogeneous but almost constantly combines typical facial dysmorphism, infantile hypotonia and growth and/or intellectual delay. Other organ damage may be associated (bone, heart, lung). However, renal damage in KS remains poorly understood.

Objectives: The main objective of the study is to describe the renal phenotype of KS patients and the long-term outcome of their renal function.

Methods: This is an observational, retrospective and multicenter study on 9 French university hospitals (Toulouse, Montpellier, Paris Necker, Bordeaux, Lille, Tours, Nantes, Lyon, Strasbourg). We included all patients with genetically proven KS.

Results: 78 patients were included, 90% of whom were mutated for KMTD2. 35 patients (45%) presented with nephrological (88%) and/or urological (51%) damage. 87% of renal damage was morphological abnormalities. 42% of patients presented with one or more renal cysts. Urological damage was dominated by ureteral duplications (50%). During follow-up, 65% of patients presented ≥ 1 pyelonephritis. After a median follow-up of 5 years [3-7], the GFR was 104 ml/min/1.73m2 [65-132]. At last follow-up, 33% of patients had an eGFR < 90 ml/min and 5 patients had CKD. 2 patients were at stage 5 CKD.

Conclusions: Renal and urological damage is common in KS and impact morbidity (CKD, infections). It is therefore necessary to systematically screen for uro-nephrological damage in these patients.

950 - P1.029

FAMILY HISTORY OF LITHIASIS IN THREE TYPES OF CONGENITAL ANOMALIES OF KIDNEY AND URINARY TRACT

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Aims: To demonstrate whether relatives of patients diagnosed with ureteropelvic junction obstruction (UPJO), vesicoureteral reflux (VUR) and renal agenesis have a higher frequency of urolithiasis than the ones of healthy children. To check whether the frequency of stone-causing metabolic abnormalities is high in children with UPJO or renal agenesis and in their parents.

Methods: Retrospective study in which 40 patients with renal agenesis, 47 with UPJO and 33 with VUR were included. In order to be included, patients were required to have information in their medical records on first and second generation family history of urolithiasis (FHU) and must had a renal ultrasound showing no evidence of stones. For patients diagnosed with renal agenesis and UPJO, the values of calcium/creatinine, citrate/creatinine and calcium/citrate ratios were collected, in addition to the calciuria and citraturia of their parents. A survey was carried out among the relatives of 82 healthy children who attended their regular follow-up at their respective primary care centers on the island of Tenerife.

Results: The frequency of hypercalciuria in children with renal agenesis was 25.4%; if cases with hypocitraturia and elevated calcium/citrate ratio are added, the frequency of metabolic disturbances causing urolithiasis in renal agenesis amounted to 51.7%. In children with UPJO hypercalciuria was present in 26.8% of cases at the end of follow-up; adding all stone-causing abnormalities, the frequency rose to 53.6%. The prevalence of FHU in first and second degree relatives was in a narrow range from 60% (renal agenesis) to 63.6% (VUR), being 61.7% for UPJO. The frequency of FHU in healthy children was 28.1% ($p < 0.001$). The frequency of stone-causing metabolic abnormalities determined in the parents of the patients was very high: 78.3% (UPJO) and 80% (renal agenesis). In UPJO and VUR the results were very similar in terms of FHU, being more frequent in the maternal family (72.4% in UPJO and 71.4% in VUR); also, episodes of lithiasis had been much more frequent in the mothers than in the fathers of the patients. In renal agenesis there were no such gender discrepancies.

Conclusions: Hypercalciuria in UPJO, VUR and renal agenesis may be of genetic origin. Our results raise the question of whether there is any etiological connection between lithiasis or prelithiasis and at least the three CAKUT malformations studied.

954 - P1.030

24-HOUR AMBULATORY BLOOD PRESSURE MONITORING IN A PEDIATRIC POPULATION WITH LOW NEPHRON MASS

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Aims/Purpose: Hypertension is described as the most frequent complication in low nephron mass population, although there are conflicting data on the prevalence in the pediatric population.

Methods: We conducted a retrospective study in a pediatric population with low nephron mass: 98 patients with single kidney (SK) defined as anatomical, functional, or acquired absence of one of the two kidneys and 18 patients with unilateral renal hypoplasia, with functional contribution between 5-30% on DMSA scintigraphy. Patients underwent office blood pressure measurements and 24-hour Ambulatory Blood Pressure Monitoring (ABPM). Values were compared with a healthy pediatric reference population.

Results: At both office and ABPM measurements, all blood pressure values were significantly higher in the low nephron mass population than in the healthy one, while maintaining median values in the normal range. At ABPM, nighttime blood pressure values were particularly high; a finding corroborated by the 61% of non-dipper patients. No significant differences were found between SK patients and patients with unilateral renal hypoplasia for any of the pressure variables. A significant correlation emerged between office SBP and both 24h ABPM SBP and diurnal ABPM SBP, while correlation between office DBP and 24h ABPM DBP. 9.8% of patients were found to be hypertensive at office measurement versus 22.4% found at ABPM, in both cases much higher prevalence than the healthy population (1.6-3.2%). 15% of the patients presented masked hypertension after the ABPM measurement, while 11.2% presented white coat hypertension. Moreover, we retrospective evaluated 42 pediatric patients with SK who repeated a second ABPM, without therapy or lifestyle modifications. 40% of them were found to be hypertensive at the first evaluation and only 21% after the repetition of the ABPM, including 2 patients who were normotensive at the first measurement. A significant reduction in blood pressure values was observed, with a reduction in hypertensive prevalence at repeat ABPM.

Conclusion: Our analysis showed a high prevalence of hypertension and impaired nocturnal pressure regulation in the pediatric population with reduced nephron mass. SK and unilateral renal hypoplasia presented an overlapping prevalence of hypertension, and management for this complication could be similar. ABPM could be a good method to monitor the prevalence of hypertension in the pediatric population with SK with the limitation that a single ABPM could lead to overestimation.

976 - P1.031

LATE ONSET OF POSTERIOR URETHRAL VALVES IN BOYS WITH VOIDING DISORDERS

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Background: Posterior urethral valves (PUV) is an obstructive developmental anomaly in the urethra and genitourinary system of male patients. The large majority of patients with PUV are diagnosed soon after birth or in the first year of life following investigations for an antenatally detected hydronephrosis or urinary tract infection. Rarely, the diagnosis is missed until adolescence or adulthood.

Aim: The aim of the study was to show that late-diagnosed posterior urethral valves may be the cause of voiding disorders in adolescents.

Methods: We reviewed the hospital records for patients with PUV treated in 2018-2023. Only those patients diagnosed, treated surgically, and followed clinically at our two centers were included.

Results: The study involved 21 boys with delayed diagnosis of PUV. The median age at presentation was 10 years and 3 months. 19 patients had voiding disorders manifested by enuresis, daytime incontinence, urgency and increased voiding frequency. Only two of them had recurrent urinary tract infections. All of them had urodynamic examination or micturating cystourethrogram that demonstrated bladder outlet obstruction . A urethral valve ablation was performed in all cases.

Conclusions: Physicians should consider posterior urethral valves as a cause of voiding disorders in older boys.

992 - P1.32

EVALUATION OF GRAFT SURVIVAL OF CHILDREN WITH KIDNEY TRANSPLANTATION WITH AND WITHOUT CONGENITAL KIDNEY AND URINARY SYSTEM ANOMALIES

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Aim: In the childhood age group, 51% of chronic kidney disease cases are due to congenital anomalies of the kidney and urinary system (CAKUT). This study aimed to compare the factors affecting the graft survival of kidney transplant children CAKUT and non-CAKUT and to determine the graft survival rates for both groups.

Materials and Methods: This study retrospectively examined the transplant records and patient information management system of the Izmir Tepecik Training and Research Hospital, Child Nephrology Clinic, for patients under the age of 18 who underwent kidney transplantation with and without congenital anomalies of the kidney and urinary system between the years 2002 and 2017. A comprehensive database was created by analyzing demographic, clinical, laboratory, biopsy, imaging, surgical, treatment data, and complications of these patients.

Results: 23 patients with congenital anomalies of the kidney and urinary system (CAKUT) and 20 patients without CAKUT were included. Tubulocystic diseases in the study group were more frequent as the cause of end-stage renal disease (ESRD) compared to glomerular diseases, dysplasia, posterior urethral valves (PUV), and vesicoureteral reflux (VUR). The most commonly encountered complication in both groups at one month was acute tubular necrosis (ATN). The primary causes of graft dysfunction (AGD) were infections at 67.6% and rejection at 14.5%. The AGD causes were not statistically different between the groups. The follow-up duration was longer in the group without CAKUT compared to the group with CAKUT. After the third year post-transplant, the non-CAKUT group exhibited a rapid increase in weight standard deviation score, which was statistically significant. In this study, no significant difference was observed between patient groups with and without CAKUT in terms of events during the transplant follow-up process.

Conclusion: Our study demonstrates that post-transplant infections remain a concern for both children with CAKUT and non-CAKUT. It also draws attention to the long-term risk posed by antibody-mediated rejections in both groups. Based on these findings, there is a need for new treatment regimens that reduce infections and suppress rejections to enhance graft survival.

Keywords: kidney transplantation, children, congenital anomalies of the kidney and urinary system, graft survival

1028 - P1.033

NECROTIZING PYELONEPHRITIS WITH UNKNOWN CONGENITAL DYSPLASIA AT PRESENTATION

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Aims/Purpose: Necrotizing pyelonephritis is a rare and serious infection. In adults, more than 90% of the patients have diabetes mellitus. Other predisposing factors are urinary tract obstruction and immunosuppression. There are few pediatric published cases of necrotizing pyelonephritis.

Methods: Case description of a patient case admitted to Oslo University Hospital, Norway.

Results: A 14-year-old girl with no prior medical history attended the local hospital with 4 days history of right loin pain and fever. Pyelonephritis was suspected and intravenous cefotaxime initiated. Due to clinical and biochemical worsening, she was transferred for hemodialysis. On admission, she was awake and circulatory stable; 88 beats/min, 37.5 ˚C, blood pressure 98/53 mmHg. Biochemical findings: s-creatinine 638 mol/L, s-carbamide 42 mmol/L, s-C-reactive Protein (CRP) 185 mg/L. Blood culture showed Staphylococcus aureus sensitive to clindamycin, linezolid and oxacillin. Urine culture revealed Group-B streptococcus 50.000-100.000 units/mL, and S.aureus 1000-10.000 units/mL. Ultrasound showed a swollen right kidney, 19 cm, with loss of corticomedullary differentiation, heterogeneous echogenicity, impaired perfusion and subcapsular fluid. The left kidney was small, dysplastic with hyperechoic, thin parenchyma, and loss of corticomedullary differentiation. She was diagnosed with right-sided necrotizing pyelonephritis due to S.aureus and a previously undiagnosed dysplastic left kidney. No obvious entry point for the infection was found. Cefotaxime was changed to linezolid the second day due to clinical worsening, and corticosteroid was added for three consecutive days. She received 4 sessions of hemodialysis. After 1 week with linezolid monotherapy, she had increased loin pain, relapsing fever episodes, and increasing CRP; Clindamycin was added. MRI confirmed the findings of ultrasound. PET at day 10 of treatment, showed only renal findings with scattered areas of increased cortical and subcapsular uptake suggestive of persistent inflammation hence intravenous antibiotics was continued for a total of 3 weeks. At follow up 6 weeks she was clinically well and s-creatinine 165 mol/L. Further information on the anatomical predisposition is pending radiological investigations and genetics.

Conclusion: To our knowledge, this is the first description of necrotizing pyelonephritis caused by S. aureus in a pediatric patient with the need of hemodialysis.

1031 - P1.034

THE USEFULNESS OF MAGNETIC RESONANCE UROGRAPHY IN THE DIAGNOSIS OF HYDRONEPHROSIS

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Purpose of the study: The study presents a summary of the experiences of one center in use of functional magnetic resonance urography (MRU) in the diagnosis of hydronephrosis in children.

Methods: From 03/2021 to 01/2023 there were 112 MRU examinations performed in the Magnetic Resonance Laboratory of the Upper Silesian Childrens' Health Center. In the MRU method, dynamic imaging is obtained after intravenous administration of a contrast agent (gadolinium compound). Dynamic sequences show the degree of contrast enhancing and elimination of contrast, similarly to radionuclide diagnostics. Images of the renal parenchyma, contrasting, secretion and excretion of the contrast are obtained by repeated scanning in a specific time, max 15-60 minutes. This allows to measure the split function of the kidneys (differential renal function - DRF) and the determination of excretion curves. The functional assessment in MRU is comparable to that obtained in dynamic renal scintigraphy, with additional precise anatomical assessment of the urinary system.

Results: The analyzed group included 36 boys and 23 girls. Average age was 6.18 ± 6.16 years. In 48 children (81.3% of the group) significant obstruction in urine outflow was found. In 3 cases, significant hypofunction (less than 15% DRF) of the hydronephrotic kidney was found - repair operations were abandoned, in 2 children nephrectomy was performed taking into account clinical indications. In 35 (59.3%) of children from the analyzed group, the MRU examination was the basis for qualification and performing surgical treatment.

Conclusions: 1. MRU examination is a non-invasive diagnostic method allowing for precise anatomical assessment of the defect with simultaneous functional assessment (secretion and excretion).

2. Correct qualification for MRU examination based on the clinical picture and sonography allows to resign from other, invasive methods imaging, such as classic urography, computed tomography or scintigraphy test (application of the ALARA rule).

3. MRU examination is a diagnostic tool helpful in proper qualification children with hydronephrosis for further treatment - surgery or further clinical observations without invasive procedures.

1046 - P1.035

THREE CASES WITH OHVIRA SYNDROME

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Aims/Purpose: Ohvira Syndrome. The association of obstructive hemivagina and ipsilateral renal agenesis is called OHVIRA syndrome and is extremely rare. It is a congenital anomaly of the genitourinary system. It is the result of abnormal development of the müllerian ducts around the eighth week. The double uterus may appear as didelfis, bicornuate or partial/full septate. It is characterized by unilateral cervico-vaginal obstruction (obstructed hemivagina, unilateral cervical atresia) and renal agenesis on the same side.

Methods: We aimed to present three cases with OHVIRA syndrome, two of whom were investigated for dysmenorrhea and the other one was found incidental while being followed up with a diagnosis of renal agenesis.

Results: One of the patients who was 12 years old was decided to have septum resection, the other patient who was 12 years old was operated for ovarian cyst when she presented with dysmenorrhea. 14-year-old patient had single vagen, no septum, uterus didelfis

Conclusion: Pelvic usg should be performed in female patients diagnosed with renal agenesis in terms of genital anomalies that may accompany

1104 - P1.036

URINARY TRACT INFECTIONS IN SPECIFIC CLINICAL SITUATIONS - RESULTS OF THE ESPN SURVEY

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Aims/Purpose: There are limited data on urinary tract infections (UTI) in specific clinical situations – adolescents, teenage pregnancy, diabetes, cystitis cystica, eosinophilic cystitis, kidney transplantation, oncology and immunosuppressed patients. The aim of this survey was to obtain data to what extent pediatric nephrologists are involved in the management of these categories of patients and to determine different practical approaches in the absence of guidelines and recommendations for their management.

Methods: The ESPN working group on CAKUT/UTI and bladder dysfunction endorsed a questionnaire consisting of 38 questions related to UTI in specific clinical situation. This survey was distributed to European pediatric nephrologists through the ESPN mailing list.

Results: The survey was completed by 235 European pediatric nephrologists. Treatment duration of afebrile UTI in adolescents was mostly 4-7 days (60.2%)). The most commonly used antibiotics to treat UTI were nitrofurantoin (30.2%), cephalosporins (28.5%), and sulfamethoxazole/trimethoprim (16.2%). Kidney ultrasound (39.1%) and VUR screening (53.61%) were performed by a radiologist in cases of recurrent UTIs and pyelonephritis. Only 32% of pediatric nephrologists had experience treating patients with cystitis cystica, and only 21.4% had experience with eosinophilic cystitis. Screening for asymptomatic bacteriuria (AB) in kidney transplant patients was indicated by 51.1% of nephrologists. AB treatment practice always differed (17.0%), only the first 3 months (17.0%), only the first 6 months (23.0%), or never (22.1.%). MCUG (49.4%) was a preferred method of VUR detection in kidney transplant patients. AB in pediatric oncology patients was screened for in 23.8% of nephrology practices with 32.3% in favor of treating patients. Pediatric nephrologists feel there are absent or insufficient guidelines for UTI management in specific clinical situations: adolescents (56.6%), pregnant teenagers (56.6%), eosinophilic cystitis (60.8%), diabetic children (55.7%), kidney transplant patients (43.4%), oncology patients (52.3%) and immunosuppressed (57.0%) children.

Conclusion: Pediatric nephrology clinical practice varies between countries and years of experience within Europe. The treatment guidelines on UTI in the above mentioned conditions are direly needed.

1106 - P1.037

DIFFERENCES IN AGE GROUPS AND CLINICAL MANIFESTATION OF E.COLI AND NON-E. COLI-INDUCED PEDIATRIC ACUTE PYELONEPHRITIS

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Aim: To evaluate the differences between E. Coli and Non-E. coli-induced paediatric acute pyelonephritis (APN) by analysing age groups and clinical findings.

Methods: The research method is a retrospective study. Medical history data was collected of children with APN treated at LUHS Kaunas Clinics Department of Children diseases in 2020-01-01 – 2021-12-31 (n = 270). The subjects were divided into four age groups: 28 days to 6 months, 7 months to 1 year, 2 years to 5 years, and 6 years to 17 years. Significant bacterial growth in urine was detected at > 105 colony-forming units (CFU)/ml in a mid-portion urine culture and > 104 CFU/ml in a bladder catheterization culture. Statistical analysis was performed using the "IBM SPSS Statistics" program. The 2 criterion was applied. The results were considered statistically significant if $p < 0.05$.

Results: After analysing the results of 266 urine cultures, significant bacterial growth was observed in 204 (76.7 %) cultures. E. coli was the cause of 170 (83.3 %) cases of APN. E. faecalis was identified as the second most common cause of APN. APN caused by agents other than E. coli occurred more frequently in children under 6 months of age, compared to other age groups ($p = 0.01$). Additionally, non-E. coli-induced APN was statistically more prevalent in boys (20, 58.8 %), than in girls (14, 41.2 %) ($p < 0.001$), and in cases lacking leukocyturia ($p = 0.02$). All patients with non-E. coli representatives such as E. faecium and S. agalactiae, in the urine culture were diagnosed with hydronephrosis by ultrasound examination ($p = 0.03$). It was found that in cases where causative agent was not E. coli, more changes were observed in renal ultrasound examination, although the results were not statistically significant.

Conclusion: Non-E. Coli-induced APN was more frequently observed in younger patients and those lacking leukocyturia. It was found that agents other than E. coli are associated with changes in renal ultrasound, but a statistically significant result was not achieved.

1127 - P1.038

A SURPRISING CONNECTION: RIGHT THORACIC ECTOPIC KIDNEY ALONGSIDE PULMONARY AGENESIS

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Aims/Purpose: Evaluation of rare association between right lung agenesis and kidney ectopia.

Methods: We report the case of a six-month-old female infant who presented with acute pneumonia associated with parapneumonic pleurisy and right atelectasis. Subsequent CT evaluation demonstrated agenesis of the right lung and right main bronchus, dextrocardia, and an ectopic and completely malrotated right kidney located in the right hemithorax, posterior to the cord, transdiaphragmatically herniated. Also, cardiological evaluation certified dextrocardia, the presence of patent foramen ovale with left-right sunt, and suspicion of right pulmonary artery hypoplasia. The radioisotopic study using 99Tc-DMSA confirmed the presence of renal tissue with normal function on the right lung's topography.

Results: We managed a case with multiple congenital anomalies, discovered incidentally following an acute infectious episode. Kidney ectopia is a congenital renal anomaly characterized by the kidney's presence in a different position or location. It has an incidence between 1 in 1000 and 5000 births per year. However, thoracic renal ectopy is a rare site, with approximately 200 cases reported worldwide at the moment.

Conclusion: Even though it is a rare occurrence, it shows that it is paramount to perform a thorough clinical examination in order to advance the suspicion of such a diagnosis. Using appropriate imagistic methods for a complete description, we can establish the proper management of these patients.

1137 - P1.039

CLINICAL AND RADIOLOGICAL COMPARISON OF PATIENTS WITH CONGENITAL AND ACQUIRED RENAL PARENCCHYMAL DAMAGE ASSOCIATED WITH MODERATE AND SEVERE PRIMARY VESICOURETERAL REFLUX

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Aim: To compare demographic, clinical, radiological parameters and treatments of patients with moderate (stage 3) and severe (stage 4-5) VUR who has congenital renal parenchymal damage, acquired renal parenchymal damage and has normal renal parenchymal structure (NP).

Materials and Methods: We scanned patients' files and patient information management system retrospectively for demographic, clinical, radiological parameters and treatments of children between January 2010- January 2020 and diagnosed as moderate and severe primary VUR. We include149 patients and 218 renal reflux units (RRU) with moderate and severe VUR.

Results: In this study, the congenital parenchymal injury (CPI) group had a male gender majority (%72,5) and the acquired parenchymal injury (API) group had a female gender majority (%73,8) ($p < 0.001$). Age of diagnosis were earlier in CPI group (mean age 7,75 months old) and normal parenchymal (NP) group (mean age 4 m.o.) than API group (mean age 36 m.o.) ($p < 0.001$). Patients with severe VUR seemed to get diagnosed by ANH (Antenatal Hydronephrosis) in CPI and NP groups and by UTI in API group (p: 0.002). Severe VUR patients were mostly followed up with continuous antibiotic prophylaxis (CAP) in the NP group and with surgical treatment in the API and CPI groups ($p < 0.001$), but no difference was found in surgical treatment types. In severe VUR patients, there was no difference in the number of UTIs under CAP treatment. The most common type of surgery in the mild API group was STING ($p = 0.034$). In the study, pelvicaliectasis/hydronephrosis was found most frequently in the dysplasia CPI group in the renal US at the time of diagnosis, and it was found to be significant for the subtypes of the CPI group ($p = 0.046$). Surgical treatment was mostly observed in the dysplasia CPI group and it was found to be significant ($p = 0.002$).

Conclusion: Moderate and severe VUR will present with either renal parenchymal damage (CPI and API, which occurs with 2 different pathophysiological mechanisms) or normal renal parenchyma. In this study, antenatal diagnosis or diagnosis between 0-6 months, ANH without UTI or incidental diagnosis, kidney size and percentile loss in renal US, very low renal uptake in DMSA scintigraphy at the time of diagnosis, no more than 5% loss of split function in follow-up DMSA despite previous UTI, and detection of severe VUR in VCUG were found to be suitable parameters for CPI.

Key words: congenital parenchymal damage, acquired parenchymal damage, UTI, VUR

1143 - P1.040

CLINICAL CHARACTERISTICS AND TREATMENT RESPONSES OF CHILDREN WITH PRIMARY ENURESIS

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Aim / Purpose: Enuresis is the most common urological problem in childhood. It significantly affects the quality of life of both the patient and caregivers, emphasizing the need for a multidisciplinary approach and timely initiation of appropriate treatment methods. In this study, we aimed to evaluate the clinical characteristics and treatment outcomes of patients with primary enuresis.

Methods: Patients aged 5-18 years diagnosed with primary enuresis in our clinic between 1 April 2021 and 1 April 2023 were included. Data including age, gender, onset of enuresis, daytime urinary incontinence history, lower urinary tract symptoms, constipation and/or fecal incontinence, family history of enuresis, treatment methods, and treatment responses were retrospectively analyzed.

Results: Of 50 children (22 female, 28 male) diagnosed with primary enuresis, the median age at presentation was 7.8 years (IQR 6.1 – 8.9), and the median follow-up period was 13.9 months (IQR 6.9 – 21.2). Thirty-three patients (66%) had nocturnal enuresis only, while 17 patients (34%) had both night and daytime enuresis complaints. Twenty-nine patients (58%) had non-monosymptomatic enuresis (NMSE), while 21 patients (42%) had monosymptomatic enuresis (MSE). Fifteen (30%) patients fully responded to behavioral therapy at third month. Out of the patients who did not respond completely to behavioral therapy (n = 35), 32 of them were started on desmopressin, and 3 of them started on anticholinergic treatment (oxybutynin) due to the findings of overactive bladder. Of the 32 (64%) patients who received desmopressin, 14 patients responded fully, and 8 patients responded partially in the first month. Among patients who did not fully respond to desmopressin (n = 18), 11 (61%) fully responded in the third month with the combination of oxybutynin. The median age of patients who responded fully or partially to desmopressin therapy in the first month was significantly younger than those who did not respond at all (7.8 vs. 9.4 years, p =0.03).

Conclusion: Early intervention and early therapy may improve treatment response. Behavioral therapy should be the first-line treatment and pharmacotherapy should be considered in cases of inadequate response. Combination therapies may be beneficial for patients not achieving a complete response with monotherapy. Prospective large-scale studies on alternative agents and their efficacy in resistant enuresis cases are warranted.

1150 - P1.041

ANHYDRAMNIOS IN FETAL NEPHROPATHY: A NON CONVENTIONAL INDICATION TO AMNIOINFUSION

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Aims/Purpose: Anhydramnios in fetal nephropathies, besides being predictor of severe renal impairment, might also represent a cause of further functional renal deterioration because of fetal dehydration related to the reduced availability of fluids. Herein, we explore the efficacy of amnioinfusion in a CKD patient with anhydramnios.

Methods: A 36-year-old woman underwent routine US examination at 20 gestational weeks (GW) showing a fetus with slightly enlarged kidneys with normal parenchymal echogenicity and normal amniotic fluid index (AFI). At 33GW the fetus kidneys were both significantly enlarged, hyperechogenic with multiple cysts and empty bladder. Anhydramnios was also observed. She underwent two amnioinfusions at 34GW aimed at providing fluids to the fetus to avoid dehydration-related renal functional worsening.

Results: The procedures were followed by an increase in AFI, fetal cardiac stroke volume and bladder filling. At birth (at 36GW, BW 3130 gr), despite severely impaired renal function, the child wasn't anuric. A diagnosis of severe bilateral renal dysplasia without associated uropathy was established. During perinatal period the baby required significant amounts of fluids to avoid dehydration and to promote sub-normal growth. Dialysis was postponed well beyond the neonatal period and was started at 6 months of life.

Conclusion: With the present case report, we just want to emphasize the apparent paradox of congenital nephropathies that may exhibit anydramnios (equivalent to anuria) during fetal period but after birth are often characterized by polyuria. It is well known that in both acute and chronic nephropathies, dehydration invariably worsen renal function and that in these conditions rehydration can revert it, at least partially. Amnioinfusion might represent a therapeutic option to prevent fetal and/or neonatal anuria aimed at postponing dialysis in severe fetal nephropathies associated with anhydramnios.

1215 - P1.042

RISK FACTORS OF REDUCED DIFFERENTIAL RENAL FUNCTION IN CHILDREN WITH VESCICULO-URETERAL REFLUX

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Aims/Purpose: Reflux nephropathy constitutes the renal scarring induced by vesicoureteral reflux (VUR), possibly associated with congenital renal dysplasia and/or recurrent episodes of urinary tract infections (UTIs). The effects of these factors on reduced renal function are not well explored. This study aims to determine the risk factors of reduced differential renal function (DRF) in children with VUR.

Methods: This retrospective study comprised of children with VUR, followed up at a tertiary hospital during the last 10 years. Data regarding age, sex, VUR grade and ultrasound renal dysplasia were collected. Differential renal function was assessed using DMSA scintigraphy or MAG3 renogram scan. The number of UTIs observed before scintigraphy exam were recorded.

Results: 51 children, 27 boys and 24 girls, with a median age of 0.58 years at VUR diagnosis, were included in this study. Median VUR grade was III (I-V). Scintigraphy was performed within a median time of 0.41 years after VUR diagnosis. 40 patients presented UTIs with a median number of 1 episode (range 1-4). Renal dysplasia was reported in 7 patients. Mean DRF was 44.7% (range 13-50). 26 (50.9%) patients presented DFR < 45%. In linear regression analysis, lower DFR was correlated to VUR grade ($r2 = 0.156$, $p = 0.004$) and presence of renal dysplasia ($r2 = 0.388$, $p < 0.001$). No significant correlation was observed between DFR and number of UTIs ($r2 = 0.035$, $p = 0.221$). In multivariate linear regression analysis, renal dysplasia ($p < 0.001$), VUR grade ($p = 0.033$) and older age at VUR diagnosis ($p = 0.047$) were correlated to lower DFR. Moreover, in subgroup analysis based on VUR grade (high grade: IV-V and low grade: I-III) and sex no correlation was observed between number of UTIs and DRF.

Conclusion: Renal dysplasia, VUR grade and older age at VUR diagnosis are the main determinants of reduced DRF in children with VUR. On the other hand, UTIs do not seem to determinately affect DFR.

1259 - P1.043

DIFFERENT FACES OF RENAL ARTERY STENOSIS: REPORT OF FOUR CASES

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Purpose: Renal artery stenosis (RAS) in children is a rare condition involved in the etiology of arterial hypertension. We present four different aspects of RAS.

Results: Case 1: An 17-year-old girl presented with incidentally diagnosed arterial hypertension (180/100 mmHg). Upper and lower extremity blood pressures (BP) were similar. Laboratory tests showed chronic disease anemia, mild elevation in C-reactive protein and erythrocyte sedimentation rate. Renal doppler ultrasonography (USG) revealed normal renal arteries. Abdominal computed tomography angiography (CTA) revealed 75-80% stenosis in the proximal left renal artery and circular wall thickening reaching to 7 mm in diameter in the descending aorta at the infrarenal level. The patient was evaluated as Takayasu arteritis. Case 2: 11-year-old male patient was admitted to emergency care unit with sudden onset numbness in the left face and left arm, and shifting of the corner of the mouth. His BP was 200/110 mmHg. Left side facial paralysis was detected. Hematological and biochemical markers, cranial CT, renal doppler USG, cranial magnetic resonance imaging (MRI) were normal. CTA showed left RAS and string of beads appearance. According to radiological findings; he was diagnosed as fibromuscular dysplasia. Case 3: 8-year-old male patient was admitted to hospital with an asthma attact and high BP was detected. His blood pressure was 157/98 mmHg. After the treatment of asthma attact; his pulmonary symptoms were resolved but he was still hypertensive. Doppler USG revealed stenosis of the bilateral renal arteries. CT angiography showed bilateral double renal arteries, stenotic appearance in bilateral renal arteries, and post-stenotic dilatation on the right side. The patient was evaluated as bilateral renal artery stenosis. Case 4: 14-year-old female patient diagnosed with chronic renal failure due to congenital nephrotic syndrome. She received peritoneal dialysis for 4 years then she had hemodialysis treatment for 8 years. A living kidney transplant was performed from her mother. Due to delayed graft function with low urine output, hypertension and high creatinine levels; renal doppler USG showed graft renal artery stenosis on the 3rd day. The diagnosis was confirmed by CT angiography and the patient was treated with an expandable stent by interventional radiology. After the stent, urine output increased and creatinine value decreased.

Conclusions: There are structural and acquired causes of RAS. It should be taken into consideration in the differential diagnosis of childhood and adolescent hypertension, especially in severely hypertensive patients who need multiple medications.

1336 - P1.044

CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT (CAKUT) - OUTCOME AFTER PRENATAL DIAGNOSIS

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Introduction: Congenital anomalies of the kidney and urinary tract (CAKUT) are detected in 0.2–0.76% of prenatal ultrasound examinations and account for approximately 20% of all fetal congenital defects. CAKUT remain the major cause of chronic kidney disease and end-stage renal disease in children, so it is important the early detection.The aim of this study was to analyse the suspected diagnosis of CAKUT on fetal ultrasound.

Material and Methods: Retrospective study of medical reports of infants born at Unidade Local de Saúde Póvoa de Varzim/Vila do Conde, Portugal from 2017 to 2023. Urinary Tract Dilatation (UTD) was defined based on UTD classification system, in prenatal period is defined as a renal pelvis anterior posterior diameter (APD) ≥4 mm in the second trimester and/or ≥7 mm in the third trimester. In postnatal period was considered normal when APD < 10 mm, no calyceal dilation and the renal parenchyma looks normal.

Results: In accordance with the hospitals CAKUT´s protocol, 272 children were studied, 66 % were male. UTD was diagnosed by prenatal ultrasound in 96 %. The postnatal study was normal in 80 %. The postnatal diagnosis included: ureteropelvic junction 29 %; duplex collecting system 25 %, vesicoureteral reflux 12 %, megaureter 9 % renal agenesis 6 %, and multicystic displastic kidney 1 %. Surgery was performed in 15 % of patients with CAKUT.

Conclusions: The approach after prenatal suspected CAKUT represents a diagnostic challenge. Although most of the UTD detected in the prenatal period do not correspond to CAKUT in postnatal study, early diagnosis is important in the detection of severe malformations and prevention of complications.

1355 - P1.045

ACUTE PYELONEPHRITIS IN CHILDREN: ETIOLOGY AND ANTIMICROBIAL RESISTANCE

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Introduction: Acute pyelonephritis (APN) is considered one of the most serious bacterial illnesses in childhood and represent one of the main reasons for fever and antibiotic prescription The aim of this study to describe the etiological picture of pathogens of acute pyelonephritis and the frequency of Escherichia coli (E.coli) resistance.

Material and Methods: A retrospective analysis of 563 medical records of inpatient patients with acute pyelonephritis in the 2nd Children's Hospital in Minsk for the period 2017-2021 was carried out. All children were divided into 2 groups: 1st – < 2 years old (n = 225) with a median age of 0,6 (IQR 0,3; 1,1) year and 2nd – 2-17 years old (n = 338) with age of 9,1 (4,4; 15,3) years. Each group was divided into subgroups: with and without recurrence.

Results: Positive results of urine culture were determined in 28.2% (n = 159) of patients: in 1st group in 24,4% (n = 55), in 2nd group in 40,8% (n = 104) (p < 0.001). It should be noted, that some patients received antimicrobial chemotherapy drugs during the two-week period before hospitalization for various infectious diseases (otitis media, acute respiratory viral infections, etc.): in 1st group, 24.4% (n = 13), in 2nd group, 26.0% (n = 27) (p =0.67). In most cases, urine sampling for sowing was carried out within 1 day from the moment of hospitalization. Gram-negative flora was detected in 90,5% (n = 144) of cases: in 1st group, 94,5% (n = 52), in 2nd group, 88,4% (n = 92) (p =0.21). In both groups, the main etiological agent of acute pyelonephritis was E.coli: in 1st – 72,7% (n = 40), in 2nd – 81,7%. Less common in 1st group P.mirabilis and E facium in 5% of cases, Kl.oxytoca and P. aeruginosa in 4% respectively, in 2nd group: S.saprophyticus in 4%, P.mirabilis, E facium, S.aureus, S.epidermidis, C,freundii in 2% of cases each. The greatest resistance from E.coli in children in 1st group without relapse of APN was observed in a combination of amoxicillin with clavulanic acid – 47%, cefuroxime – 46% and ceftriaxone – 45%; with relapse APN: ceftriaxone – 60%, amoxicillin with clavulanic acid – 50% and 40% each in cefotaxime and co-trimoxazole. In the 2nd group without relapse of APN: amoxicillin with clavulanic acid –50%, cefuroxime – 27%, and 20% each in ceftriaxone and cefotaxime; with relapse of APN: cefazoline – 60%, cefuroxime – 40% and amoxicillin with clavulanic acid in 33% respectively.

Conclusion: Our study confirms that the main causative agent of acute pyelonephritis is E.coli, predominant in females under the age of 2 years and in males in the older age group. Drugs for the initial therapy of acute pyelonephritis have a high frequency of resistance, especially in children under 2 years of age.

1383 - P1.046

EARLY SIGNS PREDICTING SURGICAL INTERVENTION IN CHILDREN WITH URETEROPELVIC JUNCTION OBSTRUCTION

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Aims/Purpose: Ureteropelvic junction obstruction (UPJO) accounts for 20-30% of antenatal hydronephrosis. Management of UPJO varies from conservative monitoring to the elective surgical intervention in selected cases. However, identifying the candidates for early surgical intervention versus conservative approach remains challenging. This study aimed to determine the factors of the properly selecting patients for surgical intervention.

Methods: In this retrospective study, among 266 patients with UPJO, 51 patients (38 males) who diagnosed with antenatal hydronephrosis and no systemic disease or concomitant urinary pathology were included. Patients were divided into two groups whether they underwent surgery. Demographic data, kidney length (standard deviation score, SDS), pelvis anterioposterior diameter (PAP), parenchymal thickness and echogenicity of affected and contralateral kidneys in postnatal first sonographic images and scintigraphic findings (normal, dilated non-obstructive, partial obstruction, total obstruction) of 38 patients with surgical intervention and 13 patients without surgical intervention were noted. Sonographic images were evaluated using urinary tract dilatation (UTD) classification.

Results: The median age at the last visit was 6.08 (3.17; 9.17) years, and the median follow-up duration was 68.5 (33.9;109.9) months. UPJO was commonly observed on the left side (n = 42, 82%). While sex, age at admission, median height SDS and body mass index SDS did not differ between the patients with or without surgical intervention, the age at last visit was higher and the follow-up duration was longer in the surgical intervention group (p =0.016 and p =0.018, respectively). Patients with surgical intervention had higher affected kidney size SDS and PAP diameter compared without surgery (p =0.011 and p =0.018, respectively). However parenchymal thickness, echogenicity, UTD score, or scintigraphic findings of the affected kidney did not differ between the two groups. According to the ROC analysis results, postnatal first ultrasound (USG) revealed that a PAP diameter over 17.5 mm predicted surgery with 71% sensitivity and 62% specificity.

Conclusion: Our study reveals that although there is no significant difference in scintigraphic findings between children who underwent surgery for UPJO and who did not, kidney length and PAP diameter on the first postnatal USG have significant differences in predicting the operation.

1395 - P1.047

ASSESSMENT OF AWARENESS LEVEL OF PRIMARY CARE PHYSICIANS ABOUT URINARY TRACT INFECTIONS IN CHILDHOOD

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Aim/ Purpose: Childhood urinary tract infection (UTI) is a significant public health issue that can lead to chronic kidney disease. This study aimed to assess the knowledge and awareness levels of primary care physicians (PCP) about UTIs in children.

Methods: This cross-sectional study was conducted between July 2021 and October 2021. Ninety-two PCP from 18 institutions in central districts of Ankara with at least two years of experience at university, training and research hospitals, state hospitals, PHCs, or private practices completed a 16-item questionnaire on UTI definition, symptoms and signs, diagnostic criteria, and treatment approaches. Data were retrospectively analyzed.

Results: Of the participants (52 female,40 male) with a median age of 38 years (IQR 31-44), 63 (68.5%) worked at PHC, 17 (18,5%) at training and research hospitals, 9 (9,8%) at university and 3 (3,3%) at state hospitals. Thirty-seven physicians (40%) had 2-5 years, 17 (18,5%) had 5-10 years, 26 (28,3%) had 10-15 years and 12 (13%) had > 15 years of professional experience. When asked about the pediatric care workload, 5 (5.4%) had none, 16 (17.4%) had < 10 patients/ week, 43 (46.7%) had 10 - 50, 18 (19.6%) had 50-100, 6 (6.5%) had 100-200, and 4 (4.3%) had > 200 pediatric patients/ week. The median percentage of correct answers was 63% (IQR 54.5 – 81.8). Pyuria was correctly identified by 75%. The most common pathogens causing UTIs and symptoms suggestive of UTIs in infants were correctly identified by 71%. About urine culturing methods, 48% rate of incorrect response was obtained. Ultrasonography was the firstly preferred imaging method by 80%. Twenty-eight percent of the participants were not aware of the hospitalization indications in children with UTI. There was no statistically significant difference for gender, workplace, years of professional experience, and number of children examined per week ($p = 0.58$, $p = 0.48$, $p = 0.25$, $p = 0.42$, respectively) in terms of correct answer percentage.

Conclusion: UTI is a commonly encountered problem in children and there is still a need for improvements in the awareness level of PCPs regarding UTI in our country. Continuing medical education and in service training programs on pediatric UTIs will help to treat patients properly, prevent complications which could lead to serious morbidities in adulthood.

1441 - P1.048

URINARY TRACT INFECTIONS CAUSED BY EXTENDED-SPECTRUM-LACTAMASE-PRODUCING ENTEROBACTERIA: A REAL PUBLIC HEALTH PROBLEM

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Aims/Purpose: Describe the epidemiological, clinical, bacteriological, and evolutionary profile of Urinary tract infections (UTIs) (especially due to E-SBLE) in Tunisian children hospitalized in the pediatric department of CHU sahloul,Sousse.

Methods: A retrospective descriptive monocentric study concerning children hospitalized for the management of UTI in the pediatric department of CHU Sahloul between 2018 and 2023.

Results: 383 patients were included. An ESBL-secreting bacterium was found in 80 cases (20.9%). The mean age of the children was 11 months. The sex ratio (boys/girls) was 0.59. A particular background was found in 160 patients, including chronic constipation in 106 patients (27.3%), bladder instability in 12 patients (3.1%), and immunosuppression in 7 patients (1.8%). Prior antibiotic therapy before hospitalization was found in 157 patients (41%). 118 children (30.8%) had been hospitalized in the previous year. 21 patients had recent surgery (5.5%). A malformative uropathy was found in 33 patients (8.6%) notably the vesicoureteral reflux (in 20 patients).80 patients had a history of urinary tract infection (20.9%).The predominant symptomatology was fever (98% of patients), back pain (53.7%), lower urinary tract symptoms (42.3%), and gastrointestinal disorders such as diarrhea and vomiting (29.5%). The main bacteria found were: Escherichia coli (80.4%), Klebsiella pneumoniae (12.3%) and Proteus mirabilis (2.3%). 49.1% of strains were resistant to amoxicillin-clavulanic acid, 21.3% were resistant to cefotaxime, and 79% were resistant to cotrimoxazole. 139 patients (36.3%) started empirical antibiotic therapy, while 244 (63.7%) did not receive treatment until the antibiogram was obtained. The most commonly used empirical antibiotic therapy was cefotaxime + gentamicin in 45 patients (32.6%). 378 patients recovered (98.7%) entirely. Only 5 patients developed ulterior complications.

Conclusion: The development of bacterial resistance in the UTIs remains a constantly evolving phenomenon and represents a threat to health that must be controlled to optimize therapeutic management.

1455 - P1.049

RESULTS OF POSTNATAL EXAMINATION AND FOLLOW-UP OF CHILDREN WITH PRENATALLY DIAGNOSED URINARY TRACT DILATATION

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Aims/Purpose: Determining the etiology, postnatal course, and need for surgical management in children with prenatally diagnosed hydronephrosis born in Faculty Hospital Hradec Králové.

Methods: A retrospective study of 48 patients with PNH born between 2018 – 2023 in the Faculty Hospital in Hradec Králové. The cohort includes 36 boys (75%) and 12 girls (25%), median gestational age is 39 GW (min. 36 - max. 41). Postnatal sonographic and urine examinations were performed in all patients. Other imaging and laboratory examinations were only performed in indicated cases.

Results: PNH was described bilaterally in 11 of the 48 cases (26%), right-sided PNH in 15 cases (36%), and left-sided PNH in 15 cases (36%). In 3 cases the affected side was not indicated. In 2 of the children the diagnosis was later established to be multicystic kidney dysplasia. The timing of first postnatal sonographic kidney examination was decided based on the severity of prenatal findings: Day 1 (D1) of life in 1 case (2%), D2 in 5 cases (10%), D3 in 6 cases (12,5%), D4 in 20 cases (42%), D5 in 10 cases (21%) and D6 in 6 cases (12,5%). Results of the first postnatal examination were consistent with the prenatal findings in 18 cases (37,5%), in 5 cases other inborn defects were determined (10,5%). A higher grade dilation was found in 21 cases (44%) and a lower grade in 4 cases (8%). Surgical management by the pediatric urologist was required in 17 children (35%) – 10 cases of pyeloplasty, 1 incision of ureterocele, 1 nephrouretectomy, 1 ectopic megaureter resection, 1 hemi-nephroureterectomy, 2 ureterostomy and 3 ureter reimplantation. Antibiotic prophylaxis was indicated after diagnosis confirmation in indicated cases during the first months of age in 43 patients (89,5%). Acute pyelonephritis was diagnosed in 8 cases (17%) during follow-up.

Conclusion: PHN has multiple etiologies and a thorough postnatal examination is vital for the optimal management, indicating surgical management if necessary and establishing an appropriate follow-up scheme.

76 - P1.050

BARIATRIC SURGERY AS BRIDGING THERAPY TO KIDNEY TRANSPLANTATION IN AN OBESE ADOLESCENT

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Purpose: The prevalence of obesity in children and adolescents is increasing, including in those with end stage kidney disease (ESKD). Obesity may increase the risk of complications during dialysis and may be associated with poorer short- and long-term outcomes after transplantation. Bariatric surgery has been found to be safe and effective in adults on dialysis. We report successful bariatric surgery in an adolescent on haemodialysis.

Methods: A fourteen-year-old with ESKD due to reflux nephropathy commenced peritoneal dialysis with a BMI of 32 kg/m2. The transplant surgeon was reluctant to add the patient to the deceased-donor waiting list due to obesity. While on peritoneal dialysis for 12 months her weight increased by 36 kg and BMI increased to 48 kg/m2. Peritoneal dialysis was ceased, and haemodialysis was initiated, however the patient gained further weight. After trialling multiple interventions for weight loss and multidisciplinary assessment, she was deemed suitable for gastric sleeve bariatric surgery.

Results: Our adult bariatric surgery team has experience in performing this procedure in adults as bridging therapy to kidney transplantation, but this was the first paediatric patient. Our patient successfully underwent surgery (laparoscopic sleeve gastrectomy) without any post-operative complications and has continued thrice weekly haemodialysis. The renal dietician provided a nutrition plan with pureed meals for the first few weeks post-surgery and ongoing supplements. She has lost 35 kg over five months post-surgery and the weight loss has made it possible for her to be activated on the deceased donor list for kidney transplantation.

Conclusion: Our report highlights that peritoneal dialysis can cause significant glucose absorption with additional calories up to 1300 kcal/session and this needs to be considered when choosing dialysis modality in patients with pre-existing obesity. As per international guidelines, bariatric surgery should be considered early in obese adolescents when conservative treatment failure puts them at risk of prolonged dialysis. To the best of our knowledge, this was the first adolescent patient (in Australia and maybe worldwide) who received bariatric surgery to enable listing for kidney transplantation. We have shown that significant weight loss can be achieved in an adolescent with ESKD. Careful monitoring of weight loss and nutritional needs by a multidisciplinary team is required to do so in a safely manner.

173 - P1.051

SURVIVAL RATES OF PAEDIATRIC DIALYSIS PATIENTS UP TO 5 YEARS IN TURKEY: FINDING FROM NATIONAL DATABASE

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Aims/Purpose: Dialysis is one of the essential kidney replacement therapies for paediatric patients with stage 5 chronic kidney disease. However, it has high long-term mortality, which varies between countries. The objective of this study was to determine the 5-year survival rates of patients who underwent peritoneal dialysis (PD) or haemodialysis (HD), using the national data system.

Methods: The national database of the Turkish Ministry of Health was used to evaluate survival rates of paediatric patients (< 18 years of age) receiving dialysis between 2006 and 2022 in Turkey.

Results: The study enrolled 1002 children with a mean age of 12.64 ± 4.82 years. Of the patients, 539 (53.8%) were on HD and 463 (46.2%) were on PD. The age of patients at dialysis initiation was lower in those on PD compared to those on HD (6.20 ± 5.06 years vs 10.70 ± 4.47 years; p < 0.001). During the first 3 years of dialysis, haemoglobin levels were higher in PD group than HD group, but this difference was no longer observed in the fifth year. Although C-reactive protein levels were comparable during the first four years of follow-up, they were found to be higher in patients on HD at the fifth year of dialysis (3.35 vs 2.12 mg/dL, p =0.038). The mortality rate on dialysis was 25.8 per 1000 patient-years. The survival probabilities for HD and PD patients at 1-, 3-, and 5-years were 92%, 77%, 72%, and 86%, 77%, 68%, respectively. Table 1 presents the survival probabilities at 1-, 3-, and 5years based on the dialysis method, age groups, and primary kidney disease. The Kaplan-Meier curves used in the survival analysis showed that the unadjusted mortality rate was similar between HD and PD patients (Log-rank test, p =0.939).

Conclusion: Based on the data from our country, the 5-year survival rate for paediatric patients on dialysis was approximately 70%; HD and PD did not differ from each other.

Table 1. Survival rates of 1-, 3-, and 5-year according to dialysis modality, age groups and primary kidney disease (HD haemodialysis, PD peritoneal dialysis, CAKUT congenital anomalies of the kidney and urinary tract)

Time	Dialysis modality (95% CI)		Patient age (years) (95% CI)			Primary kidney disease (95% CI)	
	HD	PD	≤ 6	6-12	≥12	CAKUT	Other
1-year	92% (88-96)	86% (82-90)	79% (69-90)	84% (76-92)	90% (86-94)	90% (84-95)	86% (82-90)
3-year	77% (71-83)	77% (71-82)	67% (49-85)	73% (63-82)	84% (80-89)	82% (72-93)	78% (74-83)
5-year	72% (64-80)	68% (60-76)	56% (38-74)	63% (49-77)	78% (72-84)	78% (66-90)	70% (61-76)

56 - P1.052

EARLY DETECTION OF ARTERIOVENOUS FISTULA COMPLICATIONS IN PEDIATRIC CHRONIC KIDNEY DISEASE PATIENTS

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Aims/Purpose: We aimed to evaluate the value of the inflammatory markers; Interleukin-10 (IL-10), hs CRP, and tumor necrosis factor- (TNF-), for early detection of arterio-venous fistula (AVF) complications, in pediatric patients on regular hemodilaysis (HD) HD, based on the effect of neointimal hyperplasia results in vascular stenosis and subsequent thrombosis, which lead to vascular access failure, where the previously mentioned inflammatory markers may play a role in the process neointimal hyperplasia and subsequent complications

Methods: It was an prospective cohort study, where we included 59 pediatric chronic kidney disease patients' stage 5, on regular HD (CKD5d), who were following up regularly with us for 1 year. Patients with nonfunctioning AVFs due to complications as thrombus occluding fistula, infections, or large aneurysm, were excluded from the beginning of the study. Monitoring of VA by pre-cannulation physical examination was performed to detect the physical signs of dysfunction, at least once per month according to KDOQI guidelines. Venous pressure (VP) and trans-membrane pressure (TMP) were recorded at each HD session, to detect any abnormalities and to record the pressure changes with the appearance of any AVF complications. Doppler ultrasound (DUS) was performed routinely every 3 months for all HD patients, & at the time of development AVF complications. Blood samples for measuring IL10, TNF, hs CRP were collected from the patients every 2 weeks for 12 months, prior to HD sessions, where we included the most recent samples prior to, and at the time of development complications, which were clinically and radiologically confirmed.

Results: The mean (± SD) age of our patients was 13.97 (± 2.65) years, where we had 39 (56.5%) males, and 30 (43.5%) females, with a median (IQR) HD duration of 4.0 (5.0) years. On assessing the AVF complications, 33 patients (55.9%) had experienced complications, where thrombosis was the most common reported one (17 patients, 28.8%), followed by aneurysm formation in 14 patients (23.7%), while 6 patients (10%) had stenosed AVF, early VA failure in 2 patients (3.4%),1 patient (1.7%) had pseudoaneurysm, and another patient (1.7%) had perivascular hematoma. Mean serum levels of Hs-CRP, TNF-, IL-10 were elevated at timing of early development of complication, in comparison to their baseline levels, meanwhile serum IL10, and TNF alpha were significantly higher among patients who developed AVF stenosis. The baseline hs-CRP had related positively with AVF diameter at the time of the development of the complications.

Conclusion: The inflammatory markers have no clinically applied role in early detection of AVF abnormalities, therefore, physical examination and DUS are deemed sufficient.

174 - P1.053

THE USE OF PERITONEAL DIALYSIS IN NEWBORNS WITH AKI. THE FIRST EXPERIENCE OF NATIONAL CHILDREN'S MEDICAL CENTER

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Critically ill newborns with acute kidney injury (AKI) are at high risk of mortality due to associated complications, including symptomatic uremia, metabolic and electrolyte abnormalities, and fluid overload. Management of these children is supportive, and renal replacement therapy (RRT) indicated for patients with severe kidney damage. Peritoneal dialysis (PD) is a method of RRT that can improve short- and long-term outcomes of newborns with acute kidney injury. PD is widely available in resource-limited countries because it requires less technical expertise, does not require vascular access, requires fewer resources, and is more cost-effective than HD and CRRT. Nevertheless, many developing countries do not use it because of absence PD solutions, appropriate PD catheters and the lack of experience with usage of handmade solutions and manual PD. In this article, we describe our first experience in using manual PD in newborns with AKI.

Aims: Summarize and analysis of the experience of using PD in children born full-term and premature with AKI, admitted to the National Children's Medical Center (NCMC).

Methods: A retrospective analysis of the medical records of 24 patients receiving RRT using the PD method who were admitted to the NICU of the was conducted. For all children included in the study, recorded: age, gender, birth weight, main diagnosis, body weight changes, and initial creatinine and urea levels at the time of initiation of PD, duration and complications of PD, and outcome.

Results: The gestational age of the studied children at birth ranged from 32 to 41 weeks (37.1 ± 4.1). Of these, 10 (40.0%) were girls and 14 (60.0%) were boys. Almost all children included in the study were full-term, except one (4.16%). Body weight at birth varied from 2400 to 5300g (3300 ± 1130). The main diagnosis in 20 children was congenital pneumonia with severe asphyxia at birth, in three patients - neonatal sepsis with severe asphyxia at birth, in 1 patient - congenital nephrotic syndrome. The majority of patients (80%) were in extremely critical condition at the time of initiation of RRT. To carry out RRT using the PD method was used 2.3% dialysate solution prepared manually, and a NG tube used as a PD catheter installed in the pelvic cavity. The duration of PD varied from one to 8 days (3.4 ± 1.2). Mostly reported complications of PD is mechanical block of PD catheter, with peritonitis developing in two cases, but with rapid resolution. The overall mortality rate of patients receiving PD was two (8.3%), but mortality was not due to the direct PD procedure and its complications.

Conclusion: Initiating RRT in a critically ill child requires a team approach of nephrologists, ICU doctors, surgeons, and other specialists caring for the child. The accumulation of experience and its subsequent critical analysis contributes to the expansion of the practice of using PD even in low-source countries with the absence of ready consumables.

197 - P1.054

PREDICTIVE FACTORS OF POOR NUTRITIONAL STATUS IN CHILDREN ON CHRONIC HEMODIALYSIS

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Aims: Children with kidney failure (KF) are prompt to undernutrition with subsequent growth failure. The aim of this study was to assess probable correlates of normalized protein catabolic rate (nPCR) in children on chronic hemodialysis (HD).

Methods: This prospective study included all 20-year-old or less patients undergoing chronic HD at our pediatric HD unit between 1st June 2023 and 30st November 2023. Patients included had been on HD for more than 3 months and were clinically stable. For each patient, baseline characteristics were recorded along with their echocardiogram findings. nPCR value, expressed in g/kg/day, was calculated using the modified version of Borah's equation: nPCR = 5.43 ×UGR/(TBW_PD×10) +0.17, where:

TBW_PD: post dialysis total body water, expressed in deciliters (dL) and calculated using the formula: TBW_PD = 5.8 × PDW, PDW being the post dialysis weight, expressed in kilograms (Kg)

UGR (mg/min) = Urea generation rate, calculated as followed:

UGR = (BUN_PreD × TBW_PreD-BUN_PD ×TBW_PD)/T, where PreD_BUNand PD_BUN refer to blood urea nitrogen's (BUN) pre-dialysis' and post dialysis' measurements, respectively.TBW_PreD refers to pre-dialysis total body water expressed in deciliters (dL) and calculated as followed:

TBW_PreD = 5.8 ×PreDW, where preDW refers to pre-dialysis weight, expressed in kg.

T is the time, expressed in minutes, from the end of one dialysis treatment to the beginning of the next. We used pre- and post-dialysis BUN from the same session to calculate nPCR, as suggested by some studies [5-7].

Our study included a univariate and a multivariate analysis. A p value less the 0.05 was considered statistically significant.

Results: A total of 28 patients were included with a mean age of 14.82 ± 3.2 years old and a sex-ratio of 1.33. Eighteen patients (64.3%) had a mean nPCR < 1g/kg/day. On multivariate analysis, a low 3-months dry body weight gain was strongly correlated with a mean nPCR < 1g/kg/day (OR:12- 95% CI: 2.75-145.48). Patients with a single pool KT/V < 1.2 and those exhibiting left ventricular hypertrophy were more likely to have a nPCR value < 1g/kg/day (OR:21.92 and 7.5, 95% CI: 1.28 – 375.23 and 1.27-44.08, respectively). A first hour refill index > 1.7 ml/kg/h/% was also correlated with a low nPCR (OR:11.57- 95% CI: 1.15-116.63).

Conclusion: Pressure and volume control along with dialysis adequacy are promising factors in improving nutritional status and clinical outcomes in children with KF.

Key words: Children-Hemodialysis-protein catabolic rate –dialysis adequacy- refill index – Left ventricular hypertrophy

236 - P1.055

ACUTE RENAL FAILURE IN CHILDREN: PREDECTIVE FACTORS FOR EXTRARENAL REPLACEMENT THERAPY

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Aim: Acute renal failure (ARF) is rarer in children than in adults, but its frequency is not well known and is certainly underestimated. The aim of our study was to analyse the factors predictive of recourse to extrarenal replacement therapy (ERRT) during ARF in children.

Methods: Our study was a cross-sectional, descriptive, retrospective study conducted in the paediatric wards of Charles Nicolle Hospital in Tunis. Patients under 18 years of age who presented with ARF over a 31-year period (January 2001-December 2022) were included.

Results: We collected 111 cases, with an average age of 6.5 ± 5 years. Presenting symptoms were dominated by infectious presentations in 35 patients (31.5%). Hypertension was present in 59.6% of cases, and edema in 43.5%. Oligo-anuria was present in 41.8% of cases. Extra-renal signs were present in 28% of cases, with purpura being the most frequent in 65.3% of cases. Stage 3 AKI according to the KDIGO 2012 classification was noted in 53 patients (47.7%). The etiology of AKI was functional, obstructive, and organic in 10.9%, 0.9%, and 88.2% of cases, respectively. Hemolytic uremic syndrome was the most common etiology of AKI (31.4%). End-stage renal disease (ESRD) was indicated in 40% of children, with peritoneal dialysis being the most frequently used technique in 29 cases. Progression to chronic renal failure was noted in 20 cases (18%), with end-stage renal disease in 11.2% of cases. The independent predictive factors for recourse to renal replacement therapy were: age less than two years ($p < 0.01$), dyspnea, cough, and convulsions as the chief complaint ($p < 0.01$), hypotrophy, oligo-anuria, the presence of extra-renal signs ($p < 0.01$), a higher creatinine level ($p < 0.01$), significantly lower hemoglobin ($p = 0.01$), natremia ($p = 0.02$), and calcemia levels ($p < 0.01$), the presence of schistocytes ($p = 0.05$), and an undiminished C3 factor (< 0.01). The vascular origin of acute renal failure was the main factor predicting recourse to treatment (< 0.01).

Conclusion: Several predictive factors were identified in our study. Early management of high-risk patients would improve prognosis.

360 - P1.056

THE PHOSPHATE LEVEL CHANGES AS PREDICTIVE FACTOR OF TUMOR LYSIS SYNDROME

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Aim: Tumor lysis syndrome (TLS) is a serious emergencies in onco-hematology patients, and one of the most common complications is the acute kidney injury (AKI). The aim of our study was the TLS analysis from the nephrological point of view, supplementing it with one of the most difficult decisions, the dilemma of the need for renal replacement therapy (RRT).

Material and Methods: During the 11 year period of retrospective national clinical research, children with leukemia and lymphoma were examined in four pediatric clinics in Hungary. After appropriate selection process, a total of 31 pediatric patients were included in our study. Patients were also subgrouped according to the "traditional" tumor lysis syndrome criteria (laboratory /clinical) and nephrologically, according to pRIFLE criteria (mild (pRIFLE: 0, R, I)/ severe (pRIFLE: F) AKI subgroup).

Results: Significant differences were found between the changes in parameters of phosphate homeostasis and urea levels in both classifications. Compared to the age-specific normal phosphate ranges, hypophosphatemia was common (19/31 cases) before the development of TLS, while hyperphosphatemia was the most common (26/31 cases) in the post-TLS period. The degree of daily change in serum phosphate level was significant in the nephrology subgroups, but the peaks of serum phosphate level show only a moderate increase. The calculated cut-off value of daily serum phosphate level increase before AKI was 0.32 mmol/L per ROC analysis for severe TLS–AKI. The detailed 24-hour urinalysis data of eight patients indicated only temporarily increased phosphate excretion, parallel to elevated serum phosphate levels and the development of renal failure.

Conclusion: The most important predictive parameter for severe renal involvement was the daily change in serum phosphate, which may help to select at-risk patients, where RRT may be necessary and encourage its earlier initiation.

769- P1.057

ACUTE KIDNEY INJURY IN SUICIDE ATTEMPT DUE TO OVERDOSE OF BISMUTH SUBCITRATE

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Bismuth salts, especially colloidal bismuth subcitrate, are widely used to treat peptic ulcers and chronic gastritis. The reported toxic effects caused by overdose of bismuth salts include nephropathy, encephalopathy, osteoarthropathy, gingivostomatitis and colitis. The concentration of bismuth in the kidney, and its retention time is higher than in other organs and nephrotoxicity is the most frequent serious manifestation.

Case Presentation: We report a female adolescent with acute kidney injury after bismuth subcitrate intoxication due to suicide attempt. She was first admitted to the National Toxicology Center and next day transferred in the psychiatric hospital. Third day after ingestion of 3,2 g of bismuth subcitrate, she started to vomit and became oliguric and was admitted in our hospital. Renal replacement therapy was started 56 hours after overdose ingestion of bismuth subcitrate. Two days later, the stool became blue-black colored. Continuous hemodiafiltration and five single pass albumin dialysis were performed during two weeks. Urine output progressively increased and renal function improved. Clinical outcome was favorable and after 21 days, the patient was discharged from the hospital. Bismuth in urine remained detectable even two years after ingestion of bismuth subcitrate.

Conclusion: Bismuth intoxication is a rare cause of acute kidney injury which is usually reversible if early diagnosed and properly treated. Clinicians should be aware that acute renal failure could occur after bismuth intoxication.

982 - P1.058

BRIDGING THE GAP BETWEEN KNOWLEDGE AND PRACTICE: EFFICACY OF AN EDUCATIONAL LEAFLET ON VASCULAR ACCESS PRESERVATION IN PAEDIATRIC NEPHROLOGY PATIENTS

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Aims: Vascular access preservation (VAP) is crucial for paediatric patients with chronic kidney disease (CKD) requiring frequent venous access. Proper VAP strategies can minimize complications and improve long-term outcomes in this vulnerable population. We aimed to assess knowledge and practices related to VAP and evaluate the impact of an educational leaflet on patients' understanding and willingness to adopt VAP strategies.

Methods: A single-centre, single-arm, pre-post interventional study was conducted over a 6-month period. We recruited 26 patients aged 6-18 with CKD requiring regular venous access. Participants completed a custom-designed questionnaire assessing VAP knowledge and practices before and after receiving an educational leaflet (developed based on existing guidelines and expert opinion, focusing on key VAP strategies). The questionnaire assessed participants' knowledge, ideal vs. actual blood taking practices, and willingness to engage in VAP behaviours. Descriptive statistics and McNemar's test were used to analyse the data.

Results: Pre-intervention, only 38.5% (10/26) of participants were aware of VAP, having received advice from healthcare professionals. 61.5% (16/26) of participants reported that blood was usually drawn from the elbow crease, and 57.7% (15/26) reported using the dominant arm. Post-intervention, 92.3% (24/26) demonstrated improved knowledge of VAP strategies ($p < 0.001$), with the mean knowledge score increasing from 2.46/5 to 3.08/5 (25.2% increase). Willingness to engage in VAP behaviours increased post-intervention, with participants willing to notify phlebotomists about VAP increasing from 38.5% (10/26) to 80.8% (21/26) ($p = 0.002$), and those willing to wear a VAP wristband increasing from 0% to 76.9% (20/26) ($p < 0.001$). Post-intervention, participants correctly identified the back of the hand (84.6%, 22/26) and non-dominant arm (80.8%, 21/26) as ideal sites for venous access. However, 61.5% (16/26) reported that blood is still usually drawn from the elbow crease, and 57.7% (15/26) reported continuing to use the dominant arm.

Conclusion: This study showed the leaflet effectively improved patient knowledge and promoted behavioural changes crucial for VAP. Despite patients' improved knowledge and willingness to adopt VAP strategies after the educational intervention, there remains a significant discrepancy between ideal and actual blood taking practices, highlighting the need for sustained education and systemic engagement of healthcare professionals, including phlebotomists. Future research should assess the long-term impact of educational interventions on patient outcomes and focus on identifying and addressing barriers to implementing VAP strategies in clinical practice.

1019 - P1.059

ENCAPSULATING PERITONEAL SCLEROSIS ON PERITONEAL DIALYSIS PATIENTS : FAVOURABLE OUTCOME OF EARLY TREATMENT, A CASE REPORT

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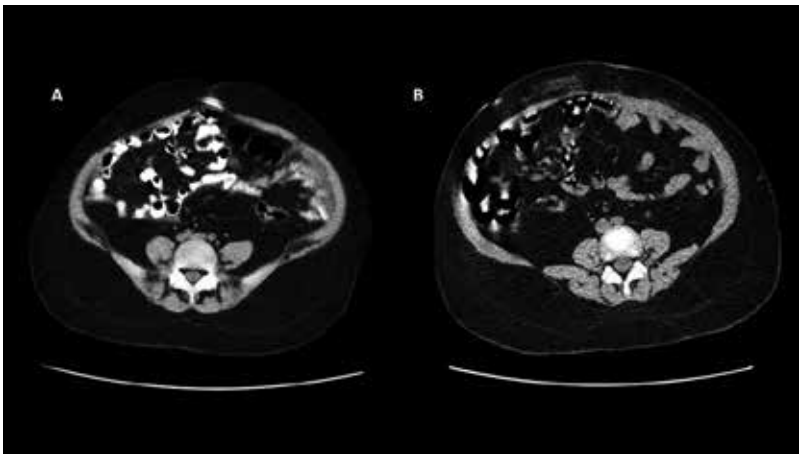
Aims/Purpose: Encapsulating Peritoneal Sclerosis (EPS) is a devastating but rare complication of long-term peritoneal dialysis (PD). The disease is characterized by extensive thickening and fibrosis of the peritoneum resulting in the formation of a fibrous cocoon leading to intestinal obstruction. EPS is a potentially fatal condition with serious consequences such as loss of the PD method and possibly the inability for a future transplantation. EPS occurs in patients who are on PD usually for a long period of time but rarely EPS is observed in patients on PD for a shorter period of time and can also be seen even after transplantation. We report the case of a 5-years old girl who developed EPS two years after starting PD.

Methods: We report the case of a 5-years old girl who developed EPS two years after starting PD. This patient was diagnosed suffered by EPS after a severe episode of peritonitis. Due to loss of clearance adequacy a peritoneal equilibration test (PET test) was performed which revealed a change in the patient's profile. The patient underwent an abdominal CT scan which revealed findings compatible with incipient EPS. Fortunately, the patient had no clinical symptoms of intestinal obstruction. Treatment with low dose of prednisolone and tamoxifen was initiated. The peritoneal catheter removed and the patient switched to hemodialysis.

Results: Six months later, during a follow-up, the CT scan of the abdomen revealed a partial resolution of the imaging findings. Two years later PS lesions completely resolved and the patient successfully transplanted from a living donor.

Conclusion: We would like to emphasize that high clinical suspicion is required in order to identify the EPS early in PD patients and treat it conservatively, as it seems that early therapeutic intervention can have beneficial effects.



A: CT scan at the time of EPS diagnosis - B: CT scan 6 months later

1082 - P1.060

SCLERODERMA RENAL CRISIS IN A CHILD: DIFFICULTIES OF DIAGNOSIS AND TREATMENT

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Introduction: Scleroderma renal crisis (SRC) is a life-threatening complication of systemic sclerosis with a high mortality. SRC is a very rare disease in children and is diagnosed in the presence of acute kidney injury (AKI), hypertension, microangiopathic haemolytic anaemia and thrombocytopenia, target organ dysfunction, and renal histopathology.

Material and Methods: We describe a clinical case of a teenager with SRC and thrombotic microangiopathy (TMA).

Results: 5 days after illness of respiratory infection, a 15-year-old boy developed edema, and 7 days later anemia (Hb-61 g/l) and thrombocytopenia (PLT-12710^9/l). Upon admission to the regional hospital, it was revealed that the child had gained 5 kg in weight, had hydrothorax on both sides, severe arterial hypertension, increased creatinine to 550 µmol/l and LDH to 1500 U/l, proteinuria and hematuria. With a diagnosis of atypical hemolytic-uremic syndrome, the child was transferred to a dialysis center. Upon admission, the child was started on hemodialysis, and 4 days later daily plasma exchanges (TPE). After the 2nd TPE, the child developed pulmonary edema, which required transfer to mechanical ventilation. A computed tomography of the chest demonstrated nonspecific interstitial pneumonia and bilateral pleural effusions. There was also a sharp decrease in left ventricular ejection fraction to 38%. After the 2nd TPE, the results of serological studies were obtained: ANCA, anti-GBM, anti-dsDNA and all anti-nuclear antibodies were negative with the exception of strongly positive (3+) anti-PM/Scl. Complement levels were within normal limits. TPEs were discontinued and 3 pulses of methylprednisolone therapy were performed, followed by a transition to a small dose of prednisolone (10 mg/day). After weight normalization, peripheral edema disappeared but no scleroderma skin changes were detected. The patient maintained a low perfusion index of 0,5-0,8% throughout the entire disease; a cold test was performed on the left arm with restoration of normal temperature only after 50 minutes. A kidney biopsy was performed 3 weeks after the onset of the disease and onion skin proliferation within the walls of the intrarenal arteries and arterioles, obliterative angiopathy were discovered. This allowed to finally establish the diagnosis. By this time, the boy no longer needed dialysis and creatinine subsequently decreased to 148 µmol/l. After 4 weeks, receiving 4 antihypertensive drugs (including enalapril) and prednisolone 5 mg/day, the child again showed strongly positive (3+) anti-PM/Scl and relapsed TMA. TPE sessions were resumed and IV cyclophosphamide was started.

Conclusion: Scleroderma renal crisis is a complex diagnosis that is very difficult to make without specific skin manifestations. In addition, there is no uniform protocol for the management of this pathology.

1085 - P1.061

MICROBIOLOGICAL FINDINGS IN CHILDREN WITH POSTDIARRHEAL HEMOLYTIC UREMIC SYNDROME USING TAQMAN ARRAY CARDS

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Introduction: Applying of microfluidic TaqMan Array Cards (TAC cards) has become one of the innovative direction in microbiology of the last two decades, allowing simultaneous detection of a wide range of enteropathogens (bacteria, viruses, protozoa, helminths).

Objective. Identification of the aetiology of diarrhoea in children with postdiarrheal hemolytic uremic syndrome (HUS) using real-time PCR based on TAC cards.

Materials and Methods: A total of 89 patients aged 9 months to 10 years with HUS hospitalized at the 2nd City Children's Clinical Hospital in Minsk in 2021-2023 were tested. Each fecal sample was simultaneously tested for the presence of 34 pathogens capable of causing diarrhea.

Results: Genes of enteropathogens capable of causing diarrheal syndrome were identified in 61 (68,5%) of 89 examined children with HUS. Among 43 children with identified diarrheagenic E. coli, 40 (93,0%) had Shiga toxin-producing E. coli (STEC). In all 40 cases, the presence of STEC was accompanied by the detection of type 2 Shiga toxin (Stx), in 13 (32,5%) of them in combination with type 1 Stx. In 16 patients, in addition to STEC, genes of pathogens were identified: bacterial – in 7 (Clostridium difficile – 5, Campylobacter – 1, Bacteroides fragilis – 1), viral – in 2 (noro-, adenoviruses), protozoa – in 4 (Blastocystis – 3, Gardia A – 1), a combination of 2 or more – in 3 patients. In 21 children without STEC, the following genes were identified: bacterial pathogens – in 6 (Bacteroides fragilis – 2, EPEC – 2, Campylobacter – 1, EAEC – 1), viral pathogens – in 10 (rota- 3, noro- 3, adeno- 3, sapoviruses – 1), protozoan genes – in 1 child (Cryptosporidium), in 4 children – genes of 2 or more pathogens. The detection rate of Stx E. coli increased from 38% in 2021 to 65% in 2023 and averaged 45%, which allows for an accurate diagnosis of STEC-HUS. 92,6% of children received antibacterial or intestinal antimicrobial drugs at the time of admission to the nephrology center. STEC was detected after 7,0 (5,0; 8,5) days, with a maximum of 13 days from the onset of diarrhea to stool collection.

Conclusions: The data obtained using TAC cards confirm the role of STEC as the main etiological agent of HUS. The role of other E. coli (non-shiga toxin-producing strains), as well as other pathogens, in the development of HUS requires further study.

1112 - P1.062

BEWARE OF HYPOTENSION IN INFANTS WITH PERITONEAL DIALYSIS: A CASE SERIES

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Aims/Purpose: Dialysis in infants is challenging, with high morbidity and mortality compared with older children and adults. Optimal fluid balance, while difficult in all age groups, is particularly challenging in infants, as there is less room for error and given their inability to report symptoms. The purpose of this case series is to alert clinicians to the significance of hypotension in this patient population, as early recognition and treatment can prevent potentially catastrophic consequences.

Methods: We describe a series of two patients treated with peritoneal dialysis in a single center. Case #1: A seven-month-old phenotypic female with Denys-Drash syndrome was born with end stage renal disease. Peritoneal dialysis was initiated at one week of age, maintaining electrolyte balance and fluid volume effectively. Blood pressure was normal without medications. At six months of age, weighing 5.5 kg, she underwent preemptive bilateral nephrectomy due to her increased risk of Wilms tumor. Post-operatively, intermittent hypotension was noted with arterial line measurements, while cuff measurements remained normal. Nine days after the surgery, she developed focal seizures of the upper extremities. Head CT and MRI revealed extensive ischemic injury.

Case #2: A four-month-old male with renal dysplasia due to an HNF1b mutation was born anuric and started peritoneal dialysis at one week of age. At a routine clinic visit, mother reported low blood pressures on home measurement. Physical examination, including blood pressure measurement, and laboratory tests, including lactate levels, were normal. The next day, he presented to the emergency department with fever, diarrhea weight loss, and a blood pressure reading of 70/40 mm Hg. He was ill-appearing with severe lactic acidosis. Imaging revealed a pattern of non-occlusive mesenteric ischemia. Exploratory laparotomy revealed extensive ischemic and necrotic bowel, leading to his death.

Results: This case series describes two infants treated with peritoneal dialysis who had catastrophic outcomes.

Conclusions: On review of the cases, both patients described were found to be intermittently hypotensive, suggesting that the mechanism in each case may have been hypoperfusion injury. We will highlight the importance of recognizing hypotension as a red flag in this age group and discuss other risk factors and potential contributing factors.

1113 - P1.063

PLATELET RICH PLASMA: IS IT AS SAFE AS WE THINK?

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Aims/Purpose: Platelets are the source of platelet growth factors which promote regeneration of damaged tissues. Platelet-rich plasma (PRP) is an autologous plasma product in which the concentration of platelets is several times higher than the physiologic level. PRP is widely used in medicine such as neurology for pain alleviation and regeneration of neurons.

Methods: Herein, a 4-year-old patient, who was diagnosed with acute disseminated encephalomyelitis with severe neurological sequelae and received PRP subcutaneous injection in a private center to provide neuronal regeneration was presented.

Results: The patient admitted to our hospital 5 days after PRP with fever, refusal to feed and decreased urine output. At admission, general condition was poor, tachypnea, subcostal retraction and tachycardia were present. Body temperature was 38.6 oC, blood pressure was 58/24 mmHg. There was marked coldness in all four extremities and capillary refill was markedly prolonged. Laboratory examination revealed elevated acute phase reactants and acute kidney injury. Urine output was 0.7 mL/kg per hour. He was intubated due to respiratory distress. Inotropic treatments were initiated when hypotension and circulatory disturbance did not improve despite appropriate intravenous fluid administration. Ceftriaxone was initiated, however antibiotic treatment was switched to teicoplanin due to the presence of gram-positive cocci signal in gram staining in blood cultures taken simultaneously from the right and left arm with appropriate methods before ceftriaxone. The next day, blood cultures from both extremities were obtained at the time of fever. Despite intensive supportive treatment, the patient died in the 48th hour of hospitalization. All blood cultures grew methicillin-resistant Staphylococcus epidermidis.

Conclusion: Staphylococcus epidermidis is the most common cause of primary bacteremia. Its ability to cause disease is linked to its presence in human skin flora. In cases where skin integrity is compromised, various complications may occur, from skin and soft tissue infections to bacteremia. Structures on the Staphylococcus epidermidis surface cause the immune system to overreact, triggering sepsis. The fact that Staphylococcus epidermidis sepsis developed in our patient after subcutaneous PRP injection suggests that the PRP procedure may be a risk factor. For this reason, it should not be forgotten that the PRP procedure, which can be performed easily and quickly in many health institutions today for various indications, may be associated with serious adverse events that may result in mortality. The PRP injection must be performed in competent hands, following disinfection recommendations.

1134 - P1.064

PERITONEAL DIALYSIS-RELATED PERITONITIS: CLINICAL COURSE AND OUTCOMES OVER 3 YEARS AT A TERTIARY SOUTH-AFRICAN PAEDIATRIC CENTRE

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Background: Peritoneal dialysis (PD) is the preferred treatment modality in children with kidney failure. Peritonitis remains a major complication of PD and the leading cause of treatment failure. Data on African children undergoing PD are very limited in the literature. This study aims to describe the clinical characteristics, clinical course and outcomes of children undergoing PD in a tertiary South-African centre.

Methods: Children enrolled to our chronic PD programme (Red Cross War Memorial Children's Hospital, Cape Town, South-Africa) between 1st June 2020 to 31st May 2023 were included. Socio-demographics, clinical data, and peritonitis-specific data (as per ISPD recommendations) were collected and stored on a secure anonymous database. Ethical and institutional approval was obtained to conduct this study (HREC 099/2024).

Results: In total, 26 children underwent PD for a total of 214.8 months. Mean age at PD onset was 10.1 ± 5.1 years, with a 1.01 episode per patient-year peritonitis rate, showing a four-fold increase in 2022-2023 compared to previous years (Figure 1). Of the 18 episodes of peritonitis that were found, 7 (39%) were culture negative, 8 (44%) were of bacterial origin and 3 (17%) fungal. Antimicrobial resistance occurred in 6/8 (75%) of bacterial episodes with 6 organisms identified, staph. epidermis being only present in 2 (11%) of the episodes. Mean time to first peritonitis episode was 4.7 ± 4.4 months. Medical cure was reached in 11 (61%) of patients whereas 2 (11%) and 1 (6%) had refractory and relapsing episodes, respectively. Peritonitis led to catheter removal in 7 (39%) of patients and haemodialysis (HD) transfer in 6 (33%). Mean length of stay secondary to peritonitis was 17 ± 18.8 days, with no peritonitis-related deaths reported. As of May 2023, most children were transplanted (n = 19, 73%; successfully: n = 14; failed: n = 5), 4 (15%) were still on PD, 4 (15%) on HD, 2 (8%) were transitioned to adult services and 2 (8%) unfortunately died. Children free of peritonitis episodes (46%) were living significantly closer to our centre compared to children who experienced at least one episode (17.8 ± 14.2 kms vs. 60.2 ± 57.4, p =0.005). No statistically significant difference was found for age at PD onset, time on PD, sex, time between catheter insertion and PD initiation.

Conclusions: We still report rates of PD-related peritonitis above international recommendations, especially in the last year. Peritonitis episodes carry a high burden in terms of treatment failure, hospitalisations rate, antibiotic resistance, and overall quality of life. This data will help prompt quality improvement initiatives to improve outcomes in children and young people living with kidney failure in South-Africa.

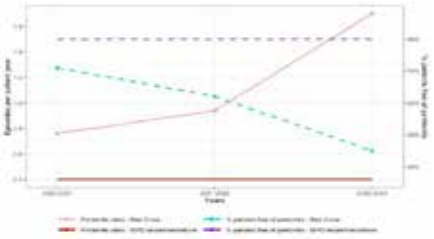

Figure 1: Yearly rates of PD-related peritonitis and percentage of patients free of episodes at Red Cross Children's War Memorial Hospital compared to ISPD standards.

1146 - P1.065

PYOCYSTIS DUE TO PROLONGED BLADDER DEFUNCTIONALISATION IN AN OLIGOANURIC CHILD WITH END STAGE RENAL DISEASE (ESRD)

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Introduction: End stage renal disease (ESRD) may result in severe anuria that leads to a defunctionalized bladder. Pyocystis is a severe form of lower urinary tract infection, described with accumulation of purulent debris within the bladder. It is rare in the pediatric population with an incidence that varied between 10-24%. We report our experience with the evaluation and management of a patient with pyocystis due to prolonged defunctionalized bladder secondary to oligoanuria.

Case Report: A 10-year-old female patient with ESRD due to congenital nephrotic syndrome who had been on hemodialysis for 5 months presented with severe, lower abdominal pain, dysuria, bloody discharge, and fever. She was febrile, tachycardic and hypertensive with lower abdominal tenderness. Uretheral catheterization drained purulent, cloudy urinary sediment. Laboratory investigations revealed slightly elevated inflammatory marker. Urine microscopy with leukorrhea and microscopic hematuria. Urine culture grew Pseudomonas aeruginosa. Abdominal ultrasonography revealed small, echogenic kidneys with new onset severe bilateral hydroureteronephrosis (HDUN) and underfilled urinary bladder containing heterogenous isoechoic to hypoechoic content with trabeculated, thick wall. She was treated empirically with intravenous ceftazidime without clinical improvement. Voiding cystouretherogam was extremely painful at 50 ml and no reflux. She had undergone diagnostic cystoscopy that revealed redness of the bladder wall with mucosal hypertrophy of the trigone and polypoid like multi-polyps in the covering the trigone and obscuring the ureteric meatus bilaterally. Pathology from the polypoid fragments revealed mucosal hyperplasia and stromal chronic inflammation. She was diagnosed with pyocystis based on clinical and radiological findings. She was treated with bladder irrigation with normal saline and antibiotic. She progressed to ESRD, became oligoanuric within few months of initiation of dialysis. We hypothesized that the state of severe oligoanuria with loss of flushing effect of the urine and subsequent accumulation of urinary debris within the contracted, small bladder. The new onset of severe HUDN suggests the diagnosis of obstructive uropathy due to physiological defunctioning of the bladder from oligoanuria. She was taught to perform clean intermittent self-catheterization with increasing volumes. Anticholinergics commenced during bladder cycling. She had careful pretransplant bladder evaluation.

Conclusion: Pyocystis is a rare complication of prolonged defunctionalized bladder. A high index of suspicion for diagnosis is indicated particularly in anuric patients on hemodialysis due to lack of characteristic presentation. Prompt diagnosis and management of pyocystis in ESRD is important to ensure recovery of the bladder and prevent complications in the post-transplant period.

1281 - P1.066

EVALUATION AND LONG-TERM FOLLOW-UP CASES WHO RECEIVED PERITONEAL DIALYSIS IN THE NEONATAL PERIOD

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Aim: To evaluate the indications, complications, results of peritoneal dialysis (PD) in newborns and long-term follow-up findings of the surviving cases over a 10-year period.

Materials and Methods: Demographic, clinical and laboratory findings for all cases upon admission, at the beginning of PD treatment and after treatment and at the last visit for surviving cases were recorded.

Results: PD support was given to 71 newborns in the mentioned period. There was an antenatal problem related to the urinary system in 34 of the cases (47.9%). When evaluated according to etiology, perinatal asphyxia was reported in 11.3%, sepsis in 16.9%, congenital heart disease in 12.7%, renal pathologies in 18.3%, hydrops fetalis in 4.2%, electrolyte imbalance in 5.6%, tumor lysis syndrome in 1.4% and metabolic disease in 23.9% of the cases. PD was performed manually in 33 (46.5%) cases. When PD type was compared according to birth weight, manual PD rate was in significantly higher in LBW cases (p =0.017). When AKI was evaluated according to n-KDIGO, 14 patients had Stage-0, 1 had Stage-1, 3 had Stage-2, and 52 had Stage-2 AKI. Among dialysis-related complications, leakage occurred in 32.4%, occlusion in 12.7%, wound infection in 2.8% and peritonitis in 16.9% of the patients. Peritoneal catheter was spontaneously displaced in 1.4%, intestinal perforation occurred in 4.2% of the cases, and catheter revision was performed in 12 patients (16.9%). 44 (62%) patients died. 21 of the surviving patients were followed up: 7 had ultrasonographic abnormalities, 5 had hypertension, 4 had proteinuria and 1 needed chronic PD.

Conclusion: Although PD treatment is an effective treatment in newborns, mortality is still significantly high in cases where PD is applied due to the severity of the underlying diseases. Since problems with kidney function may occur in surviving cases later in life, close follow-up of these cases in the following years would be appropriate.

1286 - P1.067

MILKY APPEARANCE OF PERITONEAL FLUID IN A CHILD ON PERITONEAL DIALYSIS DUE TO END STAGE RENAL DISEASE: CHYLOPERITONEUM

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Aims/Purpose: We presented a rare case of chyloperitoneum in a pediatric patient on chronic peritoneal dialysis

Methods/Results: A 4-years-old boy admitted to us with milky appearance of the peritoneal fluid (Figure 1). He was diagnosed end stage kidney disease at the newborn period due to bilateral renal dysplasia. Peritoneal dialysis was started on the first month of life with automated peritoneal dialysis using %1.36 Physioneal solution. His peritoneal dialysis course was complicated with several times of peritonitis. Due to recurrent Pseudomonas Aeruginosa infections, peritoneal catheter revision was done. He was receiving enteral feeding solutions by the way of percutaneous endoscopic gastrostomy tube for providing adequate nutrition for growth. On admission he was free of symptoms of peritonitis. Milky appearance has just started at the same day. Clinically, the infant had a healthy appearance and physical examination was non-specific. For the diagnosis of etiology of milky appearance, triglyceride (TG) level was checked. The peritoneal fluid TG level was elevated up to 1320 mg/dl. Peritonitis was ruled out with low white blood cell count in the peritoneal fluid and negative peritoneal fluid culture. Dietary modification with a medium-chain triglyceride (MCT)- based formula was done. Octreotide treatment was given at the end of first week due to persistence of chyloperitoneum. Peritoneal dialysis was continued and the milky appearance of the peritoneal fluid resolved at the end of two weeks. We checked peritoneal fluid Triglyceride levels weekly and decreased to normal values gradually (1st week; 519,8 mg/dl, 2nd week; 210 mg/dl and 3rd week; 14 mg/dl)

Conclusion: Chyloperitoneum is a rare complication in patients on PD. The etiology of the chyloperitoneum may be due to recurrent peritonitis. Initial treatment is MCT diet and if necessary octreotide treatment. Peritoneal dialysis is safe to continue in these patients.

Figure 1. Milky appearance of peritoneal fluid.

1340 - P1.068

SUCCESSFUL TREATMENT OF RHIZOBIUM RADIOBACTER PERITONITIS

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Aims/Purpose: Peritonitis is a common complication in patients on peritoneal dialysis (PD), and can lead to catheter replacement, particularly when biofilm producer bacteria are involved.

Methods: We describe a case of successful treatment of peritonitis caused by Rhizobium radiobacter in a pediatric patient undergoing PD.

Results: We report the case of a 4-year-old child undergoing PD since the first month of life due to end stage renal disease secondary to neonatal aortic thrombosis who was hospitalized for peritonitis. She presented with abdominal pain and elevation of peritoneal fluid (PF) neutrophil count. The first dialysate culture was negative. Empiric treatment with intraperitoneal (IP) amikacin and vancomycin resulted in an initial improvement, but subsequently this therapy was optimized with IP ceftazidime and iv meropenem due to clinical worsening, elevation of inflammatory markers and PF neutrophil count on day 4. For this reason, PF culture was repeated on day 5 and it was positive for R. radiobacter, which was found only in the enrichment broth, resistant to amikacin and ceftazidime, but susceptible to meropenem. The patient was discharged 14 days after admission, having completed a 10-day course of treatment. 5 days after discharge, the patient was re-admitted for peritonitis. Considering the previous positivity for R. radiobacter, empiric treatment with IP ciprofloxacin and iv meropenem was started. Dialysate culture was positive again for R. radiobacter, susceptible to cefepime, ciprofloxacin, imipenem, levofloxacin and meropenem, while hemoculture was negative. After reviewing the literature, we decided to continue treatment with IP ciprofloxacin 50 mg/L and iv meropenem for 4 weeks. Despite an initial worsening of clinical conditions with abdominal pain and an increase of PF neutrophil count, in an effort to salvage the peritoneal catheter, it was decided to complete a 4-weeks course of antibiotics and to treat the catheter locally with urokinase for three days, before switching to hemodialysis. Patient's conditions improved, PF neutrophil count decreased, and PF cultures became negative. As of date, 18 months after this episode, the patient has not had any new episodes of bacterial peritonitis.

Conclusion: R. radiobacter is an aerobic biofilm-producing Gram-negative rod found in soil and plants which has been reported to cause bacterial peritonitis in patients on PD. From our review of the literature, infections from R. radiobacter result in loss of the peritoneal catheter in 47% of cases; however, catheter preservation rates have increased from 42% (1990 – 2009) to 71% (2010 – 2024). We describe a case of successful intraperitoneal and systemic antibiotic treatment which allowed to preserve the peritoneal catheter in a 4-years-old girl, thus saving vascular accesses for future hemodialytic needs.

1350 - P1.069

ACUTE KIDNEY INJURY UPON RETURN FROM THE TROPICS

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Introduction: Multiple tropical infectious diseases can cause acute kidney injury, with malaria being the most common. Different mechanisms have been described, including acute tubular necrosis due to established hypoperfusion or direct tubular damage, thrombotic microangiopathy, and immune dysfunction with acute tubulointerstitial nephritis (ATIN) or glomerulonephritis. Due to limited resources in developing countries, diagnosis can be delayed, leading to worsened renal prognosis.

Case Presentation: We present the case of a 15-year-old girl who presented to our pediatric emergency department. Two weeks prior, in Equatorial Guinea, she experienced fever, diarrhea, and vomiting. Diagnosed with typhoid fever and malaria, she required hospital admission and received ibuprofen, ciprofloxacin, antimalarials, and ceftriaxone. During hospitalization, she underwent blood tests showing severe anemia and a renal ultrasound revealing bilateral renal hyperechogenicity. Renal function was no evaluated. The family requested discharge due to progressive clinical deterioration and traveled to Spain, where they sought care at our center. She presented with malaise, nausea, and abdominal pain. Blood tests revealed anemia without evidence of hemolysis, acute kidney injury with creatinine of 21.6 mg/dL, urea of 325 mg/dL, metabolic acidosis, and hyperphosphatemia with no other electrolyte abnormalities. Urine analysis showed mixed proteinuria (protein/creatinine ratio of 1.3 mg/ mg) with mild microscopic hematuria and 50 leukocytes/field. Antigen detection for plasmodium falciparum was found positive but with negative blood smear. She was admitted to the pediatric ICU and started on continuous hemodiafiltration. A renal biopsy confirmed ATIN with eosinophil predominance. Treatment with prednisone 1 mg/kg/day was initiated with an excellent response, leading to discontinuation of extrarenal clearance within 72 hours and normalization of renal function within a week.

Comments: ATIN is an immune-mediated cause of acute kidney injury. Multiple etiologies have been described, with drugs being the main cause. Prognosis is generally favorable when the causative agent is withdrawn early. The use of corticosteroids is controversial but appears more effective if initiated within the first few days. Our patient had received multiple treatments known to cause ATIN. The presence of eosinophils is not specific but given the absence of active malaria (negative thick smear and no signs of hemolysis), drug-induced ATIN was suspected. Suspected treatments were excluded until lymphocyte activation testing could be performed.

1405 - P1.070

QUALITY OF LIFE EXPERIENCES IN CHILDREN ON DIALYSIS: RESULTS FROM A 6-MONTH PROSPECTIVE PILOT STUDY

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Introduction: Chronic Kidney disease (CKD) is a major public health problem associated with increased health costs, morbidity, and mortality. There is a 30-fold higher mortality rate and severely impaired quality of life (QoL) in children with CKD, requiring dialysis or kidney transplant compared to the aged-match general population. Understanding patient's QoL may help improve knowledge, treatment adherence, satisfaction, and outcomes. Some evidence suggests that parent's perception of their child's QoL is poorer than that suggested by the patient themselves. The aim of this study was to understand the patient and parent's perspective and experiences of QoL on dialysis.

Methods: 6-month prospective data collection of QoL indicators in children and young people commenced on dialysis, and their parents was undertaken at a large tertiary nephrology centre. 3 validated questionnaires were used after permission (PeDs QL General Well-being Scale, PedsQL End Stage Renal Disease Module version 3 and PedsQL Paediatric Quality of Life Inventory Version 4). All domains were marked against severity scores (never, almost never, sometimes, often and almost always). Patients and parents filled out the questionnaires whilst in the waiting area for their clinic appointment or at home. All data were anonymised at collection and collated electronically.

Results: 19 participants answered the questionnaires (13 parents and 6 young people) with 3 parent-child dyads. Median time on dialysis when questionnaire filled was 8.5 months (IQR 4.25-21.8 months). All responses were of patients and parents of children and young people commenced on peritoneal dialysis. Parents were less concerned about their child's relationships with other peers or problems at school (Table 1). They were more concerned about physical functioning of their child (table 2).

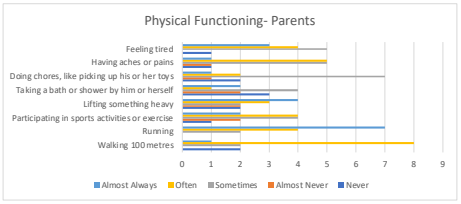

Table 1

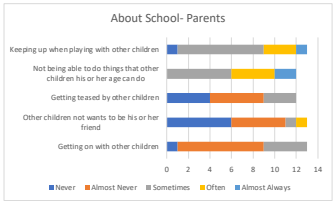

Table 2

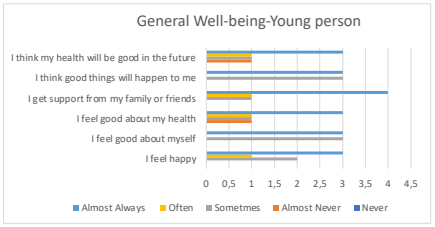

Table 3

Young people were overall generally satisfied with their current and future out look towards life (Table 3). 67% (4/6) reported that they were almost always thirsty and that they sometimes felt tired.

Conclusion: We report results from an ongoing pilot study to understand QoL indicators in children and families commenced on home dialysis. Parents and young people differ in their concerns regarding the young person's health. We aim to continue to prospectively collect data every 6 months to develop evidence and use this to advance interventions which will improve QoL of these patients and their outcomes.

1413 - P1.071

A CASE OF PRIMARY BILATERAL LYMPHOMA IN A 13 YEAR-OLD GIRL; THE CHALLENGE OF CHEMOTHERAPY IN END-STAGE KIDNEY DISEASE

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We present the case of a 13-y.o. teenager with a primary bilateral large B-cell renal lymphoma with terminal kidney failure, and we propose a practical approach to chemotherapy on dialysis. Our patient initially presented with progressive tiredness and weight loss for 4 months. An initial work-up evidenced severe hypertension and terminal kidney failure with a creatinine of 820umol/l (eGFR 7ml/min/1.73m2), hyperuremia (40mmol/l), hyperkalemia (6.3mmol/l), hyperphosphatemia (2.06mmol/l), severe metabolic acidosis (pH 7.28, Bic 14mmol/l), and isolated nephrotic-range proteinuria (A/P =254 mg/mmol). Renal echography showed bilateral dedifferentiated enlarged kidneys with a nodular infiltrating structure. A full-body PET scan showed isolated hypermetabolism of both kidneys, and a kidney biopsy led to the diagnosis of a high-grade bilateral large B-cell renal lymphoma. This presentation is rare, as it is mainly observed in adults. It usually presents with unilateral lesions without end-stage kidney disease. In the literature, we found a sole pediatric case: a 4y.o. boy with a similar clinical presentation, temporary need for dialysis, and favorable clinical evolution after chemotherapy (South, 2018). Our patient was enrolled for an inter-B-NHL ritux 2010-B (high-risk) chemotherapy protocol, based on COP pre-phase, 2 courses of R-COPADM induction, followed by 2 courses of R-CYM consolidation. The challenge was to combine the chemotherapy regimen, especially the use of Cyclophosphamide (CyP) and methotrexate (MTX), with the treatment of end-stage kidney disease. CyP and MTX have been adapted to eGFR at 50% of standard doses. Hemodialysis was tailored to grant an exposure of at least 12h for CyP, and 24-48h for MTX while avoiding overexposure and toxicity. Standard hyperhydration protocol was reduced to avoid volume and salt overload and worsening hypertension. MTX residual levels were suboptimal in the first cycle, resulting in severe mucositis with pain and hemoptysis. The adaptation of our dialysis protocol (Figure 1) with sequential daily hemodialysis to target lower MTX residual levels at 48h and 72h while granting sufficient chemotherapy exposure permitted us to achieve full remission and minimize chemotherapy complications. Based on the full-body PET/CT-scan complete remission was achieved after R-CYM1 course with only healing nodules persisting. The patient remains in complete remission 7 months after completing her treatment. eGFR improved until it stabilized at 24ml/min/1.73m2. Hemodialysis was discontinued 2 months after the end of chemotherapy. Despite CKD, the patient remains stable, active in sports, and without complaint. Residual hypertension is managed with low doses of Nifedipine and hyperkaliemia with oral potassium binders.

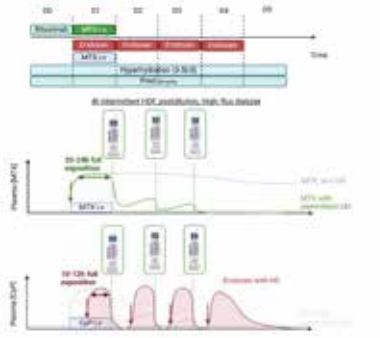


Figure. Scheme of the tailored high-flux hemodialysis to optimize MTX and CyP exposure

1414 - P1.072

ACUTE KIDNEY INJURY AS THE INITIAL MANIFESTATION OF ACUTE LYMPHOBLASTIC LEUKEMIA

João Simões[1], Mafalda Cabral[1], Pedro Silva[2], Ximo Duarte[3], Fernando Caeiro[4], Helena Viana[4], Miguel Cristovão[5], Mário Góis[4], Rute Baptista[1]

[1]Central Lisbon University Hospital Centre, Lisbon, Portugal., Paediatric Nephrology Unit., [2]Central Lisbon University Hospital Centre, Lisbon, Portugal, Paediatric Intensive Care Unit, [3]Portuguese Oncology Institute Francisco Gentil, Lisbon, Portugal., Paediatric Unit, [4]Central Lisbon University Hospital Centre, Lisbon, Portugal., Nephrology Department, [5]Central Lisbon University Hospital Centre, Lisbon, Portugal., Pathology Department

Aims/Purpose: Acute kidney injury (AKI) in acute lymphoblastic leukaemia (ALL) is usually multifactorial and associated with tumour lysis syndrome, drug-induced nephrotoxicity, and sepsis. Symptomatic AKI due to leukemic infiltration of the kidneys as the initial presentation of ALL is rare. We report a case of a T-cell ALL presenting as symptomatic AKI to highlight this rare and severe disease presentation.

Case: A 17-year-old previously healthy male was admitted to the hospital in his homeland country, Cape Verde, with an eight-day history of left flank pain, vomiting and fever. The patient was edematous, hypertensive, and oliguric. Laboratory workup was positive for anaemia, metabolic acidosis, hyperkalemia and altered renal function (serum creatinine 13 mg/dL, urea 230 mg/dL). Kidneys were enlarged, echogenicity was increased and corticomedullary differentiation was decreased. Assuming a presumptive diagnosis of AKI due to acute glomerulonephritis, haemodialysis and methylprednisolone pulses were initiated. After two weeks, he was discharged home asymptomatic, with normal renal function. After six weeks, he was readmitted due to vomiting, fatigue, and facial oedema. Hypertension (140/75 mmHg) and cervical adenopathies were noted. Haemodialysis was restarted and the patient was transferred to our hospital. Laboratory workup showed anaemia (10 g/dL), leucocytosis (13870/uL) and lymphocytosis (8670/uL) with 20% of blast cells on the peripheral blood smear. Serum creatinine was 6 mg/dL (eGFR 20 mL/min/1.73 m2). The patient promptly underwent a bone marrow aspirate and renal biopsy. Acute T-cell lymphoblastic leukaemia with diffuse and extensive infiltration of the renal parenchymal was diagnosed (figure 1). With the first dose of dexamethasone, tumour lysis syndrome developed. Continuous venous-venous haemodiafiltration was needed for 36h. Chemotherapy initiation (vincristine and daunorubicin) was withheld for two days. Two weeks after chemotherapy initiation, serum creatinine was within the normal range for age (0.88 mg/dL). One month later, the patient passed away due to refractory septic shock (OXA-48-producing Klebsiella pneumoniae). Post-mortem histopathology showed a normal kidney parenchyma with no neoplastic infiltration (figure 2).

Conclusion: T-cell ALL presenting as severe AKI due to kidney leukaemic infiltration is rare and leads to delayed diagnosis and treatment. The normalisation of kidney function two weeks after treatment initiation suggested a reduction in the initial extensive and diffuse leukaemic neoplastic infiltration of the kidneys, which was documented by post-mortem histopathology.

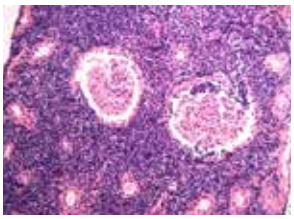


Figure 1. Diffuse extensive infiltration of the renal parenchyma by T lymphocytes (infiltration of the interstitium, invasion of Bowman's spaces and disruption of tubular architecture).

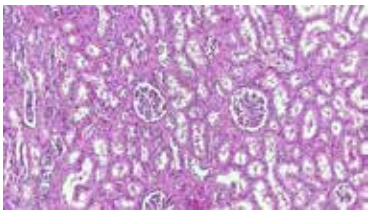


Figure 2. Normal renal parenchyma on post-mortem specimen.

58 - P1.073

THINK REANAL, THINK WISE

Dina Sallam[1]

[1]*Faculty of Medicine, Ain Shams University, Pediatric Nephrology, Cairo, Egypt*

Aims/Purpose: Leukocytoclastic vasculitis (LCV) is a cutaneous, small-vessel vasculitis, usually confined to the skin with rare extracutaneous systemic manifestations in the form of renal and GIT involvement. LCV can also cause kidney damage, typically manifesting as microscopic hematuria and proteinuria, & rarely IgA nephropathy. We have reported a case of multi-systemic LCV in adolescent, who presented initially with infection induced TMA, that was associated with attacks of bleeding/rectum, where GIT endoscopy revealed an active inflammatory bowel disease (IBD), which was refractory to medications. Vasculitis skin rash appeared, where renal & skin biopsy confirmed the diagnosis of multi-systemic leukocytoclastic vasculitis.

Methods: A 13-year-old male, who presented initially with gastroenteritis & bloody diarrhea that induced acute kidney injury (AKI) & microangiopathic hemolytic anemia, and diagnosed as Thrombotic Microangiopathy (TMA), hemodialysis sessions were needed for over 2 weeks period, but he had persistent unimproved hematological & renal manifestation, where therapeutic plasma exchange (TPE) started, with partial improvement. During which he developed attacks of bleeding/rectum not responded to medical management, where lower GIT endoscopy revealed cobble stone appearance grossly in transverse colon, with an active inflammatory bowel disease (IBD), Crohn's, on microscopic examination, upon which IBD management was started without marked response. Patient developed skin rash that was proved to be vasculitis rash.

Results: Skin biopsy confirmed the diagnosis of LCV, whereas renal biopsy revealed fragmented RBCs trapped in thrombi in the subendothelium, & mesangium, with arteriolar changes, & ischemic collapse of capillary tufts with cortical necrosis. Revision of his colonic biopsy revealed colonic leukocytoclastic vasculitis with mucosal ulceration, where he was diagnosed as a case multi-systemic leukocytoclastic vasculitis. IV Pulse steroid for together with Mycophenolate mofetil (MMF) showed marked improvement of his renal, & GIT manifestations, where follow up over 2 years showed marked improvement.

Conclusion: This case reported is unique, where individuals with LCV are characterized by a high propensity for renal dysfunction, including kidney damage, typically manifesting as microscopic hematuria and proteinuria, while presenting as TMA is a very rare presentation of LCV, which was not previously reported, up to our knowledge.

59 - P1.074

THE UGLY FACE OF SHUNT NEPHRITIS

Dina Sallam[1]

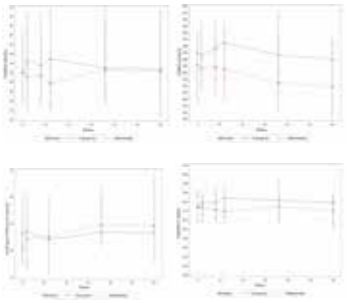
[1]*Faculty of Medicine, Ain Shams University, Pediatric Nephrology, Cairo, Egypt*

Aims/Purpose: Shunt nephritis is a rare immune complex-mediated reversible glomerulonephritis due to infected ventricular shunts, most commonly ventriculo-peritoneal shunts (VP) for the treatment of hydrocephalu (HCP). Although infection of CSF is common, shunt nephritis is rare, however remains a life-threatening disorder with a high possibility of the development of glomerulonephritis (GN), chronic kidney disease (CKD) & death. Antibiotic treatment alone is generally ineffective in resolution of GN, but removal of the shunt is usually, associated with improvement of GN.

Methods: We have reported four cases with shunt-nephritis that had occurred in consequence of infected VP shunt for treatment of hydrocephalus. The clinical courses, immunological, and histological findings were different in the reported cases, however the same management by removal of the shunt system led to an improvement of the laboratory parameters & clinical symptoms in 3 patients.

Results: Two cases had VP shunt at infancy for managing HCP, where thery presnted with acute kidney injury (AKI), shunt dysfunction, high fever & hematuria. CSF analysis was +ve for staphylococcus coagulase & staphylococcus aureus, where a 1 month course of antibiotic hadn't improve the symptoms. Renal biopsy showed Membranoproliferative glomerulonephritis (MPGN). Shunt removal with insertion of new one, was associated with marked improvement of AKI with normalization of complement levels. The 3rd case was a 7-year-old girl had VP shunt inserted since the age of 3 months, came with sepsis, convulsions, AKI & consumed C3. CSF analysis revealed streptococcal pneumonia, & renal biopsy showed diffused proliferative GN with 50% crescentic formation. Patient needed parenteral antibiotic course for 14 days, twice hemodialysis session & pulse steroid without improvement, however shunt removal & insertion of new one was associated with marked improvement of symptoms, and she diagnosed as shunt nephritis. The 4th case was 18-year-old female had VP shunt at age of 10, came with came with manifestation of increased intracranial pressure, and fever of 1 month duration. Initial investigations revealed sepsis, AKI & consumed C3. Antibiotic couldn't manage her AKI. Renal biopsy showed MPGN. CSF analysis was +ve for coagulase-negative Staphylococcus. VP shunt was removed & 1 month course of antibiotic was given without improvement of her AKI and she turned into CDK stage 3.

Conclusion: The importance of regular moniroting of VP shunt and high index of suspicion for early recognition of this reversible form of glomerulonephritis is important



60 - P1.075

THROMBOTIC MICROANGIOPATHIC DILEMMAS: COVID RELATED CASE REPORT THE UGLY FACE OF A COMMON AUTOIMMUNITE DISEASE

Dina Sallam[1]

[1]*Faculty of Medicine, Ain Shams University, Pediatric Nephrology, Cairo, Egypt*

Aims/Purpose: The long-term complications of COVID-19 infection & Multisystem inflammatory syndrome in children (MIS-C) on immune system are still unknown, however there're reports on development of autoimmune disease, highlighting their immune-related nature. MIS-C can induce Thrombotic Microangiopathy (TMA), by inducing endothelial dysfunction, platelet activation, & microthrombi formation, whereas SLE induces TMA/Thrombotic thrombocytopenic purpura (TTP), with ADAMTS13 activity < 10%, or 2ry TMA with ADAMTS13 activity ≥ 10%, where SLE/TTP carries a bad prognosis.

Methods: Our case is one of its kind, where a 12-year- old girl, who was previously infected with SARS-CoV-2, presented with new-onset SLE, associated MIS-C & 2ry TMA/TTP. She presented with convulsions, oliguria, heart failure, impaired kidney function, microangiopathic hemolytic anemia, pancytopenia, highly elevated LDH, & was diagnosed as TMA.

Results: COVID serology was +ve for IgG, & -ve for IgM, & -ve SARS-CoV-2 PCR, a diagnosis of MIS-C was postulated. Further investigations revealed low C3, C4, +ve ANA, anti-ds DNA & anti-phospholipid Antibodies. Brain imaging showed left cerebellar calcification. Echocardiography showed biventricular dysfunction with EF 30%, where the diagnosis of SLE according to Euler/ACR criteria was confirmed, with 2ry TMA. Emergency hemodialysis, PRBCs transfusion, pulse steroid with total plasma exchange (TPE), were initiated without marked improvement. Rituximab was started on 4th day, but she had generalized convulsion, arrythmia & sudden death occurred. Results of ADAMTS13 activity was < 1%, with +ve autoantibodies, so diagnosis of TMA/TTP was confirmed.

Conclusion: TMA are a diverse group of disorders that causes microvasculature thrombosis, which is inherited, or acquired 2ry to SLE or COVID-19 infection, where high index of suspicions should be raised for early diagnosis and prompt management, meanwhile COVID-19 infection can induce the development of autoimmune diseases. Herein we raise the question of cause of TMA/TTP, was it 2ry only SLE, or to the previous COVID-19 infection & MIS-C, and if this SLE itself was 2ry also to the previous COVID infection, or all it was by chance?

61 - P1.076

UNCOMMON RENAL PRESENTATION OF A COMMON AUTOIMMUNE DISEASE

Dina Sallam[1]

[1]*Faculty of Medicine, Ain Shams University, Pediatric Nephrology, Cairo, Egypt*

Aims/Purpose: Renal tubular acidosis (RTA) is common in adults with primary Sjögren syndrome, but up to our knowledge, it is reported in very few pediatric patients. Here we report a case of a female patients who presented with bilateral recurrent parotitis, unexplained attacks of quadriparesis & polyurea, that proved to be distal type RTA with hypokalemia induced paresis, that was associated with dry mouth and eyes, where clinical and investigations criteria confirmed the diagnosis of Juvenile Sjögren Syndrome with 2ry d-RTA.

Methods: A 13-year-old female, presented with bilateral recurrent painful facial swelling at angle of the mouth, raising ear lobules, making a facial disfigurement, in addition to repeated attacks of quadriparesis, polyurea. Her history revealed dysphagia to solid food, where she needed to drink plenty of water to swallow solid food, with eye burning sensation. Examinations revealed bilateral parotitis, with was non obstructing, she had dry mouth Repetitive saliva swallowing test & dry eye by Schirmer's test, proximal muscle weakness and polyurea.

Results: Investigations revealed hypokalemia, which was the cause of her quadriparesis, normal anion gap metabolic acidosis, and medullary nephrocalcinosis, where she was diagnosed as distal type Renal tubular acidosis (RTA). Immunological markers: high titers of anti-Ro/SSA & anti-La/SSB antibodies, ANA titer ≥1:320 with a positive rheumatoid factor. So, the diagnosis of Juvenile Sjögren Syndrome with distal RTA was confirmed & treatment was started in the form of Corticosteroids + mycophenolate mofetil in addition to the symptomatic treatment of hypokalemia, distal RTA &dry mouth & eye, with marked improvement of the patient's condition.

Conclusion: Juvenile Sjögren Syndrome should be considered in adolescent female with otherwise unexplained RTA. A more in-depth investigations of other renal manifestations is needed, where renal biopsy may be of a great importance in excluding renal damage and the need for immunosuppressive medications.

66 - P1.077

NEPHROTIC SYNDROME AS A PARANEOPLASTIC SYNDROME

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[1]UHC" Mother Teresa" Tirana, Pediatrics, Tirana, Albania, [2]University of Medicine, Pediatrics, Tirana, Albania

Aims/Purpose: The association of nephrotic syndrome (NS) and different malignancies is well recognized, but few cases find a specific link between Hodkin lymphoma(HL) and NS. It has been demonstrated that glomerular injury can be found as a complication in these malignancies.

Methods: We report a very rare case of a child that NS preceded the diagnosis of HL by 12 months. Case: 7 years old girl diagnosed with NS, which responded very well to supportive care and steroids. There were no adenopathy or other manifestation of HL. No relapses during 12 months. When she was on minimal dose of prednisone, just 5 mg every other day, in a routine control, a right cervical lymphadenopathy was observed. The child was referred to oncohematologist. The diagnose of Hodkin lymphoma was made by biopsy.

Results: Actually the child is under treatment according to the protocol for HL. Her condition is stable in both terms(nephrologic and oncologyc)

Conclusion: This report raise awareness of a potential association between HL and NS in pediatric patients, for a careful evaluation and follow-up.

92 - P1.078

PONTOCEREBELLAR HYPOPLASIA TYPE 1B AND ATYPICAL HEMOLITYC UREMIC SYNDROME - PRESENTATION OF TWO CLINICAL CASES AND LITERATURE REVIEW

Petya Markova[1], Galia Zlatanova[2], Georgi Bukov[1], Katerina Gaberova[1]

[1]Medical University, Faculty of Medicine, Pediatrics and Medical genetics, Plovdiv, Bulgaria, [2]Medical University of Sofia, Pediatrics, Sofia, Bulgaria

Aims/Purpose: Atypical hemolytic-uremic syndrome is a rare disease characterized by microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury, most often due to genetic disorders leading to uncontrolled activation of the complement system. Very often it is preceded by an infection, which is a trigger for its development. Pontocerebellar hypoplasia type 1b is a severe autosomal recessive neurological disorder resulting from a mutation in the EXOSC3 gene, characterized by a combination of cerebellar and spinal motor neuron degeneration starting at birth. Generalized muscle weakness, progressive microcephaly, global developmental delay and brainstem involvement are characteristic. The disease is characteristic of the gypsy population.

Methods: We present two children of gypsy origin, with pontocerebellar hypoplasia type 1b, who in early infancy, during the course of an infection, manifested hemolytic-uremic syndrome. In a review of the literature, two more children of gypsy origin were described, with pontocerebellar hypoplasia 1b and aHUS after SARS-COV-2 infection, with no effect of Eculizumab therapy.

Results: Genetic testing of one of the children did not reveal any mutations in the complement system. Two clinical cases described in the literature are also not found. This raises the question of the pathogenesis of aHUS in these children.

Conclusion: Children with pontocerebellar hypoplasia type 1b are predisposed to the appearance of aHUS in the course of infection. Knowing this type of co-morbidity contributes to a better knowledge of this syndrome and the follow-up of these children. Further studies are needed to clarify the pathogenesis of HUS.

96 - P1.079

A RARE CAUSE OF HEMATURIA IN THREE PEDIATRIC PATIENTS

Athanasia Chainoglou[1], Ioannis Koutras[2], Ioannis Goulas[1], Antonios Gkantaras[1], Kleo Evripidou[1], Chrysovalantis Mariorakis[3], Sofia Goutou[1], Kyriaki Charpantidou[1], Vasilios Kotsis[4], Stella Stabouli[1]

[1]Hippokratio Hospital, Aristotle University of Thessaloniki, 1st Department of Pediatrics, Thessaloniki, Greece, [2]Hippokratio General Hospital of Thessaloniki, Radiology Department, Thessaloniki, Greece, [3]Hippokratio General Hospital of Thessaloniki, Pediatric Surgery Department, Thessaloniki, Greece, [4]Papageorgiou General Hospital, Aristotle University of Thessaloniki, 3rd Department of Internal Medicine, Thessaloniki, Greece

Aims/Purpose: Nutcracker syndrome (NS) is a rare cause of hematuria, either microscopic or macroscopic. It is a result of the compression of the left renal vein (LRV) between the aorta and the superior mesenteric artery (SMA).

Methods: We present the cases of three children with recurrent episodes of hematuria without proteinuria.

Results: The first two are siblings, brother and sister, 13 and 14 years old, respectively, who presented with persistent microscopic hematuria without proteinuria. Biochemistry of kidney function and immunological tests were normal. Doppler ultrasound in both patients showed a dilatation of the left renal vein with a marginal high compression ratio of the LRV suggesting the presence of NS, which was confirmed by magnetic resonance angiography (MRA) with the presence of an angle between the aorta and the SMA of ≤250. The third patient is a 10-year-old boy with history of hypercalciuria well controlled under treatment with diuretics and potassium citrate who suddenly presented recurrent episodes of painless, gross hematuria after intense exercise and spontaneous resolution in the next 1-6 hours. Biochemistry, urine calcium levels, kidney imaging including Doppler ultrasound were normal. Further investigation with MRA showed pressure phenomena on the LRV and an angle between the aorta and the SMA of 29-300 indicating nutcracker syndrome. All patients were tall and lean with a low body mass index (≤ 16 kg/m2). Due to the mild symptoms and the young age of the patients, conservative treatment with weight gain and avoidance of intense or excessive exercise was advised with resolution of symptoms during follow up (range 12-20 months).

Conclusion: Nutcracker syndrome demands high suspicion for its diagnosis in absence of evident or common cause of hematuria. In pediatric patients with mild symptoms, conservative treatment has favorable outcome.

102 - P1.080

A CHALLENGING CASE OF LUPUS NEPHRITIS WITH MALIGNANT HYPERTENSION AND CHRONIC KIDNEY DISEASE

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[1]Alberta Children's Hospital, Pediatric Nephrology, Calgary, Canada, [2]Ghent University Hospital, Pediatric Nephrology and Rheumatology, Ghent, Belgium, [3]Alberta Children's Hospital, Pediatric Rheumatology, Calgary, Canada

Aims/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by antibodies directed against self-antigens, resulting in multi-organ damage. Up to 20% of SLE patients are diagnosed during childhood (cSLE), and 40 to 70% of these patients will develop kidney involvement, known as lupus nephritis (LN).

Methods: Case description.

Results: A Caucasian 12-year-old girl, previously healthy, presented with nephrotic-range proteinuria, hypertension, and chronic kidney disease. Apart from increased exertional fatigue, mild periorbital oedema, and headaches, her medical history was unremarkable. Clinical examination only revealed malignant hypertension. Significant laboratory findings included a decreased kidney function (creatinine 122 umol/L, urea 9.3 mmol/L), hypoalbuminemia, antinuclear antibody (ANA) 1:40, normal complement (C3/C4), and negative extractable nuclear antigen (ENA)/anti-double stranded DNA/anti-phospholipid antibodies. Kidney biopsy was compatible with immune complex-mediated glomerulonephritis with membranoproliferative and membranous features, consistent with ISN/RPS Class IV+V lupus nephritis. Following this diagnosis, the patient underwent treatment with corticosteroids, mycophenolate mofetil, and hydroxychloroquine. Since diagnosis, her hypertension has consistently been difficult to manage despite multiple antihypertensive agents and good adherence. Currently, she is receiving treatment with six different antihypertensive medications: an angiotensin-converting enzyme inhibitor, angiotensin II receptor blocker, calcium channel blocker, alpha-blocker, beta-blocker, and thiazide diuretic. However, blood pressure control remains insufficient. Furthermore, her nephrotic-range proteinuria worsens despite Renin-Angiotensin-Aldosterone System blockade. Due to insufficient disease control, a repeat kidney biopsy was performed two years after her initial diagnosis, revealing ISN/RPS class IV LN with marked chronic changes. Extensive imaging (doppler ultrasound, echocardiography, Magnetic Resonance (MR) Angiography brain/abdomen/carotids, MR heart, and conventional abdominal angiography) and genetic studies for SLE came back negative.

Conclusion: The primary goal of LN treatment is to preserve kidney function, reduce morbidity and mortality associated with chronic kidney disease, and minimize medication-related side effects. Our case of LN is highly atypical, as our patient exhibits no systemic manifestations of SLE, along with negative autoantibodies and normal serum complement levels. Additionally, we have yet to establish good control of her blood pressure and proteinuria despite multiple attempted treatments. Our case highlights the challenges of managing kidney involvement in cSLE and the difficulty in tailoring treatment strategies to individual patients.

120 - P1.081

ATYPICAL HEMOLYTIC UREMIC SYNDROME TRIGGERED BY SHIGA TOXIN-PRODUCING ESCHERICHIA COLI INFECTION

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Aim: Argentina has the highest incidence of Shiga-toxin producing E. coli Hemolytic Uremic Syndrome (STEC-HUS) in the world; therefore, in our country STEC is always the first etiology suspected faced with a patient with HUS. The aim of this case report is to raise awareness about the unusual situation in which STEC triggered an atypical HUS.

Case Report: A 11- year-old boy was admitted to the hospital due to vomiting without diarrhea. Laboratory tests showed: hematocrit 28% hemoglobin 9g/dl, LDH 1415 IU/l, platelets 48000/mm3, schistocytes +, Urea 182 mg/dl, creatinine 3.4 mg/dl, C3 50 mg/dl (RV: 90-120 mg/dl). He became anuric and hemodialysis was initiated. PCR multiple for Shiga-toxin in stools in the local laboratory was negative. After 14 days without neither hematologic nor kidney improvement a dose of monoclonal anti C5 antibodies was prescribed. After that, we received from the National Reference Laboratory PCR Real Time in stools positive for Stx 2 and Lipopolysaccharide antibodies 0145 IgM- /IgG +. With these results eculizumab was withdrawn assuming that the patient had an STEC-HUS. The patient continued without neither hematologic nor kidney improvement and 2 weeks later further laboratory results showed very high titers of anti FH antibodies by ELISA (8500UA/ml, RV < 100 UA/ml). Eculizumab was re-initiated, adding prednisone and mofetil mycophenolate. Genetic test performed by the next generation sequencing and multiplex ligation-dependent probe amplification revealed a homozygous deletion in the CFHR1 and CFHR3 and a heterozygous variant of uncertain significance in CFI. During the following 2 weeks he normalized hematological parameters. He withdrew hemodialysis after the second dose of Eculizumab and normalized the renal function and the titers of anti FH antibodies 2 months later. After 6 months, with the patient in total remission, eculizumab was discontinued, whereas continued receiving prednisone during the first year and mofetil mycophenolate for 2 years without relapses. Currently he is in remission and free of treatment.

Conclusion: Atypical HUS is a diagnosis of exclusion and STEC-HUS is the most important diagnose to rule out. Exceptionally, both situations can coexist and STEC can be the trigger of the disease in children with a genetic predisposition.

128 - P1.082

CAN A COMBINATION OF HETROZYGOTIC MUTATIONS IN GENES ASSOCIATED WITH THE DEVELOPMENT OF NEPHROTIC SYNDROME BE A CAUSE OF STEROID RESISTANCE?

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Objective: A demonstration of a clinical case of a 9-year-old female patient with steroid-resistant, secondary steroid-sensitive nephrotic syndrome.

Description of the case: The early onset of NS in a patient at the age of 3 years was accompanied by massive edema, ascites, proteinuria up to 3.6 g/l, hypoproteinemia, and hyperlipidemia. While taking prednisolone 60 mg/m2 for 6 weeks, remission was not achieved (proteinuria remained up to 3 g/l), a pulse therapy with prednisolone 30 mg/kg/48h was performed, which led to a decrease in protein loss up to 0.6- 0.8 g/l, however, after the end of the pulse therapy, proteinuria reached the nephrotic level again. This condition was regarded as steroid resistance, and therefore a nephrobiopsy was performed and a picture of MCD and FSGS was revealed. After a gradual dose reduction and discontinuation of prednisolone, trace proteinuria remained at 0.3 g/l. Next was the development of 5 relapses of NS over 6 years, three of which developed during the long-term remission and responded to prednisolone 60 mg/m2, which was regarded as secondary steroid sensitivity. In two cases proteinuria persisted at a dose of prednisolone 60 mg/m2, which required pulse therapy with prednisolone with a positive effect. During the inter-relapse period and up to the present day, proteinuria remains at 0.2-0.6 g/day. Taking into account the rarely relapsing course of NS, nephrobiopsy results, complications from steroid therapy mycophenolate mofetil 900 mg/m2 was prescribed. During observation, renal function remained intact (GFR 98.3-141 ml/min/m2 based on creatinine), height > 97th percentile, Cushing, no signs of osteoporosis. Ultrasound: kidney volume > 97th percentile, the parenchyma is thickened and not clearly differentiated. Signs of labile systolic arterial hypertension (enalapril 0.27 mg/kg is prescribed). Due to the atypical course of the disease, whole exome sequencing was performed and previously undescribed missense mutations were identified in genes potentially related to the phenotype: DAAM2, LAMB2, PTPRO. All identified mutations occur in a heterozygous state in genes encoding proteins of the glomerular basement membrane or podocytes and are associated with autosomal recessive nephrotic syndrome of different types.

Conclusions: NS associated with mutations in these genes is inherited autosomal recessively, and therefore isolated heterozygous mutations cannot be the cause of the described phenotype. However, an early onset, the persistence of trace proteinuria in the inter-relapse period, a positive response only to high doses of prednisolone, BMI or FSGS according to nephrobiopsy indicate a high probability of genetic mediation. The question of whether multiple heterozygous mutations in genes responsible for the development of phenotypically similar diseases can be the cause of their development or a potentiating factor requires further study.

141 - P1.083

THE NATURAL HISTORY OF IGA NEPHROPATHY IN A SINGLE CENTRE COHORT OF CROATIAN CHILDREN SHOWS BENEFICIAL COURSE WITH THE ABSENCE OF COMPLETE RENAL RESMISSION

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Aims/Purpose: IgA nephropathy (IgAN) is a complex disease diagnosed only upon evaluation of a kidney biopsy. There is a substantial heterogeneity of clinical presentation and pathological features between geographical locations, with fewer data available for region of central and southern Europe. We aim to provide a conscientious description of a paediatric IgAN cohort from a centre caring for most of the Croatian paediatric patients.

Methods: Single centre retrospective study of children newly diagnosed as IgAN since 2011 in a tertiary referral centre for paediatric nephrology of the Republic of Croatia.

Results: Total of 17 (11 M) paediatric patients were included, of which 16 were Caucasians and 1 of Roma origin. All had proteinuria (> 150 mg/day/1.73m2) and hematuria (> 5 RBC/mm3 in uncentrifuged urine), with the mean age of 12.3 ± 3.6 years at the time of the biopsy. The median value of proteinuria was 214 mg/day/1.73m2 (162 – 484), and of eGFR 90 mL/min/1.73m2 (75 – 111). The results of the biopsy in terms of MEST-C score showed M1 in 4, E1 in 0, S1 in 5, T1 in 4, T2 in 0, C1 in 2 and C2 in 0 of the patients. The IF was positive for IgA and C3 in all patients, and C1q in 1. There was significant large positive relationship between C3 intensity values and proteinuria (r = 0.55, p =0.02), and non-significant small negative between eGFR (r = -0.12, p =0.44), respectively. Hypertension was present in 3 (18%) patients. The median risk of a 30% decline in eGFR or progression to ESRD 5 years after biopsy was 8.12% (4.67 – 13.90). Initial presenting episode was treated with ACEi in 8 (47%) and with glucocorticoids in 4 (24%) patients. There was no significant difference in proteinuria (p =0.21) or risk of decline in eGFR or progression to ESRD (p =0.12) among treated and untreated patients. In all except 1 of the treated patients proteinuria reached a target of < 150 mg/day/1.73m2 during the median time of 11 (6 – 21) months. The median follow up was 5.1 (2.3 – 9.5) years. During the follow up 5 patients experienced first relapse of proteinuria, 3 had second and 0 had third relapse. Tonsillectomy was performed in 2 patients with a substantial improvement in haematuria episodes reported by caregivers. Omega-3 was used in 2 patients. While none of the patients developed CKD during the follow up, none have reached complete renal remission.

Conclusion: All the patients in our cohort had indolent disease with non-nephrotic range proteinuria, along with low risk of progression to ESRD after biopsy. Yet, regardless of the treatment options, none achieved full renal remission due to the persistent haematuria. The scarcity of available information about the course and outcome of this intricating disease in children emphasizes the need for additional reports of well characterized cohorts from around the globe, which might provide further reassurance and support for patients, their families and physician.

169 - P1.084

COVID-19 IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME : A CASE SERIES

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Aims/Purpose: COVID-19 is a highly infectious respiratory disesase that can cause significant morbidity and mortality, especially in patients with underlying chronic conditions and those in immu-compromised states. This raises concerns about susceptibility and clinical outcome in children with underlying Idiopathic Nephrotic Syndrome (INS) due to its often relapsing clinical course and the need for immunosuppression. This case series study aims to describe the impact of COVID -19 in children with INS from a single centre.

Methods: This is a retrospective cohort study of 20 patients with INS who had COVID-19 infection. The demography, clinical presentatoins, treatment modalities and clinical outcome were analyzed. Statistical analyses were performed to identify factors associated with relapse of NS during the COVID-19 infection.

Results: The mean age at diagnosis of INS and at onset of COVID-19 infection were 5.1 ± 2.7 years and 10.4 ± 4.5 years respectively. Six patients (30%) had Steroid Resistant Nephrotic Syndrome (SRNS) while the remaining 14 patients had Steroid Sensitive Nephrotic Syndrome (SSNS). Thirteen patients (65%) were on one or more immunosuppressants during the COVID-19 infection. Age, gender, histopathological findings, and specific immunosuppressants used did not correlate significantly with relapse of NS. Four patients(20%) had relapse of NS during the COVID-19 infection with significantly higher incidence in SRNS (p =0.032). Hospitalisation was needed for three patients while one patient developed Acute Kidney Injury (AKI) as a complication during the COVID-19 infection. None of the patients require respiratory support.

Conclusion: COVID-19 did not trigger a relapse in most of the patients with INS and the COVID-19 infection ran a mild clinical course. Nevertheless the risk of relapse was higher and AKI can be a possible complication in SRNS patients with concomitant COVID-19 infection.

178 - P1.085

RADIOLOGIC RENAL INVOLVEMENTS IN PEDIATRIC CROHN DISEASE

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Aims/Purpose: Crohn disease (CD) is a type of the inflammatory bowel disease (IBD) describing a group of disorders characterized by chronic inflammation of gastrointestinal tract. Among the extraintestinal manifestations seen in IBD, renal involvements have been reported in 4% to 23% of the patients. Although nephrolithiasis (NL) and glomerulonephritis (GN) are known to be common, there has been few discussion about radiologic findings of renal manifestations in CD. In this study, our aim was to analyze the characteristics of radiologic renal involvements in pediatric patients with CD.

Methods: A retrospective study was performed in patients who were diagnosed with CD at age under 18 years in Samsung Medical Center from 2019 to 2023. Primarily, the formal reading of radiologic image including ultrasonography (US), computed tomography (CT) and magnetic resonance image (MRI) were reviewed. Medical records including sex, age, and laboratory findings were consecutively reviewed in CD patients with confirmed abnormal radiologic findings in kidneys.

Results: A total of 41 (4.9%) out of 827 patients diagnosed with CD presented abnormal findings of kidneys on radiologic evaluations. Their mean age at the time of renal diagnosis was 13.0 ± 3.6 years with male-to-female ratio of 33:8. The mean pediatric Crohn disease activity index (PCDAI) was 23.4 ± 15.1 at the time of renal diagnosis. Renal cyst (22/45, 48.9%) was the most common finding followed by parenchymal heterogeneity (16/45, 35.6%) and NL/nephrocalcinosis (NC) (2/45, 4.4%). Though renal cysts have no specific implications clinically, parenchymal heterogeneity designated ischemic change of kidneys, predominant at the initial diagnosis of CD. About 70% (11/16) of patients with parenchymal heterogeneity showed spontaneous resolution within mean duration of 164 days while only one and none patient for renal cyst and NC/NL, respectively. One patient with persistent parenchymal heterogeneity who also demonstrated hematuria and proteinuria was pathologically confirmed IgA nephropathy.

Conclusion: Disease activity of CD might cause renal parenchymal heterogeneity and it is mostly reversible. However, once the lesion is detected, patients should be monitored for their renal function and urinary abnormalities as persistent radiologic abnormality might be a clue for diagnosis of GN or chronic kidney disease (CKD).

179 - P1.086

DESING AND METHOD OF KOREAN PEDIATRIC COHORT STUDY FOR IMPROVING OUTCOME IN NEPHROTIC SYNDROME (KEYNOTE): A NATIONWIDE PROSPECTIVE COHORT

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Aims/Purpose: The childhood nephrotic syndrome (NS) exhibits variable courses and prognoses, with treatment approaches differing among clinicians. Frequent relapses can lead to complications from both medications and the disease itself, significantly reducing the quality of life for patients and their families. Moreover, despite continuous treatments, some patients progress to end-stage kidney disease, yet no biomarkers are currently available to predict treatment response for NS. Previous studies have shown that clinical manifestations and medication response in NS vary across races and regions. Therefore, this cohort study aims to comprehend the characteristics of Korean pediatric NS patients.

Methods: Children with nephrotic syndrome will be recruited from all 28 pediatric nephrology centers across Korea. The eligible participants will undergo evaluation for clinical data including physical examination, laboratory findings, medications, and pathologic or genetic findings at diagnosis, as well as 1/3/6 months after diagnosis, and annually thereafter. Samples of buffy coat, serum, urine, and kidney tissue will be stored for further exploration of NS biomarkers. Additionally, information on steroid response, number of relapses, cumulative dosage of medications (steroids, cyclosporine, tacrolimus, and cyclophosphamide), and drug-related complications will be collected. Events such as infection, peritonitis, fracture, Stevens-Johnsons syndrome, thromboembolism, acute kidney injury, death, renal event (including doubling of creatinine, 50% decline in glomerular filtration rate, or initiation of renal replacement therapy), and cardiovascular event will also be collected.

Results: The data obtained from this cohort will be analyzed to determine the incidence, and risk factors for relapse, medication response, complications, and progression to chronic kidney disease.

Conclusion: As the first nationwide cohort for pediatric NS in Korea, the KEYNOTE will contribute to a comprehensive understanding of the clinical manifestations, as well as the short-term and long-term complications, prognosis, and risk factors associated with NS.

185 - P1.087

RES(E)T AND RELAXATION - INTRACTABLE HYPERNATRAEMIA

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Aim/Purpose: Sodium and water homeostasis is regulated by vasopressin (AVP) release from the anterior pituitary and its antidiuretic action on the kidney. Osmoreceptors detect changes in plasma tonicity. The osmotic threshold (or osmostat) for AVP release is ~285 mOsmol/kg H20.

Results: A 3-y boy with global developmental delay, cerebral palsy and G-tube dependence presented with pneumonia. The plasma sodium (PNa) improved from 154mmol/L to 151mmol/L with increased water intake. On follow up, PNa was 157mmol/L: he was admitted for further investigations. There was persistent sialorrhea and diaphoresis, but no medication changes, excess water losses or increased salt intake. He had stable vitals, 100g drop in weight and unremarkable examination. With no intervention, repeat bloodwork showed PNa 150mmol/L, plasma osmolality (POsm) 309 mOsm/kg H20, urine osmolality (UOsm) 1019 mOsm/kg and FeNa 0.5%. All other serum electrolytes and renal indices were unremarkable. Active increase in free water intake above his usual total fluid intake resulted in a PNa nadir of 146mmol/L, with urine osmolality of 187 mOsm/kg (Figure 1). These data show evidence of free water loss while still hypernatremic. After returning to his TFI, PNa settled around 151 mmol/L, with UOsm 600 mOsm/kg, and has remained stably high ever since.

Conclusion: We describe a case of hypertonic hypernatremia and concomitant highly concentrated urine, indicating excellent urinary concentrating ability and adequate ADH production, effectively ruling out diabetes insipidus. Once PNa dropped below 150mmol/L (but never less than 146), enhanced free water excretion was invariably observed. We hypothesized that these findings are in keeping with an osmostat that is reset at a higher POsm to trigger ADH release: a rarer form of reset osmostat (RO), which is more commonly associated with hyponatremia (type C SIADH). We estimate that the threshold is ~150mmol/L instead of the usual 145. The etiology remains unclear with no hypothalamic lesion and no evidence of anterior pituitary dysfunction, and perhaps long term hypodipsia contributed. An overview of published literature on reset osmostat hypernatremia will be discussed. RO should be considered when dealing with a patient with an unusually difficult-to-control dysnatremia, when there is evidence of normal kidney function, and intact urine diluting and concentrating ability.

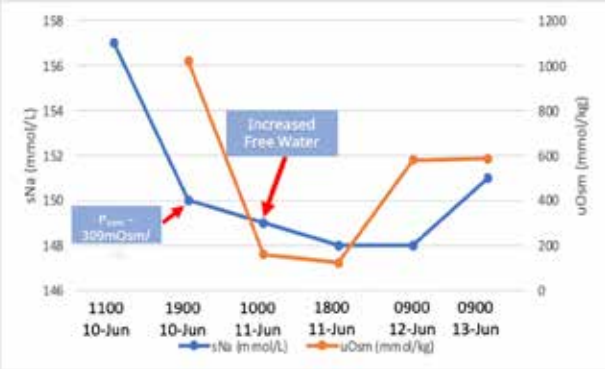

Figure 1

193 - P1.088

PEGCETACOPLAN FOR THE TREATMENT OF PEDIATRIC COMPLEMENT 3 GLOMERULONEPHRITIS: A CASE REPORT

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Aims/Purpose: Complement 3 glomerulopathy (C3G) is an ultrarare glomerular disease that includes two subgroups, C3 glomerulonephritis (C3GN) and dense deposit disease (DDD), both of which involve dysregulation of the complement system. Amplification and propagation of the complement cascade results in downstream assembly of the membrane attack complex (C5b-9) and ultimately culminates in glomerular deposition of C3 and C5 breakdown products and subsequent renal parenchymal damage. Without targeted disease-modifying medications, the prognosis for C3G is poor. Pegcetacoplan binds to C3 and its activation fragment C3b, thus controlling the cleavage of C3 and generation of downstream effectors. This case report describes our experience using pegcetacoplan in a pediatric patient for treatment resistant C3GN.

Methods: Narrative report of a pediatric case from a US referral hospital.

Results: A previously healthy 9-year-old boy was referred to our center for a second opinion and evaluation of refractory membranoproliferative glomerulonephritis following several inpatient admissions for acute kidney injury and edema. Despite treatment with high dose of prednisone 40 mg/day and mycophenolate mofetil 500 mg twice daily for immunosuppression and amlodipine, lisinopril, hydrochlorothiazide, and fluid restriction for difficult-to-manage edema, he continued to have nephrotic range proteinuria, with a urine protein-to-creatinine ratio (uPCR) of 10 g/g, a serum creatinine of 0.4 mg/dL, a low serum C3 level (35 mg/dL), and anasarca. Given the concern for refractory C3GN following a steroid taper and tacrolimus trial with modest response (reduced proteinuria), we initiated pegcetacoplan 540 mg twice weekly for 1 week followed by 648 mg twice weekly. Laboratory values before pegcetacoplan initiation included a uPCR of 1.1 g/g, serum creatinine of 0.87 mg/dL, serum albumin of 4.7 g/dL, and serum C3 level of 30 mg/dL. Clinically significant improvements in serum C3 levels (142 mg/dL) and uPCR (422 mg/g) were observed within 1 week (Figure 1). Within 3 months of starting pegcetacoplan, all immunosuppressive and antihypertensive medications were discontinued completely. No adverse effects of pegcetacoplan were reported. A kidney biopsy after 6 months of pegcetacoplan treatment showed mesangial and focal endocapillary proliferative glomerulonephritis with isolated C3c deposition by immunofluorescence, consistent with previous C3GN diagnosis. However, this biopsy showed a reduction in endocapillary hypercellularity, capillary wall double contour formation, and glomerular C3c deposition by immunofluorescence.

Conclusion: In this pediatric patient, compassionate use of pegcetacoplan was associated with rapid clinical improvement without adverse effects, and clinical effectiveness was confirmed by laboratory and histologic results within 6 months of treatment initiation.

207 - P1.089

A RARE KIDNEY INVOLVEMENT OF LYSINURIC PROTEIN INTOLERANCE: MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS

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Aims/Purpose: Lysinuric protein intolerance (LPI) is a rare inherited metabolic disease with multisystem involvement. Kidney involvement is a serious complication. Generally, it begins with mild proteinuria, and hematuria and can progress to end-stage kidney disease. Although tubular impairment, nephrocalcinosis, and chronic tubulointerstitial nephritis are the most common types of kidney disease, glomerular diseases are very rare.

Methods: Case report

Results: An 11-year-old girl was diagnosed with hemophagocytic lymphohistiocytosis (HLH) while being investigated for recurrent fever, hepatosplenomegaly, and inability to gain weight. The urinary amino acid analysis was compatible with the diagnosis of LPI. L-citrulline, L-carnitine, and sodium benzoate were initiated. During the next two years, her clinical status remained stable. At the age of 13 years, liver biopsy was performed because of the ascites in the abdomen, elevated transaminases and prolonged prothrombin time, and macrovesicular steatosis and incomplete cirrhosis were detected. Shortly thereafter, she came to the clinical attention with nephrotic syndrome (hypoalbuminemia, proteinuria 502 mg/2/hour) and low complement levels [C3: 48 mg/dl (79-152), C4: < 1.67 mg/dl (16-38)]). Serum creatinine and urine output were normal. Kidney biopsy revealed immune complex membranoproliferative glomerulonephritis (IC-MPGN) (Figure). No infectious disease, systemic immune disease, or malignancy was detected as a cause of IC-MPGN, and C3 nephritic factor was negative. She received pulse methylprednisolone treatment (15 mg/kg/day, 3 days), and then oral prednisolone (0.5 mg/kg/day). Complete remission was achieved with steroid treatment which was discontinued within 18 months, and no relapses were observed during the 3 years of follow-up.

Conclusion: Immune dysregulation is a known entity in LPI and frequently leads to serious complications such as HLH, autoimmune diseases, and pulmonary alveolar proteinosis. The underlying mechanism of IC-MPGN in LPI is still obscure; however, immune dysfunction is thought to play an important role. This case highlights that immune-mediated glomerulonephritis can be observed in LPI patients due to immune dysregulation and hyperinflammation, and immunosuppressive treatment provides significant benefits in the management of the disease.

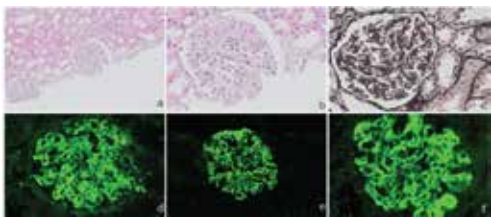

Figure: Mesangial hypercellularity with increase in mesangial matrix (Hematoxylin and Eosin, scale bar = 100 µm) b. Irregular thickening of glomerular basement membranes (Hematoxylin and Eosin, scale bar = 50 µm) c. Glomerular basement membrane double contours (Jones Methenamine Silver, scale bar = 50 µm) Irregular granular capillary loop and mesangial immunofluorescence staining with C3 (d: scale bar = 50 µm), IgG (e: scale bar = 50 µm), IgM (f: scale bar = 50 µm).

208 - P1.090

ACUTE POST INFECTIOUS GLOMERULONEPHRITIS ASSOCIATED TO SCABIES IN CHILDREN-HOW RARE IS RARE?

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Acute post infectious glomerulonephritis (PIGN) secondary to scabies in children is extremely rare and even rarer are the reported histopathological lesions on renal biopsy. Early diagnosis is necessary in order to prevent disease progression and also early treatment is necessary to avoid further complications. In PIGN, the underlying disease treatment ultimately leads to renal recovery.

Aim: The aim is to provide more details of the clinical features and the histopathologic characteristics, and to increase the vigilance among physicians in patients with PIGN secondary to systemic scabies.

Results: We report the cases of two brothers aged 13 years and 11 years admitted in our hospital. The first one was admitted in the ICU department for seizures, malignant hypertension and oligo-anuria, and the other one was hospitalized in the nephrology department with the suspicion of acute glomerulonephritis: hematuria, nephrotic range proteinuria, hypoalbuminemia, low C3, arterial hypertension and variable azotemia. Clinical examination revealed typical lesions for Sarcoptes Scabiei skin infection in both siblings confirmed by dermoscopy. The older brother was diagnosed with posterior reversible encephalopathy syndrome (PRESS) by magnetic resonance imaging. He also had a degree of renal dysfunction with nephritic range proteinuria, microscopic hematuria, and hypoalbuminemia. Kidney biopsy of both patients was suggestive for PIGN. The patients were treated with oral Ivermectine and local sodium benzoate with good renal neurological and dermatological outcome.

Conclusions: PIGN associated with scabies is easily misdiagnosed due to its rarity in clinical practice. Early diagnosis and treatment is necessary to prevent disease progression.

Keywords: Acute post infectious glomerulonephritis; scabies; children.

215 - P1.091

EPIDEMIOLOGICAL AND CLINICAL CHARACTERISTICS OF PEDIATRIC ACUTE KIDNEY INJURY: A MONOCENTRIC STUDY

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Aims: Acute kidney injury (AKI) is not uncommon in pediatrics. The aim of our study was to determine the clinical and epidemiological characteristics of children hospitalized for AKI.

Methods: It was a monocentric, retrospective, descriptive, analytical study conducted at the pediatric department of Charles Nicolle Hospital in Tunis over a period of 21 years (from January 1, 2001, to December 31, 2022). Patients included in our study met the following criteria: age ≤ 18 years at the diagnosis of acute kidney injury (AKI). Diagnosis of AKI according to the criteria of the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines. Patients not included in our study were those: having chronic kidney disease (CKD), and those who had one or more emergency renal replacement therapy (RRT) sessions for an indication other than AKI.

Results: We collected 111 cases of AKI, the mean age of the patients was 6.5 ± 5 years, with a range from 1 day to 16 years. The majority of children were over 6 years old, accounting for 52.3% of the cases. An age range between 2 and 6 years was found in 22.5% of cases, followed by the age group of 1 month to 2 years in 17.1% of cases. Neonatal AKI was noted in 8.1% of cases. The reasons for consultation were predominantly: signs of infection in 31.5% of cases, hematuria in 30.6% of cases, and gastroenteritis in 28.7% of cases. Hypertension was observed during physical examination in more than half of the cases (59.1%). The average systolic blood pressure was 12.4 ± 2 mmHg (range: 7 to 19 mmHg). The average diastolic blood pressure was 7.7 ± 2 mmHg (range: 5 to 12 mmHg). edema was found in 38 cases (43.5%). Most of patients, 65 (58.2%), had preserved diuresis, while 25 (22.8%) were anuric and 21 (19%) were oliguric. The median creatinine level in our sample was 200 µmol/l (range: 37 to 1688 µmol/l), with a mean of 333 µmol/l. The progression to chronic kidney disease was noted in 31 cases. The transition to end-stage renal disease was observed in 12 patients, representing 11.2% of the total number of patients and 38.7% of those who progressed to chronic kidney disease. Nine patients (8.1%) had died, including 5 boys (55.6%) and 4 girls (44.4%). The median age of the deceased children was 1.2 years (range: 18 days to 9 years).

Conclusions: AKI is common in pediatrics, and clinical presentations vary. Early diagnosis is essential for improving prognosis.

234 - P1.092

ECULIZUMAB IN TREATMENT OF SHIGA TOXIN-PRODUCING ESCHERICHIA COLI HEMOLYTIC UREMIC SYNDROME IN CHILDREN - FIRST EXPERIENCE AT OUR HOSPITAL

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Aims/Purpose: Hemolytic uremic syndrome (HUS) is one of the leading causes of acute kidney injury, which requires renal replacement therapy in children. Specific therapy for Shiga toxin-producing Escherichia coli (STEC) HUS does not yet exist. Introducing anti C5 monoclonal antibody in therapy for atypical HUS had revolutionary changed the disease outcome, while the role of anti-complement therapy in STEC HUS is not yet clear. Our aim was to present our experience with Eculizumab in treatment of children with STEC HUS.

Methods: During 2023, between June 1st and October 1st, twelve children with HUS were treated in our Hospital. Two patients (16,7%) with confirmed STEC HUS and extremly severe clinical presentation received Eculizumab.

Results: At the moment of Eculizumab administration, both patients had multi-organ involvement (kidney, central nervous system, heart, lungs, pancreas) and were on mechanical ventilation, renal replacement therapy and inotropic support. The first patient, a 6 year-old boy received Eculizumab on the 8th hospital day (the 10th day since the disease started), after 4 plasma exchanges and after rapid worsening of the clinical course with multi-organ failure, which was accompanied by short-term cardiac arrest. The second patient, a 7 year-old boy received Eculizumab on his 3rd hospital day (the 6th day since the disease started), after 2 plasma exchanges due to clinical deterioration predominantly of the central nervous system and heart function. In the first 24 hours since drug administration, significant clinical improvement in both patients was observed. In both patients, plasma exchanges were stopped after the first dose of Eculizumab. The first patient was discharged on the 35th hospital day, after 3 doses of Eculizumab (eGFR 69 ml/min/1.73 m2, UPCR 3.62 mg/ mg, hypertensive, with slighty elevated amylase and lipase, other findings were normal). The second patient was discharged on the 19th hospital day, after 2 doses of Eculizumab (eGFR 212 ml/min/1.73 m2, UPCR 2.84 mg/ mg, other findings were normal). One month after discharge, the first patient received an additional dose of Eculizumab, while the second patient received three aditional doses each one month apart. After 6 months since the disease start, both patients had normal clinical and laboratory findings, except the second patient still had mild proteinuria (UPCR 0.6 mg/ mg).

Conclusion: In our two patients with STEC HUS and severe multi-organ involvement, in our opinion, Eculizumab was life saving therapy.

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ETIOLOGIES OF PEDIATRIC ACUTE KIDNEY INJURY: EXPERIENCE FROM A PEDIATRIC NEPHROLOGY DEPARTMENT

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Aim: Acute kidney injury (AKI) is not uncommon in pediatrics, with diverse etiologies, some of which compromise the patient's life prognosis. The aim of this study was to investigate the main causes of AKI in a Tunisian reference center.

Methods: This was a monocentric, retrospective, descriptive, analytical study conducted at the pediatric department of Charles Nicolle Hospital in Tunis over a period of 21 years (from January 1, 2001, to December 31, 2022). Patients included in our study met the following criteria: age ≤ 18 years at the diagnosis of AKI, diagnosis of AKI according to the criteria of the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines. Patients not included in our study were those having chronic kidney disease, and those who had one or more emergency renal replacement therapy sessions for an indication other than AKI.

Results: We collected 111 cases of AKI. Among them, we identified: functional AKI in 12 cases (10.9%), with multi-organ failure present in 50.2% of cases, perinatal asphyxia, severe dehydration, and post-operative AKI in 16.6% of cases each. Obstructive AKI was identified in only one male case. The etiology was obstructive urinary lithiasis due to adenosine phosphoribosyltransferase deficiency. Parenchymal and vascular AKI were present in 98 cases (88.2%), with a mean age of 6.8 ± 5 years (range: 3 days to 13.8 years). These cases of parenchymal AKI were distributed as follows: hemolytic uremic syndrome (HUS) represented 31.4% of all AKI cases and 47.8% of parenchymal and vascular AKI in our study. This included: post-infectious HUS in 15 cases (42.3%), immunologic HUS in 18 cases (51.4%), and neonatal HUS in 7 cases (6.3%). Glomerular nephropathy was identified in 35 patients (19 boys and 16 girls), accounting for 31.5% of AKI cases and 35.7% of parenchymal AKI cases. These glomerular nephropathies with AKI were mainly manifested by: post-infectious acute glomerulonephritis (AGN) in 20 patients (18%), rapidly progressive glomerulonephritis (RPGN) in 15 patients (13.6%).

Conclusion: The prognosis of AKI closely depends on the underlying cause, highlighting the importance of early etiological diagnosis.

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BLOOD PRESSURE PROFILE IN TYPE 1 DIABETIC CHILDREN AND ADOLESCENTS: RELATION TO ALBUMINURIA

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Aims: to examine the characteristics of ambulatory blood pressure (ABP) including blood pressure variability (BPV) and its association with albuminuria in type 1 diabetic (T1D) children and to identify potential predictors of high – normal albuminuria and microalbuminuria.

Methods: ABP monitoring was performed in 201 T1D children and adolescents (mean age 14.7 ± 3.8 years) with T1D duration over one year (Table 1). The level of albuminuria was assessed as albumin/creatinine ratio (ACR) and patients further classified as low-normal, high-normal or microalbuminuria.

Results: Fifteen (7.5%) T1D children were hypertensive using office blood pressure (BP) and 10 (5%) according to ABP. T1D subjects had elevated 24-hour systolic BP (SBP) and diastolic BP (DBP) (+0.2 and + 0.3 SDS) and nighttime SBP and DBP (+0.6 and +0.8 SDS) compared to reference values (Figure 1). Patients with microalbuminuria had significantly higher 24-hour, daytime and nighttime DBP compared to normoalbuminuric subjects (Table 2). There was a high percentage of non-dippers (74.1%). Nighttime diastolic BPV was significantly higher in subjects with high-normal compared to low-normal albuminuria (p =0.01). A weak correlation was found between ACR and daytime DBP SDS (r = 0.29, p < 0.0001) and nighttime DBP SDS (r = 0.21, p =0.003). Age and nighttime diastolic BPV were predictors of high-normal albuminuria while nighttime DBP was strong predictor for microalbuminuria.

Conclusion: T1D children have impaired BP regulation although most of them do not fulfill the criteria for sustained hypertension. There is an association between diastolic ABP and diastolic BPV with rising levels of albuminuria pointing on a clear connection between BP and incipient diabetic nephropathy.

Table 1.

Variable	total	low normal albuminuria	high normal albuminuria	P	microalbu-minuria	P
N	201	158 (78.6%)	36 (17.9%)		7 (3.5%)	
Age (y)	14.7 ± 3.8	14.9 ± 3.8	13.2 ± 3.9	0.017	16.4 ± 1.5	0.336
Sex (m %)	44.8	55.7	55.6	0.865	42.9	0.777
BMI (kg/m2)	21.2 ± 5.3	21.5 ± 5.5	50.6 ± 19.7	0.074	21.4 ± 1.6	0.622
Diabetes duration (y)	6.9 ± 4.2	6.9 ± 4.3	6.8 ± 4.1	0.894	5.4 ± 3.1	0.337
HbA1c (%)	8.2 ± 1.6	8.0 ± 1.4	8.5 ± 1.7	0.131	10.5 ± 2.5	0.006
eGFR (ml/min/1,73m2)	117.6 ± 18.4	116.6 ± 17.6	119.9 ± 22.1	0.346	126.6 ± 14.7	0.189
Office SBP (mmHg)	112.0 ± 12.4	112.2 ± 12.5	109.5 ± 11.7	0.214	121.4 ± 9.9	0.034
Office DBP (mmHg)	70.6 ± 8.9	70.4 ± 8.9	70.7 ± 8.6	0.860	72.9 ± 9.1	0.429

Table 2.

Variable	All patients (n = 201)	Low normal albuminuria (n = 158)	High normal albuminuria (n = 36)	p	Microalbuminuria (n = 7)	p
24-h SBP SDS	0.2 + 0.7	0.2 + 0.7	0.2 + 0.8	0.93*	0.2 + 0.8	0.84*
24-h DBP SDS	0.3 + 1.1	0.2 + 1.1	0.3 + 1.0	0.76*	1.2 + 0.6	0.03*
daytime SBP SDS	-0.0 + 0.7	-0.0 + 0.7	-0.0 + 0.7	0.92*	-0.1 + 0.8	0.77*
daytime DBP SDS	-0.2 + 1.1	-0.2 + 1.0	-0.3 + 1.0	0.88*	1.0 + 1.4	< 0.01*
nighttime SBP SDS	0.6 + 0.7	0.6 + 0.7	0.6 + 0.8	0.66*	0.8 + 0.5	0.52*
Nighttime DBP SDS	0.9 + 0.9	0.9 + 0.9	0.9 + 0.6	0.95*	2.3 + 0.6	< 0.01*

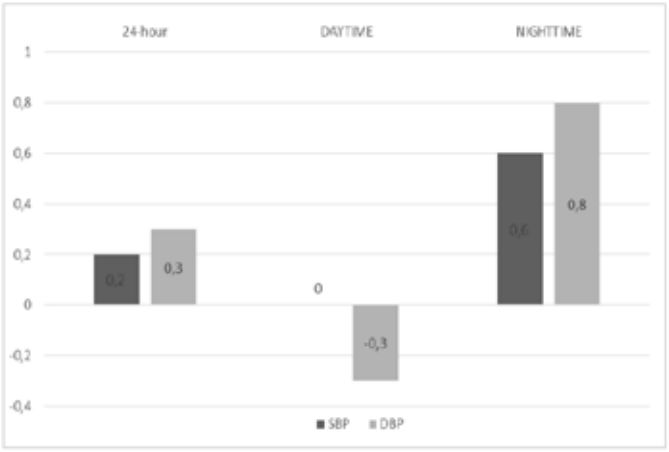

Figure 1.

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RHEUMATOID PURPURA NEPHRITIS IN CHILDREN: PREDICTIVE AND PROGNOSTIC FACTORS

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Aims: Rheumatoid purpura (RP) is the most common vasculitis in children. Nephropathy determines the prognosis of this disease. The aim of our study is to analyze the epidemiological, clinicobiological, histological, therapeutic and evolutionary particularities of rheumatoid purpura nephritis (RPN), as well as her associated prognostic factors.

Methods: This was a retrospective, analytical study that included children (age≤18 years) followed in the paediatric department of Charles Nicolle Hospital in Tunis for RP over a 19-year period (2002-2019).

Results: A total of 99 patients were included (61 males and 31 females), with a sex ratio of 1.6. The mean age at diagnosis of RP was 6.85 ± 3 years). Sixty-four children developed kidney damage, with a median onset of 46.3 days (range: 1 to 700 days). Edema was present in 37.5% of cases. Ten patients had hypertension (15.6%) at the time of initial diagnosis. Macroscopic hematuria was present in 31.2% of cases. Mean creatinine clearance was 108.2 ± 25 ml/min/1.73m^2 (extremes: 58.6 and 179.6 ml/min/1.73m^2). Renal biopsy was performed in 32 patients; the most frequent histological type in our series was M1S1E0C0T0 according to the Oxford classification. Corticosteroid therapy was prescribed in 38 children (59.3%) and immunosuppressive therapy was required in 15 patients with severe nephritis. The mean follow-up in children with nephritis was 4.6 ± 3.5 years (extremes: 3 months and 15 years). Remission was achieved in 37 patients (57.8%), while 2 patients developed an end-stage renal disease. Only one child died at the age of 10 (3 months after the diagnosis of the nephritis and 2 months after the initiation of dialysis). After multivariate analysis, the risk factors identified for the occurrence of nephritis were advanced age and the presence of digestive hemorrhage. However, only advanced age was a poor prognostic factor.

Conclusion: Kidney damage in PR is common. Identifying predictive and prognostic factors such as advanced age or the presence of digestive hemorrhage would enable us to tailor treatment and prevent or slow the progression to end-stage renal failure.

288 - P1.096

ECULIZUMAB USE IN PATIENTS WITH PNEUMOCOCCAL-ASSOCIATED HEMOLYTIC UREMIC SYNDROME AND KIDNEY OUTCOMES

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Aims/Purpose: The aim of the study was to describe the course and kidney outcomes of pneumococcal-associated hemolytic uremic syndrome (P-HUS) in patients with and without eculizumab treatment.

Methods: We analyzed demographic, clinical, and laboratory data of patients with P-HUS from our center.

Results: The cohort consisted of 4 females and 3 males. All patients had pneumonia. Four were given eculizumab (days 1–3). The eculizumab group required a shorter duration of dialysis and mechanical ventilation (medians 20 vs. 28.5 and 30 vs 38.5 days, respectively) compared with the non-eculizumab group, but this was still much longer than normally reported; the thrombocytopenia resolution was similar in both groups (medians 10 vs. 8 days). Chronic kidney disease (CKD) was correlated with the duration of dialysis and mechanical ventilation duration at 1 year ($r = 0.797$, $P = 0.032$ and $r = 0.765$, $P = 0.045$) and last follow-up ($r = 0.807$, $P = 0.028$ and $r = 0.814$, $P = 0.026$, respectively); our scoring system showed even stronger correlations ($r = 0.872$, $P = 0.011$ and $r = 0.901$, $P = 0.0057$, respectively). The eculizumab group showed slightly better 1-year and last follow-up CKD stage (2.75 vs. 3, $P = 0.879$ and 2.5 vs. 3.67, $P = 0.517$).

Conclusion: Despite the fact that the eculizumab group showed better outcomes, eculizumab does not seem to improve the course of P-HUS compared with previous reports. Kidney outcomes are strongly correlated with the duration of dialysis and mechanical ventilation duration.

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CLINICAL CHARACTERISTICS OF CHILDREN WITH ACUTE POST-STREPTOCOCCAL GLOMERULONEPHRITIS AND RE-EVALUATION OF PTIENTS WITH ARTIFICIAL INTELLIGENCE

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Aims/Purpose: Acute post-streptococcal glomerulonephritis (APSGN) is the leading cause of acute glomerulonephritis among children. It may present as acute nephritic syndrome, nephrotic syndrome and rapidly progressive glomerulonephritis. ChatGPT (OpenAI, San Francisco, California, USA of America) has been developed as a chat robot supported by artificial intelligence. In this study, we evaluated whether artificial intelligence can be used in the follow-up of APSGN.

Methods: Clinical characteristics of patients with APSGN were noted from patient records. Twelve questions about APSGN were directed to ChatGPT 3.5. The accuracy of the answers was evaluated by researchers. Then, the clinical characteristics of the patients were transferred to ChatGPT 3.5 and it was examined how the follow-up would be managed by it.

Results: A total of 11 patients were included in the study. The mean age was 9.08 ± 3.96 years. Eight (72.7%) patients had elevated creatinine and 10 (90.9%) had hematuria and/or proteinuria. Hypertensive encephalopathy, nephrotic syndrome and rapidly progressive glomerulonephritis were observed in three different patients. Normal creatinine values were achieved in all patients. Questions assessing the definition, epidemiologic characteristics and pathophysiologic mechanisms, diagnosis and treatment of APSGN were answered correctly by ChatGPT 3.5. Also, all patients were diagnosed with APSGN and the treatment steps applied by clinicians were similarly recommended by ChatGPT 3.5.

Conclusion: The information and guidance provided by ChatGPT for APSGN may be a valuable resource in the care and management of patients. With artificial intelligence applications, clinicians can review their decisions and create more effective treatment plans.

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EVALUATION OF SCHOOL ACHIEVEMENTS IN ADOLESCENTS WITH PRIMARY HYPERTENSION

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Aims/Purpose: Primary hypertension (HT) is a global public health problem with increasing prevalence in recent years. HT may have cause decreased neurocognitive functions and learning difficulties. In this study, clinical characteristics of adolescents with primary HT were examined and the relationship between semester grade point average (GPA) and HT was evaluated.

Methods: This is an observational, cross-sectional, descriptive study conducted on adolescents with primary HT attending high school. Patient records (number of hospital visits, HT-related complaints, blood pressure measurements, and laboratory tests) were evaluated retrospectively. End-of-semester report card grades of Mathematics, Turkish Language and Literature and English courses were noted, and compared with the clinical characteristics of the patients.

Results: The study included 83 patients with a mean age of 15.6 ± 1.2 years. Patients with higher body mass index had lower grades in Mathematics ($p = 0.007$) and Turkish Language and Literature ($p = 0.004$). Patients with HT-related symptoms such as headache, epistaxis and palpitations had lower GPAs for all courses. Also, patients with hyperuricemia or proteinuria had lower semester GPAs compared to patients with normal serum uric acid levels or without proteinuria ($p < 0.05$). GPAs for Mathematics ($p = 0.000$) and Turkish Language and Literature ($p = 0.006$) decrease as the number of hospital visits increases.

Conclusion: HT may cause not only cardiovascular complications but also decreased neurocognitive functions through various mechanisms and may have a negative impact on academic skills. Therefore, HT should be followed up with a multidisciplinary approach and intensive efforts should be made to approach the goal of normotension.

331 - P1.099

CASE REPORT: IGA VASCULITIS NEPHRITIS ASSOCIATED WITH NEPHROTIC SYNDROME AND RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

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Background: IgA Vasculitis (Henoch Shconlein Purpura) is the most common small vessel vasculitis during childhood. It is characterized by a purpuric rash, arthritis/arthralgia and abdominal pain. Approximately 50% of patients develop renal manifestations termed as IgA Vasculitis Nephritis (IgAVN). These most commonly including isolated microscopic hematuria or non-nephrotic proteinuria, while full-blown nephrotic syndrome affect ~20% of cases. Rapidly Progressive Glomerulonephritis (RPGN) is the rarest manifestaion of IgAVN.

Methods: A 5-years-old, previously healthy male, developed nephrotic range proteinuria two weeks after presenting with a typical purpuric rash, arthritis of the ankles, abdominal pain, and normal urinalysis. Within two weeks from initial presentation, proteinuria up to 5 gr/day, hypoalbuminemia up to 2.9 mg/dL, hypertriglyceridemia, and hypercholesterolemia were abruptly followed by worsening of kidney functions with increase of creatinine up to 1.66 mg/dL. An urgent kidney biopsy showed more than 50% cellular cresents, extensive endocapillary proliferation, fibrinoid necrosis, and acute tubular injury, with massive mesangial deposition of C3&IgA. In accordance with KDIGO-2021 and SHARE-2019 guidelines for the treatment of IgAVN associated with RPGN, the patient was managed with intra-venous (IV) pulse methylprednisolone followed by IV Cyclophosphamide every two weeks and oral prednisone.

Results: Within two weeks under this therapeutic combination, there was a dramatic improvement of kidney function, with a decrease of serum creatinine to 0.48 mg/dL, but yet with clinical and laboratory signs of ongoing nephrotic syndrome.

Conclusion: RPGN is rare presentation of IgAVN. Our case presents rapid improvement of kidney function in response to combination therapy of IV high dose glucocorticoid and cyclophosphamide therapy. The long-term effect of this regimen on resolution of nephrotic syndrome and remains to be seen.

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BE AWARE OF DIFFERENT MANIFESTATIONS OF VASCULITES

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Vasculitis, defined as inflammation in a blood vessel, may occur as a primary process or secondary to an underlying disease, manifesting with a wide range of clinical symptoms. Given the multisystem nature of vasculitis, various pediatric subspecialties, including rheumatology, dermatology, nephrology, pulmonology, and cardiology, may be involved in diagnosis and ongoing care.

Our case involved a boy, one and a half years old, hospitalized initially for pulmonary disease. Subsequently, he experienced recurrent pulmonary exacerbations characterized by cough, labial cyanosis, breathing difficulties, and high fever. He also presented with severe anemia necessitating blood transfusion (Htc: 18%). These exacerbations occurred frequently, requiring treatment 2-3 times a month.

At two years and five months old, he exhibited resistant, recurrent obstructive bronchitis. A pulmonologist suggested a possible diagnosis of Haemosiderosis with an undefined etiology. Fiberoptic endoscopy revealed regular nasal, pharyngeal, and laryngeal mucosa, as well as regular tracheobronchial epithelium. Cultures of aspirate were sterile, and bronchoalveolar lavage (BAL) showed regular epithelial cells, along with macrophages and lymphocytes. Macrophages tested positive for lipid with Sudan III stain and for iron with Perls' stain, confirming hemosiderophages.

After approximately five years of treatment with fluctuations in lung condition and persistence of hematuria and proteinuria, a kidney biopsy was performed. The biopsy revealed Extracapillary Glomerulonephritis with initial crescents, with negative immunofluorescence findings. Also immunology labs were pos for pANCA vasculitis. Started treatment for Poliangitis microscopica with Pred, CyC, AZA. During treatment boy got some skin characteristic changes. Suspecting sensitivity to AZA (Azathioprine), treatment was switched to MMF (Mycophenolate Mofetil) for maintenance, and changes improved.

Conclusion: Prompt recognition and treatment of vasculitis are crucial, as these conditions can be severe and life-threatening without appropriate management. Recent adult guidelines recommend kidney biopsy in cases like ours, even without strong biopsy indications.

341 - P1.101

AN UNUSUAL CASE OF NEPHROTIC SYNDROME AND DIABETES MELLITUS TYPE 1 IN ADOLESCENT BOY

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Frequently relapsing nephrotic syndrome (FRNS) appears to be complicated and difficult to treat with corticosteroids alone, so need for immunosuppressive agents is common. The outcome of FRNS may be poor and with major treatment toxicity. But treatment FRNS together with other chronic disease in children seems to be much more difficult problem.

Aim: Was to review the case of a child with FRNS and diabetes mellitus, type 1 (T1D), followed in paediatric department of Vinnytsya Regional Children's Hospital, Ukraine.

Methods: We have a follow up of the patient with FRNS and T1D, determined clinically, laboratory in a Vinnytsya Regional Children's Hospital.

Results: A 13-year-old boy presented with severe generalized oedema and the results of laboratory tests revealed normal creatinine, hypoproteinemia, hypoalbuminemia, and nephrotic range proteinuria (3.3 g/day). A diagnosis of relapse of NS was made, and steroid treatment (prednisolone 60 mg/day) was started. From the history it is known that the boy was diagnosed FRNS in 2017, got several courses of steroid therapy and mycophenolate mofetil as steroid-sparing agent for 2 years. This episode of relapse of NS was associated with COVID-19 infection. He achieved remission of NS after 2 weeks of steroids, but at this period glucosuria appeared. Additional blood tests showed hyperglycemia without ketonemia, low level of C-peptide, glycated A1c fraction of haemoglobin was 6.9%. Pancreatic islet cell autoantibodies were positive (Glutamic acid decarboxylase and ZnT8 (zinc transporter) antibodies), which exclude steroid-induced diabetes. T1D was suspected and insulin therapy was initially introduced. During alternate day dosing of prednisolone, he started to take just long-acting insulin, so further long follow-up is needed to understand the course of both diseases.

Conclusions: Patients with FRNS are at high risk of drug-induced glucose metabolism disorders, because of their long-term use of diabetogenic medications, particularly glucocorticoids. But despite of this, we should also think about possibility of other types of diabetes mellitus in such patients. More studies are necessary for realising the impact of chronic hyperglycaemia on patients with FRNS.

373 - P1.102

EVALUATION OF AMBULATORY BLOOD PRESSURE MONITORIZATION VARIABLES IN PEDIATRIC PATIENTS WITH PRIMARY HYPERTENSION

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Aims/Purpose: The aim of this study is to evaluate the effect of obesity and target organ damage on the data obtained with ambulatory blood pressure monitorization (ABPM) in children diagnosed as primary hypertension (HT).

Methods: Ninety-four patients, ages of 5-18, diagnosed as primary hypertension by ABPM and etiologic study in the Department of Pediatric Nephrology/Erciyes University Faculty of Medicine during the years 2021-2022 were included the study. The ABPM records were examined retrospectively. Results of primary HT subgroups and healthy control group were compared.

Results: According to the ABPM variables average systolic pressure (ASP), average diastolic pressure (ADP), average arterial pressure (AAP), and all blood pressure (BP) loads in the HT group were found to be significantly higher than in the healthy control group. Forty-five percent of primary HT patients had obesity. Primary HT patients with obesity were compared to patients without obesity for all the ABPM variables and only day systolic standard deviation (SD) value found to be significantly higher in patients with obesity than in without obesity. Other ABPM variables were similar in patients with and withhout obesity. In the hypertension group, a positive relationship was found between body mass index (BMI) and night and total ASP, total and day systolic SD, night systolic and average SD. Night systolic blood pressure (SBP) load, night ASP and night- day systolic SD values had a positive relationship between left ventricular mass index (LVMI).

Conclusion: In primary HT patients, the increase in BMI effects ASP however the ABPM data of primary HT patients with obesity are similar to the patients without obesity except for systolic SD values. In particular, the increase in night SBP load and day-night systolic BP variability is associated with the increase in left ventricular mass index.

401 - P1.103

EFFICACY AND PROTOCOLS OF VINCRISTINE IN PEDIATRIC SRNS

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Aims/Purpose: Nephrotic syndrome (NS) is a glomerular disorder causing proteinuria. While corticosteroids are the first-line treatment, some children develop steroid-resistant NS (SRNS). This study aimed to evaluate the efficacy and safety of vincristine, a potential second-line therapy, in pediatric SRNS.

Methods: A literature review was conducted on vincristine use in pediatric SRNS. Studies were identified through searches in the PubMed database using relevant keywords. Studies evaluating the efficacy and safety of vincristine in children with SRNS were included.

Results: Several studies reported on the use of vincristine for SRNS but none were randomized control trials (RCTs). Dosing protocols varied, with most studies using weekly or bi-weekly intravenous pulses for several weeks. Complete remission rates ranged from 21% to 36%, with some studies showing a significant reduction in proteinuria. Vincristine was generally well-tolerated, with side effects like jaw pain, constipation, and mild hair loss reported.

Conclusion: Vincristine shows promise as a second-line therapy for pediatric SRNS. Existing data suggests moderate efficacy, a favorable safety profile, and potential proteinuria reduction. Further research with larger, well-designed RCTs is needed to confirm these findings and optimize vincristine treatment protocols for pediatric SRNS.

450 - P1.104

A RARE CAUSE OF ACUTE KIDNEY INJURY: INFECTIVE ENDOCARDITIS

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Introduction: Infective endocarditis (IE) is a disease caused by bacterial infection of the endocardial surface of the heart. It may rarely present with glomerulonephritis and acute kidney injury (AKI) in children. Here, we present a case who was referred to us with a pre-diagnosis of hemolytic uremic syndrome (HUS) and later on diagnosed as IE.

Case: A 6-year-old male patient was applied to a local hospital with the complaints of bloody diarrhea, fever and dark urine. Ceftriaxone was started and due to the presence of anemia, thrombocytopenia and renal dysfunction, the patient was referred to our hospital with a preliminary diagnosis of HUS. Physical examination revealed pale appearance, dental caries, 4/6 pansystolic murmur in the mesocardiac focus and hepatosplenomegaly. Laboratory tests showed; Hb: 6,1 g/dl, PLT: 50x109 /L, creatinine: 0,81 mg/dl, BUN: 17 mg/dl, Na:141 mmol/L, K: 2.6 mmol/L. Urinalysis showed hematuria and proteinuria. There were no signs of intravascular hemolysis (Normal LDH and haptoglobulin levels and absence of schistositis on peripheral smear). The diagnosis of HUS was excluded. He had hypocomplementemia (C3:0.7 g/L (0.9-1.2)), elevated rheumatoid factor level (115 IU/ml (0-14)) and nephrotic range proteinuria (48 mg/m2/h). Abdominal ultrasound revealed hepatosplenomegaly and increased size and parenchymal echoes of both kidneys. Echocardiography showed a 2.5 mm perimembranous ventricular septal defect (VSD) and a vegetation with a diameter of approximately 23 x 4 mm, which was seen to enter the RA with valve motion adhering to the anterior tricuspid valve liflet (Figure 1). The patient was diagnosed as IE according to Duke criteria and appropriate antibiotic treatment was started. Blood cultures were negative. Antifungals were added to the treatment of the patient with persistent fever. Fever returned to normal on the 16th day of hospitalization. Creatinine level progressively increased and reached 1.8 mg/dl, probably associated with IE-related glomerulonephritis and drug toxicity. Echocardiography showed a significant regression in vegetation in the 3rd week (Figure 2). In the fourth week of antibiotic therapy, hepatosplenomegaly regressed; renal function, anemia and thrombocytopenia improved. Treatment was continued for about 6 weeks. At discharge, serum creatinine was returned to normal (0.46 mg/dl), hematuria and proteinuria were completely resolved.

Conclusion: IE is rarely seen in children and may present with different clinical findings. IE should be kept in mind in children with congenital heart disease presenting with AKI.

Figure 1(A, B). Apical-4 space imaging shows vegetation on the tricuspid valve

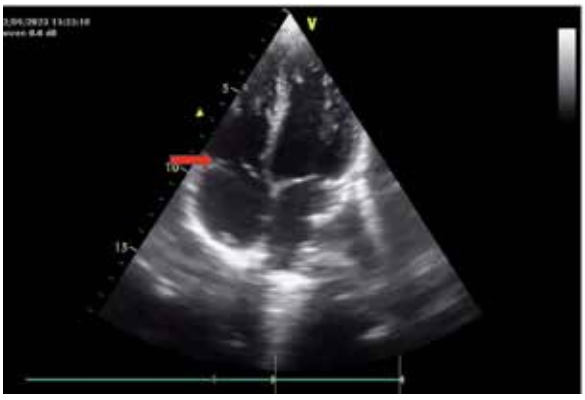

Figure 2. Regression of vegetation on the tricuspid valve in the apical-4 space after treatment

452 - P1.105

FROM CLINICAL TO GENETIC: MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS TYPE 3 AND AUTOIMMUNE DISEASE WITH GENETIC BASIS IN A PAEDIATRIC PATIENT

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Aims/Purpose: Monogenic lupus a recognised rare systemic and rheumatological diseases of childhood. It represents a rare, chronic, autoimmune disorder with multisystemic and renal involvement usually in the form of nephritis and haematuria. Our purpose is to present a patient with a histological diagnosis of membranoproliferative glomerulonephritis type 3, who after discontinuation of immunosuppressive treatment started with systemic symptomatology and biochemical alterations with complement consumption and positive ANAs.

Patient Methods & Results: We present a patient who was under follow-up in another centre. At 3 years of age with 2 months of intermittent macroscopic haematuria and nephrotic range proteinuria when infections, C3 and C4 in the normal range and negative autoimmune study. At 4 years of age, he persists with subnephrotic proteinuria (0.5-1 mg/ mg) and first renal biopsy reports IgA nephropathy. He received corticotherapy for 9 months without response, and double RAAS blockade was added without improvement. At 9 years of age and given the persistence of proteinuria, a new renal biopsy was performed and reported as membranous nephropathy, restarting corticosteroids and adding mycophenolate. At our centre, we received the patient at 13 years of age and he persisted with subnephrotic proteinuria and normal renal function. The histological material was reviewed and both samples showed a glomerulonephritis due to immunocomplexes (C3+, C4+ IgA+++, IgG and IgM+) with a mesangiocapillary pattern. The ultrastructural study showed subendothelial, intramembranous and subepithelial dense deposits. Diagnosis of membranoproliferative glomerulonephritis type 3 was made, patient was treated with cyclophosphamide without success. Then, rituximab with partial response and early relapse. Subsequently, a complete and sustained response was achieved with ciclosporin. In 2021, immunosuppressive treatment was tapered, presenting systemic symptoms with skin and joint involvement, weight loss and fatigue. The biochemical study showed for the first time, complement consumption (C3, C4 and CH50) with positive ANA. Genetic study showed two heterozygous variants in the DNASE1L3 gene.

Conclusion: The DNASE1L3 gene is located on chromosome 3p14.3 and loss-of-function mutations have been associated with monogenic SLE. This disorder has an autosomal dominant or recessive inheritance pattern and would explain the clinical features of our patient.

471 - P1.106

A SYSTEMATIC REVIEW OF ACUTE KIDNEY INJURY IN INFANTS WITH PATENT DUCTUS ARTERIOSUS

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Aims/Purpose: Acute kidney injury (AKI) is common and associated with poor clinical outcomes in neonates, affecting nearly a third of infants admitted to a neonatal intensive care unit (NICU). Premature infants and infants with a very low birth weight are particularly predisposed to acute kidney injury. The presence of a patent ductus arteriosus (PDA) may result in an inequitable distribution of cardiac output, which may compromise end-organ perfusion. Both conservative management and intervention have the potential to exacerbate AKI. This systematic review sought to assimilate the existing literature pertaining to the study of AKI in infants with PDA.

Methods: A systematic review of existing literature was performed using PRISMA methodology. A search was run across three separate reputable databases, OVID Medline, SCOPUS and PUBMED. Studies pertaining specifically to the incidence of, factors contributing to, and outcomes associated with AKI in newborns with PDA were searched for. The search conducted included years between 1946 and Q1-2024. No language restrictions were applied. Keywords were mapped to subject headings. The reference lists of included articles were examined for potential eligible studies.

Results: n = 199 abstracts were identified, which was reduced to n = 130 upon removal of duplicates. n = 108 were excluded in initial screening, leaving n = 22 eligible for full-text review. n = 5 were excluded at this stage, leaving n = 17 eligible for inclusion. The articles took varying approaches to the definition of both AKI and the haemodynamic significance of a PDA. 70% of studies utilised the KDIGO criteria, whilst smaller numbers used nRIFLE, AKIN and NIDDK criteria. Only 65% of studies defined their criteria for a haemodynamically significant patent ductus arteriosus (hsPDA), 17% used ductal diameter in isolation and the remaining utilised a combination of measurements, most commonly ductal diameter and Left Atrial-Aortic Root ratio.

Conclusion: There is a paucity of literature pertaining to the incidence of AKI in infants, in the setting of a hsPDA. Whilst there has been a clear trend towards the coherent use of a single approach to determine acute kidney injury, there is a wide variance in the approach to echocardiographic assessment of a PDA for haemodynamic significance. All studies pertaining to neonatal AKI should use the KDIGO definition. The degree of heterogeneity in approach taken in existing literature calls for prospective studies, which utilise both serum creatinine and urine output for AKI classification and the use of a robust PDA scoring system to accurately categorise the relationship between AKI and a hsPDA.

479 - P1.107

COBALAMIN DEFICIENCY AS A RARE CAUSE OF THROMBOTIC MICROANGIPATHY : A CASE REPORT

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Introduction: Thrombotic microangiopathy (TMA) is characterized by microvascular thrombosis that causes thrombocytopenia, Coombs-negative hemolytic anemia, and end-organ destruction. Thrombotic microangiopathy caused by several pathogenetic mechanisms among which Shiga toxin-producing Escherichia coli infections and complement dysregulation are the most common. However, very rarely disorders of cobalamin metabolism can present with TMA. Here we report a case TMA associated with cobalamin deficiency.

Case: A 2,5 year-old girl presented to the emergency department with pallor and weakness. Her past medical history was unremarkable. She was hypertensive on admission. The laboratory tests revealed anemia, thrombocytopenia low haptoglobin and increased lactic dehydrogenase, urea and creatinine. Peripheral blood smear revealed schistocytes. A comprehensive evaluation for infection and autoantibodies was negative. Complement fractions of C3 and C4 were also normal. She was diagnosed with atypical hemolytic uremic syndrome and was initiated on therapeutic plasma exchange and supportive therapy. As her blood pressure could not be controlled with oral amlodipine, doxazosin and propranolol, first iv esmolol and then oral minoxidil were added to her treatment. The patient underwent genetic analysis. Initially treated with eculizumab, the patient's hematologic parameters worsened, along with kidney failure. Subsequently, the patient experienced seizures and was started on antiepileptic therapy. Although vitamin B12 levels were within normal range, hyperhomocysteinemia, hypomethioninemia, and increased urinary excretion of methylmalonic acid were detected. Based on these findings, the patient was diagnosed with thrombotic microangiopathy (TMA) associated with cobalamin deficiency. Specific treatment with intramuscular hydroxocobalamin, betaine, and folic acid was initiated. Following treatment, the homocysteine level decreased. In patient, next generation sequence analysis revealed a homozygous pathogenic missense variant, NM_015506:c.484 G > T(p.Gly162Trp) in the MMACHC gene. After fourteen days of treatment, hematologic parameters normalized, but non-oliguric renal failure persisted, although it did not require hemodialysis.

Conclusion: Trombotic microangipathy associated with cobalamin deficiency is very rare. Multidisciplinary approach is essential for TMA due to its rarity and potential severity. We strongly recommend including plasma homocysteine determination in the diagnostic work-up of any patient with TMA in order to ensure timely diagnosis and effective treatment.

522 - P1.108

MAJOR ADVERSE CARDIOVASCULAR EVENTS IN YOUNG ADULTS WITH GLOMERULONEPHRITIS: THE NEED FOR A BRIDGING BIOMARKER FOR PAEDIATRIC CARDIOVASCULAR RISK

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Aims/Purpose: A diagnosis of glomerulonephritis (GN) is commoner in children and young adults. This group of immune mediated diseases alongside immunosuppressive treatment and progression of proteinuric kidney impairment can increase the risk of cardiovascular disease. In adults with GN routine cardiac biomarkers Troponin I and NTproBNP can predict incident major adverse cardiovascular events (MACE) (HR 1.79; 95% CI 1.70, 1.88, p < 0.0001) and (HR 1.99; 95% CI 1.86, 2.14, p < 0.0001) respectively. We aimed to investigate the prognostic significance in predicting incident MACE in young adults within 5 years of GN diagnosis.

Methods: A retrospective cohort study was performed using electronic medical records from a global federated research network database, TriNetX, accessed on April 3rd 2024. Young adults aged 16-22 years with a diagnosis of all-cause GN identified by International Statistical Classification of Diseases coding (ICD-10) were included with data censoring for MACE invoked prior to the index event of GN. Cardiac biomarkers were the first reported result after the diagnosis of GN. Cohorts were grouped according to biomarker-specific thresholds NTproBNP > 400pg/mL and Troponin I > 18 ng/L and 1:1 propensity-score matched for age, gender, and co-morbidities (hypertension, diabetes mellitus and smoking status). Logistical regression produced hazard ratios with 95% confidence interval for 5-year incident of the primary composite outcome MACE: ischaemic heart disease, angina pectoris, acute myocardial infarction, heart failure, Atrial fibrillation, stroke, and all-cause mortality. All statistical analysis was performed on the TriNetX online platform.

Results: The propensity score matching identified 264 children and young adult patients (Mean age 15.2 years SD ± 3.3, 49% male). There were 40 composite MACE events, 20% across both cohorts. The table shows the outcomes, hazard ratio (HR), and 95% confidence interval (CI) for NTproBNP and Troponin I above the threshold level.

Outcome	Number with outcome	Hazard Ratio	95% CI	P-value
NTproBNP > 400pg/mL				
MACE	10	1.71	(0.65, 4.50)	0.481
Ischaemic Heart Disease	10	4.32	(0.48, 38.72)	0.932
Heart failure	10	1.53	(0.34, 6.85)	0.958
Death	10	1.43	(0.50, 4.12)	0.231
Troponin I > 18 ng/L				
MACE	10	1.85	(0.56, 6.07)	0.385
Ischaemic Heart Disease	10	0.57	(0.11, 3.13)	0.447
Heart failure	10	2.23	(0.37, 13.37)	0.920-
Death	10	-	-	

Conclusion: Cardiac biomarkers routinely used in adult settings cannot be used to predict incident MACE in young adults diagnosed with glomerulonephritis. These results highlight the need to identify a bridging biomarker for paediatric extrapolation of cardiovascular disease in this at risk population.

533 - P1.109

A CONNECTION BETWEEN MEMBRANOUS NEPHROPATHY AND AUTOIMMUNE HEPATITIS. PRESENTATION OF TWO CASES

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Aims: Membranous nephropathy (MN) is rare in children and often secondary to a systemic condition such as an autoimmune disease (systemic lupus erythematosus) or an infection (hepatitis B). Primary MN due to known autoantibodies (anti-PLA2R) is even less common, especially before puberty. Management of both types of MN differ. MN is not typically associated with autoimmune hepatitis (AIH). The aim is to present 2 pediatric cases with these 2 conditions.

Methods: Retrospective charts review.

Results: A 5-year-old boy presents with nephrotic syndrome which requires steroids and mycophenolate mofetil to achieve complete remission. Two years later, 2 months after mycophenolate discontinuation, he comes in with acute liver failure due to AIH with anti-liver cytosol antibody type 1 (anti-LC1), treated with steroids and azathioprine with resolution of the liver dysfunction. Proteinuria remains negative up to 3 years later when he has a relapse of his nephrotic syndrome and his kidney biopsy shows a MN lesion with negative anti-PLA2R antibodies and negative PLA2R immunostaining. Partial remission with steroids is achieved and enalapril is started. Liver enzymes intermittently increase throughout the course requiring steroids and an increase in the azathioprine dose. Proteinuria is currently well controlled (6 years after kidney biopsy) with enalapril 20 mg and azathioprine 75 mg every 24 hours. A 9-year-old boy with celiac disease and suspicion of inflammatory bowel disease is diagnosed with AIH (negative antibodies) and treated satisfactorily with steroids and azathioprine. Two years later he presents with steroid-resistant nephrotic syndrome with evidence of MN on kidney biopsy (negative anti-PLA2R antibodies). Due to lack of response after 6 weeks of steroids he was started on enalapril but this was discontinued 6 months later due to negative proteinuria. Hepatitis is well controlled on methylprednisolone 4 mg every 48 hours (azathioprine was discontinued due to neutropenia). He has positive ANA antibodies in the last few appointments with no symptoms.

Conclusion: MN and AIH are likely connected in these cases. Whether their MN is secondary to the AIH or there is a primary MN in the context of a systemic autoimmune dysregulation is unclear. It is possible that their anti-PLA2R antibodies are negative because of their maintenance immunosuppression or there may also be unknown autoantibodies against the podocyte. Spontaneous remission rate of primary MN is higher in children compared to adults, but it can also be a cause of steroid-resistant nephrotic syndrome. Secondary MN is likely to recover once the cause is removed. Regardless of the mechanism our patients had a favorable kidney outcome.

534 - P1.110

IMMUNITY OF CHILDREN WITH STEROID-DEPENDENT NEPHROTIC SYNDROME

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Aims/Purpose: Idiopathic nephrotic syndrome is a disease that requires immunosuppressive (IMS) therapy that often lasts for years. The aim of the study was to assess the influence of prolonged IMS therapy on immunity and vaccine competence in children with steroid-dependent nephrotic syndrome [SDNS].

Methods: Vaccination status and medical history was obtained from 36 children with SDNS. Serum IgG levels as well as serum specific antibodies against HBs antigen and against Tetanus were assessed in remission.

Results: Mean age of the studied group, in which boys predominated [21/36] was 146 [26-241] months. All patients had received at least one steroid-sparing immunosuppressive agent. All patients completed their vaccination course against HBV. More than one third [11/28] of examined patients had incomplete vaccinations status against Tetanus [usually one dose was missing]. Only 10/22 received vaccination against COVID. Mean serum IgG was 7,29 [G/l]. Decreased serum IgG was noted in 17/36 children, but was decreased more than 50% of the lower reference range in only 2. Mean serum anti HBs titers were 11,8 [mIU/ml]. In 9/36 children the antibodies exceeded the protective value of 10 mIU/ml]. 11/36 children had very low serum antiHBs antibody (< 1,0 mIU/ml). Mean antibody titers against Tetanus were 1,73 [IU/ml]. In all 29 children they were above the protective value of 0,1 IU/ml.Five patients had suffered from severe infections that required hospitalization. No subject had acquired HBV or Tetanus infection.

Conclusion: Child's vaccination status at idiopathic nephrotic syndrome onset and during further course of disease requires assessment. Children with SDND who receive IMS therapy require systematic screening for serum IgG levels and protective titers of vaccination induced antibodies .

543 - P1.111

ADRENAL INSUFFICIENCY IN CHILDREN WITH NEPHROTIC SYNDROME TREATED WITH HIGH DOSES OF GLUCOCORTICOIDS

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Aims/Purpose: Pediatric patients with nephrotic syndrome are treated with high doses of Glucocorticoids (Gc) for 4 weeks followed by gradual tapering. The incidence of iatrogenic adrenal suppression following this treatment has not been addressed in Denmark before.

Methods: We prospectively included fourteen children with nephrotic syndrome from October 1st 2019 until 31st December 2023 from the pediatric departments at two university hospitals of Copenhagen.

A non-fasting Adrenocorticotropic hormone (ACTH) stimulation test with 250 µg was performed after tapering to the lowest dose of Gc. Gc was not taken on the day of the test. Serum ACTH was measured at 0 minutes. Normal reference range 1.2-16.7 pmol/l. Serum cortisol was analyzed by using High Performance Liquid Chromatography at 0, 30 and 60 minutes. A response above 440 nmol/l at any time was considered normal, 400-440nmol/l was classified as borderline. Patients with adrenal insufficiency were treated with hydrocortisone 3 times daily, if a borderline response only when ill or in need of surgery, until a normal response. The stimulation test was repeated every 3 months until normal.

Results: Fourteen patients were included. Four patients (28%) had an insufficient response. Two of these patients had low ACTH (0.7 pmol/l). Two patients (14%) had a borderline response. ACTH was normal in one patient and missing in one patient.

ACTH test	Recurrent nephrotic syndrome	(Yes/no) Age (years, months)	Gender (1 = boy, 2 = girl)	ACTH (pmol/l)	S-Cortisol (nmol/l) at 0 minutes	S-Cortisol (nmol/l) at 30 minutes	S-Cortisol (nmol/l) at 60 minutes
Normal	Yes	17.2	1	-	392	590	696
	No	7.4	2	4.4	146	481	548
	Yes	8.0	1	-	168	-	764
	No	1.10	2	6.0	246	475	-
	Yes	3.4	1	3.5	90	434	484
	Yes	2.8	1	-	112	481	523
	No	8.9	2	2.5	202	527	627
	Yes	3.5	1	1.1	73	618	692
Borderline	No	14.1	2	7.3	185	-	400
	Yes	3.8	1	-	55	343	422
Pathologic	No	2.3	1	0.7	18	284	399
	Yes	7.7	1	-	170	-	346
	Yes	5.2	2	0.7	4	120	158
	No	12.6	1	5.3	135	344	385

Conclusion: We found that 28% patients with nephrotic syndrome treated with high doses of Gc showed adrenal insufficiency. We recommend to perform an adrenal function test in these patients before discontinuing the Gc treatment.

573 - P1.112

DOES NEPHRECTOMY AFFECT PATIENT SURVIVAL IN PATIENTS WITH CONGENITAL NEPHROTIC SYNDROME SECONDARY TO NEPHRIN MUTATIONS?

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Aims: The management of congenital nephrotic syndrome (CNS) aims to maintain intravascular volume and ensure healthy growth. NPHS1 mutations are one of the most important causes of CNS and prone to severe complications such as haemodynamic instability, recurrent infections, thromboses and impaired growth. We aimed to investigate the effect of unilateral/bilateral nephrectomy in Turkish patients with CNS secondary to NPHS1 mutations.

Methods: This longitudinal cohort study recruited 29 pediatric patients (14 females, 15 males) with homozygous or compound heterozygous NPHS1 mutation from 10 different pediatric nephrology centers in Türkiye. Among 29 patients, 16 of them underwent nephrectomy while 13 patients were managed conservatively. The clinical parameters and survival of these two groups were compared.

Results: Median age of diagnosis was 29 days (IQR; 11-62 days). While number of albumin infusion was 16 (IQR; 12-28) days per month, number of infection and hospitalization in a year were 2 (IQR; 1-4) and 4 (IQR; 2-6), respectively. All patients were receiving angiotension converting enzyme inhibitor treatment (ACEi). Sixteen patients (8 females, 8 males) underwent nephrectomy (13 unilateral, 3 bilateral) at median age of 6.5 (IQR; 4.25-11.75) months. One year after nephrectomy, serum albumin increased and eGFR decreased compared to baseline ($p = 0.008$ and $p = 0.025$, respectively) and the need of albumin infusions (day/month), number of infection and hospitalization decreased ($p = 0.001$, $p = 0.0027$ and $p = 0.004$, respectively). Kidney replacement therapy (KRT) was commenced in 10 patients (62.5%). Thirteen patients (7 females, 6 males) were followed-up conservatively. One year after diagnosis, serum albumin level increased ($p = 0.034$) when compared to those at the time of diagnosis, eGFR decreased but did not reach statistical significance ($p = 0.328$) when compared to baseline. Besides, the necessity of albumin infusion (day/month) decreased ($p = 0.007$) whereas, the number of infection and hospitalization remained unchanged ($p = 0.589$ and 0.5, respectively). In this cohort, KRT was performed in 10 patients (76.9%). At last visit, serum albumin level was higher in patients with conservative management compared to the nephrectomy group (4.3 (IQR; 3.6-4.6) vs 3.8 (1.9-4.25), $p = 0.031$). During follow-up, 4 patients died (two patients from conservative management group, two patients from nephrectomy group) ($p = 0.91$).

Conclusions: Although there is no evidence to suggest routine nephrectomy in patients with CNS secondary to NPHS1 mutation, it may be still beneficial in selected cases.

593 - P1.113

STEROID-SENSITIVE NEPHROTIC SYNDROME IN TWIN SISTERS

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Aims/Purpose: Idiopathic steroid-sensitive nephrotic syndrome (SSNS) is most often encountered in sporadic cases of minimal change disease (MCD). Only rare cases of familial forms of MCD have been reported. The scarcity of familial NS has precluded unraveling the underlying genetic defect and candidate gene approaches have been unsuccessful. We report identical twin sisters with SSNS.

Methods: We show clinical data of twin sisters who contemporaneously developed SSNS and review the related literature.

Results: Female monozygotic twins with normal prenatal ultrasound findings, normal amount of amniotic fluid, normal common placenta, and normal female phenotype were born preterm at 33+5 gestational week. Twin A was hospitalized at the age of 4 years due to generalized edema. Laboratory findings showed severe hypoproteinemia (38 g/L) and hypoalbuminemia (14 g/L), severe proteinuria (24-hour urine total protein / creatinine; 3,036 mg / 270 mg), and normal serum creatinine and complement levels. Treatment was started with deflazacort 60 mg/m2/day for 4 weeks followed by tapering and slow reduction. Negative conversion of proteinuria was achieved at two-week of therapy. Two months later, however, dose of steroid was increased because of mild proteinuria, then, tapered successfully. Two months later after the initial onset of nephrotic syndrome in twin A, twin B was admitted due to generalized edema. Laboratory findings showed hypoproteinemia (54 g/L) and hypoalbuminemia (31 g/L), severe proteinuria (24-hour urine total protein / creatinine; 3,668 mg / 310 mg), and normal serum creatinine and complement levels. We treated her with deflazacort as twin A, and in tapering. Negative conversion of her proteinuria was achieved at 8-day of therapy. During ten years twin A and twin B have shown frequent and infrequent relapsing steroid-sensitive features, respectively. The identical twins possessed the identical HLA antigens; HLA-A24,33, HLA-B44.5, HLA-C07,14, and HLA-DRB1 07,14. In genetic studies targeted for podocyte molecules, such as, NPHS1, NPHS2, PLCE1, ACTN4, CD2AP, WT-1, TRPC6, LAMB2, were all negative.

Conclusion: We reports a pair of identical female twins who contemporaneously developed idiopathic SSNS. We found that they showed familial feature, however, genetic defects of podocyte molecules were not detected yet.

595 - P1.114

EXPERIENCE WITH DARATUMUMAB IN A STEROID-RESISTANT NEPHROTIC SYNDROME RECURRENCE CASE AFTER KIDNEY TRASPLANTATION

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Aims/Purpose: Steroid-resistant nephrotic syndrome continues to pose a therapeutic challenge, especially in refractory cases to multiple lines of treatment. Recently, studies supporting the use of new therapies based on the inhibition of potential circulating humoral permeability components are emerging. We present a clinical case in which we evaluate the effectiveness of one of these treatments.

Methods: We present a kidney transplant patient secondary to a steroid-resistant nephrotic syndrome with a refractory recurrence of his primary disease. We conducted a review of recent related literature on emerging therapeutic options in cases refractory to multiple lines of treatment. After evaluating the available options, a regimen of intravenous daratumumab administration was agreed.

Results: We present a 20-year-old patient with idiopathic steroid-resistant nephrotic syndrome onset at the age of 11 years and a renal biopsy consistent with diffuse and segmental glomerulosclerosis with cellular predominance. Following a difficult course with refractory proteinuria unresponsive to multiple treatments including therapeutic apheresis, the patient progressed to end-stage renal disease, initiating hemodialysis 10 months after initial diagnosis. Ten months later, he received a deceased donor kidney transplant. Recurrence of nephrotic syndrome occurred 2 months after transplant, requiring plasma exchange and immunoadsorption with partial response and two doses of ofatumumab, achieving complete remission of the disease by the second year after transplantation. At 19 years old, the patient experienced a new relapse of nephrotic syndrome in the context of acute infections and poor therapeutic adherence, with diffuse global glomerulosclerosis observed on a new renal biopsy, with pedicle fusion on electron microscopy but no signs of graft rejection. Treatment with corticosteroids, cyclosporine, everolimus, losartan, rituximab, and plasma exchange did not improve the nephrotic syndrome. Plasma exchange was replaced with immunoadsorption, achieving complete remission of proteinuria, but relapse occurred after discontinuation of this technique, requiring at least one session weekly to maintain remission. In order to discontinue immunoadsorption, we treated with 4 doses of daratumumab after a successful experience in a team in Paris. The patient experienced a complete remission in proteinuria at 6 month with stable renal function and no need for new apheresis.

Conclusion: Daratumumab is a human IgG1k monoclonal antibody targeting CD38 antigen (present on the membrane of plasma cells). Currently indicated as an effective treatment in multiple myeloma, new studies are proposing this new therapeutic option in cases of corticosteroid-resistant nephrotic syndrome, although for now those patients who seem to benefit the most are the ones who respond to immunoadsorption.

607 - P1.115

NON LUPUS FULL HOUSE NEPHROPATHY: A CASE REPORT

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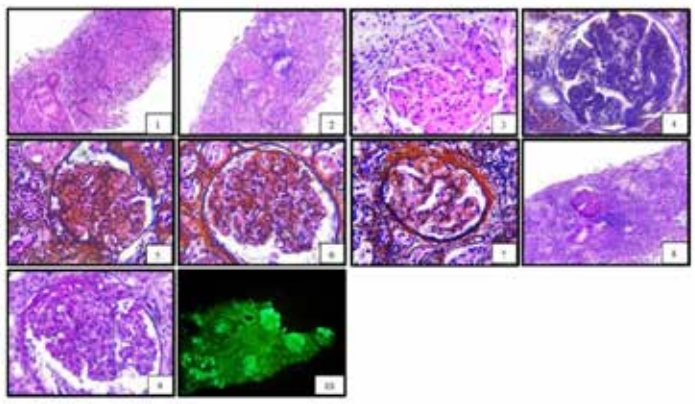
Aims/Purpose: To describe the clinical presentation of a rare pathology for which there is no therapeutic consensus

Methods: Full house nephropathy refers to the detection of deposits of IgA, IgG, IgM, C3, and C1q in the renal biopsy with immunofluorescence (IF), almost pathognomonic of lupus nephritis. However, in patients with negative serology for autoantibodies, it is called non-lupus full house nephropathy. It is believed that their physiological bases may be similar, but more studies are required for prognosis and treatment purposes.

Results: A 12-year-old male began experiencing fever, nausea, vomiting, fainting, and dysarthria. A doctor took a capillary blood glucose level, which was reported as 170 mg/dl, and ordered additional tests to rule out diabetes mellitus. Hematuria (164cel) and nephrotic proteinuria (191.6 mg/m2/h) were detected, without nephrotic syndrome or abnormalities in kidney function. Hypertension and glucosuria were ruled out. There is no family history or medication use reported. A renal biopsy was performed, which reported membranoproliferative glomerulonephritis mediated by immune complexes with full house immunofluorescence. Negative ANA, no complement consumption, 18 negative immunospecificities. Rheumatologic and infectious pathologies are ruled out. Renal ultrasound shows loss of corticomedullary relationship and left renal hypoplasia. Cranial MRI is normal. The prednisone was tapered off, and cyclophosphamide was started at a dose of 750 mg/m2 (4 doses), along with mycophenolate acid at a dose of 750 mg/m2 subcutaneously, and rituximab at a dose of 375 mg/m2 subcutaneously (2 doses), with no response. An inhibitor of the angiotensin-converting enzyme (IECA) was started, and there was a decrease in massive proteinuria to nephrotic levels. Later, Tacrolimus was started at a dose of 0.1 mg/kg/day, and there was a significant decrease in nephrotic proteinuria (from 47 to 26.3 mg/m2/h).

Conclusion: Full house non-lupus nephropathy, treated with immunosuppressants as for SLE, few case series report favorable results; but improvement was observed in the corticosteroid- resistant nephrotic syndrome treatment algorithm. This report is made because it is infrequent, for prognostic and treatment purposes.



1-3. H&E: Hypercellularity in the endocapillary region, leukostasis, and subendothelial deposits. Minimal tubular atrophy and interstitial fibrosis.

4. Masson: Hypercellularity in the endocapillary region, leukostasis, and subendothelial deposits.

5-7. Jones: Hypercellularity in the endocapillary region, leukostasis, and subendothelial deposits. Irregularities in the basement membranes with duplication. Minimal tubular atrophy and interstitial fibrosis.

10. Immunofluorescence: Mesangial and subendothelial immunocomplex deposits.

610 - P1.116

THE ROLE OF TUMOR NECROSIS FACTOR RECEPTOR 1 AND TUMOR NECROSIS FACTOR RECEPTOR 2 IN PREDICTING DIABETIC NEPHROPATY IN CHILDREN WITH TYPE 1 DIABETES MELLITUS

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Aim: Diabetic Nephropaty (DN) is one of the most important long-term complications of Type 1 Diabetes Mellitus (T1DM). Microalbuminuria is a late indicator of DN, so biomarkers that can detect kidney damage at an earlier stage are needed. We aimed to investigate the role of serum Tumor Necrosis Factor Receptor (TNFR) 1 and TNFR2 levels in the early diagnosis of diabetic nephropathy in children followed up with the diagnosis of T1DM.

Material and Methods: Children between the ages of 10 and 18, T1DM (n = 46) and control group (n = 35) were included in the study. Demographic and anthropometric characteristics of the case group, duration of diabetes, presence of retinopathy and neuropathy, family history of diabetes, hypertension and kidney disease, laboratory parameters (HbA1c, urea, creatinine, estimated glomerular filtration rate (eGFR), C-reactive protein, cholesterol, triglyceride, TNFR1, TNFR2 and 24-hour urine microalbumin) were examined and compared with the data of the control group. Case group was divided into subgroups and compared according to the presence of microalbuminuria, duration of diabetes and glycemic control status.

Results: T1DM group and the control group were similar in terms of gender, age, weight, height, body mass index standart deviation score (SDS). The avarage duration of diabetes was 5.52 ± 3.08 (2-16) years. eGFR was significantly higher in the T1DM group (142.07 ± 27.55 mL/min/1.73m^2) than in the control group (130.46 ± 18.61 mL/min/1.73m^2) (p:0.026). Serum TNFR1 and TNFR2 was not different between the patient and control groups. TNFR1 and TNFR2 levels were not different in the patient group according to the presence of microalbuminuria and glycemic control status. Serum TNFR1 and TNFR2 levels were significantly higher in patients with diabetes duration of less than five years (p:0.012, p:0.030).

Conclusion: Higher levels of serum TNFR1 and TNFR2 in the first five years of DM may suggest that these inflammatory markers may be diagnostically valuable in the very early stages of diabetic nephropathy.

Table 1. Comparison of Type 1 Diabetes Mellitus Patient and Control Group Data

	T1DM (n:46)	Control (n:35)	p
	(n:46)	Control	t, p
Gender (M/F)	(n:35)	p	p:0,523
Age (years)	14,30 ± 2,43	13,82 ±2,61	t:-0,844, p:0,401
Weight SDS	0,21 ± 1,24	-0,02 ± 0,91	t:-0,956, p:0,342
Height SDS	0,14 ± 0,97	-0,14 ± 0,63	t:-1,611, p:0,111
BMI SDS	0,13 ± 1,24	0,11 ± 0,88	t:-0,078, p:0,938
eGFR (mL/min/1.73 m^2)	142,07 ±27,55	130,40 ± 18,61	t:-2,271, p:0,026*
CRP (mg/L)	1,37 ± 1,68	1,10 ± 1,42	t:-0,766, p:0,446
TNFR-1 (ng/dL)	15,12 ±10,45	15,21 ±10,47	t:0,40 p:0,968
TNFR-2 (ng/dL)	13,72 ±13,31	19,08 ±16,71	t:1,605, p:0,113

x: Arithmetic mean, SDS: Standard deviation score, BMI: Body mass index, CRP: C-reactive protein, TNFR: Tumor Necrosis Factor Receptor. Independent samples t-test was applied. *p<0.05, ** p<0.01, *** p<0.001 are significant.

623 - P1.117

PREVALENCE OF HYPOTHYROIDISM IN MONOGENIC STEROID RESISTANT NEPHROTIC SYNDROME

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Purpose: Despite a chronic progressive course, there is a scarcity of data on thyroid dysfunction in children with monogenic steroid resistant nephrotic syndrome (SRNS) during the nephrotic stage and after its resolution. The purpose of this study was to determine the natural history of thyroid dysfunction in children with genetic SRNS.

Methods: A retrospective observational cohort study of patients with SRNS at the pediatric nephrology unit, Shaare Zedek Medical Center between January 1995 and October 2023. Thyroid function was routinely tested during 3 disease stages- the nephrotic stage, dyalisis treatment and post kidney transplantation. Hypothyroidism was defined according to age corrected elevated thyroid stimulating hormone (TSH) levels. Levothyroxine dose, defined as maximal dosage per body weight, was reported for each disease stage.

Results: Study population included 45 participants with SRNS, genetic mutation was diagnosed in 40 (89%). The majority of patients with genetic diagnosis - 27 (68%) - had NPHS1 or NPHS2 mutations. NPHS1/2 patients (NPHS) were diagnosed with NS at a significantly younger age compared to other participants—median 1 month (IQR-0-12) vs 26 months (IQR- 93), $p < 0.05$. Hypothyroidism during NS was documented in 20/40 (50%) cases, with a significantly higher prevalence among NPHS (17/27, 63% vs 3/13, 23% in other genetic causes, $p = 0.02$). Ninety-four percent of patients with hypothyroidism remained levothyroxin dependent during dialysis, despite being anuric. After kidney transplantation, 9/12 (75%) NPHS patients still required levothyroxine treatment, but at significantly lower doses- median maximal dose 52 mcg/kg (IQR 42) during nephrotic state, vs 13 mcg/kg (IQR 15) after transplantation ($p < 0.001$).

Conclusion: In our cohort, hypothyroidism was highly prevalent among children with monogenic SRNS, mainly with mutations in NPHS1 or NPHS2 genes. Contrary to most previous studies, we found that hypothyroidism persisted after dialysis initiation and kidney transplantation despite resolution of proteinuria, suggesting additional pathophysiological mechanisms, which merits investigation.

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630 - P1.118

B12 VITAMINE DEFICIENCY: PSEUDO-THROMBOTIC MICROANGIOPATHY OR THROMBOTIC MICROANGIOPATHY?

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Aims/Purpose: Severe vitamin B12 deficiency or defective cobalamin metabolism may lead to symptoms mimicking thrombotic microangiopathy (TMA). The vitamin B12 deficiency has been termed as pseudo-TMA and the defective cobalamin metabolism as metabolic mediated (MM)TMA. The ineffective erythropoiesis with hemolytic pattern, reduced platelet production, and endothelial injury with organ damage result from toxic byproduct of B12 dysmetabolism. The aim of the case report is to differentiate between pseudo-TMA and TMA.

Methods: case report.

Results: We describe a girl with short bowel syndrome due to necrotizing enterocolitis and > 40 cm resection of the ileum on parenteral nutrition for 2 years since her birthday. With the switch to enteral nutrition she was diagnosed with B12 deficiency solved by B12 intramuscular substitution. At 13-years of age, the B12 therapy was discontinued by the family due to non-adherence. After 6 months without B12, the girl was admitted to hospital with hematuria, heavy hemolytic anemia (Hb 45g/l), thrombocytopenia (18), increased schistocytes (0.010), LDH (71ukat/l), creatinine (81umol/l) and Cystatin C 1,27 (mg/l). Other tests proved low eGFR (1.1 ml/s/1.73m2), C3 (0.77g/l), C4 (< 0.08g/l), AH50 (< 5), CFH (47), normal ADAMTS13 (78 %) and CFI (76), negative a-CFH. Her personal history revealed 17 episodes of hemolytic anemia with thrombocytopenia and increased creatinine associated with 2 episodes of acute kidney injury, 1 episode of respiratory failure, and 2 episodes of deep vein thrombosis. Due to heavy anemia she needed a blood transfusion. Since then she has been treated with high doses of B12. Anemia, thrombocytopenia and LDH have been gradually improved with the therapy. However, low levels of CFH (< 50) and eGFR (0.8 ml/s/m2) have persisted. The following genetic analysis excluded MM-TMA and confirmed disposition to atypical hemolytic uremic syndrome (aHUS): homozygous mutation in exon 10 of CFH gene (c.1419G > A/p.Ala473), 3 variants of homozygous risk haplotype MCPggaac (c.-547A > G, c.-261A > G, c.1127+638G > A) in promoter area and intron 12, homozygous risk haplotype CFH-H3 in exon 9 of CFH gene and heterozygous pathogenic mutation in exon 1 of MBL2 gene (c.161G > A/p.Gly54Asp).

Conclusion: The patient´s history, laboratory tests, and especially genetic analysis confirmed aHUS. Thus, genetic analysis may discriminate aHUS from pseudo + MM TMA, however, B12 deficiency with a toxic effect on endotel may have triggered clinical symptomatology.

633 - P1.119

CHANGES TO STANDARD CORTICOSTEROID REGIMEN TO TREAT RELAPSES IN CHILDHOOD STEROID-SENSITIVE NEPHROTIC SYNDROME AFFECT THE TIME TO NEXT RELAPSE: A SECONDARY ANALYSIS USING THE PREDNOS 2 DATABASE

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Aims/Purpose: Using a large controlled trial database of children with steroid-sensitive nephrotic syndrome (SSNS), this study aimed to investigate the effect of changes to standard steroid relapse treatment on time to next relapse.

Methods: The PREDNOS2 randomised controlled trial comprised 365 children followed for 12 months. Of these, 153 children relapsed at least twice within the trial duration. In five relapses, there was spontaneous remission, leaving 148 children with first and second treated relapse for analysis. Time to next relapse was defined as time from the start of the first relapse to the start of the second. The steroid regimens used to treat the first relapse were recorded as standard (60 mg/m2/d until remission followed by 40 mg/m2 on alternate days for 4 weeks) or non-standard in the trial case record form (CRF). According to free text in the CRF, non-standard regimens were classified as delivering more steroid (longer courses and/or higher doses) or less steroid (shorter courses and/or lower doses) by two independent senior doctors. Nineteen records where there was disagreement or unclear data were excluded. Analyses of the time to the next relapse in each treatment group were performed using the Kaplan-Meier and log-rank tests.

Results: A total of 129 children were included: 43 (33%) received standard regimens, 72 (56%) received more steroid and 14 (11%) received less steroid. The median (IQR) times to the next relapse were 45 (28-97) days, 77 (47-115) days and 100 (72-162) days for children who received less, standard and more steroid respectively. The time taken for all children to relapse was 131, 345 and 291 days in the less steroid, standard and more steroid groups respectively. Kaplan-Meier analysis of each treatment group demonstrated that children in the less steroid group had a significantly shorter time to the next relapse than the standard and more steroid groups. Also, children in the more steroid group relapsed later than the standard group (log-rank $P < 0.002$).

Conclusion: Children with relapsing SSNS receiving less steroid to treat a relapse experience an earlier subsequent relapse. Giving more than standard steroid prolongs the time between relapses but at the potential cost of greater steroid toxicity. Children who receive less steroid to treat relapses may inadvertently receive higher cumulative doses due to earlier relapses. The importance of standardised relapse regimens highlighted; large clinical trials to determine effects of changes to standard doses are urgently needed.

635 - P1.120

ROLE OF ULTRASTRUCTURAL ANALYSIS IN THE ROUTINE HISTOLOGICAL DIAGNOSIS OF KIDNEY DISEASES IN CHILDREN: CASE HISTORY ANALYSIS OF A SINGLE TERTIARY CENTER

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Aims/Purpose: To describe the contribution of electron microscopy (EM) in the diagnosis of paediatric kidney disease by processing data from a single reference centre between 2000 and 2020.

Methods: We analysed 513 paediatric kidney biopsies for which EM was required. Renal transplant patients, repeated biopsies in same patients and cases of IgAN or IgAVN already diagnosed at light microscopy (LM) and immunofluorescence (IF) were excluded.

In view of the light microscopy and IF data the ultrastructural analyses were divided into the following groups: 1 - negative IF, histology without significant changes; 2 - idiopathic nephrotic syndrome (i.e. negative IF, MCD/FSGS at LM); 3 - mesangial hypercellularity predominant C3 at IF; 4 - negative or no IF independently to histological features; 5 – various histological pattern and IF with predominant IgG (including full house pattern); 6 - LM with predominant tubulointerstitial alterations.

The contribution of EM to the final diagnosis was also defined as:

Necessary: final diagnosis not possible without EM

Supportive: EM does not change the initial diagnosis, nevertheless it provides important information

Not helpful: EM does not prove necessary or decisive in the diagnostic definition

Finally, histological diagnoses were considered in more detail, analysing the usefulness of EM both in association with the six etiopathological groups and, subsequently, with regard to the individual preliminary histological diagnoses.

Results: Among the entire cohort, EM was necessary in 234 patients (46 %), supportive in 201 patients (39 %) and not helpful in 78 patients (15 %). Within the six clinical/histological groups, a particularly important role of EM was observed in group 1 and group 4 (necessary in 95.7 % and 87.9 % of cases respectively), whereas it was not helpful in the majority of patients in group 6 (66.7 %). Regarding the individual histological diagnoses, in group 1 EM proved useful especially in diagnosing cases of inherited GBM diseases. In group 2, on the other hand, EM was diagnostically supportive in most cases of podocytopathy, while in group 3 it proved supportive in the differential diagnosis of C3 glomerulopathies. Group 4 turned out to be very heterogeneous, with EM distinctly helpful in compensating for the lack of IF. As for group 5, the cases of SLE are certainly worth mentioning, for which EM proved to be mainly supportive (identification of Class V renal involvement). In group 6, finally, there are 21 patients with signs of tubular damage, for most of whom (14) EM proved to be not helpful.

Conclusion: EM is confirmed as a valid diagnostic technique for paediatric glomerular pathologies. Since it was helpful (necessary or supportive) in 85 % of the patients considered, its systematic use in the analysis of paediatric kidney biopsies certainly continues to be justified.

648 - P1.121

RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS IN CHILDREN, A SINGLE CENTER EXPERIENCE

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Aims/Purpose: Rapidly progressive glomerulonephritis (RPGN) is a rare cause of chronic kidney disease in children. Here we report a single center experience in ANCA-associated nephritis treatment and one case of overlap of anti-glomerular basement membrane nephritis and AAN.

Methods: We reviewed the records of all children admitted to the pediatric nephrology department of our clinic with RPGN during the 2015–2024 year.

Results: Retrospective analysis (2015–2024) revealed 18 children (7 boys) with RPGN; 16 had biopsy-proven AAN; one girl was diagnosed with anti-GBM nephritis; and in one girl, we diagnosed AAN in CKD 5 stage on hemodialysis. The median age of diagnosis was 14.1 years (range 4,5–17,8), the median time from first symptoms to first admission and biopsy was 3,5 months (from 25 days to 3,25 years), and the median age of onset was 13.5 years (IQR 9,67–14,8). It should be mentioned that patients with delayed biopsy had more sclerotic lesions. ANCA screening was done before biopsy in 13 cases, and 4 were negative. In our analysis, all patients were ANCA positive (12 anti-MPO, 6 anti-PR3), and one patient had anti-MPO and anti-GBM antibodies. All children had a GFR decrease at onset (Me 28 ml/min/1,73m2, IQR 15,8–43,8). Most of the children were treated with oral steroids (13), pulses of methylprednisolone (9) before biopsy; 6 started cyclophosphamide (CP), 2 started mycophenolate mofetil (MMF), and 1 received rituximab (RTX) due to alveolar hemorrhage. Systemic manifestations were observed in 10 cases: 8 had alveolitis, 4 had skin rash, 4 had fever, 2 had ocular involvement (uveitis and orbital pseudotumor), and 3 had arthralgia. In our clinic, all patients were treated with oral prednisolone 0.3–1.5 mg/kg (up to 80 mg/day), and 17 started immunosuppression (the treatment was delayed in one case because of infection). The induction schedule included CP (5), MMF (3), RTX (4), or both RTX and CP (4). During follow-up (FU) (Me 21,6, IQR 9.4-35,3 months) 10 of the patients decreased creatinine more than 50% after the induction course. We observed two patients with severe kidney failure and diffuse extracapillary glomerular lesions, glomerulosclerosis, and Bowman capsule rupture in one of them. Both children were on dialysis but started immunosuppression due to lung involvement and had a partial recovery of kidney function. One of them now has CKD 3 (after 13 months of FU), and the second started peritoneal dialysis 80 months after onset. During FU 3 girls reached CKD stage 5 and received kidney grafts. The presence of crescents in 75% of glomeruli was associated with a progressive decrease of GFR, despite immunologic remission.

Conclusion: Despite the presence of unfavorable biopsy results, partial recovery of kidney function is possible in cases of early start of immunosuppression.

650 - P1.122

SHRUNKEN PORE SYNDROME IN PAEDIATRIC NEPHROLOGY PATIENTS

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Aims: Shrunken Pore Syndrome (SPS) has been described in adults as the reduction in glomerular filtration of 3-50 kDa molecules such as cystatin C compared to filtration of smaller molecules like creatinine. The estimated renal glomerular filtration (eGFR) by serum cystatin C and creatinine concentration ratio eGFRcys/eGFRcrea ≤ 0.7 defines this disorder. The aim of our study is to assess and describe the existence of this condition in paediatric nephrology patients.

Methods: Longitudinal retrospective study in which we analysed 87 patients (58 males, 29 females), with different diagnosis (glomerulopathy, congenital anomalies of kidneys and urinary tract (CAKUT) with and without parenchymal loss, ciliopathies, acquired parenchymal loss, tubulopathies,...) followed up in the Paediatric Nephrology department. We calculated eGFRcys/eGFRcrea ratio at two different time points (t1 and t2). eGFR was calculate using the full age spectrum (FAS) equations and CKIDU25 equations.

Results: The number of patients with eGFRcys/eGFRcrea ratio ≤ 0.7 varies depending on the equations used for eGFR calculation: 4/87 with FAS (4.5%) and 8/86 with CKIDU25 (9.2%). This 8 patients with ratio ≤ 0.7 measured by CKIDU25 at t1 diagnosis were: haemolytic uremic syndrome (n = 1), Alport disease (n = 1), CAKUT with parenchymal loss (n = 3), history of acute kidney injury requiring renal replacement therapy (n = 2) and haematuria with non-definitive diagnosis (n = 1). 75% (6/8) of patients with ratio ≤ 0.7 had an eGFR < 90 ml/min/1.73m2 at the time of measurement; and the group was younger compared to patients with > 0,7 ratio (median of 2 years old ± 6 in the group with ratio ≤ 0.7 compared to 11 years old ± 7; p < 0,005). The ratio became > 0.7 in 62.5% of these patients at t2 (5/8) remaining only with ≤ 0.7 ratio one patient with Alport disease and one of the patients with history of acute kidney injury.

Conclusion: SPS is present in paediatric nephrology patients and the percentage varies depending on the equation used to calculate eGFR. SPS seems to be related with eGFR < 90 ml/min/1.73m2. Some cases of SPS in paediatric population could be transient. It does not seem that this condition is congenital associated with malformations, since all our cases with CAKUT without parenchymal loss have a ratio > 0.7, and patients with CAKUT with parenchymal loss who had abnormal ratio in the first determination regained index > 0.7 in the follow up.

661 - P1.123

VACATION IN EGYPT AS MAJOR RISK FOR SHIGA TOXIN ESCHERICHIA COLI INFECTION IN CHILDREN. DATA FROM THE ITALKID-HUS NETWORK

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Aims/Purpose: Hemolytic uremic syndrome (HUS) is a severe thrombotic microangiopathy that may develop as a complication of Shiga toxin-producing Escherichia coli (STEC). In individual cases the source of infection often remains unknown. During 2023 we observed several cases of infection in children returning from vacations, thus we evaluated the association between travelling and STEC infection.

Methods: We analyzed all Shiga toxin-positive children identified by the ItalKid-HUS Network surveillance system in 2023. Families of infected children were contacted and a short questionnaire regarding recent travels abroad was administered. The exposure time was considered since the 3rd day after the arrival abroad until the 5th day after the return home. A self-controlled case series design was used to calculate relative risk.

Results: Of 43 cases with STEC infection, 11 developed HUS. Twenty-three subjects did not travel abroad, while 20 had travelled to several destinations. For 12 subjects we identified a specific association between exposure time and travel (10 to Egypt, 1 to Kosovo and 1 to Albania), Thus 23% of all cases of STEC infection were acquired during a short vacation in Egypt defining a relative risk of 133-folds higher than the general risk. Serotype analysis excluded the possibility of an epidemic given the different identified strains. Exposures analysis didn't provide evidence of a single potential source of the infection.

Conclusion: Children travelling to Egypt are exposed to a high risk of STEC infection. Specific actions by Egyptian health authorities are needed to identify the source of infection to develop effective preventive measures.

713 - P1.124

INSIGHTS INTO AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE: A CASE STUDY OF THREE SIBILING

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Aims/Purpose: To present a case study involving three asymptomatic sisters diagnosed with ADPKD through targeted examination prompted by a positive family history, highlighting the importance of family screening and early detection.

Methods: This abstract draws upon existing research and literature to provide background information on autosomal dominant polycystic kidney disease (ADPKD), including its genetic basis, clinical manifestations, prevalence, and potential complications.

Results: The case under consideration involves three asymptomatic sisters, aged 4, 8, and 10 years, who were diagnosed with polycystic kidney disease through targeted examination prompted by a positive family history. Their father was monitored for bilateral cystic kidney disease and his mother suffered from polycystic kidney disease discovered due to arterial hypertension and underwent a kidney transplant at the age of 53. All the above-mentioned three sisters had ultrasound scans revealing bilateral renal cysts ranging in size from 3x2 mm to the largest 20x10 mm. The ultrasound examination of the urinary system revealed hyperechoic parenchyma in both kidneys, lacking corticomedullary differentiation. Both the 10-year-old and 8-year-old sisters exhibited normal ambulatory blood pressure monitoring (ABPM), except for the absence of nocturnal dipping in the 10-year-old sister. There was no indication for therapy introduction. Blood tests, screening for proteinuria, glomerular filtration rate, and serum creatinine were regularly monitored. Heart, abdomen, and urinary system ultrasounds were also done for each of them. The overall renal function was normal during monitoring in all three sisters. Also, no hepatic, pancreatic, or splenic cysts were found with the abdomen ultrasound. The ADPKD is assumed so a genetic analysis utilizing Next Generation Sequencing (NGS) methodology was conducted. The sequence analysis revealed a heterozygous frameshift variant PKD1 c.11803del, p. (Ala3935Profs*10) in two sisters, aged 4 and 10. A variant is classified as likely pathogenic, based on the established association between the gene and the patient's phenotype, the variant's absence in control populations, and variant type (frameshift). 8 years old sister was heterozygous for TTC21B c.1593_1595del, p. (Leu532del), which is VUS. In two sisters aged 4 and 10, in whom PKD1 c.11803del, p. (Ala3935Pros*10) mutation was found, brain magnetic resonance imaging (MRI) was performed for intracranial aneurysms, which was not confirmed by examination.

Conclusion: Due to increasing knowledge about genotype-phenotype correlation, genetic testing is important in adults with ADPKD, especially in children with an early manifestation of the disease. As well as long-term monitoring for timely therapeutic intervention in case of proteinuria, hypertension or chronic renal failure development.

719 - P1.125

USE OF MYCOPHENOLATE MOFETIL AND CYCLOPHOSPHAMIDE AS AN ANTI-RELAPSE THERAPY IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME

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Aims/Purpose: The efficacy of corticosteroid therapy in idiopathic nephrotic syndrome (INS) is widely recognized, but concerns about steroid toxicity during long-term treatment and the effectiveness of anti-relapse therapy with different medications remains challenging. The aim of this study is to assess the anti-relapse effectiveness of Mycophenolate Mofetil (MMF) in children with INS.

Methods: Eleven patients between the ages of 2 and 11 were studied, of whom 9 were diagnosed with minimal change disease (MCD) and 2 patients with primary focal segmental glomerulosclerosis (FSGS). All 11 patients were initially treated with 60 mg/m2 per day of prednisolone for 6 weeks, followed by 40 mg mg/m2 alt day for 6 weeks. Initially, all patients achieved complete remission. However, during the second relapse, hormone resistance was observed in both cases, and focal segmental glomerulosclerosis was confirmed. Among the 9 patients with MCD, frequent relapse variants occurred along with steroid toxicity. Subsequently, all patients were treated with cyclophosphamide at a dosage of 2 mg/kg/day, with a maximum cumulative dose of 168 mg/kg . In 6 patients with MCD relapses occurred 2-8 weeks after discontinuation of treatment with cyclophosphamide. In 3 patients cyclophosphamide treatments were stopped within a week due to serious side effects such as leukopenia, and thrombocytopenia. In cases of FSGS, complete remission was not achieved. Considering the above treatment with MMF was initiated. Each patient received an initial dosage of MMF 1200 mg/m2 daily dose (up to a maximum of 1 g twice daily) for one year. Prednisolone was prescribed at a dosage of 1 mg/kg every other day (maximum dosage 40 mg every other day) during the first 8 weeks of MMF. This was followed by 0.5 mg/kg every other day (maximum dosage 20 mg every other day) for another 8 weeks.

Results: In cases of focal segmental glomerulosclerosis, treatment with MMF resulted in partial remission, with a reduction in proteinuria by 60-70%, and normalization of albumin and lipid levels in the blood. However, after discontinuation of MMF treatment, one patient developed nephrotic syndrome after 4 weeks, and another after 6 weeks. In patients with frequently relapsing minimal change disease who were treated with MMF, remission was sustained for 8 months after discontinuation of corticosteroid therapy. In the course of 1 year of MMF treatment, not a single side effects were observed, however, 1 to 3 months after the discontinuation of treatment, disease relapse occurred.

Conclusion: In patients with frequently relapsing minimal change disease long-term therapy with MMF results in significant steroid sparing. However, long-term remission did not develop after withdrawal of MMF. In the case of FSGS neither cyclophosphamide nor MMF had an effect and remission was not achieved.

724 - P1.126

EXPLORING MICROHEMATURIA IN PEDIATRIC PATIENTS: A CASE STUDY OF DIAGNOSTIC COMPLEXITY AND GENETIC CONSIDERATIONS

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Aims/Purpose: To present a case study of an 11-year-old girl with incidentally discovered asymptomatic microhematuria, and to highlight the diagnostic challenges and considerations in identifying the underlying cause of microhematuria, including the role of genetic tests and kidney biopsy.

Methods: This case study serves to illustrate real-world applications of the information discussed and provides practical insights into the diagnostic and management challenges associated with microhematuria.

Results: An 11-year-old girl, previously treated for phlegmonous appendicitis, has been monitored for four years due to incidentally discovered asymptomatic microhematuria during school enrollment. Initial extensive laboratory tests showed normal urea and creatinine, without significant proteinuria or hypercalciuria. Glomerular filtration rate was normal. While ANA was positive, ANCA was negative, and complement components were normal. Ultrasound revealed normal kidneys and urinary tract. No familial hematuria was detected. Over the follow-up period, persistent microhematuria of glomerular origin persisted alongside proteinuria lasting over six months. Light microscopy showed normal kidney tissue, with negative immunofluorescence. Electron microscopy revealed variable glomerular basement membrane thickness (160 – 470 nm, mean 274 nm, standard deviation 62 nm) with focal splitting, indicative of Alport syndrome. Next-generation sequencing failed to identify mutations causing Alport syndrome but revealed variants of unknown significance, including LAMB2 c.5039C > T (p.Ala1680Val). Despite lacking active treatment, the patient maintained normal kidney function over a one-year follow-up, with only persistent microhematuria. Extensive examinations for additional Alport syndrome characteristics yielded negative results, and the patient exhibited normal vision, hearing, and neurological development. Alport syndrome results from mutations in genes encoding type IV collagen manifesting with kidney disease, and variants like thin basement membrane nephropathy. Initial signs usually include childhood microhematuria and sensorineural hearing deficits. While typically X-linked, some cases may occur sporadically, necessitating genetic testing for diagnosis. Although our patient's clinical presentation and biopsy findings align with Alport syndrome, genetic testing failed to confirm it, implicating LAMB2 variants. The literature suggests LAMB2 mutations can lead to kidney disorders resembling Alport syndrome.

Conclusion: The effects of LAMB2 variants on kidney function remain uncertain, necessitating regular nephrological monitoring to anticipate potential kidney failure. Hence, the importance of genetic testing, especially in the absence of familial history, in diagnosing symptoms consistent with Alport syndrome is underscored.

748 - P1.127

ACUTE KIDNEY INJURY DUE TO RHABDOMYOLYSIS ASOCCIATED WITH INFLUENZA A H1N1 INFECTION IN A PEDIATRIC PATIENT

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Aims/Purpose: Raise awareness of the importance of recognizing kidney complications in the context of influenza A infection in pediatrics.

Methods: Review of the clinical history of a pediatric patient suffering from rhabdomyolysis in the context of influenza A who developed acute kidney injury, treated in a tertiary hospital.

Results: A 13-year-old girl presented with high fever, cough, runny nose, asthenia, and myalgia for 4 days. The parents report an affectation of the general condition and oligoanuria in the last hours, with scarce and choluric urination. No personal or family history of interest. The physical examination revealed poor general condition, pale-jaundiced color, cough with nasal mucus without oropharyngeal exudate and pretibial edema. Presence of arterial hypertension for age, sex and height (147/90 mmHg, Pc > 99/Pc > 99). Complementary tests: Blood tests highlight: Leukocytes 5,920/mm3, Neutrophils 4,550/mm3. Hemoglobin 13.5 g/dL, Platelets 111,000/mm3. Urea 81 mg/dL, creatinine 2.18 mg/dL [FGe(Schwartz 2009): 29.5 ml/min/1.73m2], total proteins 5.8 g/dL, GOT 4705 U/L, GPT 1179 U/L, Total bilirubin 1.1 mg/dL, CK 163,914 U/L, High-sensitivity Troponin T 20.3 pg/mL, CRP 21.04 mg/L, albumin 3.7 g/dL, haptoglobin 216 mg/dL, without schistocytes. Urinary systematic: Density 1,015, pH 6.5, Proteins 3+, Bilirubin 1+, remainder negative. Urinary sediment: Presence of myoglobinuria, abundant granular casts. Protein/creatinine index 1.67 mg/ mg. Normal coagulation. Venous blood gases: metabolic acidosis (pH 7.32, HCO3 16.5 mmol/l). Respiratory virus PCR: positive for influenza A H1N1. Normal chest x-ray. Abdominal ultrasound: Hyperechogenic kidneys, with poor cortico-medullary differentiation. Clinical evolution: Admitted to the Pediatric Intensive Care Unit with acute kidney injury in the context of rhabdomyolysis due to influenza A. Requires diuretic treatment with IV furosemide, hyperhydration and administration of 1/6 M IV sodium bicarbonate. Respiratory and hemodynamically stable. Cessation of fever in the next 48 hours. It was decided not to start treatment with oseltamivir due to the time of symptomatic evolution and because it is nephrotoxic. Progressive improvement in renal function with biochemical normalization, disappearance of associated hypertension and onset of spontaneous diuresis on the 3rd day of admission. Discharged with subsequent normal renal function.

Conclusions: Influenza A infection can cause serious kidney complicatios (acute kidney injury, hemolytic uremic syndrome, acute postinfectious glomeulonephritis, tubulointerstitial nephritis), as well as muscle (rhabdomyolysis), cardiac (fulminant myocarditis) and/or neurological (encephalitis) complications. Knowing these complications to diagnose and treat them early is essential to improve the prognosis of these children.

754 - P1.128

PROGNOSTIC FACTORS IN ANCA-ASSOCIATED VASCULITIS IN CHILDREN: THE EXPERIENCE OF TWO MAJOR ITALIAN CENTERS

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Aims/Purpose: This retrospective study aims to analyze the demographic profile, clinical presentation, treatment patterns, and long-term outcomes in pediatric patients diagnosed with renal involvement in ANCA-associated vasculitis (AAV).

Methods: Data from pediatric patients diagnosed with biopsy-proven renal involvement AAV between January 1999 and January 2024 were retrospectively analyzed. Clinical records from two major Italian pediatric nephrology centers were collected and analyzed. Demographics, clinical presentation, laboratory findings, treatment regimens, and outcomes were examined. Renal biopsies were categorized based on the Berden's histopathological AAV classification (1).

Results: Twenty-seven pediatric patients were enrolled. The median age at diagnosis was 12.7 years, with a slight female predominance (63%). Granulomatosis with polyangiitis was the most common clinical variant (48.1%), followed by microscopic polyangiitis (25.9%) and renal-limited vasculitis (25.9%). Anti-MPO autoantibody was found in 44.4% of the patients, anti-PR3 in 37%, while 11.1% of the patients were ANCA negative. One MPO-ANCA positive patient presented also with anti-GMB autoantibodies. Pulmonary and ear, nose, and throat involvements were common extrarenal manifestations A significant proportion of patients (33.3%) progressed to end stage kidney disease (ESKD). Histopathological classification emerged as a significant predictor of one-year estimated glomerular filtration rate (eGFR), with the crescentic class associated with the poorest outcomes (p value 0.002). Creatinine at onset and amount of proteinuria at onset were both correlated with reduced eGFR at 1 year (p value < 0.05). Anaemia at onset (Hb < 10 g/dL) was also predictive of worse renal outcomes (p value < 0.05). Therapeutic regimens at onset did not predict outcome, but the need for renal replacement therapy at onset was associated with poorer one-year eGFR (p value 0.00003).

Conclusion: This retrospective analysis provides valuable insights into the demographic profile, clinical presentation, treatment patterns, and long-term outcomes in pediatric AAV with renal involvement. The study highlights the importance of renal histopathology and early identification of risk factors for adverse outcomes in pediatric AAV management. Further prospective studies are warranted to validate these findings and refine risk prediction models for improved patient care.

References

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772 - P1.129

HEMOLYTIC UREMIC SYNDROME IN CHILDREN WITH OUTCOME 6 MONTHS AFTER THE DISEASE ONSET - EXPERIENCE OF OUR CENTER

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Aims/Purpose: Hemolytic-uremic syndrome (HUS) is one of the most common causes of acute renal failure in children, which requires acute dialysis. The most common form of the disease is Shiga toxin-producing Escherichia coli (STEC) HUS. Most patients with STEC HUS fully recover renal function, but 15-20% have chronic sequelae such as proteinuria and hypertension. The most common extrarenal manifestation of the disease is involvement of the central nervous system (CNS). The aim of our study was to examine the course and outcome of the disease in children with HUS at discharge and at follow-up 6 months after the onset of the disease.

Methods: This retrospective study included 12 patients with HUS, treated at University Children's Hospital, Belgrade, Serbia, during the year 2023, in the period from June to October. The data were obtained from the patients' medical records. Descriptive statistics methods were used for data processing.

Results: The examination was performed in 12 patients, median age was 6.5 years (IQR 2-13.5). Male to female ratio was 7:5 (58.3%:41.7%). The first symptoms of the disease appeared 1-8 days before hospitalization (average 4.41 ± 2.1). One patient (8.33%) died on the second day of hospitalization, due to the rapidly progressive course of the disease with primarily involvement of the CNS. In the surviving 11 patients, hospitalization lasted 7-35 days (average 19.1 ± 9.3). In 10/12 patients (83.3%), stool examination using PCR and/or ELISA technique was performed and the diagnosis of STEC HUS was confirmed in 9/12 (75%). One patient had a negative test result (previously received antibiotics parenterally). In two patients the stool was not examined (one died on the second day of hospitalization, the other did not have a stool during the first 7 days of hospitalization). Renal replacement therapy (RRT) by hemodialysis was required in 9/12 patients (75%). The need for RRT ranged from 1-22 days (average 9.25 ± 8.5). During hospitalization, 10/12 patients (83.3%) had hypertension. Seven patients had extrarenal manifestations of the disease: CNS 7/12 (58.3%), lungs 3/12 (25%), heart 3/12 (25%), pancreas 2/12 (16.7%), intestines 1/12 (8.3%). At discharge, in 11 surviving patients, 8 (72.7%) had eGFR < 90 ml/min/1.73m2; all patients had pathological proteinuria (UPCR > 0.21), from which 5 patients had nephrotic range proteinuria (UPCR > 2.1); 4 patients had hypertension. At the follow-up 6 months after the onset of the disease, one patient had eGFR < 90 ml/min/1.73 m2, 4/11 (36.3%) patients had proteinuria of non-nephrotic range, no patients had hypertension, however 4 patients were on ACE- inhibitor therapy due to pathological proteinuria.

Conclusion: The most common cause of HUS in children is STEC infection. Recovery of renal function in children with HUS is complete in most cases. Proteinuria is the most common sequela of the disease. Although rare, fatal outcome is possible.

792 - P1.130

URINARY LIVER FATTY ACID BINDING PROTEIN AS A PREDICTOR OF ACUTE KIDNEY INJURY IN PEDIATRIC ONCOLOGY PATIENTS TREATED WITH NEPHROTOXIC AGENTS

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Aims/Purpose: Acute kidney injury (AKI) is a common complication in pediatric oncology patients, and is often caused by nephrotoxic drugs. We aimed to assess whether levels of urinary liver fatty acid binding protein (L-FABP) can be an early biomarker for cytostatic induced AKI.

Methods: A cross-sectional study was performed in children treated with cisplatin or ifosfamide. AKI was defined as at least 25% decrease in the estimated glomerular filtration rate from pre-treatment within 48 hours after chemotherapy. For each patient, five serum and four urine samples were obtained immediately before and at 2, 6, 24 and 48h after treatment.

Results: Of 38 patients, 12 (31.6%) experienced AKI within 2 days following the chemotherapy. Significant rise of urinary L-FABP excretion in comparison with the baseline was observed 2h after chemotherapy administration, with highest urinary levels of L-FABP detected 6 h following the chemotherapy administration in AKI (4.4-fold) and non-AKI (8.2-fold) group of patients, respectively. However, there was no statistically significant difference in urinary L-FABP levels between AKI and non-AKI group of patients. The ROC AUCs for measured urine L-FABP adjusted according to urine creatinine concentrations did not show value greater than 0.7, indicated unacceptable sensitivity and specificity in detection of chemotherapy induced nephrotoxicity.

Conclusion: Our study suggest that despite the early and significant increase of urinary L-FABP excretion after chemotherapy administration, this biomarker do not provide satisfactory diagnostic accuracy in early prediction of acute kidney damage in patients treated with cisplatin and ifosfamide. Further research should determine urinary L-FABP diagnostic and prognostic utility.

794 - P1.131

A RARE KIDNEY INVOLVEMENT IN JUVENILE DERMATOMYOSITIS: FOCAL SEGMENTAL GLOMERULOSCLEROSIS

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Aims/Purpose: In juvenile dermatomyositis (JDM), renal involvement is rare and there is scarce data in the literature. In most cases, renal involvement was observed concomitantly with the diagnosis of JDM. We report a patient in whom focal segmental glomerulosclerosis (FSGS) was diagnosed nine months after the diagnosis of JDM and while he was still under immunosuppressive therapy.

Methods: Case report

Results: A 14-year-old male was admitted with symptoms including proximal muscle weakness, calcinosis, and skin manifestations consistent with JDM. Laboratory tests revealed elevated levels of creatine kinase (CK) and lactate dehydrogenase. Whole body MRI findings, muscle and skin biopsies confirmed the diagnosis, with positive NXP-2 in the myositis panel. Following the JDM diagnosis, the patient received methylprednisolone (MPZ) pulse therapy and a single dose of intravenous immunoglobulin (IVIG). Maintenance therapy included prednisolone and methotrexate. During follow-up, elevated CK levels and weakness recurred and another pulse MPZ treatment was given. Despite treatment, he experienced ongoing proximal muscle weakness and difficulty in swallowing. Three weeks after JDM diagnosis adalimumab was initiated and an additional IVIG dose was given. Adalimumab resulted in improved muscle strength and skin findings. After nine months, while he was under treatment with adalimumab, MTX, and a tapering regimen of prednisolone, with stable clinical course and preserved renal function, nephrotic-level proteinuria was detected. The 24 hour urine protein was 4644 mg/day (96 mg/m2/h) and albumin 5400 mg/day (111 mg/m2/h). Kidney biopsy revealed focal segmental glomerulosclerosis (FSGS), mesangial cellular proliferation and mild matrix increase. Immunofluorescence staining yielded negative results. Monthly pulse MPZ treatment for total three doses was initiated and MTX was replaced with cyclosporine. After two doses of monthly pulse MPZ treatment, his spot urine protein to creatinine ratio decreased to 0.27 mg/ mg. Low dose steroid was given between MPZ pulses. Currently he is under adalimumab, siklosporin, prednisolone and enalapril; and he is clinically stable.

Conclusion: Toxic effect of myoglobinuria and autoimmune reactions are thought to be involved in kidney involvement in JDM. Modification of immunosuppressive treatment provides significant benefits in the management of kidney involvement in JDM.

821 - P1.132

PROFILES OF CHILDREN WITH POSTENFECTIOUS NEPHRITIS IN A SINGLE CENTER

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Aims/Purpose: This study aims to evaluate clinical features and laboratory parameters in children with postinfectious nephritis.

Methods: Children, diagnosed with postinfectious nephritis in a single center during the last thirthy years, were evaluated in terms of clinical features and laboratory data retrospectively. Proteinuria and glomerular filtration rate (GFR) were evaluated during last follow-up visit.

Results: 81 patients (53 boys and 28 girls) with mean age 8.5 years included in the study. Edema and macroscopic hematuria were the major presenting symptoms. Majority of patients (93.8 %) had upper respiratory tract infection history. Median follow-up time was 12 months. 19 patients (23.5%) underwent kidney biopsy. Proteinuria levels during first month and last follow up, serum creatinine levels of children who underwent biopsy were found to be higher than in children without biopsy ($p < 0.05$). In the same group total protein and albumin levels were significantly lower than in children without biopsy. Steroid, antihypertensive and diuretic treatments were required in 15 (18.5 %), 20 (24.6 %) and 26 (32.1 %) of children respectively. There was dialysis requirement in five patients with rapidly progressive course. Laboratory and clinical features including creatinine levels, proteinuria, systolic and diastolic blood pressure levels were all significantly decreased at first month of diagnosis when compared to the presenting levels ($p < 0.05$). Last follow up GFR and proteinuria were seen to be significantly improved.

Conclusion: Abnormal clinical and laboratory findings of children with postinfectious nephritis generally improves in one month. Kidney biopsy can be needed in selected cases especially if those are not improved.

851 - P1.133

THE GOODPASTURE SYNDROME IN CHILDREN AND ADOLESCENTS: A SINGLE CENTER EXPERIENCE

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Aims/Purpose: Goodpasture syndrome is a rare autoimmune disease due to the action of anti-GBM antibodies on the alpha-3 subunit of type IV collagen, resulting in the development of RPGN and lung involvement with bleeding. Lungs and kidneys are affected together in 60 % of patients, in 20-40 % only renal involvement develops, in 10 % only lung disease occurs. The pediatric population does not show predominance due to gender, it affects children of different ages and most of them progress to ESRD. In the years 2010-2023, we treated 5 patients diagnosed with Goodpasture syndrome in our center.

Methods: Retrospective assessment of the course, treatment, laboratory parameters: creatinine, eGFR (Schwartz formula), anti-GBM antibodies

Results: Age: median 16 years 8 months (1 year 5 months - 18 years 3 months). Main symptoms: acute kidney failure, pulmonary hemorrhage with the development of respiratory distress. Complications: hypertension, anemia, catheter sepsis, venous thrombosisDuration from first symptoms to start of treatment: median 11 (8-22) days. eGFR at the time of diagnosis (patient 1-5): 9, 37, 12, 0, 102 ml/min/1.73 m2. Renal biopsy performed in 4 patients with evidence of rapid progressive glomerulonephritis and presence of crescents. Treatment: corticosteroids, cyclophosphamide (CP), plasmapheresis (PF)/ immunoadsorption (IA). Number of PF/IA cycles (patient 1-5): 18 IA, 11 PF, 26 PF + 16 IA, 1 x PF + 12 IA, 8 IA +3 PF. Anti-GBM antibody level at time of diagnosis/ after completion of PF/IA (patient 1-5): 18887/ 766, 269/7, 195/44, 748/57, 211/8 CU. eGFR after administration of last cyclophosphamide dose (patient 1-5): 36, 97, 12, 0, 114 ml/min/1.73 m2. 4 patients developed AKI with subsequent development of CKD. 2 patients required hemodialysis, one developed ESRD with the need for chronic HD and subsequent kidney Tx. The development of pulmonary impairment occurred in 4 patients.

Conclusion: In all patients, there was a significant decrease in anti-GBM antibodies during treatment, which was helped by a series of immunoadsorptions or plasmapheresis. The level of anti-GBM antibodies stabilized at a low level after the end of basic therapy. 80 % of our patients developed renal impairment, 80 % developed pulmonary impairment, 20 % developed only renal and 20 % developed only pulmonary symptomatology. The youngest patient was 1 year and 5 months old and showed a many times higher level of anti-GBM compared to the other patients. All patients were treated with corticosteroids, CP and PF/IA. Remission was achieved in all patients. Only one developed ESRD with subsequent kidney Tx before the 19th birthday.

884 - P1.134

PREVALENCE AND DETERMINANTS OF ANTI-TISSUE TRANSGLUTAMINASE ANTIBODIES IN PATIENTS WITH IDIOPATHIC STEROID SENSITIVE NEPHROTIC SYNDROME

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Aims/Purpose: Uncontrolled studies suggest that restriction of gluten or other food antigens reduces the frequency of relapses in patients with difficult-to-treat steroid-sensitive nephrotic syndrome (NS). The prevalence of celiac disease in patients with steroid-sensitive NS has not been tested formally.

Methods: This cross-sectional observational study examined the prevalence of positive serology for celiac disease, defined as anti-tissue transglutaminase (anti-tTG) antibody ≥20 RU/ml, in children with idiopathic steroid sensitive NS. Following IRB approval and informed consent, anti-tTG antibodies were tested by a commercial ELISA (EUROIMMUN, Perkin Elmer, USA) in samples collected in remission, remote from relapse and/or therapy with high doses of prednisolone. The frequency of relapses and clinical features of celiac disease were compared between patients with and without positive celiac serology. Patients with positive serology underwent upper gastrointestinal tract endoscopy to document the severity of duodenal histological abnormalities using modified Marsh criteria.

Results: Of 274 patients with steroid-sensitive NS screened in remission, 250 (76% boys) were enrolled at median age of 106 (interquartile range 80-142) months. During disease span of 61 (46-89) months, frequent relapses or steroid dependence were observed in 52% and 24% patients, respectively. Five patients had positive celiac serology, indicating a prevalence of 2% (95% CI 1.11-5.14%), which was similar to the prevalence in healthy north Indian children [risk difference 1.0 (95% CI -0.84-2.84%); P =0.22]. There were no significant differences in the frequency of relapses and symptoms of food allergy between patients with or without positive serology. Patients with positive serology had significantly lower anthropometric standard deviations cores for weight (median -1.58 vs. -0.20), height (-2.4 versus -0.66) and body mass index (-0.58 vs. 0.26). Three patients, all with anti-tTG antibody > 300 IU/ml, had duodenal histology indicating celiac disease.

Conclusions: The prevalence of positive celiac serology in children with steroid-sensitive NS is low and comparable to healthy Indian children. Positive serology does not relate to the severity of disease or symptoms of allergy/atopy. Overt duodenal histological changes are limited to patients with high-titer anti-tTG antibodies. Patients with steroid-sensitive NS with low anthropometric indices might merit evaluation for celiac disease.

901 - P1.135

FACTORS INFLUENCING REMISSION OF STEROID RESISTANT NEPHROTIC SYNDROME IN INDONESIAN CHILDREN

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Aims/Purpose: To determine the remission rates and factors influencing remission in pediatric steroid-resistant nephrotic (SRNS) syndrome patients at Cipto Mangunkusumo National Hospital.

Methods: This study is a retrospective cohort study conducted at Cipto Mangunkusumo National Hospital. The evaluated factors included gender, age of onset of nephrotic syndrome, use of calcineurin inhibitor (CNI) immunosuppressants, type of resistance, and histopathological findings.

Results: A total of 150 subjects were included in this study (table 1). The remission rate in pediatric pediatric steroid-resistant nephrotic patients was 74.6%, consisting of 51,3% complete remission and 23,3% partial remission. The factors influencing remission (table 2) in pediatric SRNS were CNI immunosuppressant therapy (p =0.001, adjusted OR 4.309, 95% CI 1.773-10.470).

Table 1. Characteristics of subjects

Characteristics	n = 150	**Characteristics**	n = 150
Gender, n (%)		**Histopathology (n=64)**	
Male	100 (66,7)	MCD	10 (15,6)
Female	50 (33,3)	FSGS	36 (56,3)
Resistance type n (%)		DMS	3 (4,7)
Primary	41 (27,3)	MPGN	12 (18,8)
Secondary	109 (72,7)	PGN	2 (3,1)
GFR at SRNS diagnosis (mL/min/1,73 m2)	122,5 (17,5;428,0)*	MN	1 (0,7)
UPCR (mg/gram) n= 86	7740,3 (308,0;77229,1)*	**Remission status**	112 (74,6)
Immunosupressant therapy, n (%)		Complete	77 (51,3)
Cyclosporine	121 (80,7)	Partial	35 (23,3)
Cyclophosphamide	9 (6,0)	Duration to achieve remission (days)	66 (13;194)*
Mycophenolate mofetil	17 (11,3)		
Cyclosporine and MMF	2 (1,3)		
Cyclophosphamide dan MMF	1 (0,7)		

GFR, glomerular filtration rate; SRNS, steroid-resistant nephrotic syndrome; UPCR, urine protein creatinine ratio; MCD, minimal change disease; FSGS, focal segmental glomerulosclerosis; DMS, diffuse mesangial sclerosis; MPGN, mesangioproliferative glomerulonephritis; PGN, proliferative glomerulonephritis; MN, membranous nephropathy. *min-max

Table 2. Factor influencing remission in SRNS patients

Characteristics	Subjects (n=150)		Univariate			Multivariate		
	Remission (n=112)	Non remission (n=38)	OR	95% CI	p value	OR	95% CI	p value
Gender, n (%)								
male	70 (70)	30 (30)	0,44	0.186-1.059	0,097a	0.467	0.190-1.146	0.096
female	42 (84)	8 (16)						
SRNS onset (years)*	4,4 (1-17,1)	3,4 (1,2-17,6)			0,854b			
Resistance type, n (%)			0,898	0.397-2.031	0,962a			
primary	30 (73,2)	11 (26,8)						
secondary	82 (75,2)	27 (24,8)						
Histopathology, n (%)			1,684	0.322-8.822	0,712c			
MCD	8 (80)	2 (20)						
Non-MCD	38 (70,4)	16 (29,6)						
Immunosuppressants			4.442	1.849-10.676	0,001a	4.309	1.773-10.470	0.001
CNI	99 (80,5)	24 (19,5)						
Non-CNI	13 (48,1)	14 (51,9)						

aChi square test, bMann-Whitney test, cFisher test. *median (min-max). MCD, minimal change disease; CNI, calcineurin inhibitor

Conclusion: The factor influencing remission in pediatric patients with SRNS is the administration of cyclosporine, which belongs to the class of CNI.

904 - P1.136

IG A NEPHROPATHY, CASUISTRY OF OUR UNIT

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Aims/Purpose: IgA nephropathy is the primary glomerulonephritis, second cause of pediatric renal glomerulopathy. It is characterized by deposition of mesangial IgA. Unlike adults, its long-term prognosis is less known, with the possibility of spontaneous remission or developing renal failure.

Methods: Retrospective and descriptive study of cases diagnosed using clinical and pathological criteria from 2017 to the present.

Results: A total of 15 diagnosed patients are presented (women 20%, men 80%) with an average age at diagnosis of 9.2 years. Family history 26.66%. Clinically they presented : hematuria (13.34%), hematuria and proteinuria with or without alteration of eGFR (60%), Proteinuria (20%). Purple Scholein Henoch (HSP) 26,66%. Mean age at diagnosis, 11 years and the time elapsed until biopsy was 1.6 years; mean creatinine levels at diagnosis 0.566 mg/dl (range 0.23-1) with an eGFR by Schwartz < 90 ml/min/1.73 m2 (13.33%). . Albuminuria was observed in 57.14% of cases and proteinuria in 86.7%, with 13.3% being in the nephrotic range. C3 (6.66%) and C4 (26.66%) hypocomplementemia was evident, which normalized in all cases. A biopsy was performed in 66.66%. Treatment: 40% of the cases received treatment: steroids (20%), ACE inhibitors (46.66%) and immunosuppressants (6.6%). Schwartz eGFR > 90 ml/min/1.73 m2 and BP < P95 in all cases. In patients > 14 years old we found CKD EPI eGFR > 90 ml/min and Schwartz eGFR < 90 ml/min/1.73 m2. ERCG1 A1 (26.6%), ERCG1A2 (33.3%), ERCG2A1 (26.66%), ERCG2A2 (6.6%) and ERC G2 A3 (6.6%). All of them antitransglutaminase antibodies, negative.

Conclusion: IgA nephropathy is a common entity with a benign prognosis in most cases, although it can progress to chronic kidney disease. In our series, the need for treatment was not correlated with the decrease in eGFR at diagnosis, and was more frequent (57.14%) in the case of HSP debut.

906 - P1.137

WHAT HIGH BLOOD PRESSURE WAS HIDING

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Aims/Purpose: Highlight the importance of screening for high blood pressure in pediatric age as a marker of not only renal but also systemic pathology.

Methods: Review of the clinical history of a pediatric patient with arterial hypertension with associated oncological pathology treated in a tertiary hospital.

Results: We present the case of an asymptomatic 12-year-old adolescent referred to consultation for study after being diagnosed with arterial hypertension in a routine check-up. Absence of personal and family history of interest. The physical examination revealed good general condition with normal cardiopulmonary auscultation and, at abdominal level, palpation of a deep, non-painful periumbilical mass. Systolic and diastolic blood pressure in Pc > 99/Pc > 99 for age, height and sex in a sustained manner. Complementary tests: Blood analysis with normal complete blood count and biochemistry, including kidney (plasma creatinine 0.65 mg/dl [eGFR(Schwartz 2009): 95.3 ml/min/1.73m2]), liver and lipid profiles. ESR and PCR negative. Systemic/urinary sediment negative. Abdominal ultrasound: heterogeneous solid retroperitoneal mass with hyperechoic foci (which could correspond to calcifications), at the umbilical level and in intimate contact with the aorta and mesenteric arteries and vena cava, in the midline with a slight left deviation, measuring 46 x 43 x 30 mm (craniocaudal, transverse and anteroposterior diameter). Findings confirmed by abdominal MRI, suggesting as the first possibility a tumor of apparently low-grade neural origin (schwannoma, ganglioneuroma, less likely paraganglioma). Study of tumor biomarkers and negative hormones. Negative metaiodobenzylguanidine scintigraphy. Normal renal Doppler ultrasound. Negative urine catecholamines. Antihypertensive treatment with amlodipine was started with good blood pressure control. Complete excision of the tumor mass was performed. The pathological anatomy analysis revealed a study compatible with ganglioneuroma. Favorable clinical evolution, blood pressure normalization after the intervention, with withdrawal of the antihypertensive medication.

Conclusions: It is important to screen for high blood pressure in the pediatric population. Among the secondary causes of arterial hypertension, oncological pathology stands out, being able to diagnose tumors such as neuroblastoma, pheochromocytoma, Wilms tumor, paraganglioma or ganglioneuroma; some of them with evil behavior. Early diagnosis and treatment improves the vital prognosis of these patients. In the case of our patient, the hypertension was due to vascular compression, with resolution after tumor excision, the ganglioneuroma being a tumor of neuronal origin with benign behavior.

914 - P1.138

HEMATURIA, VENOUS RENAL THROMBOSIS AND NEPHROTIC SYNDROME AS INITIAL MANIFESTATION OF CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME

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Aims/Purpose: Catastrophic antiphospholipid syndrome (CAPS) is a rare and severe form of antiphospholipid syndrome (APS) characterized by thrombotic microangiopathy, thrombocytopenia, and microangiopathic hemolytic anemia. The objective is to know the clinical manifestations, diagnosis and treatment.

Methods: We report an 8-year-old female patient with no relevant personal history, who presented with macroscopic hematuria, right flank pain and persistent fever. She was diagnosed of febril urinary tract infection and started antibiotic treatment 48 hours ago. On physical examination she only had right flank pains with normal blood pressure. In blood test she presented thrombocytopenia (90.000/mm3), normal renal and hepatic profile and negative acute phase reactants. Renal ultrasound revealed an enlarged right kidney with inflammatory changes. Given initial suspicion of acute pyelonephritis, he was admitted with empiric intravenous antibiotic therapy after collecting urine and blood cultures. During admission she started with petechiae in the lower limbs, abdominal collateral circulation and ascites, and continued with macroscopic hematuria and proteinuria in nephrotic range. Blood test revealed persistent thrombopenia (up to 66.000/mm3) and a nephrotic biochemical pattern with hypercholesterolemia and hypoalbuminemia. Cultures were negatives. Doppler ultrasound revealed a thrombus in right renal vein (RDV), with extension to the inferior vena cava (IVC) that subsequently advanced up to 2 cm from the right atrium. The study was expanded with angioTAC, which showed evidence of pulmonary thromboembolism, so treatment with low molecular weight heparin was initiated and the etiological study was expanded, showing positive ANA, positive lupus anticoagulant, negative antiDNA, anticardiolipin antibodies, antibeta2glycoprotein I, and C4 hypocomplementemia.

Results: Given the suspicion of CAPS associated with underlying Systemic lupus erythematosus (SLE), we started treatment with bolus doses of IV-steroid associated with hydroxychloroquine, acetylsalicylic acid, mycophenolate, enalapril and atorvastatin, with decrease of thrombus size and progressive improvement of proteinuria without other signs of nephropathy. She is currently asymptomatic, with no new episodes of thrombosis and remission of proteinuria, maintaining treatment with anticoagulation, mycophenolate, hydroxychloroquine and atorvastatin.

Conclusion: Pediatric CAPS is a rare (< 1% of patients with APS) and potentially serious systemic autoimmune disease that requires early diagnosis and aggressive treatment. Most cases are associated with infections, surgical procedures and SLE outbreaks, so it is important to carry out an exhaustive study and long-term follow-up.

917 - P1.139

ACUTE POST-INFECTIOUS GLOMERULONEPHRITIS IN TUNISIAN CHILDREN: A 10-YEAR RETROSPECTIVE STUDY

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Introduction: Despite the improvement of socioeconomic conditions, acute post-infectious glomerulonephritis (APGN) remains a prevalent cause of acute glomerulonephritis in Tunisian children. This study aimed to describe the clinical and evolutionary features and identify prognostic factors for severity.

Methods: A descriptive retrospective analysis was conducted on pediatric patients diagnosed with acute postinfectious glomerulonephritis and admitted to the pediatric department of CHU Sahloul Sousse over a decade (2013–2023).

Results: Fifty-two patients were included, with a mean age of 7.7 years. The majority (96%) had a recent history of upper respiratory tract or cutaneous infection, most commonly tonsillitis (46%). Staphylococcus was suspected as the causative agent in 8 cases. Gross hematuria was the primary presentation mode (86.5%), followed by hypertension (51.9%) and edema (21%). Oliguria was noted in 18 children (34.6%). Acute renal failure developed in 42% of patients. Renal biopsy was performed in 10 cases, with 3 cases of RPGN managed with IV methylprednisolone. Diuretics were utilized in 23 cases .The use of other antihypertensive drugs in was necessary in 15 cases. The average time for the disappearance of gross hematuria was 8 days. The average hospital stay was 9 days, with no instances of progression to chronic renal failure or mortality.

Conclusion: APGN continues to be a significant kidney disorder among Tunisian children. Timely identification and efficient treatment of related infections could potentially reduce its occurrence.

951 - P.140

HANTAVIRUS INFECTION AS A CAUSE OF ACUTE KIDNEY INJURY IN CHILDREN - CASE SERIES

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Introduction: Haemorrhagic fever with renal syndrome (HFRS) is a zoonotic disease caused by hantaviruses and it is clinically characterized by fever, coagulation abnormalities and renal dysfunction. In Poland hantavirus infections are mainly caused by the Puumala and Dobrava serotypes. Most cases are reported in the adult population in south-eastern part of the country, recognized as endemic area of hantavirus prevalence. The disease has been thought to be rare in children.

Purpose: The purpose of this study was to evaluate the incidence, clinical course and outcomes of haemorrhagic fever with renal syndrome in the population of patients admitted to two regional reference centres in Subcarpathian and Lower Silesian Voivodeships.

Materials and Methods: We analyzed the cases of hantavirus infection in patients treated in the Department of Paediatrics at Clinical District Hospital in Rzeszów and in the Department of Paediatric Nephrology at University Hospital in Wrocław.

Results: Eight cases of HFRS in children between ages 13 and 17 (2 girls and 6 boys) were diagnosed between July 2021 and February 2024. Four patients were living in rural regions in south-eastern, and 4 in southwestern part of Poland. All patients presented with fever and gastrointestinal symptoms, followed by acute kidney injury (AKI). Thrombocytopenia was present in 7 patients. Three children required short course of intermittent haemodialysis. All patients survived, with complete recovery of kidney function.

Conclusions: Hantavirus infection should be considered as one of possible causes of acute kidney injury in children, especially in the setting of fever and thrombocytopenia. Limited prevalence of HFRS in the paediatric population in Poland might be associated with low awareness of the disease. Further studies on hantavirus infections are needed to raise awareness of the disease and prevent future outbreaks.

Key words: acute kidney injury, thrombocytopenia, hantavirus, haemorrhagic fever with renal syndrome

957 - P1.141

PARENTAL WILLINGNESS REGARDING COVID-19 VACCINATION FOR YOUTH WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Aims/Purpose: To assess parental attitudes towards COVID-19 vaccination among youth diagnosed with systemic lupus erythematosus (SLE) and to determine the factors linked with parental willingness to vaccinate their children.

Methods: We conducted a single-center survey between May 2023 and January 2024. Primary caregivers of youth under 21 years old diagnosed with SLE before turning 18 were eligible. Participants completed a validated questionnaire designed to measure their willingness to vaccinate their child with SLE against COVID-19 and their attitudes towards the COVID-19 vaccine using the modified Vaccine Hesitancy Scale (VHS), where higher scores indicate increased hesitancy (a score of ≥ 3 indicates high hesitancy).

Results: Seventy-four caregivers, primarily parents (87.8%), with an average age of 46.0 ± 8.9 years, participated in the survey. The average age of youths with SLE was 16.1 ± 3.2 years. Among the participants, 66.2% expressed willingness to vaccinate their child with SLE against COVID-19, while 13.5% were uncertain, and 20.3% were unwilling. Similarly, 68.9% of participants were open to receiving the COVID-19 vaccine themselves, with 16.2% unsure and 14.9% unwilling. Parental willingness to vaccinate their child with SLE was comparable to their willingness to vaccinate themselves (p =0.71). At the time of the study, 93.2% of participants and 94.6% of children with SLE had received at least one dose of the COVID-19 vaccine. Parental attitudes towards the COVID-19 vaccine, depicted in Figures 1, predominantly displayed positive sentiments, with an average overall VHS score of 2.43 ± 1.04.

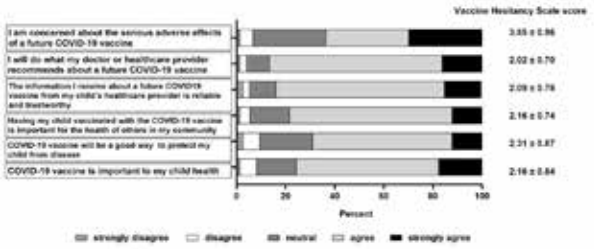

Figure 1 Parental attitudes towards the COVID-19 vaccine

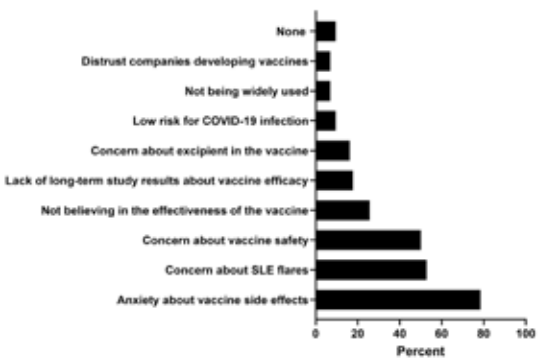

Figure 2 Parental concerns regarding COVID-19 vaccination

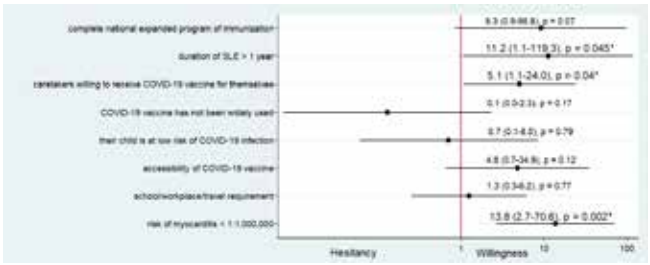

Figure 3 A multivariate logistic regression model for factors associated with parental willingness to vaccinate their child against COVID-19

Primary concerns regarding COVID-19 vaccination, shown in Figure 2, centered around potential side effects (78.4%), followed by concerns about SLE flares (52.7%). Multivariate analysis, incorporating factors that significantly differed between caregivers willing and hesitant to vaccinate their child with SLE, was employed to identify factors associated with parental willingness to vaccinate their child against COVID-19. Three factors—disease duration of more than one year, parental willingness to vaccinate themselves, and a myocarditis risk below 1:1,000,000—were significantly associated with parental willingness to vaccinate their child (Figure 3).

Conclusion: These results provide valuable insights into opportunities for healthcare professionals and patient advocacy organizations to enhance vaccine acceptance for future outbreaks of COVID-19 and other emerging infectious diseases.

959 - P1.142

ACUTE INFECTION-RELATED GLOMERULONEPHRITIS IN CHILDREN: A NEW ERA OF STREPTOCOCCUS?

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Aims/Purpose: The rate of acute post-streptococcal glomerulonephritis (GN) (the most common cause of acute GN in children) has decreased over the last few decades due to the use of antibiotics, improved socio-economic status and hygiene. We are seeing an increase in the number of cases of patients with acute GN during the period of decreasing number of patients with covid 19. Aim: to analyze the data of patients with acute GN over a 10-year period (2014-2023) to clarify the possible reasons for the increase in incidence.

Methods: 52 children (14 girls, 38 boys) aged 3-15 years were under the observation at the Belarus National Center for Pediatric Nephrology (2nd Children's Hospital Minsk). Retro- and prospective analysis was done.

Results: During the period 2014-2021, we observed an annual number of cases from 3 to 5; from 2022-2023, the number dramatically increased to 20. The connection with streptococcal infection has been confirmed in 45% before the covid 19 pandemic and in 80% as the incidence of covid 19 decreases. Acute GN developed after an infection of the pharynx and respiratory organs of various localizations (sinusitis, otitis, pneumonia), associated with streptococcus (culture from the pharynx, growth of antibodies against streptococcus). Acute onset with complaints of headache, deterioration of condition, loss of appetite and the development of nephritic syndrome: moderate proteinuria (1-2 g/l), hematuria from micro- to macrohematuria, moderate swelling of the eyelids, face, arterial hypertension (in 78%), low C3 complement were seen. There were no significant differences in the onset, clinical and laboratory parameters, course of the disease and its outcomes when comparing 2014-2021 vs 2022-2023.

Conclusion: According to the data from a number of researchers (Pubmed database), over the past decades there has been a significant decrease in the number of cases of acute GN in children which we observed among our patients until 2021. We noted an increase in the number of cases without changes in the clinical course and outcome of the disease in 2022-2023 (n = 20) vs previous 8 years (n = 32), probably associated with a change in the structure of infectious disease pathogens associated with COVID 19. Future prospects for the prevention of streptococcal pharyngitis and post-infectious systemic complications include the development of a vaccine against Streptococcus pyogenes.

996 - P1.143

A CASE THAT IS HISTOPATHOLOGICALLY COMPATIBLE WITH POSTINFECTIOUS GLOMERULONEPHRITIS AND CLINICALLY IGA VASCULITIS

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Aim: A patient who presented with a preliminary diagnosis of IgA vasculitis and underwent renal biopsy in follow-up, and was found to have post-infectious glomerulonephritis histopathologically, is presented.

Case: A 15-year-old male patient presented with abdominal pain, vomiting, and complaints of rash on the legs that started five days ago and gradually worsened (Fig1). It was learned that the patient did not have any illness in the past two to three months. No specific features were found in the patient's personal and family history. On physical examination, there was intense palpable purpura extending from the ankles to the hips and severe abdominal tenderness. The patient was hospitalized with a preliminary diagnosis of IgA vasculitis. Kidney function tests were normal, protein and erythrocytes were negative in routine urine analysis, fecal occult blood was positive, and ultrasound showed normal findings except for edema in the duodenojejunal bowel wall. Antistreptolysin O (ASO) and complement 3 (C3) levels were found to be normal. The patient, who was considered to have IgA Vasculitis with gastrointestinal and skin involvement, did not start steroid treatment. On the fifth day of hospitalization, the patient developed darkening of urine color, and erythrocytes +++, protein +++, and proteinuria of 192 mg/m2/hour were detected in routine urine analysis. Urinary ultrasound and renal Doppler ultrasound were evaluated as normal. Simultaneous kidney function tests remained normal. A kidney biopsy was performed on the patient considering IgA Vasculitis kidney involvement. Three days of pulse methylprednisolone intravenous treatment were administered, followed by oral prednisolone at a dose of 60 mg/day. The kidney biopsy result was reported as postinfectious glomerulonephritis. Immunofluorescence examination showed staining of IgG and C3, with IgA being negative. No pathogen was detected in throat culture. On the tenth day of hospitalization, the patient, who was found to have streptococcus pneumonia as the causative agent in the respiratory panel, had a low C3 level.

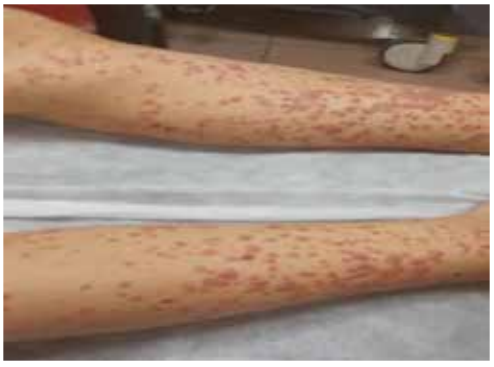

Fig 1.

Conclusion: This case presented with typical IgA Vasculitis clinically, and post-infectious glomerulonephritis was detected in the biopsy performed considering renal involvement. C3 level decreased on the 10th day of follow-up. Therefore it is an interesting case

Keywords: Ig A vasculitis, postinfectious glomerulonephritis,

997 - P1.144

EVALUATION OF THE EFFICACY AND SIDE EFFECTS OF CLASSICAL IMMUNOSUPPRESSIVE TREATMENTS AND RITUXIMAB TREATMENT IN PEDIATRIC PATIENTS WITH A DIAGNOSIS OF STEROID -DEPENDENT NEPHROTIC SYNDROME

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Aims: The aim of this study is to evaluate the effectiveness of classical immunosuppressive therapy and rituximab (RTX) treatment in patients with steroid-dependent nephrotic syndrome (SDNS).

Method: Patients aged 0-18 years who were followed up with a diagnosis of SDNS were included in this study, and the data of 35 patients were evaluated retrospectively.

Results: When the patients were evaluated, 23 (65.7%) were male and 12 (34.3%) were female. The age at diagnosis was 54.1 ± 39.6 months, and the follow-up period was 120.4 ± 66.4 months. While the patients' height percentiles were -0.63 ± 1 SDS and weight percentiles were 0.12 ± 0.88 SDS at the time of diagnosis, their height percentiles were -1 ± 1.11 SDS and weight percentiles were -0.09 ± 1.2 SDS at the last visit. Glomerular filtration rate (GFR) at the time of diagnosis was 146.5 ± 29.4 ml/min/1.73m2, GFR at the last visit was 146.2 ± 32.1 ml/min/1.73m2 and no significant change was detected. While the average number of attacks was 5.2 ± 3, patient attack scores were calculated as 0.05 ± 0.05. A total of 59 biopsies were performed in 35 patients, and 27 biopsies were performed recurrently. Initial biopsy results showed minimal lesion disease (MLH) in 21 patients (65.6%), focal segmental glomerulosclerosis (FSGS) in 3 patients (9.4%), diffuse mesangial proliferation in 4 patients (12.5%), and IgM nephropathy in 4 patients (12.5%). The most common reason for recurrent biopsy indications was cyclosporine (CSA) toxicity in 14 rebiopsies (51.8%). An increase in the rate of FSGS from 9.4% to 28.1% was detected in the pathological diagnoses of rebiopsies. Steroid toxicity was observed in 14 patients (40%); Cushingoid phenotype (42.9%) and osteoporosis (35.7%) were most frequently observed. CSA-related toxicity was observed as hair growth in 5 patients (15.6%) and gingival hyperplasia in 1 patient (3.1%). Considering the treatment distribution in terms of steroid withdrawal agents, the most frequently used agent was CSA in 32 patients (91.4%), while the least used agent was levamisole in 1 patient (2%). 31.4% of the patients received cyclophosphamide(CYC), 22.8% mycophenolate mofetil (MMF), and 17.1% RTX. While the highest attack-free period with CSA was 42.4 ± 32.1 months, the lowest attack-free period with MMF was 24.2 ± 17.5 months. The attack-free period after RTX was found to be 26.1 ± 14.5 months, but this period was associated with the short follow-up period after RTX. When 6 patients receiving RTX were examined, all of them had previously used CSA, 3 patients (50%) had used CYC, and 2 patients (33.3%) had used MMF.

Conclusions: With early and appropriate treatment, kidney functions, growth and development can be preserved. Recurrent biopsies show that patients develop renal findings, with FSGS becoming more intense over time. RTX is still in the foreground in terms of attack-freeness after the start of treatment.

1014 - P1.145

COLLAGEN TYPE III GLOMERULOPATHY; A RARE AGGRESSIVE KIDNEY DISEASE IN A YEMENI ADOLESCENT GIRL

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Introduction: Collagen type III glomerulopathy (CIIIG), also termed as collagenofibrotic glomerulopathy, is a non-immune-mediated glomerular disease characterised by abnormal accumulation of type III collagen fibrils within the mesangial matrix and subendothelial region. Clinical features of CIIIG are nephrotic range proteinuria, edema, and hypertension. The disease ultimately progresses to end-stage kidney disease (ESKD), often within 10 years of onset.

Case Presentation: A twelve-year-old Yemeni girl presented with nephrotic range proteinuria, edema, hypertensive encephalopathy, and kidney failure requiring dialysis. Clinical examination did not show nail or bone abnormalities. Kidney biopsy revealed 16 out of 19 glomeruli were globally sclerosed by light microscopy. Electron microscopic study showed a diffusely thickened irregular capillary basement membrane showing subepithelial, subendothelial, and mesangial fibrillary deposits compatible with type III collagen depositions. Consequently, the patient was diagnosed as a CIIIG case.

Managment and Outcome: The patient was initiated on dialysis therapy for a period of two months. Kidney transplantation was subsequently performed, and the patient has experienced two years of graft function with no reported complications.

Discussion: Collagen type III glomerulopathy is an extremely rare disease, and its origin and pathogenesis remain elusive. Currently, only case reports are available, mainly from Japan. However, subsequent reports included people of European and African descent. Approximately 101 cases have been reported in the literature. Herein, we presented the first CIIIG case reported in a Yemeni adolescent female, furthering our understanding of the disease. Within the current literature on CIIIG, reports of successful kidney transplantation remain scarce. Our patient's case expands this limited collection, demonstrating the viability of transplantation in select CIIIG patients with appropriate matching donors.

1030 - P1.146

SECONDARY NEPHROTIC SYNDROME DURING PENICYLLAMINE TREATMENT - A SOMEWHAT FORGOTTEN COMPLICATION. HOW SHOULD IT BE TREATED?

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Aim of the Study: Analysis of the clinical course of nephrotic syndrome (NS) during penicillamine therapy in a 17-year-old girl with type 1 diabetes and Wilson's disease.

Case report: A 17-year-old girl with diabetes type 1 diagnosed at the age of 8. and Wilson's disease diagnosed at the age of 16, was admitted to the Nephrology Department in Katowice, Poland with suspicion of NS. One month before hospitalization, the girl noticed increasing peripheral oedema and an increase in body weight about 5 kg. Six months earlier, the patient was hospitalized in the Gastroenterology Department due to jaundice. Liver failure with hepatorenal syndrome was diagnosed (laboratory tests included increased creatinine level - eGFR 47ml/min/1.73m2, anemia, cholestasis, increased INR, hypoproteinemia, hypoalbuminemia, proteinuria - without DUB assessment). After being transferred to the Department of Gastroenterology, Hepatology, Eating Disorders and Pediatrics in Warsaw, Wilson's disease was diagnosed and penicillamine treatment (3 x 250 mg) was started. At discharge, trace proteinuria with normoalbuminemia was detected, and from then until the diagnosis of NS, she remained without urine tests follow-up.On admission to the Nephrology Department, physical examination revealed severe swelling of the lower limbs. Laboratory tests confirmed NS with a daily protein loss of 9 g. Ultrasound examination revealed a liver with slightly increased, heterogeneous "granularity" and cholelithiasis. Due to the suspicion of drug-induced NS, penicillamine was discontinued and zinc supplementation was started as an alternative treatment for Wilson disease. At the same time, a kidney biopsy was performed - ultrastructure examination revealed membranous nephropathy. ACE-inhibitor treatment and antithrombotic prophylaxis were continued with gradual regression of proteinuria observed until full remission of NS at 7 months after its diagnosis.

Conclusions:

1. One of the side effects of penicillamine is proteinuria (10-30%), which progresses to NS in 70% of cases (most often as a late complication).

2. The morphological basis of the disorders is most often membranous nephropathy.

3. The basis of treatment is the removal of the causative factor and symptomatic treatment, without steroid therapy or immunosuppression. However, the time to achieve remission of NS often exceeds 6 months.

1032 - P1.147

ANCA-POSITIVE GLOMERULONEPHRITIS RELATED TO INFECTIVE ENDOCARDITIS IN A 15-YEAR-OLD GIRL

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Purpose: Presentation of a clinical case study of a 15-year-old female patient with congenital heart disease, after multi-stage cardiac surgery, who developed infective endocarditis complicated by ANCA-positive glomerulonephritis.

Methods: Case report

Results: The presented patient was born with congenital heart defect combining pulmonary atresia, hypoplasia of the left pulmonary branch, ventricular septal defect, aortopulmonary collateral circulation to the left lung and right-sided aortic arch. She underwent multi-stage cardiac surgery, including implantation of pulmonary homograft. Currently, at the age of 15, she presented with infective endocarditis, complicated by nephritic syndrome with impaired renal function (eGFR 40 ml/min) and proteinuria as high as 5.7 g/day. Antineutrophil cytoplasmic antibodies (ANCA) directed against Proteinase-3 (PR3) were detected at high titer (122 RU/ml). Combined antibiotic therapy gave a relief from fever but did not show influence on renal symptoms. Glucocorticoid therapy including methylprednisolone intravenous pulses was started and kidney biopsy was performed, which revealed crescents in 50% of glomeruli with negative IgG/IgA attaining – the picture of pauci-imune crescent glomerulonephritis. The steroid therapy resulted in eGFR stabilization at 70 ml/min and reduction of proteinuria around 1.5 g/day. At that time the girl underwent homograft reconstruction of the right ventricular outflow tract. Abundant bacterial vegetation were found at pulmonary valve. After surgery a general clinical improvement was achieved but without further resolution of renal symptoms. Thus, Immunosuppression based on mycophenolate mofetil was added to the treatment. It is continued without any complications and after 3 months a full normalization of kidney function (eGFR > 90 ml/min) and reduction in proteinuria below 0.5 g/day were achieved.

Conclusions: Despite advances in diagnosis, antibacterial treatment and improved cardiac surgical techniques, infective endocarditis remains a serious clinical problem. It can cause numerous complications, including ANCA-positive crescent glomerulonephritis. It's treatment is challenging but proper combination of causative treatment (cardiac surgery) with balanced immunosuppression may significantly improve the patient's outcome.

1039 - P1.148

CAN THE DOSING INTERVAL OF ECULIZUMAB BE EXTENDED IN PATIENTS WITH HAEMOLYTIC UREMIC SYNDROME?

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Aims/Purpose: Eculizumab is particularly important in the treatment of haemolytic uremic syndrome (HUS). Data on patient selection, duration of treatment and long-term effects of eculizumab in treatment of HUS are limited. Discontinuing treatment abruptly may cause a relapse. The objective of this study is to present the clinical data of patients with HUS who have undergone mutation studies in our clinic. Additionally, we aim to share the single-centre experience of patients who received eculizumab treatment and whose treatment dose interval was extended.

Methods: The study included paediatric patients who had been diagnosed with HUS and whose complement genetics had been studied. In patients with stable clinical and laboratory findings, the interval between eculizumab treatments was extended by one week every three months after collaborative assessment by 4 paediatric nephrologists. Haemoglobin, platelet count, lactate dehydrogenase, serum creatinine, haematuria and proteinuria were checked before each change.

Results: There were a total of 48 paediatric HUS patients and 37 of them received eculizumab. The median age of HUS patients at diagnosis was 1.86 years (IQR 1.03-4.29), and the median follow-up time after diagnosis was 3.79 years (IQR 1.41-7.89). Mutations affecting the complement system were found in 33 patients (68.7%). Renal replacement therapy was administered to 68.8% of patients. Fresh frozen plasma was infused in 95.8% of patients and plasma exchange was performed in 41.7%. For patients received eculizumab, the median time between diagnosis and eculizumab administration was 6.0 days (IQR 5.0-8.0). Eculizumab treatment was discontinued in seven patients, the dose was not changed in six patients, and the dose interval was extended in 24 patients (Figure 1). The median time to first dose change in the extended dose interval group was 12.2 months (IQR 5.0-20.7). A genetic anomaly was identified in 16 of the 24 patients who underwent dose modification. In all but three of the 16 patients with a genetic mutation whose dose interval was extended, the mutation was present in a single allele. Two of the 3 patients with homozygous mutation were identified as VUS in the databases. The median interval of eculizumab use was 5 weeks (IQR 4-8) at the last follow-up. The serum creatinine and the urine protein to creatinine ratio at the last follow-up visit were similar in patients who had their eculizumab interval extended and in those who used eculizumab according to the protocol (0.62 mg/dL vs 0.80 mg/dL; p =0.268 and 0.23 mg/ mg vs 0.16 mg/ mg, p =0.574).

Conclusion: In patients with stable clinical and laboratory findings and low genetic risk, the eculizumab treatment interval may be extended with close monitoring.

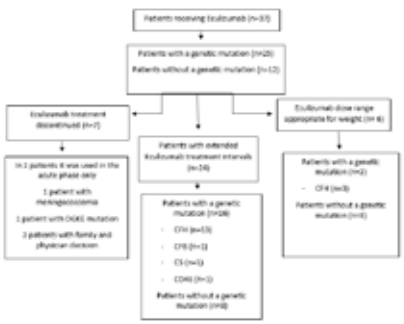

Figure 1. Distribution of the patients according to the eculizumab treatment regimens

1042 - P1.149

PAEDIATRIC ANCA-ASSOCIATED VASCULITIS. EMERGING PERSPECTIVES ON TREATMENT

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Aims/Purpose: ANCA-associated vasculitis (AAV) encompasses a spectrum of systemic immune-mediated conditions characterized by the inflammation of small blood vessels. While predominantly diagnosed in adulthood, these diseases can also manifest in childhood, albeit rarely. Notably, more than 75% of patients experience kidney involvement, particularly marked by rapidly progressive glomerulonephritis (RPGN). Appreciating the intricacies of renal involvement in pediatric AAV is crucial, as it profoundly influences prognosis and guides personalized therapeutic approaches.

Methods: Retrospective, observational review of patients diagnosed with AAVs at our center from the year 2021 to 2024. Diagnostic and therapeutic data were extracted to present patient histories succinctly.

Results

	Case 1	Case 2	Case 3	Case 4
Gender	Female	Female	Female	Female
Age at diagnosis (years)	12	13	12	9
ANCA specificity	PR3	PR3	MPO	MPO
Kidney biopsy	Pauci-immune, necrotizing glomerulonephritis with 83% crescents, pauci-immune	Pauci-immune, necrotizing glomerulonephritis with 21% cellular crescent	Pauci-inmune, extracapillary glomerulonephritis with 21% crescents, with 47% global glomerulosclerosis and segmental glomerulosclerosis lesions	Evolved pauci-inmune, extracapillary glomerulonephritis with 36% globally sclerosed glomeruli, 31% fibrous and fibrocellular crescents
Main kidney symptoms at diagnosis	Macroscopic haematuria Subnephrotic-range proteinuria Decline kidney function (eGFR 13.23 mL/min/1.73m2)	Microscopic haematuria No kidney function decline	Microscopic haematuria Decline kidney function (eGFR 38.38 mL/min/1.73m2)	Microscopic haematuria. Non-nephrotic proteinuria. Decline kidney function (eGFR 23.6 mL/min/1.73m2)
Systemic Features	Alveolar hemorrhage	Fatigue, arthritis, anemia, optical perineuritis, bloody nasal discharge, alveolar hemorrhage	Fatigue Anemia	Cutaneus purpura. Abdominal pain.
Induction phase treatment	Corticoid steroids Rituximab Cyclophosphamide Plasma Exchange	Corticoid steroids Cyclophosphamide	Corticoid steroids Rituximab	Corticoid steroids
Maintenance phase treatment	Prednisone Mycophenolate mofetil Azathioprine Belimumab	Prednisone Rituximab	Prednisone Rituximab	Prednisone Mycophenolate mofetil Azathioprine
Kidney Outcome	Kidney transplant Peritoneal dialysis	No need for renal replacement therapy	No need for renal replacement therapy	Hemodialysis

Conclusion: Although vasculitis is a rare disease, the early use of rituximab in a similar way to insights gleaned from adult studies, it can modify the short and long-term prognosis of these patients.

1066 -P1.150

STEROID-RESISTANT NEPHROTIC SYNDROME AND SECONDARY THROMBOTIC MICROANGIOPATHY IN A GIRL WITH IGA-NEPHROPATHY

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Aims/Purpose: IgA-nephropathy (IgAN) is one of the most common glomerular diseases in children which characterized by variable clinical presentation and progression to end-stage kidney disease in adults. Steroid resistant nephrotic syndrome (SRNS) at the onset of IgAN and secondary thrombotic microangiopathy (TMA) as a complication of the disease are very rare. Therefore, the data regarding efficacy of immunosuppressive treatment and kidney outcome in children with SRNS due to IgAN and secondary TMA are scarce.

Methods: We present a case of IgAN in a girl with SRNS and secondary TMA.

Results: A 13-year-old girl presented with SRNS with hematuria, hypertension and acute kidney injury not related to hypovolemia (eGFR 50.5 ml/min/1.73 m2). Serum levels of complement C3, C4; antinuclear factor; anti-double stranded DNA, antinuclear, antineutrophil cytoplasmic, anti-SSB/La and antiphospholipid antibodies, including lupus anticoagulant, anticardiolipin and anti--2-glycoprotein-1 were within the normal values. Kidney ultrasound found enlarged kidney size (BSA-related volume of both kidneys > 97 percentile) with increased echogenicity of parenchyma. Kidney biopsy revealed IgAN with segmental sclerosis of 8% (2/25) glomeruli, moderate mesangial and endocapillary proliferation (M1E1S1T0C0). Treatment with cyclophosphamide iv has been postponed for 2 months due to recurrent infections (bronchitis, sinusitis, COVID-19-associated pneumonia), complicated by Coombs-negative hemolytic anemia (Hb up to 72 g/l), thrombocytopenia (up to 105×10*9/l) and elevated serum level of creatinine (up to 128 µmol/l). Her ADAMTS 13 serum level was normal (91%), there were no extrarenal involvement and flow cytometry didn't reveal a paroxysmal nocturnal hemoglobinuria (PNH) clone, so primary forms of TMA (thrombotic thrombocytopenic purpura and hemolytic uremic syndrome) and PNH were excluded, and secondary TMA was diagnosed. After transfusions of fresh plasma (10 ml/kg) her blood tests normalized and eGFR increased (69 ml/min/1.73 m2). Treatment with cyclophosphamide iv (500 mg/m2/monthly for 6 months) induced complete remission of SRNS in the girl. In order to maintain remission of the disease treatment with mycophenolate mofetil (900 mg/m2/d) was started and continued for 2 years. At the last follow-up at the age of 16 years the girl had long-term complete remission of SRNS and improvement in kidney function (eGFR 83 ml/min/1.73 m2).

Conclusion: Treatment with cyclophosphamide iv and MMF of SRNS due to IgAN in the girl induced long-term complete remission. Secondary TMA in the index case might be related to IgAN and infections, including SARS-CoV-2. The mechanism of TMA in IgAN is poorly defined, however, endothelial injury or podocytopathy could be suspected.

1068 - P1.151

A NATIONWIDE COHORT STUDY OF HEMOLYTIC UREMIC SYNDROME IN POLISH CHILDREN POPULATION

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Aims/Purpose: During last decades significant advances in management of HUS especially the atypical form were achieved, however we still need guidelines, which show a full consensus on management recommendations to achieve the best treatment options.

Methods: The final cohort of analyzed 438 patients is derived from the one source: Polish Registry of HUS – pediatric study. The cases were registered from January 2012 to December 2023 with the participation of 12 Clinical Centers responsible for the treatment of these children in the country. Additionally, patients with an active form of the disease undergoing previously chronic treatment were included into the registry. For the first time in Poland, eculizumab was used in 2017/2018, so we compared era pre- and post eculizumab implementation.

Results: The average age of patients at onset was 2.6 (1.32-5.49) years. Sixty seven (15.3%) children were diagnosed under 1 year of age. There was no difference in incidence between boys: 206 (47%) and girls: 232 (53%). Thirty four (7.8%) children had a recurrent syndrome.

Typical form of HUS was diagnosed in 301 (68.7%) children, atypical in 137 (31.3%) children. 248 (56,6%) children received renal replacement therapy. The mean glomerular filtration rate on admission was 14.5ml/min/1.73 m2. Oligo/anuria was present in 263 (60%) children. The mean concentration of complement components at admission was: c3: 92.0 mg/dl, c4: 17.0 (12.15-22.00) mg/dl, mean hemoglobin concentration: 7.30 (6.50-7.95)g/dl, mean platelet count: 34.00 (22.00-55.00) G/l. 218 (50.11%) children had arterial hypertension. Plasma infusions were used in the treatment of 153 children (35.0%), 203 (46.5%) with packed platelets, 406 (92.9%) with packed red blood cells, and 64 (14.7%) with plasmapheresis. Eculizumab was administered to 89 (20.3%) children. Mean time of observation was 1.92 (0.64-3.90) years. Final eGFR has improved after 2018.

Conclusions: The incidence of HUS over the evaluated years was comparable in subsequent years. After 2018 all centers had the possibility to use eculizumab in aHUS in first days after admission, which improved the outcome.

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1077 - P1.152

DOES THE DURATION OF B-CELL DEPLETION INFLUENCE THE LONG-TERM OUTCOME OF PEDIATRIC PATIENTS WITH STEROID DEPENDENT IDIOPATHIC NEPHROTIC SYNDROME?

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Aim/ Purpose: Rituximab (RTX) has proven its efficacy for relapse prevention in steroid-dependent nephrotic syndrome (SDNS). However, the impact of the B-cell depletion duration on long-term outcome remains unclear. The aim of this study was to compare patients who had undergone short-term B-cell depletion (one course) with those who had undergone long-term depletion (18 months) and to analyze the long-term course of nephrotic syndrome.

Methods: In this multicenter retrospective study, we included patients with SDNS who received RTX before the age of 18 years between 2008 and 2017 and outcomes were long-term remission without immunosuppressive treatment or relapse at least two years after the last anti-CD20 infusion and adverse events.

Results: 117 children (age at first RTX infusion 11.6 years [7.7 - 14.3]; 65% boys), including 48 (41%) treated with short B-cell depletion vs. 69 (59%) with long depletion, were included. There was no difference in age or oral immunosuppressive therapy prior to RTX between the two groups. Two years after the last infusion, 68% of patients with short B-cell depletion were in remission vs. 65% of patients with long depletion (p =0.7). No difference was observed in adverse events, with respectively 8% and 11% infectious complications (p =0.56) and 33% vs. 47% (p =0.11) prolonged hypogammaglobulimenemia in the two groups. At last follow-up (median duration of follow-up after the last RTX infusion: 6.7 years [3.7 – 9.8]), 78/117 (66%) patients were in long-term remission, of whom 58% had received a long B-cell depletion versus 40% among the 38 patients with still active SDNS (p =0.06).

Conclusions: Duration of B-cell depletion does not appear to influence long-term disease activity of SDNS, but remains effective in preventing relapses with acceptable medium term adverse events in patients treated with long-term B-cell depletion.

1083 - P1.153

TREATMENT DILEMMA OF A PATIENT WITH RARE LAMB3 MUTATION AS A CAUSE OF A STEROID-RESISTANT NEPHROTIC SYNDROME CO-OCCURRING WITH DIGEORGE'S SYNDROME

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Aim: Steroid-resistant nephrotic syndrome (SRNS) is a heterogeneous disease with a number of genes discovered as its underlying cause, only a few cases describing laminin mutations. We present a rare case of a child with SRNS with novel LAMB3 mutation and DiGeorge syndrome.

Methods: A clinical, laboratory and molecular genetic data (whole-exome sequencing using next-generation sequencing) was correlated. Case: A 20-month-old boy with DiGeorge syndrome, epilepsy, hearing impairment, congenital heart disease, hypotonia and psychomotor retardation, presented with edema during respiratory tract infection. Nephrotic syndrome was diagnosed with hypoalbuminemia (16g/l), hypercholesterolemia (6.2 mmol/l), proteinuria (41 g/l) and erythrocyturia (23/µl). Additionally – a decreased kidney function (eGFR 65 ml/min/1,73 m2) was revealed. Ultrasound displayed inhomogeneous hyperechogenicity of renal parenchyma with unspecific radiant lines and diminished cortico-medullar differentiation. According to his mother, proteinuria had been seen in the dipstick tests since first months of life. Steroid therapy was introduced, though the patient presented the resistance. Kidney biopsy was postponed due to patient's unstable condition. Genetic analysis identified a heterozygous nonsense, pathogenic variant in LAMB3 (c.1903C > T, p.Arg635Ter) in chromosome 1, encoding laminin subunit beta 3, typically causing epidermolysis bullosa. The boy did not present epidermolysis bullosa, but was more prone to skin lacerations. Administration of other immunosuppressive agents has been deferred due to the patient's recurrent infections, a common complication observed in individuals with DiGeorge syndrome. Nephroprotection with ramipril was successfully introduced.

Conclusions: Although LAMB2 has been described as a susceptible gene associated with congenital NS, there is limited scientific data reporting LAMB3 mutation as a possible cause of disorder in a glomerular basement membrane structure. While LAMB3 mutations typically cause Herlitz junctional epidermolysis bullosa or amelogenesis imperfecta, we present a unique case linking LAMB3 to SRNS, underscoring the necessity for further research into laminin's role in SRNS.

1079 - P1.154

THE LINK BETWEEN COVID-19 AND ACUTE GLOMERULONEPHRITIS

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Aims/Purpose: This study explores AGN incidence, manifestation, clinical features, outcome, and potential influences on disease development.

Methods: A retrospective study comparing the incidence of post-COVID-19 AGN in children aged 3-12 years was carried out by the Republican Center for Pediatric Nephrology in Minsk. The male to female ratio among the 34 kidswas 2.4:1. Clinical information was gathered from health records, concentrating on symptoms of confirmed SARS-CoV-2 infection. Standard testing was run, and when necessary, kidney biopsies were conducted.

Results: For all 34 patients: (2018-2020 n = 13, 2021-2022 n = 7, 2023 n = 14) AGN developed after an infection of the pharynx and respiratory organs of various localizations (sinusitis, otitis, pneumonia), in some associated with streptococcus (culture from the pharynx, growth of ASLO). AGN incidence increased significantly between 2022 and 2023, from 0.20 to 0.90, which may have something to do with the COVID-19 pandemic. Acute onset with complaints of headache, deterioration of condition, loss of appetite and the development of nephritic syndrome: moderate proteinuria (1-2 g/l), hematuria from micro- to macrohematuria, moderate swelling of the eyelids, face, hypertension (in 75%). There were no significant differences in the onset, clinical and laboratory parameters, course of the disease and its outcomes when comparing patients who fell ill in 2018-2020 and from 2021 to mid2023. The results reveal a significant increase in pediatric patients' risk of developing AGN after COVID-19. These kids had a high incidence of immune-complex AGN, which was linked to streptococcal infections. In children with a history of COVID-19, hematuria, proteinuria, and reduced renal function were common manifestations of AGN symptoms. Genetic studies point to a possible inherited tendency affecting the severity of AGN after COVID-19.

Conclusion: According to the data of a number of researchers (Pubmed plus data from my own research), over the past decades there has been a significant decrease in the number of cases of AGN in children due to the rational use of antibiotics, improvement of socio-economic and hygienic conditions, which we observed until 2020. We noted an increase in the number of cases without significant changes in the clinical course and short-term outcome of AGN in 2021-07.2023 (n = 21) vs 2018-2020 (n = 13) which may be due, on the one hand, to a change in the immune response after Covid-19 possibly including immune-related harm and direct effects of the virus on kidney tissue, and on the other hand, to a change in the structure of pathogens after the pandemic. Additionally, it is possible that certain genetic tendencies interacting with COVID-19 could clarify why some people have a higher risk for severe AGN

1086 - P1.155

STEROID-RESISTANT NEPHROTIC SYNDROME DUE TO KIDNEY AMYLOIDOSIS: CASE PRESENTATION

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Aims/Purpose: Amyloidosis is the rare condition to cause nephrotic syndrome in children. The purpose of our work was to increase understanding of this problem in children.

Methods: We present a case of steroid resistant nephrotic syndrome in 15 year old girl due to amyloidosis.

Results: Patient A presented to our hospital with the complaints of progressive proteinuria for 9 months. Past medical history was remarkable for congenital heart disease – bicuspid aortic valve without stenosis. Two years before at a routine check-up anemia and elevated ESR up to 65 mm/hr were found. Further assessment at Republican Center for Pediatric Oncology and Hematology revealed hepatosplenomegaly with nodular changes according to MRI and lymphadenopathy. Biopsy of suspicions foci in liver and sternal punction shown no evidence of malignancy. ANA and ANCA were negative. Primary immunodeficiency has been ruled out. Anemia and elevated ESR persisted over time and proteinuria appeared with the tendency to progress for which the patient has been sent to the nephrological center. At hospitalization patient appeared to be pale with mild urtical rash on the back. Periorbital and ankle edema were present. BP was not elevated. Laboratory investigation revealed nephrotic syndrome: serum protein level of 49 g/l, albumin level of 22 g/l, cholesterol 8 mmol/l, 24 hour proteinuria varied from 3,67 to 7,87 g. Kidney function was normal. CRP slightly elevated only in first analysis with further normalization with antibacterial treatment but ESR remained constantly elevated up to 40 mm/hr. Prednisolone treatment 80 mg/day was ineffective and daily transfusions of albumin were needed. Kidney biopsy was performed which revealed positive staining with Kongo red at the areas of mesangial expansion and within the thickened walls of afferent arterioles. Diagnosis of the Kidney amyloidosis, secondary steroid resistant nephrotic syndrome was made. Treatment with colchicine 0,5 mg twice a day and ACEi (enalapril 10 mg daily) was initiated with gradual withdrawal of prednisolone. During three years of follow-up patient remained stable with the treatment prescribed. Proteinuria persisted but was not higher than 2,1g/24 hr. Hypoproteinemia and hypoalbuminemia were mild and didn't require albumin transfusion. ESR remained elevated up to 40 mm/hr and mild anemia persisted but multiple interdisciplinary assessments and investigations failed to reveal the origin of inflammatory process. Neither hypertension nor decline in GFR were present. Patient has been transferred under the supervision of the adult nephrologist at the age of 18 years.

Conclusion: Early biopsy and timely diagnosis of kidney amyloidosis let us stabilize the condition of the patient and avoid side-effects of prolonged use of corticosteroids.

1094 - P1.156

NEPHROPATHIA EPIDEMICA IN AUSTRIAN CHILDREN

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Aims/Purpose: Hantavirus infections are reported from many European countries with highly variable annual incidences. Nephropathia epidemica (NE) is caused by Puumala virus (PUUV) infections and is a mild form of haemorrhagic fever with renal syndrome. Infections occur through inhalation of aerosols from rodent faeces, urine or saliva. Clinical manifestations of PUUV infection range from subclinical to severe, with an urgent need for intensive care treatment particularly in adults. Low absolute lymphocyte counts and dyspnea were associated with a severe course of infection in Austrian adults (Hatzl et al, Emerg Infect Dis, 29(5), May 2023). We performed a retrospective analysis of all Austrian children with serologically verified NE between 2008-2021.

Methods: All children younger than 19 years with positive PUUV serum antibody testing were evaluated. Clinical, laboratory, and radiologic data were obtained from the electronic healthcare data system and medical charts. We defined a severe course of PUUV infection by oxygen saturation < = 90% in room air and/ or intensive care unit admission. This study was approved by the institutional review board of the Medical University of Graz.

Results: The study comprised 38 children (10 girls, 28 boys). All patients were hospitalized, 35/38 were treated in the southeastern part of Austria. Median age of patients was 15.5 years (range 3-18). Annual incidences ranged from 0-15 (in the peak year 2012). Children presented throughout the year, 10/38 in June. A temperature of > = 38,5˚C occurred in 87% of the patients. Additional symptoms were arthralgia (68%), gastrointestinal symptoms (63%), transient visual disturbances (55%), cough (15%), and epistaxis (13%). Two patients developed dyspnea. Duration of hospitalization was median 6 (range 2-17) days. Thrombocytopenia was documented in 92% children. Lymphocytopenia was observed in 42% of patients. Acute kidney injury (AKI) emerged in 35/37 children, highest plasma creatinine levels were median 2.15 mg/dl (range 0.69-11.96), corresponding to a decrease of calculated GFR to median 25.39 (range 6.22-79.01) mL/min/1.73m2. Both patients with dyspnea had low absolute lymphcyte counts, and fulfilled our criteria for a severe clinical course: Patient 1 was diagnosed with interstitial pneumonia in high resolution-computed tomography. Patient 2 needed intensive care for severe abdominal pain and conservative managment of severe AKI (minimal calculated GFR 6.22 mL/min/1.73m2).

Conclusions: Our cohort showed the typical NE features including fever, thrombocytopenia, and AKI. Visual disturbances and arthralgia were seen as frequent as in adults. Low absolute lymphocyte counts and dyspnea were associated with a severe course of PUUV in NE. Awareness of this emerging infectious disease is mandatory to avoid kidney biopsies and renal replacement therapy by early adequate conservative management.

1095 - P1.157

EFFICACY AND SAFETY OF MEDICAL THERAPY IN CHILDREN WITH IGA NEPHROPATHY: A NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Aims/Purpose: This network meta-analysis aimed to synthesize the current evidence regarding the efficacy and safety of medical therapy in children with IgA nephropathy.

Methods: A computerized search from inception to the end of April 2023 was conducted on the following databases: CENTRAL, MEDLINE Core Database, MEDLINE via PubMed, SCOPUS, and Web of Science, using the relevant key terms. The included studies were randomized controlled trials (RCTs) comparing immunomodulators, anticoagulants, and statins, with data analyzed using R software and the Metainsight tool. The quality of each study was assessed using the Cochrane Risk of Bias 2 tool. Efficacy outcomes such as urinary protein excretion and creatinine clearance, as well as safety outcomes, were synthesized.

Results: Seven RCTs were included. The combination of immunomodulator therapy plus anticoagulant/antiplatelets significantly reduced urinary protein excretion (mean difference, MD = -1.03 g/dL, 95% CI: -1.90 to -0.16, Figure 1) and improved the grade of hematuria (MD = -1.20, 95% CI: -2.12 to -0.28, Figure 2). Anticoagulant/antiplatelets plus statins were found to increase creatinine clearance significantly (MD = 27.90 ml/min per 1.73 m2, 95% CI: 14.28 to 41.52), and immunomodulator therapy alone significantly reduced the percentage of glomeruli showing crescents (MD = -10.56%, 95% CI: -20.83% to -0.29%). In terms of safety, combination therapy reduced the risk of elevated blood pressure (risk ratio, RR = 0.14, 95% CI: 0.03 to 0.75); however, it increased the risk of headaches (RR = 9.92, 95% CI: 1.29 to 76.21) compared to immunomodulator therapy alone.

Conclusion: The limited literature suggests that combination therapy with immunomodulators and anticoagulant/antiplatelets could benefit urinary protein and hematuria reduction in pediatric IgA nephropathy, with statins further enhancing renal function. However, clinicians should consider the increased risk of headaches associated with combination therapy. These findings highlight the need for individualized treatment approaches, balancing efficacy with patient tolerance to optimize clinical outcomes in pediatric IgA nephropathy.

Keywords: IgA nephropathy, Immunomodulators, Anticoagulants, Statins

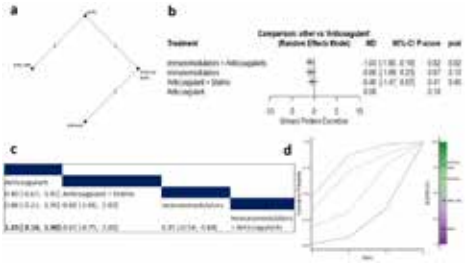

Figure 1: Network meta-analysis of Urinary Protein Excretion; a) Net graph, b) Forest plot, c) Net league table, d) SUCRA Analysis

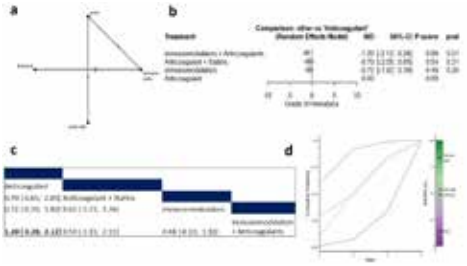

Figure 2: Network meta-analysis of the change in the grade of hematuria in morning urine; a) Net graph, b) Forest plot, c) Net league table, d) SUCRA Analysis

1116 - P1.158

ARTIFICIAL INTELLIGENCE IN CHILDREN WITH HYPERTENSION: CHATGPT 3.5 AND MICROSOFT COPILOT GPT 4.0

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Aims/Purpose: Hypertension (HT) is a major global health concern affecting people of all ages, with extensive research focused on its implications in adults but limited studies on its significance and long-term effects in children. Artificial intelligence (AI) technologies hold promise for application across various medical domains. In this investigation, we utilized ChatGPT and Microsoft Copilot GPT, two widely utilized AI platforms, to gather general insights on pediatric HT. Our aim was to assess the potential of AI in providing accurate information and guiding appropriate practices for diagnosing and managing HT in children.

Methods: We directed 25 open-ended and 5 case-based multiple-choice questions regarding pediatric HT to ChatGPT 3.5 and Microsoft Copilot GPT 4.0 in Turkish and English. The accuracy of responses provided by the AI was assessed by two researchers, a pediatric nephrologist and a pediatric cardiologist, in accordance with internationally recognized publications and guidelines. We conducted a comparison of the AI responses based on the type of AI and the language used when posing questions.

Results: The study revealed that the lowest total score obtained was 70 out of 100, which was attributed to ChatGPT 3.5 Turkish. Conversely, the highest score achieved in the study was 98, recorded by Microsoft Copilot GPT 4.0 English. The analyses revealed that when the version of the AI application remained constant, more precise responses were obtained for questions posed in English compared to those in Turkish. The scores for English questions were significantly higher compared to Turkish questions.

Conclusion: AI technologies offer significant potential for utilization across diverse medical fields. With the continual development of updated versions of AI applications, their effectiveness is notably rising, particularly in English. AI applications can serve as supplementary tools to assist clinicians in decision-making processes related to the diagnosis, treatment, and monitoring of pediatric HT, complementing their expertise rather than replacing it entirely.

1119 - P1.159

ATYPICAL HEMOLYTIC UREMIC SYNDROME: LESSON LEARNED FROM A TEN-YEAR RETROSPECTIVE STUDY

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Aims/Purpose: This retrospective study aimed to delineate the clinical and biological characteristics, potential triggers, genetic underpinnings, and treatment outcomes in pediatric patients diagnosed with atypical Hemolytic Uremic Syndrome (aHUS) over a ten-year period, in a tertiary hospital in North-East of Romania.

Methods: A cohort of 25 pediatric patients diagnosed with aHUS between 2014 and 2024 was analyzed retrospectively. Data were collected on demographic characteristics, clinical presentations, laboratory findings, complement system activity, genetic testing results, treatment modalities, and patient outcomes. Escherichia coli and Streptococcus pneumoniae related HUS cases were excluded.

Results: Our cohort comprised predominantly male patients (n = 19), with age at presentation between 4 months and 14 years old, (median age = 44 months old) with varied clinical presentations such as diarrhea (n = 16), fever (n = 8), oligo-anuria (n = 14), hypertension (n = 15) and seizures (n = 4). Significantly high IgG titers for COVID-19 were present in 5 patients. At first evaluation, normal complement system activity was observed in 7 patients. Further investigations revealed immune-mediated aHUS with anti-factor H autoantibodies in 3 patients. Genetic analysis confirmed the presence of pathogenic mutations in 5 cases and all patients presented either risk factors (genetic polymorphisms, risk haplotypes) or variants of unknown significance, in genes coding for different complement regulating proteins. Hemofiltration and plasmapheresis were performed in 15 patients. Treatment with Eculizumab (n = 19) was very well tolerated and therapy discontinuation was decided for 5 patients, with no relapse until present. 6 patients died due to disease related complications, but in all other patients, renal function progressively restored.

Conclusion: aHUS is a diagnosis of exclusion, as clinical characteristics, complement system activity evaluation and genetic testing cannot rule it out. Complement inhibitory treatment is now a standard of care, tackling this thrombotic microangiopathy in a way that restores renal function and promptly stops hemolysis process. However, timely initiation of therapy is crucial, as irreversible end-organ damage can install in the absence of complement blockade. Further investigations must be conducted regarding the interplay between infectious triggers, including COVID-19, and genetic predisposing factors, as these aspects can guide the decision of treatment discontinuation.

1125 - P1.160

HIGHLIGHTING POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME IN PEDIATRIC RENAL DISEASE: A CALL FOR VIGILANCE

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Aims/Purpose: Posterior reversible encephalopathy syndrome (PRES) represents a relatively rare encounter in the pediatric population but with a higher prevalence in the Nephrology and Oncology departments, due to treatment and disease evolution peculiarities. Our study aims to describe our experience with PRES in pediatric patients with renal disease and highlight the importance of a high index of suspicion and timely intensive supportive care initiation.

Methods: We are reporting our single-center experience on a cohort of 8 patients diagnosed with PRES in the last 5 years in our department. Data were extracted from the electronic database from the 1st of January 2019 to the 31st of December 2023. PRES was defined by the clinical presentation with reversible neurologic symptoms associated with specific neuroimaging findings, either on CT or MRI scans.

Results: The mean age at presentation was 7,7 years (range 6-12), with equal gender distribution. The most frequent preexisting pathology was represented by nephrotic syndrome (37,5%), while the others had: end-stage renal disease, hemolytic uremic syndrome, IgA vasculitis with nephritis, post-streptococcal glomerulonephritis, and multisystem inflammatory syndrome. Presentation symptoms included tonic-clonic seizures (87,5%), headaches (75%), and altered consciousness (62,5%), the blood pressure was higher than the 95th percentile for age and height in 5 out of 8 patients. 3 children were investigated solely by CT scan, while 3 had an MRI and 2 had both a CT scan and MRI. All of our patients were admitted to the ICU, and blood pressure control was attained in the first 24 hours. Six of the patients were discharged with antihypertensive therapy, and the mean number of antihypertensive medications they received at home is 1,5 (range 1-2). 50% had a follow-up MRI confirming the reversible aspect of the lesions. Only one of the patients needed chronic antiepileptic treatment with valproate.

Conclusion: Our findings are concordant with the available literature on the subject, showing that PRES seems to be more aggressive in children with kidney disease, but errors such as missed minor cases due to the lack of recognition of this entity can not be excluded. The results we presented confirm the reversible character of the pathology in the majority of cases, based on follow-up imaging studies, but highlight that in a limited number of cases, chronic changes can appear and this does not exclude the diagnosis.

1126 - P1.161

MYCOPLASMA PNEUMONIAE: A CATALYST FOR PEDIATRIC NEPHROPATHY

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Aim/Purpose: Mycoplasma pneumoniae frequently plays a role in pediatric respiratory tract infections. Despite this, it rarely cites extrapulmonary manifestations like renal involvement, which can be the only presenting symptom at the time of admission. The purpose of this paper is to showcase a series of Mycoplasma pneumoniae cases that affected the kidney and provided a variety of pathological findings.

Methods: We studied 5 patients (3 girls) aged 11–14 years with positive serological tests for Mycoplasma pneumoniae and renal involvement. The diagnosis of the infection was based on the presence of serum IgM detected by enzyme-linked immunosorbent assay (ELISA). One child had a renal biopsy, with immunofluorescence (IF) and paraffin studies.

Results: Extrarenal findings included: fever (n = 2), respiratory (n = 5), cutaneous (n = 4), hepatic (n = 3) and hematological (n = 2). Kidney involvement presented as acute nephritis (n = 2, 1 had acute kidney injury-AKI), nephrotic syndrome (n = 1) and hemolytic uremic syndrome (HUS, n = 2). Anuria (n = 2), oedema (n = 3) and hypertension (n = 2), as well as microscopic hematuria (n = 5) and proteinuria (n = 5) were among the renal symptoms. Thrombocytopenia (n = 3) characterized the HUS cases as well as the AKI patient. Hypocomplementemia was present for the C3 fraction (n = 4), while 1 patient had both low C3 and C4 levels. Confirmation of Mycoplasma pneumoniae was achieved by positive serum IgM detection with ELISA (n = 5). Both patients with HUS required hemodialysis, and one showed altered genetic findings in complement activity suggestive of atypical HUS, requiring long-term therapy with Eculizumab. Antibiotherapy was administered (n = 4) as well as supportive measures with recovery of renal function.

Conclusions: Renal involvement in pediatric Mycoplasma pneumoniae is a rare, but serious manifestation that presents with various symptoms and pathological findings. Prompt identification and management can define the outcome of these patients.

1130 - P1.162

NEXT GENERATION SEQUENCING IN CHILDREN WITH STEROID-SENSITIVE NEPHROTIC SYNDROME

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Introduction: Steroid sensitive nephrotic syndrome (SSNS) is the most common form of NS in childhood and there is growing data that genetics might play a role in the susceptibility for the disease. The aim of the study was to investigate the rate and spectrum of genetic variants in SSNS among Russian children.

Methods: We evaluated 21 (17M/4F) children with steroid-dependent and frequently relapsing SSNS. Kidney biopsy was performed in 13 (61.9%) patients. Focal segmental glomerulosclerosis (FSGS) was revealed in 7/13 (53.8%), minimal change disease in 6/13 (46.2%) of children with SSNS. Clinical exome sequencing of 73 genes, associated with SRNS was conducted using MiSeq and HiSeq 2500 platforms and bioinformatics analysis of the obtained data was performed via a custom pipeline developed in our laboratory.

Results: No likely pathogenic/pathogenic variants were identified in children with SSNS. Heterozygous variant of uncertain significance (VUS) in exon 4 in the PAX2 gene c.491C > T (p.Thr164Ile) associated with autosomal dominant FSGS, 7 (OMIM #616002) was detected in one (7.7%) 6-year-old boy with steroid-dependent NS without extrarenal involvement. Kidney biopsy was not perforemd. The variant does not occur in the Genome Aggregation Database (gnomAD) v.3.1.2, is located in a conserved site, and is predicted to have a pathogenic effect on the protein by the computer algorithms MutationTaster, SIFT, PROVEAN, Polyphen, PrimateAI, MetaSVM, DEOGEN, and FATHMM. Trio Sanger sequencing analysis detected the PAX2 VUS only in the boy and de novo variant was confirmed. The boy had complete remission, induced by prednisolone and maintained by cyclosporin with normal kidney function (eGFR 112 ml/min/1.73 m2).

Conclusions: These results demonstrate that there were no identified causative genetic variants in children with SSNS using clinical exome sequencing. We suggest that detected de novo heterozygous VUS in the PAX2 gene might be a cause of SSNS in the boy despite the previously described association only with FSGS in adults and steroid-resistant NS in children.

1140 - P1.163

BEYOND THE SURFACE: A CASE OF IGA NEPHROPATHY MIMICKING NUTCRACKER SYNDROME

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Aims: Intermittent gross hematuria associated with persistent microscopic hematuria can be a common presentation of glomerular and nonglomerular pathologies. Sometimes we have a combination of both so it is difficult to find the primary cause of these clinical manifestations.

Methods: We report the case of a 14 year old boy with a story of left varicocele, who came to a visit for incidental finding of microhematuria and one episode of gross hematuria with mild non orthostatic proteinuria; negative family history, normal physical examination and blood pressure.

Results: Laboratory examinations revealed normal renal function, absence of hypocomplementemia, and low-titerANA positivity. Farley tests consistently suggested non-glomerular hematuria, while urinary stone screening yielded negative results, and abdominal ultrasound showed no abnormalities. Due to the presence of both non-glomerular hematuria and left varicocele, Nutcracker syndrome (NS) was suspected. NS is characterized by extrinsic compression of the left renal vein (nutcracker phenomenon) and can coexist with left varicocele in 15% of cases, with 56% of left varicocele patients meeting ultrasound criteria for NS. Therefore, we performed a color-doppler ultrasound, which was inconclusive. However, 1.5 years after the first episode of gross hematuria, following a mild respiratory infection, the patient developed hypertension and nephrotic proteinuria, rapidly progressing to nephritic syndrome(hematuria, edema, and hypertension) with acute kidney injury (AKI). Therefore we performed a kidney biopsy and it revealed IgA nephropathy. According to Oxford MEST Classification (M1E1S1T0C0), a combination of intravenous steroids and mycophenolate mofetil therapy was initiated leading to resolution of gross hematuria, normalization of renal function and blood pressure, improvement of proteinuria.

Conclusions: Although all symptoms were likely attributed to IgA nephropathy, the initial presentation strongly suggested NS. Our case underscores the importance of maintaining a high index of suspicion for glomerulopathy in patients with recurrent macrohematuria, even when NS is the leading diagnosis. Despite inconclusive findings, the association between IgA nephropathy and NS is documented in the literature, though the underlying pathophysiology remains unclear.

1155 - P1.164

ACUTE GLOMERULONEPHRITIS ASSOCIATED WITH CONCOMITANT BACTERIAL PNEUMONIA

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Aims/Purpose: Post infectious glomerulonephritis is a common condition in children occurring several weeks after streptococcal infections. However, acute glomerulonephritis occurring during an active bacterial pneumonia is rare.

Methods: We describe 3 cases with pneumonia and concomitant acute glomerulonephritis. In all cases immunological tests suggested the diagnosis of post streptococcal glomerulonephritis (elevated antistreptolysin O titer, low C3, and normal C4 complement factors).

Results: Case 1. An 8-year-old boy presented with a 4-day history of fever and acute onset macroscopic of hematuria during the last 6 hours. Radiology showed consolidation in the lower 2/3 of the right lung and pleural effusion. He presented severe deterioration of renal function with severe azotemia, increase of serum creatinine > 4 mg/dl and anuria, emerging the initiation of acute dialysis. Renal biopsy revealed endocapillary proliferative glomerulopathy with infiltration of neutrophils and diffuse granular deposits of C3. Renal function fully recovered along with remission of pneumonia.
Case 2. A 6-year-old boy presented with a 9-day history of fever, a 2-day chest pain and macroscopic hematuria. Radiology showed left lung pneumonia and severe pleural effusion needing drainage. He presented blood pressure (BP) > 90th pc, hematuria, nephrotic-range proteinuria and serum creatinine levels were doubled from baseline with normal diuresis. Renal function and proteinuria gradually recovered with remission of pneumonia. Pleural fluid culture isolated Streptococcus pneumonia.
Case 3. A 6.5-year-old boy with a 3-day history of fever, under antibiotic treatment for respiratory infection, presented with macroscopic hematuria and edema and BP > 99th pc. Serum creatinine levels were triple from baseline at admission with improvement to baseline the next days. He maintained normal diuresis. Urine analysis showed nephrotic range proteinuria, which fully recovered within 3 weeks along with normalization of C3 levels.

Conclusion: Acute glomerulonephritis during bacterial pneumonia may be more frequent than previously estimated and should be considered in the differential diagnosis of children presenting with pneumonia and renal findings such as oliguria, hypertension, azotemia, and abnormal urinalysis. The outcomes are reported favorable for both pulmonary and kidney involvement.

1169 - P1.165

EXPLORING PEDIATRIC ATYPICAL HEMOLYTIC UREMIC SYNDROME IN EASTERN INDIA: A COMPELLING CASE SERIES

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Aims/Purpose: The study aims to explore the clinical features, treatment approaches, and outcomes of pediatric patients with atypical Hemolytic Uremic Syndrome (aHUS) in a tertiary care setting in Eastern India, emphasizing the challenges and effectiveness of treatment modalities in a resource-limited environment.

Methods: This retrospective case series analyzed five pediatric patients diagnosed with aHUS from January to December 2023 presenting at a tertiary care cente of Eastern part of India. The course of disease, response to treatment, including efficacy of plasmapheresis and immunomodulators was assessed, focusing on hematological remission and improvement in kidney function.

Results: The age of presentation varied from 4 to 16 years. The predominant etiology was Anti-factor H mediated aHUS, often linked to deletions in the factor H-related genes. Effective treatment outcomes were associated with early disease presentation and timely administration of plasmapheresis. Challenges included the lack of availability of Eculizumab.

Conclusion: Early detection and timely intervention with plasmapheresis and immunosuppression are critical for improving outcomes in pediatric aHUS cases. Genetic factors and delayed treatment initiation were significant barriers to recovery, highlighting the need for improved diagnostic and therapeutic strategies in resource-limited settings.

Table 1. Clinical profile and treatment outcomes of pediatric atypical hemolytic uremic syndrome cases

Serial No	Age (years)	Etiology	Treatment	Outcome-(Kidney Function)
1.	4	Anti-factor H-positive, Genetic Test- CFH (+) gene, homozygous missense variants. chr1:g.196673076C>T, c.157C>T, p. Arg53Cys	Early Plasmapheresis Followed by Immunodulators like Cyclophospha-mide, MMF, Prednisolone	Improved
2.	16	Anti-factor H negative, Genetic test showing Large homozygous deletion overlapping CFHR1 and CHFR3.	Early Plasmapheresis	Improved
3.	7	Anti-factor H- positive with Genetic defect: Hete-rozygous deletion: CFHR3 and CFHR1	Plasma infusions	Poor
4..	12	Anti-factor H, Genetic test-not done	Immunomodulators	Improved
5.	4	Genetic defect: CFH (+) gene, homozygous mis-sense variants. Anti-factor H negative	Initially Immunomodulators, Later only on Hemodialysis	Poor

1184 - P1.166

TWO NEONATAL DEATHS LINKED TO FINNISH-TYPE CONGENITAL NEPHROTIC SYNDROME

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Aims/Purpose: Finnish type congenital nephrotic syndrome (CNS) is the most severe form of nephrotic syndrome.

Methods: We report on two siblings who died shortly after birth and were later found to be affected by CNS.

Results: A non-consanguineous couple was referred to our clinic after losing two children. Both pregnancies were spontaneous, there was no evidence of maternal infection; prenatal ultrasound showed polyhydramnios in the second pregnancy. The first child, a female, was born at 33+5 weeks gestational age (GA) by emergent C-section due to absent foetal heartbeat. Weight 1870 g. The amniotic fluid (AF) was meconium stained. Apgar was 0-2-5, and resuscitation began immediately. Renal function was normal, with severe hypoalbuminemia (0.2 g/dL). Despite invasive respiratory and inotrope support and antibiotic coverage, the patient died 4 hours after birth. Death was attributed to severe respiratory distress. No further investigations were conducted. The second child, a male, was born at 33+0 weeks GA by urgent C-section due to foetal distress. Weight 1810 g. AF was meconium stained. Apgar was 3-5-8, thus resuscitation was initiated. He received invasive respiratory and inotrope support, inhaled nitrogen monoxide for pulmonary hypertension, iv bicarbonates for metabolic acidosis with hyperlactatemia, and antimicrobial coverage. He developed oedema, hypoalbuminemia (1.2 g/dL), and hyponatremia (129 mEq/L), treated with iv albumin, furosemide, and sodium. Despite treatment he remained anuric and died 48 hours later. Post-mortem examination revealed alveolar blood and marked congestion of pulmonary vessels, with no other alterations. Given the family history and atypical course, clinical exome analysis was performed, unexpectedly revealing a homozygous mutation of the NPHS1 gene (c.3387+1 G > A in intron 26), causative for Finnish-type CNS. After counselling, we tested the parents, who were found to be heterozygous carriers of the same mutation. Given the similar clinical course, we decided to analyse the dried blood spot of the first child, finding the same homozygous mutations (Fig. 1).

Conclusion: We describe the case of two siblings affected by CNS type 1 who died soon after birth due to severe respiratory distress and multi-organ failure. Despite the presence of a clinical nephrotic syndrome in the second sibling, the diagnosis was only reached post-mortem by exome sequencing. Prematurity, a larger placenta, meconium-stained AF, and lower Apgar are more frequent CNS type-1 children; however, major respiratory problems are uncommon. Nephrotic proteinuria is detectable at birth and likely begins in utero, but oedema usually develops in the first weeks of life. While we cannot rule out the presence of other unknown modifying factors, this atypical presentation increases our knowledge of CNS type-1 and may indicate the possibility of underdiagnosis in early neonatal deaths.

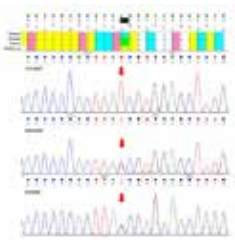

Fig. 1

1186 - P1.167

HEMATURIA CORRELATED WITH SARS COV2 INFECTION IN PEDIATRIC PATIENT

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Although respiratory and gastrointestinal symptoms are the most common manifestations of COVID-19 in symptomatic pediatric patients, it is crucial to understand that this virus may affect any organ or system. Hematuria in children is becoming more common as a result of the SARS-CoV-2 virus infection. Patients often appear with microscopic hematuria; however, gross hematuria has been reported.

Aims: At the Pediatric Clinic II in Timisoara, the renal involvement of patients with SARS-CoV-2 was systematically monitored. We have remotely followed the patients to determine their renal impairment.

Methods: The study was conducted at the Pediatric Clinic II between 2020 and 2022. During that time, 220 children diagnosed with SARS-CoV-2 infection were examined. The patients' ages varied from 9 months to 18 years. All patients had previously been hospitalized. SARS-CoV-2 was isolated from nasal swabs. In several instances, infection was diagnosed based on the epidemiological context because of symptoms and high levels of SARS-CoV-2 IgM antibodies.

Results: We identified 18 children with hematuria. Macroscopic hematuria was seen in 4 of the 18 people affected. The remaining 12 cases presented with glomerular hematuria, which included dysmorphic red blood cells. No patients had urinary tract infections when they were diagnosed. Three of the 18 toddlers had stage I acute kidney injury (AKI). These three patients made substantial improvements with conservative treatment. Urine testing showed "bearing" cells with intracytoplasmic inclusions, indicating an RNA virus infection. Twelve individuals had significantly increased inflammatory markers (indicating a systemic inflammatory response associated with SARS-CoV-2 infection, MIS-C). Macroscopic hematuria resolved, on average, within 3-5 days. All patients achieved satisfactory advancement and had no complications. Fifteen of them were periodically followed. No patient had long-term complications, and there was no indication of persistent hematuria.

Conclusions: The study's findings highlight how important it is to monitor proteinuria and hematuria in all patients with SARS-CoV-2 (especially those with MIS-C) to assess renal involvement in these cases. Furthermore, factors that can compromise renal function, such as nephrotoxic medications, hypovolemia, and septic conditions, require particular attention. In conculusion, there are multiple contributing factors to the pathogenesis of renal impairment in SARS-CoV-2 patients.

1188 - P1.168

"WILL MY CHILD GROW OUT OF NEPHROTIC SYNDROME?": PREDICTORS OF LONG TERM FOLLOW UP IN CHILDREN WITH NEPHROTIC SYNDROME

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Idiopathic childhood nephrotic syndrome is the most common glomerular kidney condition in childhood. The disease spectrum is broad, varying from a single episode to immunosuppression resistance leading to kidney failure. A common question asked by parents is whether their child would grow out of it. It was previously understood that majority of children who were responsive to immunosuppression would 'grow out of it'. However, for the more difficult to manage population there is a dearth of data available on long term risk of ongoing relapses.

Aims: To understand the factors that may predict the requirement for ongoing follow-up in children with nephrotic syndrome and transition to adult nephrology care.

Methods: Single centre, retrospective review of all patients who were discharged from a large tertiary nephrotic clinic over 11 years (2012-2023). Of the 469 patients identified, 32 were excluded (4 congenital nephrotic syndrome, 28 secondary nephrotic syndrome or proteinuria without nephrotic syndrome) and 4 were re-referred to the service hence not included in analysis.

Results: 59% (253/433) patients were male, with 45% (195/433) of Asian and 42% (183/433) of Caucasian ethnicity. 90% (391/433) of patients achieved complete remission (on steroids and/or alternate immunosuppression) and 10% (41/433) had partial response or complete resistance to all immunosuppressive therapies. 65% (281/433) of patients were discharged from clinic, at a mean age of 10 years (range of 1-18 years) at discharge. 22% (93/433) were transitioned to adult nephrology, of whom 83% (77/93) were immunosuppression sensitive. 10% (43/433) of patients moved from the clinic for other reasons including moving out of area. Of the children who were immunosuppression responsive and were discharged (n = 281), 66% (142/281) received prednisolone or one other steroid sparing medication whilst 13% (38/281) received 3 or more steroid sparing medications. Of the children who were transitioned, 48% (37/77) required 3 or more steroid sparing medications to maintain remission (p =0.079). Graph 1 represents the percentage of children discharged compared to transitioned for the number of medications used. Of the children who were immunosuppression resistant (n = 41), a higher proportion of females (65%, 27/41) were noted, compared to responsive group. 39% (16/41) developed kidney failure and 39% (16/41) were transitioned to adult care. 7% (3/41) patients died from complications of nephrotic syndrome. A genetic cause for nephrotic syndrome was found in 27% (11/41) patients with immunosuppressant resistant disease.

Conclusion: Two-thirds of patients presenting at a large tertiary nephrotic service were discharged prior to age of transition to adult care. Number of medications required over the course of treatment may be used as a predictor of requirement of ongoing nephrotic care into adulthood.

Graph 1.

1197 - P1.169

RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS (RPGN) ANCA NEGATIVE PAUCI IMMUNE IN A PATIENT WITH MICROHEMATURIA AND EPISODES OF MACROHEMATURIA FROM THE INFANCY

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Aims/Purpose: Rapidly progressive glomerulonephritis (RPGN) is an acute nephritic syndrome, with progressive loss of renal function in a short period of time. It constitutes < 15% of glomerulopathies, and histology shows epithelial crescents that evolve to fibrous. Pauciimmune (type 3 RPGN) doesn't present immunoglobulin deposits. Negative ANCA has a worse prognosis.

Methods: We report an 11-year-old boy, with a personal history of microhematuria under study between the age of 2 and 4, suspicion of IgA nephropathy, and mother with microhematuria and episodes of macrohematuria. He presented high creatinine (GFR-Schwartz 22 mL/min/1.73 m2), hypoproteinemia, normocytic anemia and hypercholesterolemia in blood test made because of knee pain. In anamnesis, he has referred episodes of macrohematuria since the age of 4, every 2-3 months, in context of infections. In the last 6 months, he has also presented nausea, fatigue, halitosis, day-night incontinence and abdominal pain. He had received ibuprofen two months before for knee pain. On physical examination, he only had uremic fetor with normal blood pressure.

Results: In diagnostic study, he had poliuria, high cratinine and urea (GFR-Schwartz 17 mL/min/1,73m2), hyperkalemia and hyperparathyroidism. The immunity study (autoantibodies, complement and immunoglobulins) was normal. Urine test had proteinuria in nephrotic range, glycosuria and hematuria. Serologies were negative and urinary tract ultrasound was normal. He started treatment for chronic kidney disease. Ultrasound-guided percutaneous renal biopsy was performed and it reported "RPGN extracapillary pauciimmune sclerotic class (> 50% of sclerotic glomeruli globally) with presence of epithelial/fibroepithelial crescents in 36% and data of acute tubular necrosis. Negative IF. Negative ANCA. The patient was treated with three bolus doses of IV-steroid on consecutive days, followed by two bolus doses of cyclophosphamide, with no improvement in renal function.

Conclusion: RPGN is a rare cause of acute kidney damage in children, especially RPGN ANCA negative pauciimune. Although prognosis is bad, early initiation of treatment with steroids and cyclophosphamide may minimize the degree of irreversible renal damage.

1198 - P1.170

VITAMIN D LEVELS IN CHILDHOOD IDIOPATHIC NEPHROTIC SYNDROME

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Aims/Purpose: Children with idiopathic nephrotic syndrome (INS) are usually managed with long-term administration of glucocorticoids, which have a negative impact on bone metabolism. Vitamin D deficiency may also negatively affect bone health. We studied 65 children with idiopathic nephrotic syndrome (INS) in remission phase, with the aim to investigate Vitamin D levels and explore potential correlations to bone mineral density (BMD) and their corticosteroid (CS) treatment .

Methods: In this cross-sectional study we enrolled 65 children with INS [mean ± SD age: 8,7 ± 3.7 years, median INS (IQR) duration: 3.8 years (2.7-5.7)], who were compared to 39 healthy children, of similar age and sex. Almost half of our patients (53.8%) were on glucocorticoids on day of examination. Parathyroid hormone (PTH), Alkaline Phosphatase (ALP) and Vitamin D levels were measured. Lumbar and total body BMD were estimated via a dual energy x-ray absorptiometry (DEXA).

Results: Children with INS, albeit being on remission phase, had lower Vitamin D levels compared to controls (21.3 ± 9.2 vs 25.4 ± 8.7 ng/ml, p =0.019). There was a difference in Vitamin D levels between those receiving and those not receiving CS at enrolment, but it didn't reach statistical significance, although the dose of prednizolone at study enrolment was rather low (median: 0.33 mg/Kg/48h, IQR: 0,21-0.78). The difference in Vitamin D levels was statistically significant for patients receiving CS during the 4 months prior to study enrolment (mean difference 4.83 ng/ml (95% CI: 0.20 to 9.46). A significant positive correlation was found between time from last CS dose and Vitamin D levels. No significant correlations were found between Vitamin D levels and either total or Lumbar Spine BMD (p > 0.05 for both measurements).

Conclusion: In the present study on children with INS on remission, lower levels of Vitamin D were found compared to healthy controls. A significant positive correlation was found between Vitamin D levels and CS treatment during the last 4 months. Moreover, time off CS treatment was positively correlated to increasing Vitamin D levels, highlighting the importance of constantly monitoring Vitamin D levels during CS treatment in these patients. Longitudinal studies are needed to determine the impact of CS treatment on Vitamin D and bone health in INS patients.

1199 - P1.171

AN UNUSUAL CASE OF A 14-YEAR OLD ADOLESCENT WITH HANTAVIRUS INFECTION IN THE MEDITERRANEAN REGION

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Aims/Purpose: Hantaviruses are a group of viruses carried by rodents, associated with two severe clinical conditions; cardiopulmonary syndrome and hemorrhagic fever with renal syndrome. We present the first reported pediatric case of hantavirus infection in our country.

Methods: A 14-year-old male presented with a two-day abdominal pain, vomiting and headache. He was hospitalized one year ago for visceral leismaniasis. His clinical examination revealed pain at the right upper quadrant. Laboratory tests revealed low platelets (1x 105/μL) and high C-reactive protein level (80 mg/L). Abdominal ultrasonography was normal. During hospitalization, the patient developed fever and progressive oliguric acute kidney injury (creatinine: 1.71 mg/dl, urine output: 0.7ml/kg/h), nephrotic-level proteinuria (5 gr/24h) and bradycardia (hear rate: 50-60/min) with normal blood pressure.

Results: The repeated abdominal ultrasonography revealed kidney edema. The patient was initially treated with intravenous cefotaxime and furosemide. Due to persistent leukopenia and thrombocytopenia the patient underwent bone marrow biopsy, considering his past medical history of visceral leismaniasis. Myelogram was normal and blood, urine, and stool cultures were negative. Serum anti-Hantavirus IgM and IgG (ELISA) were positive as well as anti-Hantavirus IgG (IFA) with a title 1:1024. Diagnosis of Hantavirus was established, and the patient was discharged on the 12th day, free of symptoms.

Conclusion: Hantavirus infection should be suspected, even in regions where Hantavirus is non-endemic, in patients with acute kidney injury and thrombocytopenia, especially in people living in poor health conditions.

1203 - P1.172

REMOTE FOLLOW-UP OF CHILDREN WITH NEPHROTIC SYNDROME AND OTHER KIDNEY DISEASES

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Background: India is the most populous country (1.4 billion) and the seventh-largest country by area. Specialist (Paediatric Nephrology) services are limited, and people frequently travel to New Delhi from far states for medical consultations. This results in increased cost burden and inconvenience to the family and child absentees from school. Tele consultations in India were not prevalent before the COVID-19 epidemic, but they evolved as a necessity during the pandemic. Post-pandemic, many families preferred to stay connected via online consultation and stay satisfied. In Paediatric nephrology, long-term follow-up is required for many asymptomatic (diseases in remission) chronic diseases and their laboratory monitoring. Telemedicine helps to reach specialist care to distant patients and their follow-ups.

Method: This is a retrospective follow-up outcome of patients who were seen online between December 2022 and March 2024. Telehealth activity with the standard face-to-face appointment through WhatsApp was done. Information was collected on patients' visits, age, sex, illness, and the reason for the consult.

Result: 200 e-consultations were done for 85 children (54 males), with an average age of 7.47 years (max 18, min 0.5 years). 90% preferred online face-to-face consults. 67% (n = 57) were Nephrotic Syndrome, mainly frequent relapsing/ steroid-dependent and steroid-resistant nephrotic syndrome on long-term immunosuppression medications. Growth, blood pressure, medications and lab reports followed, and 3.5% (n = 2) required hospital visits for albumin transfusion. Children with CAKUT (28.3%) preferred online long-term 6 monthly follow-up. The remaining cases included UTI, hypophosphatemia rickets, distil RTA, and post-kidney transplant.

Conclusion: Tele-consult has a role to play in Nephrology care. This study demonstrated that remote tele-pediatrics nephrology consult is a practicable option for the long-term follow-up of stable children with renal disorders. It has multiple benefits for patients, families, and treating teams, such as saving money and helping to keep maintenance follow-up of patients who are on long-term immunosuppression (single or multiple) therapies, especially in frequent relapsing or steroid-dependent and steroid-resistant nephrotic syndrome along with CAKUT disorders.

1207 - P1.173

LONG-TERM OUTCOME OF STEROID SENSITIVE NEPHROTIC SYNDROME

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Aims/Purpose: Nephrotic syndrome is the most frequent glomerular disease among children, where over 85% of children respond to steroid therapy. The disease however is characterised by a remitting and a relapsing course. Most published literature suggest that majority of steroid sensitive nephrotic syndrome enters long term remission around puberty. This study was undertaken to evaluate the long term outcomes of steroid sensitive nephrotic syndrome presenting to a tertiary care facility in Sri Lanka.

Methods: The details of all children presenting or referred to Teaching Hospital Peradeniya, Sri Lanka with nephrotic syndrome were obtained and updated in a data base on regular basis from 2002, with the approval of the local ethics committee. This review focused on patients recruited up to 2010, such that all patients will be above 16 years of age at present. The proportion of children who had active disease beyond 16 years were studied further, focusing on the age at onset, gender, immunosuppressive therapy, timing of response to steroids and relapse within six months of the initial diagnosis.

Results: Among the 963 patients with steroid-sensitive nephrotic syndrome presenting between 2002-2010, 209 patients (21.7%) had active disease requiring immunotherapy beyond 16 years of age. The median age at disease onset was 4.50 years (IQR 2.90, 6.00). The majority were male (67%), and 61% had relapsed within six months of the inital diagnosis. Levamisole (48%) was the most commonly prescribed immunosuppressive drug, followed by cyclosporine (26%) and mycophenolate mofetil (25%). Most patients (72%) were late responders to treatment..

Conclusion: The results suggest that over 21% of patients with childhood steroid sensitive nephrotic syndrome have active disease beyond 16 years. Late response to steroids at the disease outset may herald a protracted course of disease with activity persisting beyond 16 years.

1208 - P1.174

PREDICTORS OF SHORT-TERM RENAL OUTCOME IN PATIENTS WITH SHIGA TOXIN ASSOCIATED-HAEMOLYTIC UREMIC SYNDROME

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Aims/Purpose: Haemolytic Uremic Syndrome (HUS) caused by Shiga toxin producing E. Coli (STEC) is a rare disease characterised by abrupt onset and rapid evolution, a high mortality rate and several short and long- term complications. The ability to predict short-term outcome can be crucial for the correct management of STEC-HUS patients. Laboratory indices such as lactate dehydrogenase (LDH) and C3 complement protein, easily measurable and commonly available in the hospital setting, can provide important information. The purpose of this study is to identify possible early predictors of renal outcome derived from routine blood analysis in affected patients.

Methods: In this retrospective study, we analysed laboratory parameters of 62 pediatric patients diagnosed with STEC-HUS between 2009 and 2022, considering data gathered at two timepoints: patient admission and discharge. Multiple linear regression models were used to highlight possible correlations between levels of parameters gathered at disease onset and nephrological outcomes in terms of eGFR and levels of proteinuria at the end of the hospitalisation period.

Results: A low eGFR (< 90 ml/min/1.73m2) associated with low C3 levels (< 90 mg/dL) at diagnosis were predictive of low eGFR at discharge (PLR = 3,71, p value = 0.003). The model has a sensitivity of 69% (95% CI = 41%-89%) and specificity of 81% (95% CI = 62%-94%). Furthermore, LDH levels measured at admission were strongly correlated with synchronous proteinuria levels (adjusted R2 = 0,73, p value = 6,27e-11).

Conclusion: Based on our results, we conclude that the reestablishment of adequate renal function in patients with STEC-HUS presenting with acute kidney failure at disease onset can be predicted by eGFR together with C3 levels measured at admission. The striking collinearity between LDH levels and the severity of proteinuria suggests that LDH may be regarded as an early indicator of acute renal damage.

1218 - P1.175

VAPING INDUCED ACUTE KIDNEY INJURY AND RESPIRATORY DISTRESS IN A PEDIATRIC PATIENT

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Aims/Purpose: Kidneys can be harmed by various medications in various ways. This sensitivity of the kidneys is primarily due to their high degree of filtration capacity and the metabolism of toxic by-products. Electronic cigarettes may contain various substances and medications and, if vaporized, may also cause lung damage. In this case, a previously healthy child presenting to the pediatric emergency department with seizures, respiratory distress, and acute kidney injury (AKI) thought to be associated with electronic cigarette use were discussed.

Case: A 14-year-old male patient presented to the pediatric emergency department with complaints of generalized tonic-clonic seizures occurring three times, respiratory distress, and decreased urine output. The patient's general condition was poor and consciousness tended to sleep. Vital signs showed tachypnea (RR: 30/min), tachycardia (HR: 120/min) and hypertension (160/100 mmHg). Bilateral rales, more pronounced on the right side, were present on auscultation. The liver and spleen were non-palpable, and there was no edema. It was learned that the patient had used electronic cigarettes occasionally and most recently two days prior to his complaints. Laboratory tests showed leukocytes 23500/uL, absolute neutrophils 14500/uL, absolute lymphocytes 7200/uL, hemoglobin 12.3 g/dL, platelets 322000/uL, serum creatinine 1.18 mg/dL, albumin 4.9 g/dL, C-reactive protein 17.2. The urine color was dark and urinalysis was consistent with hematuria. Brain computed tomography (CT) and diffusion-weighted magnetic resonance imaging were normal. Thoracic CT showed consolidation with air bronchograms and ground-glass opacities in the right lower zone. The patient was commenced on broad-spectrum antibiotic therapy. Echocardiography was normal, with an ejection fraction (EF) of 70%. Within 24 hours, the patient developed anuria, a rapid rise in serum creatinine (4.8 mg/dL) and a decrease in EF. Intermittent hemodialysis was initiated. A broad viral panel for infection and an autoantibody panel for reno-pulmonary syndromes resulted negative. Rapidly progressive nephritis was treated with pulse prednisolone and plasma exchange. The kidney biopsy resulted in acute tubular necrosis. The patient began to urinate on the 15th day of follow-up. Plasmapheresis was discontinued, and treatment continued with low-dose (2 mg/kg per day) prednisolone. The patient had no recurrent seizures during follow-up, respiratory distress improved, and there was no need for intermittent hemodialysis.

Conclusion: The use of drugs, substances or electronic cigarettes should always be considered in the differential diagnosis of any patient presenting with AKI.

1219 - P1.176

KIDNEY BIOPSY IN CHILDREN WITH PROTEINURIA

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Proteinuria usually indicates a disturbance in glomerular barrier and may be an important sign of kidney disease. Asymptomatic proteinuria is thought to be a relatively common urinary abnormality in children. Kidney biopsy is not routinely indicated for patients with isolated proteinuria and there is little known about the impact of kidney biopsy on differential diagnosis and prognosis of glomerular involvement.

The aim - analysis of kidney biopsies has been done at tertiary hospital over 2022-2023 years in patients with persistent proteinuria.

Materials and Methods: Initial kidney biopsies were performed in 17 children aged 6 to 17 years, with persistent (more than 12 months) proteinuria (mean 9.6 ± 1.9 months). The diagnosis based upon the presence of abnormal ranges of protein:creatinine ratio (PCR) > 200 mg/g in morning specimen. A transient or orthostatic proteinuria were exluded before a kidney biopsy. Each patient was instructed to empty their bladder just before bed time and to collect urine immediately upon rising the next morning (the first urine specimen). Renal tissue was obtained by needle biopsy under ultrasound guidance. Renal biopsy specimens were investigated by routine light, immunofluorescence and electron microscopy. All biopsy specimens were examined and diagnosed by one of the study investigators.

Results: The renal histopathology revealed focal segmental glomerulosclerosis (FSGS) (n = 4), diffuse mesangial proliferative glomerulonephritis (n = 7), IgA nephropathy (n = 2), systemic lupus nephritis (n = 2), Alport syndrome (n = 1), thin basement membrane disease (n = 1).

Among isolated proteinuria cases and PCR ranged 200-2000 mg/g only one patient diagnosed with FSGS and 5 patients with mesangial proliferative glomerulonephritis. Those with higher level of proteinuria (PCR ≥ 2000 mg/g) 3 patients diagnosed with FSGS and 1 patient with mesangial proliferative glomerulonephritis, 2 patients with systemic lupus nephritis. Patients combined proteinuria with hematuria presented with IgA nephropathy (2 cases), mesangial proliferative glomerulonephritis (1 patient), Alport syndrome 92 patients) and 1 cases of thin basement membrane disease.

Conclusion: Renal biopsy may be indicated to clarify the cause of glomerulopathy those with proteinuria persists longer than 1 year. There is a high likelihood of detecting significant renal pathology in children with proteinuria lasts for 1 year, which may negatively affect a long-term prognosis.

1225 - P1.177

LONG-TERM CLINCAL AND PATIENT-CENTERED OUTCOMES IN 132 ADULTS WITH CHILDHOOD ONSET SYSTEMIC ERYTHEMATOSUS LUPUS

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Aims/Purpose: Childhood-onset Systemic lupus erythematosus (c-SLE) is a chronic, multisystemic autoimmune disease with more severe organ damage than adult-onset SLE. The aim of this retrospective and cross-sectional study was to evaluate long-term clinical, socioeconomic and patient-centered outcomes of adults diagnosed with c-SLE.

Methods: Patients older than 18 years old diagnosed with c-SLE between 1990 and 2019 in 4 Southwest French University Hospitals were included. Clinical evolution during childhood and after the transition to adult care were retrospectively collected through medical records. Socioeconomic data, education level and patient's perspectives on their disease were collected using a simple questionnaire survey sent to the patients.

Results: A total of 132 patients were included with a median age at diagnosis of 14 years old [IQR, interquartile range, 12-15] and 84% were female. The median disease duration was 14 years [IQR10-19]. Six patients (4.5%) died during follow-up. The most frequent organ flares were articular, cutaneous, and renal. Almost half of the patients (45%) developed organ damages over the disease course with a SLICC-damage index ≥ 1. Four patients reached kidney failure leading to kidney transplantation and 10 developed major cardiovascular disease after 18 years. The most frequent complications during adult course were severe infection (23%) and osteoporosis (12%). At last available follow-up (median age 28 years [IQR 24-33]), 51% of patients still received immunosuppressive therapy. The educational level was similar to that of the French population and 70% of patients were employed at the time of the survey. Almost all patients (92%) responded that c-SLE has strongly influenced at least one aspect of their daily life (professional, private or scholarship) and half of them (45%) stated that all three aspects were impaired. In univariate logistic regression, only SLE-related cardiovascular manifestations were associated with patient-centered outcome.

Conclusion: In this multicenter cross-sectional study, c-SLE patients developed significant organ damages over time after a long disease duration and estimated that c-SLE has highly impacted their lives despite achieving an academic and employment level comparable to the French population.

1228 - P1.178

GLOBAL LONGITUDINAL STRAIN (GLS) IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME

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Aims/Purpose: The aim of this study is to determine the relationship between global longitudinal strain (GLS) with clinical (including disease duration, cumulative dose of steroids, number of relapses), biochemical parameters, intima media thickness (cIMT) and determine the factors that influence GLS in children with nephrotic syndrome.

Methods: A cross-sectional study included 40 patients with nephrotic syndrome (mean age 11.7 ± 4.7 years). Steroid dependent nephrotic syndrome was established in 32 patients (80%), while 8 (20%) had steroid resistant nephrotic syndrome. Blood pressure based on 24-h ambulatory blood pressure monitoring (ABPM), cIMT, fasting glucose, insulin, HbA1c, lipid concentrations and echocardiography parameters (left ventricular mass index and global longitudinal strain) were measured in all children.

Results: GLS negatively associated with duration of nephrotic syndrome (r = - 0.612, p =0.000), age (r = -0.658, p =0.000), cIMT (r = -0.527, p =0.000), serum creatinine (r = -0.374, p =0.017), daytime systolic blood pressure (r = -0.457, p =0.003) and nocturnal systolic blood pressure (r = -0.536, p =0.000). Multiple linear regression showed that duration of nephrotic syndrome (R2 = 0.591, = - 0.595, p =0.003) and body mass index (R2 = 0.591, = - 0.349, p < 0.001) were independent predictors of GLS in children with nephrotic syndrome.

Conclusion: The findings of the present study suggest subclinical cardiovascular damage in patients with nephrotic syndrome. Duration of nephrotic syndrome and body mass index were independent predictor of global longitudinal str.

1236 - P1.179

ERICONS - EARLY RITUXIMAB IN CHILDHOOD ONSET NEPHROTIC SYNDROME - INCLUSION COMPLETION IS APPROACHING

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Aims/Purpose: ERICONS study is designed to assess the efficacy and safety of early rituximab (RTX) treatment in steroid-dependent nephrotic syndrome (SDNS) and frequently relapsing nephrotic syndrome (FRNS). RTX as initial steroidsparing therapy is given in order to prevent further relapses or prolong time to relapse without the use of steroids.

Methods: Design: A multi-centre, double-blind, placebo-controlled, randomized clinical trial (RCT) followed by an open label cohort study. Protocol dosing: 2 weekly infusions of 375 mg/m2 RTX. Participating centers: Gdansk (Coordinating Center), Warsaw, Wroclaw, Krakow, Lublin, Bialystok, Poznan Lodz, Zabrze, Poland. Sponsor: Medical University of Gdansk (PI A. Zurowska, M. Drozynska-Duklas). Financial support: Non-commercial Clinical Trial financed by: Medical Research Agency, Poland, Project number: 2019/ABM/01/00024. The study has been accepted by regulating agencies and bioethical committee in 2021 and registered in EudraCT: 2020-004982-37. Inclusion: 60 patients required;

Results: First Patient In (FPI) 28th December 2021. To date 40 patients have been enrolled. An equal numer of boys and girls (20:20) have been entered at a mean age of 73,1 months. 75% of the cohort has been diagnosed with SDNS, 25% with FRNS. Recruitment completion is expected by June 2025. The estimated primary completion date is June 2026.

Conclusion: Study enrollment is expected to be completed by June 2025 with 40 patients entered from FPI. It is expected that long term steroid free remission can be achieved with early introduction of rituximab in children with SDNS/FRNS, with a good safety profile.

1237 - P1.180

EARLY INTERVENTION WITH ECULIZUMAB IN ANTI COMPLEMENT FACTOR H ANTIBODIES AHUS IMPROVES OUTCOMES

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Aims/Purpose: A distinct subtype of complement dysregulation driven thrombotic microangiopathy (TMA) is the one with autoantibodies against Complement Factor H (CFH). This antibody are targeting the C-terminus of CFH, in this way inhibiting its function. This retrospective analysis of four patients aims to emphasize the advantages of early start of Eculizumab, demonstrating its superior efficacy compared to immunosuppressants or plasmapheresis.

Methods: An 11-year-old girl with marked anaemia, thrombocytopenia and acute kidney injury developed extrarenal manifestations including liver, lung, pancreas and brain, received plasma infusions, methylprednisolone, cyclophosphamide, and mycophenolate mofetil. She required 19 dialysis sessions and 12 red blood cell transfusions. Eculizumab was started on day 31 as her condition worsened. Subsequently, she showed favourable progress. A 5-year-old girl presented with TMA triad and oligoanuria. She was treated with plasma exchange (3 sessions) and needed 2 hemodialysis sessions and 5 blood transfusions. Even if the anti CFH antibodies decreased dramatically after plasma exchange, we saw little improvement in her clinical condition. Eculizumab started 8 days after symptom onset resulting in rapid improvement. A 10-year boy presented with clinical and laboratory signs of HUS, no gastrointestinal symptoms. Eculizumab was started within 24 hours of admission, with no need for dialysis. He needed 2 blood transfusions. Subsequently, he showed rapid clinical and laboratory progress, without extrarenal involvements. A 6-year-old girl with anaemia, thrombocytopenia and acute kidney injury, no diarrhea, received Eculizumab treatment within 6 hours from admission. She showed rapid favourable progress without the need of dialysis. 4 blood transfusions were needed in her case.

Results: All patients had low C3, normal C4 and anti CFH levels ranging from 678 to 15000 AU/mL. All 4 patients genetic testing revealed homozygosity for CFHR1 and CFHR3 deletion and other additional variants in C3, CD46, CFH that were considered disease modifiers. Early therapy was associated with less severe illness, less extrarenal complications and rapid positive outcomes.

Conclusion: When considering complement and its blockade, a decisive approach is crucial: initiate therapy promptly and assertively. Complement blockade should be prioritized as the initial treatment for aHUS, rather than a secondary option.

Table 1: Summary of cases

	C5 blocking blocking start	Discharge (days)	Blood	C3	CFH	Anti CFH Abs	Dialysis (days)	PLT normalization	Neurological involment	Other organs	Emotional trauma	Invasive procedures	CKD
P 1	31 days	80	12	0.7	195	678	19	45 days	YES	YES	YES –PT	YES	YES
P 2	8 days	21	5	0.5	49	10900	2	15 days	NO	NO	NO	YES	NO
P 3	24 hours	8	2	0.46	63	15000	0	5 days	NO	NO	NO	NO	NO
P 4	6 hours	6	4	0.66	61	3704	0	6 days	NO	NO	NO	NO	NO

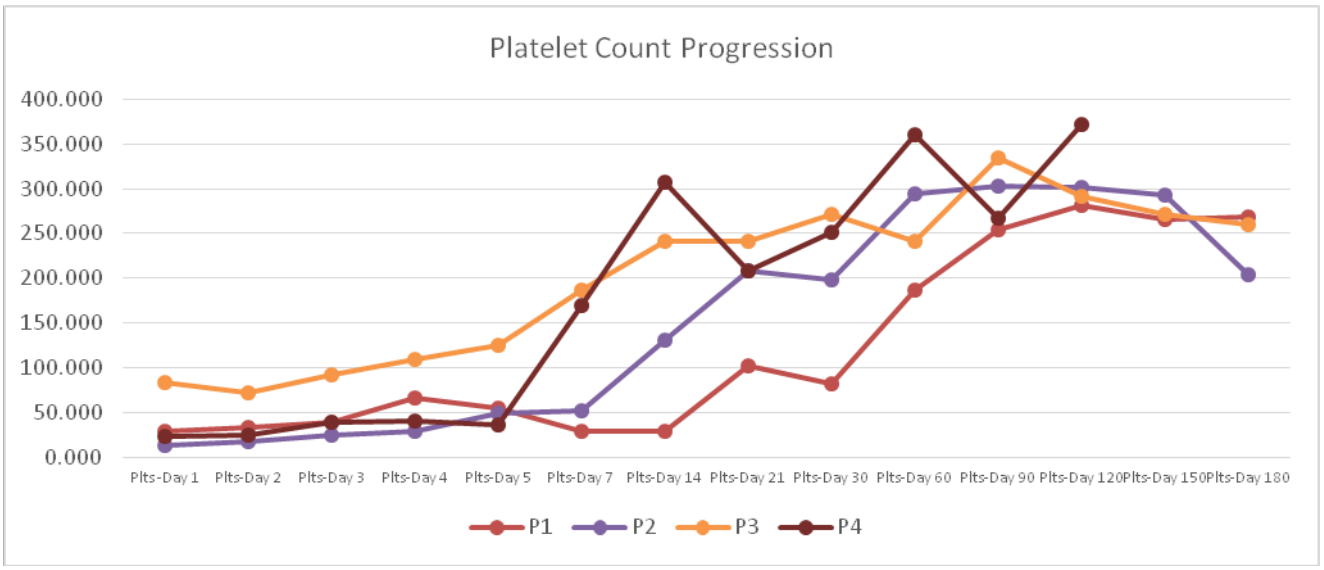

Figure1: Platelet count progression (☆= Eculizumab)

1248 - P1.181

FAVORABLE PREDICTORS OF OUTCOME WHEN CYCLOSPORINE A THERAPY IS CHANGED TO MYCOPHENOLATE MOFETIL IN STEROID RESISTANT NEPHROTIC SYNDROME

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Aims/Purpose: The induction and maintainance of remission of steroid-resistant nephrotic syndrome (SRNS) in children remains challenging. Despite calcineurin inhibitors (CNI) emerging as the therapy of choice, consensus is lacking on the optimal duration of treatment. The jury is still out on the benefit of switching to less toxic agents such as mycophenolate mofetil (MMF) to maintain CNI-induced remission. Due to the economic crisis in Sri Lanka, Cyclosporine A became unavailable, and hence a majority of children were switched MMF to maintain remission. Tacrolimus was used sparingly to reserve it for transplant recipients. This study evaluates the outcomes of these children.

Methods: Forty two children receiving Cyclosporine A for over one year were switched to MMF. Eight patients were commenced on tacrolimus as they relapsed immediately following the change or failed to enter remission following a relapse. The study focused on the relapse episodes during the preceding 12 months with Cyclosporine A and the relapse episodes with MMF in the subsequent 12-month period, along with the factors that affect the relapse rate after switching to MMF.

Results: The analysis included 34 participants with a median age of 10 years, 62% males, and 38% who had prior relapses. The Bayesian Poisson regression model showed that age, sex and histology were not significantly associated with the number of relapses following the change to MMF. However, each additional relapse before changing the drug was associated with a 62% increase in the number of relapses with MMF. In addition, each additional year of prior Cyclosporine A treatment was associated with a 64% reduction in the number of relapses. The model was fitted using the brms package in R.

Conclusion: The conversion from Cyclosporine A to MMF in SRNS appears to be more successful in patients with prior prolonged Cyclosporine A therapy with sustained remission.

1265 - P1.182

ROLE OF TACROLIMUS AND LONG-TERM OUTCOME OF MONOGENIC STEROID RESISTANT NEPHROTIC SYNDROME (SRNS) AND NEPHROTIC RANGE PROTEINURIA WITH CAKUT - A CASE SERIES

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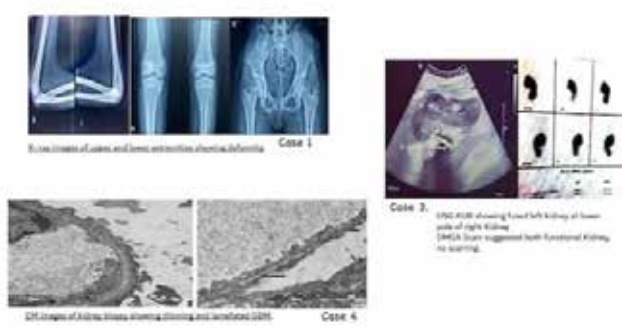
Background: SRNS constitutes 10 % of all cases of Nephrotic syndrome (NS), and more than 50% of cases without any genetic association responded well to calcineurin inhibitors (CNI)1. A report of 203 children with monogenic SRNS suggested 27.6% and 22.5% complete (CR) and partial (PR) remission, respectively, and a reduction in kidney failure risk after 6 months of CNI treatment2.

Method: This retrospective case series of 5 patients was collected from the medical records of SRNS patients treated with tacrolimus.

Result: A total of 3 monogenic SRNS and 1 with CAKUT went into CR and PR for an average of 7.4 years (max 10; min 3) after starting treatment with tacrolimus.
Case 1: A 6-year-old girl, with weight and height centiles as 75th and 90th centiles, respectively, was referred for SRNS. She also had partial bilateral elbow dysplasia. Case image 1. Renal histopathology showed FSGS. Genetic testing revealed LMX1B c.668G > A on exon 4, a heterozygous Autosomal Dominant (AD) mutation. She achieved early CR for two years, and as proteinuria reappeared after stopping tacrolimus twice, she achieved CR again for six years.
Case 2: A 1.1-year-old girl was diagnosed with SRNS course, biopsy suggestive of FSGS and genetic testing revealed positive KANK2 c.304T > C mutation. She has been in PR on tacrolimus for nine years.
Case 3: A 3 year-old-boy presented with late SRNS with a family history of albinism, had heterozygous TYR gene, chr 11:c:419T > G, (p.Leu140) remained CR on tacrolimus for three years.
Case 4: A 1.5-year-old -girl, weight and height on 90th centiles, referred for SRNS course and renal ultrasonography suggestive of crossed fused ectopic kidney—case image 2. Initially followed without immunosuppression, required admission for hypoalbuminemia and achieved CR after giving tacrolimus. Require re-initiation of tacrolimus when stopped twice and maintained remission.
All four cases have normal kidney function and no extra-renal side effects of tacrolimus.
Case 5: A 1.7-year-old girl presented with gross haematuria and anasarca. A kidney biopsy showed thinning of the basement membrane (TBM) and MCD. She was initially treated with corticosteroids as the first episode of NS. However, intermittent proteinuria and haematuria episodes persisted for the next three years. The second biopsy was suggestive of a basket weaving pattern and TBM, suggestive of Alport syndrome, and genetically reported COLA 4A5 c.2678-42A > G heterozygous X-linked dominant. Case image 3. Ear and eye examinations were normal.

Conclusion: This report describes the long-term outcome of monogenic SRNS who achieved CR or PR and maintained normal kidney function with tacrolimus. Further data is required to understand the course and management of such cases.

Cases images



1302 - P1.183

IGA VASCULITIS; RISK FACTORS FOR PROTEINURIA FOLLOWING IGA VASCULITIS IN CHILDHOOD

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Aims/Purpose: The aims of this study was to explore proteinuria development in pediatric IgA vasculitis (IgAV) patients and to create a predictive model for identifying those at risk of moderate to severe proteinuria (defined as; a urine dipstick with ≥ 2+ for protein or a urine albumin-creatinine ratio ≥ 300 mg/g).

Methods: We conducted a retrospective cohort study based on an extraction of patients from The North Denmark Region. Patients were included in the study if they were given one of the following ICD-10 codes; D69.0, D69.0A, D69.0B, D69.0C, D69.0D, D69.0E, D69.0F, D69, D69.2, D69.2D, or M31.0B. The diagnosis must have been given in the period lasting from January 1996 to March 2023, and the patients must be under the age of 18 at the time of debut. Baseline characteristics, debut symptoms, and paraclinical findings of IgAV patients, were collected from electronical medical records. Patients were grouped by proteinuria duration to assess differences. A prediction model for moderate to severe proteinuria within the first year post-IgAV onset was made using multivariate logistic regression with backward selection. This was validated via 10-fold cross-validation, yielding a receiver operating characteristic (ROC) curve.

Results: A total of 618 children and adolescent with IgAV were included in the study. A mean follow-up time of 138 months was observed within the study cohort. Those who experienced proteinuria lasting more than 6 months were notably older at debut, experienced more recurrences, and were treated with corticosteroids more frequently compared to those without proteinuria. Additionally, they more frequently suffered from severe abdominal symptoms, headaches, isolated haematuria, and persistent purpura (lasting over 4 weeks). Independent risk factors for moderate to severe proteinuria included age at debut ≥ 8.5 years (OR 4.41, 95% CI 1.27-15.39), persisting purpura (OR 9.34, 95% CI 2.75-31.75), mild proteinuria within the first month post-IgAV onset (OR 25.36, 95% CI 5.80-117.43), and isolated haematuria within the same timeframe (OR 10.88, 95% CI 2.35-50.38).

Conclusion: The following risk factors of developing moderate to severe proteinuria following IgAV in childhood were identified; age older than 8.5 years at debut, persisting purpura, mild proteinuria within the first month post-IgAV onset, and isolated haematuria within that same timeframe.

1321 - P1.184

BEST PRACTICE RECOMMENDATIONS FOR THE MANAGEMENT OF CHILDREN AND YOUNG PEOPLE WITH IMMUNOGLOBULIN A VASCULITIS: A NATIONAL, EVIDENCE-BASED, CONSENSUS APPROACH

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Aim: IgA vasculitis (IgAV) is the most frequently experienced subtype of vasculitis seen in children. Most children fully recover however chronic kidney disease (CKD) is a major consequence. The aim of this project was to develop a national, unified, evidence-based approach to the management of IgAV.

Methods: A national, fully representative multi-professional guideline development group (GDG), consisting of 28 members, adhered to pre-defined standards focused on topic areas. Using nationally accredited methods, that included open consultation, recommendations for both the initial management and the management of complications were planned. Incorporating existing international guidelines, a systematic literature review was performed and the IgAV GDG met monthly from June 2021 to October 2022 to generate agreed recommendations.

Results: A total of 66 papers were deemed relevant evidence for the initial management and 16 additional studies were revealed for complications. Any feedback obtained from open consultation was incorporated. Using endorsement from the UK Kidney Association and Royal College of Paediatrics and Child health, consensus group agreement and evidence were used to generate recommendations related to predefined key topics. These include the screening of nephritis, biopsy indications and treatment of histologically proven IgAV nephritis. The guidelines are available in detail online.

Conclusion: There is huge unmet need in the evidence-based management of IgA vasculitis. A national standardised approach to the clinical management of IgAV is a vital component towards accelerating outcomes for children and young people.

1323 - P1.185

A SEVERE HYPOCOMPLEMENTEMIC GLOMERULONEPHRITIS REQUIRING DIALYSIS: WHEN IT RAINS, IT POURS!

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Aims: We report a pediatric case of acute hypocomplementemic glomerulonephritis concurrent with pneumococcal pneumonia and nonsteroidal anti-inflammatory drug (NSAID) intake, presenting with renal failure and requiring dialysis.

Case report: In February 2024, a 7-year-old boy with an unremarkable personal and family medical history suffered an episode of vomiting, abdominal pain, and fever which was treated with two doses of ketoprofen; an episode of pharyngotonsillitis with fever had occurred a few weeks before symptom onset. On admission to the emergency department, blood and urine tests were performed which revealed renal failure (urea 114 mg/dl, creatinine 3.87 mg/dl) and complement consumption, negative antinuclear antibodies, and macrohematuria, indicative of acute hypocomplementemic glomerulonephritis. Chest X-ray showed signs of pneumonia, and urinalysis was positive for pneumococcal antigen. The association between pneumococcal pneumonia and concurrent hypocomplementemic glomerulonephritis has been described in the literature. He was hospitalized and experienced worsening renal function and decreased urine output, leading to anuria despite diuretic therapy. Peritoneal dialysis was initiated, which was discontinued after a week as his condition improved. Due to acute renal failure associated with acute glomerulonephritis, he received three doses of intravenous methylprednisolone for three days, followed by oral prednisone for seven days with rapid tapering. Kidney biopsy revealed an overall picture of diffuse acute glomerulonephritis, endocapillary proliferation (mainly neutrophilic granulocytes), with an "exudative" pattern. Extensive areas of glomerular necrosis were noted, along with diffuse acute tubular necrosis and tubular hemoglobin casts. Immunofluorescence showed diffuse granular glomerular deposits, predominantly C3-dominant. Electronic microscopy showed a mesangial-proliferative/endocapillary necrotizing pattern and markedly electron-dense deposits. Renal function was significantly improved at discharge; complement levels normalized, however macrohematuria with nephrotic-range proteinuria persisted.

Conclusion: Our patient presented with acute hypocomplementemic glomerulonephritis, renal failure, and anuria, requiring renal replacement therapy for seven days. Given the concurrent pneumococcal pneumonia, it is likely that the glomerulonephritis was secondary to the lung infection, as described in the literature. An alternative hypothesis is post-streptococcal glomerulonephritis, given a previous episode of febrile pharyngitis and the raised Antistreptolysin O titer, which could also be secondary to the inflammatory response to pneumonia. The presence of tubular damage and the serious kidney damage was probably caused by the concurrent use of NSAIDs and their associated risk of nephrotoxicity.

1325 - P1.186

PEDIATRIC ANCA-ASSOCIATED VASCULITIS CASE SERIES: IS IT COVID-19 RELATED?

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Aims: Anti-neutrophil cytoplasmic antibody associated vasculitis (AAV) are multisystemic diseases affecting small blood vessels in the body. AAV is infrequent in childhood and the knowledge is limited. Our purpose is to present our pediatric AAV cases, discuss different clinical findings and laboratory results and analyze prognosis.

Methods: Retrospective study of four pediatric patients with diagnosis of AAV admitted between August 2023-January 2024 in pediatric nephrology clinic.

Results: The age range was 6-16 years old age and three were girl. All patients had severe multisystemic involvement. Clinical and laboratory features are given in Table 1. Kidney failure was present in all cases and all had multiple sessions of hemodialysis. All cases had pulmonary involvement with different clinical severity. Bronchoscopy showed that three cases had upper respiratory tract involvement. All had positive SARS-COV2 antibody positivity. Cresentic glomerulonephritis was the main pathologic finding on kidney biopsy. Two cases had also chronic findings on kidney biopsy. Steroids, Pulse steroids, Cyclophosphamide and Rituximab (four doses) was given to all patients. One patient was complicated with Posterior Reversible Encephalopathy Syndrome secondary to hypertension. She was hospitalized in Pediatric Intensive Care Unit and received plasmapheresis. On last follow up only one case had normal eGFR, one had stage 2 chronic kidney disease and the other two cases are still having hemodialysis despite intensive immunosuppressive treatment

Conclusion: AAV are rare in pediatric population. We presented four severe pediatric cases of AAV. They all admitted in a short time period and had Covid-19 antibody positivity. MPO-ANCA positivity were related with chronical course. PR3-ANCA was related with severe pulmonary and upper respiratory tract involvement. Most had a poor prognosis despite intensive immunosuppressive treatments.

Table 1. Clinical and laboratory findings

	Case 1	Case 2	Case 3	Case 4
Age	16	13	7	6
Sex	Girl	Girl	Boy	Girl
Presenting Symptom	Fatigue, weight loss	Sinusitis, tachypnea, tachycardia	Fever, pneumonia, hematuri	Oliguria, edema
ANCA	MPO-ANCA>200	PR3-ANCA>200	MPO-ANCA>200	ANCA (-)
Kidney Involvement	Hemodialysis	Hemodialysis	Hemodialysis	Hemodialysis
Renal Histopathology	Four glomerulus was sclerotic, four had fibrous/fibrocellular crescents IF (-)	Celular crescents on 10/15 glomerulus, neutrophilic inflammation IF (-)	All glomerulus were crescentic, most were cellular. IF (-)	Six glomerulus were present, three were fibrous crescentic and three were sclerotic IF (-)
Bronchoscopic Findings	Nodular involvement, mild suglottic stenosis, severe inflammation on upper respiratory tract	Severe upper respiratory tract involvement, bronchial stenosis	Normal	Mild subglottic stenosis
Prognosis	ESRD	Normal eGFR, persistent proteinuria	Stage 2 CKD	ESRD

1334 - P1.187

IS ORTHOSTATIC PROTEINURIA REALLY BENIGN?

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Aims/Purpose: Orthostatic proteinuria (OP) is the most common cause of proteinuria in children. It's a condition in which a greater than normal amount of protein is excreted in the urine when the patient is in an upright position, and normal protein excretion occurs in the supine position. Patients with OP are followed for a long time to check the continuity of the orthostatic character of proteinuria. Our aim is to identify findings that may help in the differential diagnosis of hereditary nephropathy during clinical follow-up and to evaluate the course of proteinuria and glomerular filtration rate (GFR).

Methods: Children between the ages of 0-18 admitted to pediatric nephrology outpatient clinics with OP in between January 2009 and January 2024 screened retrospectively. After lying on back all night, the first urine protein/creatinine ratio in the morning is lower than 0.2 mg/ mg creatinine, or the absence of proteinuria in the urine collected at the nighttime (< 4 mg/m2/hour) and the presence of proteinuria in the urine collected during the daytime (> 4 mg/m2/hour) was defined as OP. In our study, patients' demographic data, 24-hour urine and biochemistry results, radiological imaging, biopsy results if performed, and disease course during follow-up were evaluated.

Results: 52 of 118 patients with OP were not included the study. 17 had Nutcracker syndrome, 13 a follow-up period of ≤3 months, 9 insufficient data, 4 low C3 levels, 3 abnormalities on renal Doppler and/ or urinary USG, 3 FMF or HSP in their medical history that could cause proteinuria. Additionally, during the follow-up, 1 patient was diagnosed with Alport syndrome, 1 patient with Thin Basal Membrane disease and 1 patient with Focal Segmental Glomerulosclerosis (FSGS) were excluded from the study. 72.7% of the 66 patients included in the study were female. The mean age at diagnosis was 10.7 ± 4.26 years, and the mean follow-up period was 50 ± 37.92 months. The mean body mass index (BMI) was 22.33 ± 7.31 kg/m^2. The median value of 24-hour urinary protein excretion at the time of admission and at the last follow-up were 10.16 mg/m2/h and 5.01 mg/m2/h respectively. A significant decrease of proteinuria determined at the end of the follow-up period (p 0.001). A statistically significant negative correlation was detected between the patients' BMI and 24-hour urinary protein excretion (p 0.05). There was no relationship between 24-hour urinary protein excretion with age, gender and GFR. During the follow-up period, there were no patients with GFR below 90ml/ m2/h, and only 13.6% of the patients had persistent proteinuria with the loss of orthostatic pattern. Additionally, 34.8% of patients had no proteinuria during the follow-up.

Conclusion: In patients with OP, proteinuria may decrease or even disappear over time. However, diseases that can progress to chronic kidney disease, such as Alport syndrome and FSGS, may also initially present with OP.

1339 - P1.188

MULTI-FOCAL BACTERIAL NEPHRITIS: REPORT OF TWO CASES

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Aims/Purpose: Acute focal bacterial nephritis characterized by a localized bacterial kidney infection that manifests as an inflammatory mass. Most children with acute focal bacterial infection have nonspecific symptoms including fever, vomiting, and abdominal discomfort.

Methods: We describe 2 cases of acute multi-focal bacterial nephritis.

Results: Case 1. A 9-year-old boy presented with fever for 4 days and 24-h onset abdominal pain. He was oriented and cooperative but appeared ill. Acute phase reactants such as erythrocyte sedimentation rate and C-reactive protein were raised, with a significant increase in serum creatinine phosphokinase levels (27.205 U/L). Kidney function parameters were normal and urine culture was negative. Computed tomography (CT) was conducted for further evaluation which showed an increase in the size of the left kidney with multiple cortical nodular lesions and perirenal adipose tissue inflammation. Diagnosis of acute focal pyelonephritis was made, and the patient was treated with intravenous antibiotics.

Case 2. A 5-year-old boy presented with a one-day history of fever, chills and dysuria. Hematologic examinations indicated high white blood cell count and high acute phase reactants such as erythrocyte sedimentation rate and C-reactive protein. Urinalysis revealed leukocyturia and urine culture was positive for Pseudomonas Aeruginosa. Kidney function remained normal. Computed tomography revealed multifocal nodular lesions in the right kidney with at least two nodular lesions of the left kidney and diffuse enlargement of bilateral kidneys. Acute focal bacterial nephritis was diagnosed. The patient was treated with antibiotics and discharged on day-15 of hospitalization. Repeated urine cultures were negative.

Conclusion: The clinical spectrum of focal bacterial pyelonephritis is vague, with no specific manifestations, and can be easily misdiagnosed. A negative urine-culture can mislead the clinicians causing them to miss a nephro-urological diagnosis. Ultrasound and computed tomography imaging are helpful in making a definite diagnosis.

1345 - P1.189

MILD ENCEPHALITIS/ENCEPHALOPATHY WITH REVERSIBLE SPLENIAL LESIONS (MERS TYPE II) IN A PEDIATRIC PATIENT DURING TYPICAL HEMOLYTIC UREMIC SYNDROME: A CASE REPORT

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Aims/Purpose: Hemolytic uremic syndrome (HUS) is a rare disease characterized by the triad of microangiopathic hemolytic anemia, thrombocytopenia and acute kidney injury. Shigatoxin-associated HUS, also known as "typical" form, is the most frequent cause of acute kidney injury in children worldwide. Neurologic complications are the most common extra-renal manifestations in typical HUS, accounting 25% of patients. They are at elevated risk of the worst outcome after the acute phase of the disease. At now, the key role of the complement system dysregulation is well known in the atypical HUS, while rising evidence underlies its involvement also in the pathogenesis of typical HUS, thus could support the "off label" use of an anti-C5-convertase monoclonal antibody (Eculizumab) for treating more severe forms of this disease. In this report, we describe an unusual neurological involvement in a patient with typical HUS.

Methods: A 5-year-old male was observed in the Pediatric Nephrology Department (Bari).

Results: After admission to our Nephrology Pediatric Unit because of asthenia, abdominal pain and vomiting, laboratory data showed hemolytic anemia, thrombocytopenia and acute renal failure. A supportive treatment was started: iperhydration with glucosaline solutions, diuretic drugs, plasma infusion and blood transfusion. After 3 days, an unusual delirium episode appeared characterized by dread, fear to the father and distress. Neurologic examination showed disorientation, nystagmus and unsteadiness. MR studies revealed ischemic lesions at the thalamus and, surprisingly, at the splenium of the corpus callosum. Consequently, we administered Eculizumab. After 24 hours, a generalized tonic-clonic seizure appeared: the patient was sudden transferred to Intensive Care Unit and treated with antiepileptic drug. He had the second MR scans that showed new ischemic lesions at the white matter. The CNS symptoms completely disappeared at the eighth day after a second Eculizumab infusion. The patient was discharged from the hospital on the 19th day without clinical CNS impairment. A follow-up MR examination on the 30th day after discharge returned to normal: it didn't show any ischemic lesions neither at the thalamus and white matter nor splenium of the corpus callosum.

Conclusion: MERS (Mild encephalitis/encephalopathy with Reversible Splenial lesions) is a transient clinico-radiological syndrome characterized by non-specific encephalopathy and specific MR imaging pattern, such as ovoid lesion in the mid-splenium of the corpus callosum (SCC). This case report describes a rare case of reversible splenial lesion and concomitant reversible white matter lesions within the scope of a STEC-HUS.

1353 - P1.190

EFFECTIVE MANAGEMENT OF RECURRING SEVERE ATYPICAL HEMOLYTIC SYNDROME INDUCED BY RECURRENT CLOSTRIDIUM DIFFICILE INFECTION IN CHILD WITH MCP GENE(CD46 HOMOZYGOUS MUTATION) WITH ORAL VANCOMYCIN AND MONTHLY IVIG THERAPY

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Aims/Purpose: To highlight the value of thorough investigation and genetic testing in the management and treatment of a patient with recurrent atypical hemolytic uremic syndrome. Additionally, to raise pediatric nephrologists' knowledge of a recently suspected trigger for recurrence in the genetic form of atypical HUS. Describe the association between MCF mutation (CD46 gene) and immune deficiency which increases the susceptibility to unusual infectious agents such as clostridium difficile and induces recurrent atypical HUS.

Methods: We describe a case presented to our hospital one year ago with severe recurrent hemolytic uremic syndrome precipitated by profuse watery diarrhea caused by relapsing Clostridium difficile infection in a previously healthy 9-year-old kid.A thorough medical history and examination were obtained. examination of his lab results and medical record, along with noting any problems, therapeutic response, and changing circumstances during the illness. A comprehensive regional and worldwide literature evaluation of similar cases was conducted among pediatric and adult patients. The genetic etiology of atypical HUS and its associated disorders were extensively studied.

Results: While the literature suggested an association between the MCP gene and immune deficiency and low IGG levels, no relationship was documented between this gene and recurrent Clostridium difficile infection, which served as a trigger for HUS episodes. However, comprehensive multidisciplinary teamwork with our patient revealed and validated the previously postulated theory about the severity and relapsing nature of atypical HUS with positive MCF (CD46 gene). Conservative management and oral vancomycin eliminated the C. diff infection and halted the triggering factor in atypical HUS episodes. IVIG also aids in boosting the patient's immune system and reducing the possibility of C. diff infection, which lowers the frequency of recurred HUS episodes.

Further research is required to validate our assumptions

Conclusion: Since Clostridium difficile is an uncommon precipitant of HUS in adults and has not been previously reported in pediatrics, our case emphasizes the need to consider it as a potential cause of HUS in pediatric patients. Vancomycin as oral therapy and supportive care are effective in curing the condition. Depending on the disease's stage, dialysis or plasma exchange may be further therapeutic choices. To determine the potential reasons for recurrent Clostridium difficile infections in children who seem healthy, a comprehensive study is necessary. Genetic testing is crucial in the management and aids in disease classification and prognostic outcome. IVIG is a potential therapy in patients with recurrent HUS of possible genetic mutation.

1356 - P1.191

FUNCTIONAL ACUTE KIDNEY AT THE DIAGNOSIS OF POST-INFECTIOUS GLOMERULONEPHRITIS IN A PEDIATRIC POPULATION

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Background and Aims: Post infectious glomerulonephritis (PIGN) is the leading cause of acute glomerulonephritis in children. There is large variability in the clinical expression at diagnosis which can range from asymptomatic microscopic hematuria to acute nephritic syndrome. AKI is common at diagnosis and conditions immediate treatments. Even if the long-term prognosis remains favorable, the functional part in AKI at diagnosis is little known and could condition the initial management. This study aims to describe the functional part in AKI at diagnosis of PIGN in the pediatric population.

Methods: We performed a monocentric retrospective analysis of children diagnosed with PIGN between 2011 and 2024 at Necker Hospital. We retrospectively collected clinical date using the full text search engine of Necker Hospital Dr Warehouse. We analyzed the frequency of the functional part in children with AKI with the use of creatinine level at diagnosis (AKI was the define with a DFG < 90 ml/min/1,73m3). AKI was defined as functional if the ratio of urinary to plasma urea was higher than 10.

Results: We included 47 patients with a diagnosis of PIGN during this period. The mean age was 6,9 2,8 years. Among the 47 patients, 35 (74%) had a AKI at diagnosis. Among AKI patients at diagnosis, we found a high proportion of functional profile with a total of 24 (68%) patients. Only one patient had an organic profile of AKI. Urinary ionogram was lacking in 10 (28%). The median level of C3 during the acute phase was 333 mg/L (193-513). All patients had a favorable evolution over time with normalization of renal function and the absence of recurrence.

Conclusions: Overall, we showed that AKI in PIGN seems to be frequently presented under a functional profile. This makes it possible to assume that a functional profile of ARI identified with the urinary ionogram should not call into question the diagnosis of PIGN and that it must be highlighted to set up the appropriate therapeutics.

1358 - P1.192

PROLIFERATIVE GLOMERULONEPHRITIS WITH MONOCLONAL IGG DEPOSITS IN AN ADOLESCENT SUCCESSFULLY TREATED WITH DARATUMUMAB

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Aims/Purpose: There is no specific treatment for proliferative glomerulonephritis with monoclonal IgG deposits (PGNMID), a disease that is very rare in the pediatric population. Here, we present a case of a boy successfully treated with 6-month course of daratumumab, a monoclonal antibody targeting CD38.

Methods: Here, we present a case of a 15-year-old boy with PGNMID, which was successfully treated with daratumumab.

Results: A 15-year-old boy presented with lower limb edema and hypertension. His laboratory results revealed hypoalbuminemia (serum albumin 22 g/l), creatinine 82 µmol/l corresponding to a mildly decreased glomerular filtration rate of 85 ml/min/1.73m2, 3+ protein in urine, and microscopic hematuria. His urine protein to creatinine ratio was 816 mg/mmol (upper normal limit 20 mg/mmol). His immunology results were remarkable only for a mildly lower complement C3 level of 0.74 g/l. A kidney biopsy showed membranoproliferative pattern glomerulonephritis with diffuse global mesangial and focal segmental endocapillary hypercellularity and duplication of the glomerular basement membrane. No necrosis or crescents were present. Immunofluorescence showed strong staining for IgG3 with kappa light chain restriction. Electron microscopy revealed mainly mesangial deposits. Protein electrophoresis and immunofixation of serum and urine did not detect monoclonal component protein. Flow cytometry of peripheral blood showed a significant plasma cell population, with high expression of CD38, but no clonal characteristics. There were elevated levels of free kappa and lambda chains in the urine and serum. Based on the flow cytometry results indicative of "low-plasma-cell-dyscrasia" and encouraging data from adult studies, we decided to treat our patient with daratumumab. We also added ramipril and amlodipine for hypertension and proteinuria. Initially, daratumumab infusion was administered once a week at the dose of 16 mg/kg. Then, every other week for another 8 weeks, the patient received subcutaneous injections, 1800 mg each, due to inaccessibility of intravenous daratumumab in our country. The treatment was generally well tolerated and there were no severe side effects. The patient only complained of transient fatigue on the day of drug administration. This therapy led to rapid and sustained reduction in proteinuria. At the end of the treatment, kidney function was normal and only mild proteinuria was present (urine protein to creatinine ratio 49.5 mg/mmol).

Conclusion: As far as we know, this is the first pediatric case of PGNMID successfully treated with daratumumab. There was a significant reduction in proteinuria and normalisation of kidney function. Based on positive experience with adults, daratumumab should also be studied in children with PGNMID.

1365 - P1.193

LOW MOLECULAR WEIGHT PROTEINURIA IN PEDIATRIC IDIOPATIC NEPHROTIC SYNDROME

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Aims: Nephrotic syndrome (NS) is characterized by proteinuria and hypoalbuminemia. While proteinuria due to albumin excretion is prominent in NS, some studies have emphasized that low molecular weight (LMW) proteinuria is also present and this may effect prognosis. Minimal change disease (MCD) was reported as the most common causes of NS. On the other hand some reports have shown that the frequency of focal segmental glomerulosclerosis (FSGS) and steroid resistance have increased in recent years. In this study, the urinary excretion of low molecular weight protein beta-2 microglobulin (2M) and alpha-1 microglobulin (1M) was evaluated in idiopathic NS. It was also investigated its relationship with glomerular filtration rate (GFR), cystatin C, serum creatinine levels and the remission states.

Methods: 82 patients with idiopathic NS, aged between the ages of 2 and 18 years, were included in the study. Demographic data and medical history were collected and laboratory investigations of serum creatinine, cystatin C, urinalysis, urine creatinine, urine 2M, urine 1M and estimated GFR (eGFR) were all investigated.

Results: The median age at diagnosis of the patients was 5 years and the male/female ratio was 2.4. At the time of inclusion, 30 of 82 patients were in remission. Renal biopsy was performed in 53 patients. FSGS was detected in 66.04% and MCD was detected in 9.43% of the patients who underwent renal biopsy. 76.83 % of patients had steroid-resistant NS and 67.31% of steroid-resistant patients were FSGS and 15,38% were membranoproliferative glomerulonephritis. Cystatin C levels were significantly low in patients with remission. No significant difference was detected between u2M and u2M/creatinine levels in patients with remission. On the other hand, median u1M (13,09 mg/L vs 5,42 mg/L) and u1M/creat ratio (17,27 mcg/ mg vs 5,43 mcg/ mg) were significantly higher in patients who were not in remission ($p < 0.001$, $p = 0.002$). In steroid resistant patients, there was no significant difference in u2M ($p = 0.507$), u2M/creat ratio ($p = 0.762$) and u1M/creat ratio ($p = 0.198$). Urinary 1M level was higher in patients with steroid-resistant NS ($p = 0.046$). There was a positive correlation between serum cystatin C and u2M/creat ratio ($r = 0.276$, $p < 0.05$) and also a positive correlation between serum cystatin C and u1M/creat ratio ($r = 0.255$, $p < 0.05$) in patients with idiopatic NS. No significant relationship was detected between eGFR and u2M or between eGFR and u1M.

Conclusion: Most of our patients with INS consisted of FSGS and steroid resistant patients. There was a positive correlation between serum cystatin C and the i2M/create ratio and i1M/create ratio. Although it is thought that low molecular weight proteinuria may be useful in predicting renal functions in NS, its lack of relationship with eGFR suggests that more studies are needed on this subject.

1367 - P1.194

COVID-19-INDUCED TUBULOINTERSTITIAL NEPHRITIS IN AN INFANT WITH MULTISYSTEM INFLAMMATORY SYNDROME

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Aims/Purpose: During the SARS-Cov-19 pandemic the incidence of multisystem inflammatory syndrome (MIS-C) increased among children. MIS-C can occur in all age groups but is rare in infants. An essential part of this condition is kidney involvement, but still little is known about the histopathology picture and proper treatment.

Methods: A case report of a 9-month-old, previously healthy female infant treated at our tertiary clinic.

Results: The girl was admitted in the winter of 2022 for MIS-C related to a previously non-symptomatic COVID-19 infection.

Table 1. Clinical symptoms and laboratory findings

Clinical signs and symptoms	High fever, vomiting, skin lesions, edema, hepatosplenomegaly, diminished urine output, high blood pressure
Laboratory findings	Blood urea nitrogen (BUN) 18 mmol/l Creatinine 239 µmol/L C-reactive protein (CRP) 150 mg/l Albumin 18 g/L NT-proBNP 6320 ng/L Urine albumin/creatinine ratio 0,2 g/mmol, microhematuria
Immunological tests	Positive COVID-19 spike protein antibodies

Table 2. Diagnostic tests

Kidney biopsy	Light microscopy demonstrated signs of tubulointerstitial nephritis with pronounced eosinophil and neutrophil infiltrates. General edema and tubular damage were significant
Kidney ultrasound	Both kidneys vastly enlarged with increased echogenicity

Treatment with intravenous immunoglobulins and three bolus doses of methylprednisolone was administered. Within four days the girl's general condition improved and creatinine levels normalized. Oral prednisolone was started to retain the anti-inflammatory effect. The child received low molecular heparin for one week, followed by low-dose aspirin. After one month, an ultrasound examination showed a total regression of spleen-hepatomegaly. Moreover, kidney size and echogenicity were normalized.

Conclusions: Acute kidney injury is one of the most harmful sequels of MIS-C, regardless of the severity of COVID-19, and, in the event of its non-recognition, can lead to a fatal outcome. However, if properly treated, it can resolve completely. For this reason, it is crucial to conduct broad diagnostics, which may include kidney biopsy, in case of even a slight suspicion of MIS-C.

1377 - P1.195

ACUTE POST STREPTOCOCCAL GLOMERULONEPHRITIS AND ATIPYCALL HEMOLYTIX UREMIC SYNDROME: A UNUSUAL ASSOCIATION

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Aims/Purpose: While Post streptococcal glomerulonephritis (APGN) with hypocomplementemia is the most common cause of glomerulonephritis in children, atipycal Hemolytic Uremic Syndrome (aHUS) is a rare disease due to dysregulation of the complement system leading to microvascular endothelial injury, thrombocytopenia, and microangiopathic hemolytic anemia. Despite their distinct etiologies, emerging evidence suggests a possible intersection between these pathways, involving complement dysregulation triggered by infectious agents.

Material and Methods: We present the case of male child who was admitted to our pediatric nephrology unit, where he underwent a complete clinical laboratory and genetic examination.

Results: A 8 years old male two weeks before admission presented pharyngeal pain and fever lasted five days. Then he presented diarrhea without blood, abdominal pain and weight increase. He was admitted on Emergency Department where showed high Blood pressure (129/89 mmHg, 99° percentile), edema without rashes, ecchymoses or petecchiae with triad of symptoms of HUS (hemolytic anemia, acute renal failure and piastrinopenia). Laboratory investigation revealed presence of schistocytes, elevated lactic dehydrogenase, reduction of aptoglobine, but also elevated antistreptolysin O title and low C3 complement. Urinalysis showed marked proteinuria and haematuria. Due to a possible overlap of aHUS and APGN. We performed, after normalization of platelets count, renal biopsy with evidence of characteristic of acute glomerulonephritis with hypercellularity and proliferation of capillary endothelium involving some glomeruli; some sub epithelial electron-dense deposits (humps) on electron microscopy. Patient was treated with glucocorticoids (as treatment strategies of APGN) and Eculizumab (as treatment strategies for aHUS) with progressive improvement of renal function but with persistence during a 4 months follow up of proteinuria. After 6 admnistration, eculizumab was discontinuated while steroid therapy was progressively decreased. Genetic analysis releaved an heterozygous mutations in the MMACHC gene(c4440G > C), while genetic analysis of the PRDX1 gene (involved in the regulation of MMACHC transcription) is underway.

Conclusions. A-HUS and APGN, although both serious renal diseases, rarely occur simultaneously in the same patient. Further studies are needed to deepen our understanding of this unusual co-occurrence, described up to now in 12 cases, and to develop optimized treatment strategies for affected patients.

1387 - P1.196

NEPHROTIC SYNDROME ASSOCIATED WITH LYMPHOID DISORDER

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Aims: we will present three different patients treated at aur center during 2022 -2024, all presented initially with nephrotic syndrome (NS). The final diagnosis was hematologic malignancy. We will describe the association between NS and hematologic malignancies, possible molecular mechanism, and clinical aspects.

Case1: A 17-year-old boy presented with edema and pleural effusion, hypoalbuminemia (albumin was 1.5 g/dl), proteinuria (protein/creatinine was 20 mg/ mg), renal function was normal. Renal biopsy demonstrated mild mesangial proliferation; immunofluorescence was negative. The patient received corticosteroids with good clinical response. The patient presented six months later with cervical lymphadenopathy; lymph node biopsy was consistent with Hodgkin's lymphoma.

Case 2: A 3-year-old boy presented with edema, hypoalbuminemia (albumin was 2.3g/dl) and proteinuria (protein/creatinine was 4 mg/ mg). creatinine at admission was 0.48 mg/dl. In the following days creatinine increased to 2 mg/dl and he developed oliguria and hypertension. Kidney biopsy demonstrated dense interstitial lymphoid infiltrates. The final diagnosis was Burkitt lymphoma.

Case 3: A 15-years old girl previously treated at aur center for Hodgkin's lymphoma with full remission since 2021.three years later the patient presented with edema, hypoalbuminemia (albumin was 1.8g/ dl) and proteinuria (protein/creatinine was 13 mg/ mg). renal function was normal. PET/CT revealed hypermetabolic retro pectoral lymph nodes. The final diagnosis was relapsed Hodgkin's lymphoma.

Conclusion: Lymphoma associated nephrotic syndrome often presents a diagnostic challenge. The molecular mechanism of both idiopathic and lymphoma associated NS is still unclear. Further investigation of the pathogenetic similarities can provide important insights.

Keywords: nephrotic syndrome, lymphoma, case reports.

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1388 - P1.197

CLINICAL CHARACTERISTICS AND OUTCOME OF ACUTE POSTINFECTIOUS GLOMERULONEPHRITIS IN CHILDREN: A PROSPECTIVE-RETROSPECTIVE STUDY

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Aims/Purpose: Evaluate the clinical characteristics, complications and outcome of post-infectious glomerulonephritis (PIGN).

Methods: This prospective-retrospective observational study was conducted from January 2018 through December 2023 at pediatric rhumatolgy en nephrology department of mother and child hospital Abderrahim Harouchi in Casablanca-Morocco. Post-streptococcal glomerulonephritis (PSGN) was diagnosed in the presence of: a) Hematuria and proteinuria b) Clinico-serological evidence of recent streptococcal infection [recent pyodermas or pharyngitis; positive antistreptolysin-O (ASO) titres, c) Low serum C3 levels, with normalization on 8 wk follow up. Clinical features, biochemical and serological investigations in the study subjects were recorded.

Results: Eighty-five cases of GNA PS were identified. There is a male predominance with a sex ratio of 3.3. The median age of onset is 6.9 years. GNA occurs seasonally; in our experience we note an autumn-winter predominance in 51.5% of cases. A concomitant Ear, Nose and Throat infection or preceding the episode was observed in 82.3% of cases, a skin infection such as impetigo in 4 cases, a pleuropulmonary infection in 5 cases and a urinary tract infection in 2 cases. The clinical presentation was dominated by hematuria in 100% of cases, edema in 36.7% of cases, hypertension in 29.4% of cases including 5 patients with threatening hypertension, oligo-anuria in 20.5% of cases. Paraclinically, acute renal failure was observed in 83.3% of patients, nephrotic proteinuria in 55.8% of cases. The evolution was favorable in all patients in the short, medium and long term. only 2 patients are required Peritoneal dialysis .

Conclusion: PIGN remains a significant contributor to morbidity in children. Prevention through screening, correct treatment of any infection likely to cause GNA and improving living conditions are the pillars of care.

1394 - P1.198

HEMOLYTIC UREMIC SYNDROME: SINGLE CENTER EXPERIENCE

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Aims/Purpose: A triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute renal dysfunction characterizes hemolytic uremic syndrome (HUS). In children most common is diarrhea-associated HUS and only in 5-10% of cases atypical HUS is diagnosed. In this paper we aimed to present clinical features, severity, management and outcomes of HUS in our unit.

Methods: Retrospective study of HUS patients admitted to our tertiary Pediatric Nephrology Unit between 2010 and 2024. From the charts were obtained demographic and clinical data regarding etiology, clinical manifestations, severity, treatment, and outcome.

Results: Thirty-two patients with HUS were admitted to our unit in this period. The study group consisted of 19 females (59%) and the median age at diagnosis was 2 years (2 months - 8 years). Frequent clinical manifestations were diarrhea 75%, vomiting 50%, hypertension 65%, oliguria 47%, and fever 28%. Shiga toxin-producing Escherichia coli was confirmed only in 6 cases (19%), 13 cases were secondary HUS due to respiratory infections and 13 cases were atypical HUS according to analysis of the complement profile. In the acute phase, renal replacement therapy was implemented in 47% of cases, equally in PD and HD. Complement blockade therapy was implemented in two children and one of the children was treated with immunosuppressive therapy due to the presence of anti-factor H antibodies. Concerning the outcome, 62% of the children had normal renal outcomes, 12.5% progressed to CKD, five children were lost from follow-up because they left the country and three children died.

Conclusions: These results confirmed a high number of secondary and atypical HUS. Complement profile testing is particularly necessary for STEC-negative HUS and when another infectious agent cannot be detected.

1396 - P1.199

NON-NEPHROTIC PROTEINURIA: IS IT A DIAGNOSTIC CHALLENGE IN PEDIATRIC NEPHROLOGY OUTPATIENT CLINICS?

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Aim: Proteinuria is defined as presence of abnormal amounts of protein in the urine and is a frequent reason for admission to pediatric nephrology outpatient clinics. In this study, we aimed to evaluate the demographic, clinical and laboratory findings of patients who were referred to the pediatric nephrology outpatient clinic due to proteinuria.

Methods: The data of patients who applied to the Pediatric Nephrology Outpatient Clinics of Ankara Bilkent City Hospital between September 2021 and August 2023 and whose ICD diagnosis code was "Isolated proteinuria" were evaluated retrospectively. Patients who were previously under follow-up due to a nephrological disease were not included in the study. The data of 143 patients were analyzed with SPSS Statistics 17.0 program.

Results: Male/female ratio was 64/79, mean age of the group was 11.48 ± 4.35, median age was 12 (min-max 1-17). Fifty-six (39.2%) patients had orthostatic proteinuria, 66 (46.2%) patients had transient proteinuria, and 21 (14.7%) patients had persistent proteinuria. Microscopic hematuria was accompanied in 13 patients. There was a family history of kidney disease in 23 (16%) patients. None of the patients had hypertension. There was a history of urinary tract infection in 9 (6.3%) patients. Hypoalbuminemia was not found in any patient. Complement 3 (C3) and complement 4 (C4) levels were examined in 74 patients. C3 was low in only 3 patients, and C4 was normal in all patients. Beta-2 microglobulin was tested in the urine of 27 patients, and elevation was detected in 5 of them. Nutcracker phenomenon was detected in 51 of 95 patients who underwent left renal vein Doppler . No scar was detected in any of the 11 patients in whom DMSA was applied. No patient had a biopsy during this period. At the last follow-up, it was observed that proteinuria improved in 82 (57.3%) of the patients, continued as orthostatic proteinuria in 37% (25.9%), and persistent proteinuria persisted in 21 (14.7%) patients. No abnormal findings were noted in any of the 25 (17.5%) patients who underwent ophthalmological examination. Hearing test was performed on 23 patients, sensorineural hearing loss was recorded in 1 patient and conductive hearing loss was recorded in 1 patient.

Conclusion: Detection of protein in urinalysis is a common condition in children, and in cases where serum albumin level and serum creatinine are normal, it is usually not accompanied by a serious underlying nephrological problem. Proteinuria in adolescent children is often caused by orthostatics and is often accompanied by the Nutcracker phenomenon. It is thought that checking the spot protein/creatinine ratio in the first morning urine sample of patients with proteinuria detected in urinalysis during routine examinations will eliminate the majority of nephrological applications due to proteinuria.

Key words: Proteinuria, nutcracker, ortosthatic

1400 - P1.200

FOCAL SEGMENTAL GLOMERULOSCLEROSIS IN THE GIRL WITH MIRAGE SYNDROME

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Aim/Purpose: MIRAGE syndrome is a rare genetic disorder caused by a mutation within the SAMD9 gene. The clinical course is complicated with multiorgan involvement. Only a few cases are reported, some of which have renal manifestations.

Methods: A case report of the patient who has been followed at our tertiary hospital since 2012.

Results: A girl was born in the 34th week of pregnancy with a birth weight of 1.2 kg. During the neonatal period, she experienced a CMV infection. As a toddler, she suffered from unclear anemia. Since the age of three, a urine test manifested moderate albuminuria with subsequently low serum albumin levels. The patient has been treated with a RAAS blockade but with limited effect.

Table 1. Diagnostic tests

Kidney biopsies	**2015**	**2020**
	Discrete changes were estimated as the initial stages of FSGS.	3 of 21 glomeruli were totally and 4 partially sclerosed; muscle hyperplasia in arterioles
GFR ml/min/1,73 m ^{2}	>90	61

Table 2. Syndromes manifestations

Clinical manifestations of the syndrome	Symptoms and signs in our patient
Myelodysplasia	Bone marrow aspirate with hypocellularity, with some maturation disturbance in all cell lines but no significant dysplasia
Infection	Upper respiratory tract infections, pneumonia
Restricted growth	Extreme weight restriction with weight 26 kg and height 149 cm at the age of 14.
Adrenal hypoplasia	Treated with Hydrocortisone
Genital phenotypes	Female genotype, no signs of puberty
Enteropathy	She experiences recurrent vomiting and diarrhea associated with malabsorption syndrome is orally and enterally nourished via gastrostomy and treated with pancreatic enzyme

The patient has skeletal deformities and scoliosis. Additionally, she has also low serum phosphate levels. The girl was diagnosed with autism with a slight mental status retardation. The magnetic resonance imaging of the brain demonstrated calcifications in white substance. Her fluid status and overall well-being significantly worsen by almost daily episodes of chills and profuse sweating.

Conclusion: The patient we present has progressive kidney disease with GFR decreasing. In some patients with MIRAGE syndrome, albuminuria of varying severity is described. However, to our knowledge, only one patient has been reported in whom kidney pathology has been confirmed by biopsy. We certainly require additional clinical data on patients with Mirage syndrome, along with multidisciplinary international collaboration, to evaluate prognosis and determine the most effective support.

1404 - P1.201

UNDERSTANDING TINU SYNDROME: A CASE REPORT IN A 15-YEAR-OLD GIRL

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Aims: Tubulointerstitial Nephritis and Uveitis Syndrome (TINU) represents a rare manifestation characterized by bilateral anterior uveitis concurrent with acute renal interstitial inflammation, occurring independently of other systemic pathologies predisposing to either interstitial nephritis or uveitis. Typically, the uveitis presents as mild, and the nephritis exhibits a self-limited course. Nonetheless, instances of chronic uveitis and progressive renal impairment have been documented, underscoring the contemporary significance accorded to TINU syndrome. Prompt identification of both nephritis and uveitis stands as a pivotal determinant for achieving therapeutic efficacy.

Case report: We present a case study of a 15-year-old girl diagnosed with TINU syndrome. Initial onset of the disease manifested at age 14 with abdominal discomfort, progressing gradually to bilateral lumbar pain. Concurrently, the patient exhibited symptoms of anorexia accompanied by significant weight loss, prompting hospital admission for further evaluation. Laboratory investigations revealed elevated serum creatinine levels alongside indicators of tubular injury in urinalysis, suggestive of tubulointerstitial nephritis. Expanded diagnostic assessment unveiled iridocyclitis. Subsequent referral to our Department facilitated a kidney biopsy, confirming the diagnosis of acute tubulointerstitial nephritis. Corticosteroid therapy initiation post-biopsy led to a progressive amelioration of creatinine levels and reduction in proteinuria. Ophthalmologic surveillance, coupled with local uveitis treatment, was diligently maintained. Notably, during subsequent follow-up evaluations, the patient exhibited complete recovery, devoid of any residual kidney impairment or uveitis manifestations.

Conclusion: TINU syndrome represents a rare yet clinically significant oculorenal inflammatory disorder, necessitating comprehensive diagnostic examination for timely recognition. TINU syndrome poses a notable threat to patient health, accounting for a substantial proportion, up to 15%, of acute kidney injury cases. Notably, the prevalence of uveitis in individuals with tubulointerstitial nephritis may surpass current estimations, particularly among pediatric cohorts. Consequently, heightened vigilance is warranted in patients presenting with nephritis, mandating further investigative protocols to either rule out or promptly initiate treatment for TINU syndrome, thereby mitigating potential disease sequelae.

1412 - P1.202

CHRONIC KIDNEY DISEASE CAUSED BY AN ATYPICAL COURSE OF BARTONELLA HENSELAE INFECTION

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Aim: Our aim is to present an atypical course of Bartonella henselae infection in a 7 year old girl who was previously operated on for pulmonary atresia.

Method, Results: She was presented with chronic kidney disease at our institution in Nov. 2023. Hepato-, splenomegaly without lymphadenomegaly was found in Oct. 2022. on a routine pediatric examination. No infectologic, hematologic, oncologic cause was revealed that time. Her cardiac state was stable, according to regular echocardiologic results. GFR was 21ml/min/1,73m^2, but urinanalysis showed no abnormality. The last previous data on her kidney function is from 2019, and it was in the normal value for her age. From Dec. 2022. she neeeded intensive care because of acute myocarditis. No causative agent was found. Hepato-, splenomegaly was still observable and it did not improve along with cardiac function. No vegetation was detected in her heart. Her GFR deteriorated during the next 8 months. Microscopic hematuria was detected twice without any degree of proteinura, but it was not seen any more. Regular echocardiologic examinations showed improvement of cardiac function, endocarditis was not detected. She had no history of fever, lymphadenopathy, skin lesions or other complains during and before this period. Nephrologic workup revealed PR3 ANCA- and mild ANA-positivity, increased c1q and MAC level, presence of amiloid A and mild hypergammaglobulinaemia. Fluctuating but constant mild elevation of CRP level with the above mentioned results increased the suspicion of chronic infection. Eventhough there was no data on close contact with cats or other animals, neither on typical symptoms of zoonosis, serologic test and PCR assay proved Bartonella hensalae infection. Ultrasonography showed multiple small echogenic lesions in the visceral organs. Echocardiography proved vegetation on the pulmonary valve this time. After 3 weeks of combined (ceftriaxon/tetracyclin and amikacin) therapy the PCR became negative and the affected pulmonary valve was changed. During the 6 weeks postoperative course of doxycyclin therapy PCR remained negative. Significant improvement of kidney function was already observable after 2 weeks of antibiotic therapy, GFR increased to 70 ml/min/1,73m^2 during the 10 weeks of treatment. With stablely negative PCR result and no signs of inflammation on FDG-PET CT scan doxyciclin therapy was stopped.

Conclusion: Bartonella infection is an underrecognised disease with variable clinical presentation. Kidney involvement is generally known as a consequance of endocarditis and with manifestation of proliferative glomerulonephritis. The successfull antibiotic treatment highlights the importance of a detailed workup for infectious diseases not only in cases of typical clinical presentation of GN, but also in cases of silent chronic kidney diseases, especially with other organ involvement.

1416 - P1.203

OUTCOMES OF STEROID RESISTANT NEPHROTIC SYNDROME IN CHILDREN IN KAZAKHSTAN: A TERTIARY MEDICAL CENTER EXPERIENCE

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Aims/Purpose: Steroid resistant nephrotic syndrome (SRNS) remains a challenging condition in pediatric nephrology. We aimed to retrospectively analyze the outcomes of SRNS cases admitted to our center.

Methods: Children from birth to 18 years of age with SRNS admitted from 2016 to 2022 were included to the study. Clinical, histopathologic data and treatment outcomes were collected and analyzed using SPSS.

Results: 178 children with SRNS were selected. Characteristics of the cohort and outcomes after 1 year on intensified immunosuppression (IIS) are presented in Table 1. Cyclosporin was used in 78% of cases as initial IIS. Older age at disease manifestation and female gender were predictive of higher probability to achieve complete remission (CR) within the 1st year ($p < 0.05$). By the end of follow-up, 35% were in CR, 17% had partial, 48% had no remission. 24% developed ESKD, 25 of them were transplanted and 3 (12%) had disease recurrence with graft loss. 12 (7.3%) children died. The overall, 1-year and 5-year ESKD-free survival rates were 90.7% and 71.8%, respectively. By multivariate Cox regression model, only no response to IIS in the 1st year was independently associated with ESKD development (Table 2).

Conclusion: This is the first analysis of outcomes in children with SRNS in Kazakhstan. We observed a high prevalence of non-responsive to IIS cases with FSGS and poor outcomes. This finding may be explained in part by selective admission of severe cases from across the country to our tertiary center.

Table 1. Characteristics of studied cohort

Characteristic	N=178	Characteristic	N=178
Gender: Male	109 (61.2%)	Kidney biopsy:	105 (59%)
Disease onset:		FSGS	84 (80%)
Age, median (IQR), mo	67 (12.5 – 117)	MCD	7 (6.7%)
Age < 1 yo	30 (16.8%)	MesPGN	7 (6.7%)
Hypertension	48 (27%)	MN	5 (4.8%)
Hematuria	69 (38.8%)	IgM-nephropathy	2 (1.9%)
eGFR (mL/min/1.73m2), median (IQR)	98 (72 – 120)	Outcome after 1 year on IIS	141 (79%)
eGFR < 60 mL/min/1.73m2	30 (16.9%)	Complete remission	40 (28.4%)
Resistance:		Partial remission	32 (22.7%)
Initial	125 (70.25%)	No remission	62 (44%)
Late	36 (19.7%)	Death	7 (5%)
Infantile NS not treated with steroids	17 (9.6%)	Time to late SRNS, median (IQR), mo	9 (6 – 18.7)
		Time to complete remission, median (IQR), mo	6 (4 – 14.7)
		Follow-up, median (IQR), mo	32 (12.5 – 67)

Table 2. Predictors for ESKD (Cox regression analysis)

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p	HR (95% CI)	p
Age at onset	0.99 (0.98-0.99)	0.01	0.99 (0.99-1.01)	0.54
Gender (Ref: boys)	1.02 (0.53-1.96)	0.964		
GFR at onset	0.98 (0.98-0.99)	0.009	0.99 (0.99-1.01)	0.79
GFR at onset <60ml/min	2.81 (1.33-5.94)	0.007	2.11 (0.62-7.18)	0.23
Hypertension (Ref: no)	1.69 (0.85-3.35)	0.131		
Hematuria (Ref: no)	0.91 (0.46-1.8)	0.781		
Initial resistance (Ref: late)	10.14 (2.34-43.94)	0.002	4.16 (0.92-18.77)	0.06
FSGS on biopsy (reference: MCD)	1.56 (0.35-6.96)	0.557		
NR after 1 year on IIS (Ref: CR+PR)	13.7 (4.86-39.11)	0.0001	8.87 (3.01-26.18)	0.0001

1419 - P1.204

VARIANTS OF NPHS2 GENE PRESENTING WITH GLOMERULAR PROTEINURIA WITHOUT AN OVERT NEPHROTIC SYNDROME

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Aims/Purpose/Introduction: Mutations of the NPHS2 gene encoding podocin are the main cause of autosomal recessive steroid resistant nephrotic syndrome (SRNS). However, it can also manifest as sporadic in both pediatric or adult patients. The R229Q polymorphism (p.R229Q) of NPHS2 gene has been increasingly identified, being only pathogenic when trans-associated to specific mutations, with a wide spectrum of clinical presentation. We report 3 cases.

Results/Case Report: The first one is a 2-years old boy with glomerular proteinuria detected after a urinary tract infection. During the follow-up presented albuminemia in the lower limit of normal (3.1 g/dL) with nephrotic proteinuria (urine protein-creatinine ratio (UPCR) of 3.3 mg/ mg) and dyslipidemia, without clinical manifestations of NS. Among others complementary tests, was submitted to a genetic study that identified the R229Q variant associated with a pathogenic mutation of NPHS2. He is under a symptomatic treatment with a statin and high doses of an angiotensin converting enzyme inhibitor (ACEI), showing an improvement in proteinuria (UPCR 0.63 mg/ mg). After his diagnosis, the family genetic screening identified the same variant in compound heterozygosity in his sister, who until now remains asymptomatic, at 16 years of age. Both parents are healthy carriers. The third case is a 11-year-old girl, who presented oscillating bimalleolar and periorbital edemas and glomerular proteinuria (UPCR 3 mg/ mg) without hypoalbuminemia. The R229Q polymorphism combined with other different pathogenic mutation of NPHS2 was identified in the genetic study and presently is requiring increasing doses of an ACEI to reduce proteinuria. Currently, the 3 patients maintain surveillance in pediatric nephrology with a normal kidney function.

Conclusion: Heterozygous NPHS2 mutations may play a role in atypical cases of SRNS with a later onset but also in isolated moderate to nephrotic proteinuria, without NS. Identifying these patients for follow-up and early treatment can mitigate or delay the progression of the disease. Further studies, which specify clinical and pathological details of the patients, will help to define whether there are specific populations that warrant systematic testing.

1424 - P1.205

THE ROLE OF DRUG MONITORING IN THE TREATMENT OF MMF AND CYCLOSPORINE A IN CHILDREN WITH STEROID-DEPENDENT NEPHROTIC SYNDROME

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The severe side effects of long-term corticosteroid therapy complicate the treatment of children with nephrotic syndrome. We conducted a single-center comparative retrospective study of the effectiveness of MMF and cyclosporine A in children with steroid-dependent nephrotic syndrome. Drug exposure is best represented by the "area under the time-concentration curve" (AUC), but it is labor-intensive and costly. Therefore, a single time-point measurement (C0) is often utilized

Objective: To demonstrate the relationship of drug monitoring of MMF and cyclosporine with afficasy in the treatment of steroid-dependent nephrotic syndrome in children

Materials and Methods: The study included 33 children with steroid-dependent nephrotic syndrome. Of these, 17 (10 male) children received cyclosporine A in mean dose 4,67 мг/кг/сут, and 16 (11 male) MMF in mean dose 1029 мг/1.73м2/сут. Duration of the disease was 3.0 vs 2.0 year (p =0.2), age of initiation of therapy was 7.0 vs 6.5 years (p =0.58) and the number of relapses before therapy was 8 vs 5, respectively (p =0.09). In both groups, the concentration of the drug was studied 12 hours after administration (C0)

Results: It was noted that in the cyclosporine A therapy group, the rate of relapses per year did not differ significantly from MMF therapy for 12 months (1.3 and 1.5 respectively, p =0.9). In the cyclosporine therapy group, the rate of relapses per year with C0 < 100 ng/ml (was greater than with C0 > 100 ng/ml (2.3 vs 0.6 respectively, p =0.01). Relapse of nephrotic syndrome was noted in 5/7 (71%) in the group of children with C0 < 100 ng/ml and in 3/10 (30%) with C0 > 100 ng/ml. In the MMF therapy group, the frequency of relapses per year was higher in children with C0 < 3 ng/ml than with C0 > 3 ng/ml (3 and 0.6, respectively, p =0.001). Relapse of nephrotic syndrome developed in all (100%) with C0 < 3 ng/ml, in 4/6 after 2 months and 2/6 after 6 months of therapy, with C0 > 3 ng/ml - in 3/10 (30%).

Conclusions: Drug monitoring of dose-dependent drugs (cyclosporine A and MMF) allows prolongation of disease remission in steroid-dependent nephrotic syndrome.

1425 - P1.206

A PATIENT WITH GLYCOGEN STORAGE DISEASE TYPE 1B PRESENTED WITH PROTEINURIA

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Aim: To describe renal manifestations in Glycogen storage disease type Ib (GSD Ib) in a pediatric patient. An 11-years-old girl with GSD Ib presented with 2 episodes of macrohematuria which resolved spontaneously. followed by persistent proteinuria (protein/creatinine was 2571 mg/g albumin/creatinine was 1740 mg/g). Blood pressure and renal function where normal. Laboratory investigation revealed increased immunoglobulin A (IGA) 457 mg/dl (reference range 61-348 mg/dl), normal complement and ANA. Renal biopsy revealed mesangial hypercellularity with segmental glomerulosclerosis. immunofluorescence demonstrated IGA deposition (++) in the mesangium, Findings consistent with IGA nephropathy. The patient commenced on ACE inhibitor and albuminuria decreased (albumin/creatinine was 76 mg/g). Two years later, on routine follow up, hypertension (139/80 mmHG), massive proteinuria (protein/creatinine 11000 mg/g, albumin/creatinine 4700 mg/g) and abnormal renal function (creatinine was 1.4 mg/dl) were noticed. Blood albumin was 3.1g/dl. A Second renal biopsy reveals findings consistent with IGA nephropathy without crescents, with no evidence of glycogen deposition.

Discussion: We present for the first time a pediatric patient with GSD Ib who developed CKD due to IGA nephropathy. The renal pathology described in adult GSD Ib patients resembles diabetic nephropathy: Glomerular hyperfiltration accompanied by microalbuminuria, in some patients evolving to proteinuria, Focal segmental glomerulosclerosis, and renal insufficiency. Other reported renal complications include nephrocalcinosis, gouty nephropathy, AA amyloid deposition, glycogen deposition and Fanconi-like syndrome.

Conclusion: IgA nephropathy may be associated with GSD Ib.

Keywords: Glycogen storage disease, IGA nephropathy, Case presentation

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1446 - P1.207

UPDATES IN ANCA - ASSOCIATED VASCULITIS

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Background: Antineutrophil Cytoplasmic Antibodies (ANCA) associated vasculitis (AAV) is a rare entity in childhood. However, renal involvement is frequent in up to 90% of cases but is not well discussed in literature.

Objectives: The aim of this retrospective study is to describe cases of AAV among the population of Pediatric Nephrology Santobono children's Hospital.

Methods: We analyzed ten patients diagnosed as AAV, in accordance with EULAR/PReS criteria. We evaluated renal function at onset, ANCA antibody titer, renal biopsy findings, proteinuria and hematuria at onset, induction and maintenance therapy performed, need for hemodialysis, need for plasmapheresis, outcome.

Results: All patients presented with acute renal failure at onset with average value of Schwartz eGFR of 32 mL/min. They showed proteinuria in non-nephrotic range with average value of 1800 mg/day. Glomerular hematuria was found in all patients. Renal ultrasound showed cortical hyper echogenicity in 70% of patients in absence of other anomalies. Three patients required at least one hemodialysis session at onset. All patients required renal biopsy with the finding of ANCA glomerulonephritis associated with extracapillary proliferation and glomerular sclerosis in more than 50% of the glomeruli in 70% of patients. All patients analyzed were ANCA-positive: 5 were affected by microscopic polyangiitis, 5 by granulomatosis with polyangiitis. As induction therapy, all patients underwent steroid pulses; in addition, Cyclophosphamide was administered in 6 patients, while Rituximab in 2 others. In a single patient, plasmapheresis was performed in association with steroid pulses and Rituximab. 70% of patients underwent in complete remission. The median follow-up of the population was 115 months instead of 70 months of those treated with Rituximab +/- plasmapheresis. At the last follow-up only 3 patients had chronic kidney disease (CKD) (one patient went on hemodialysis replacement therapy, one patient had renal transplant and one was classified as stage V CKD).

Conclusions: Renal involvement was highlighted in all the patients. Patients treated with Rituximab and/or plasmapheresis, in comparison to those treated with Prednisone plus Cyclophosphamide, did not show relapses after remission. However, the number of cases is too small, and the follow-up of patients treated with Rituximab and/or plasmapheresis is shorter than those treated with Cyclophosphamide and Prednisone. The renal outcome shows a recovery rate of 70% and this data appears to be more favorable compared with adult patients. 70% of patients do not require renal replacement therapy, showing that AAV if diagnosed in time, can be controlled using current therapeutic approaches.

1464 - P1.208

AN UNCOMMON CAUSE OF THROMBOTIC MICROANGIOPATHY IN A CHILD WITH SPINAL MUSCULAR ATROPHY TYPE 1

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Aims: Atypical Hemolytic Uremic Syndrome (aHUS) is a condition characterized by microangiopathic hemolytic anemia, thrombocytopenia and acute kidney injury. It can have genetic, infectious or drug-related causes. The differentiation between complement mediated aHUS and secondary thrombotic microangiopathy (TMA) relies on identifying a clear cause. We present a patient with Spinal Muscular Atrophy Type I (SMA) who developed TMA secondary to the infusion of Onasemnogene abeparvovec.

Methods: Case report.

Results: Onasemnogene abeparvovec (ZolgensmaR) is a gene replacement therapy that uses a non-replicating adeno-associated virus (AAV9) to introduce a copy of the SMN1 gene, which is altered in patients with SMA. Although TMA is a rare complication of ZolgensmaR, its potential morbidity warrants suspicion. The patient is a 23-month-old female with Spinal Muscular Atrophy Type 1 who was referred for the infusion of ZolgensmaR. She had received seven previous infusions of Nusinersen (SpinrazaR), another treatment for SMA. Ten days after the ZolgensmaR infusion, she presented with vomiting, fever, diarrhea, petechiae and decreased urine output. Laboratory results showed microangiopathic hemolytic anemia (hemoglobin 8.4 mg/dl, lactate dehydrogenase 4400 UI/l, schistocytes in peripheral blood, haptoglobin 7.2 mg/dl), thrombocytopenia (platelet count 45000/mm3), acute kidney injury (urea 237 mg/dl, creatinine 1.96 mg/dl), electrolyte imbalances (plasma sodium 120 meq/lt), low complement levels (C3 64 mg/dl, C4 7 mg/dl), proteinuria and hematuria with hemoglobinuria. Due to oligoanuric kidney injury, we began renal replacemente therapy. Her course was complicated by posterior reversible encephalopathy syndrome. Given the neurological involvement, refractory hypertension and low complement levels, the decision was made to perform therapeutic plasma exchange (PE). After ruling out other causes of TMA, such as Shiga toxin-producing Escherichia coli (STEC) infection and thrombotic thrombocytopenic purpura, evidence of complement inappropriately activation was suggest by low C3 serum levels and high levels of C5b9. After evidence of nonresponse, PE was stopped and complement-inhibiting therapy with Eculizumab was initiated, prescribing two doses according to the infusion protocol. Within 96 hours of first Eculizumab infusion, the patient recovered from acute kidney failure, with complete hematologic remission.

Conclusion: TMA is associated with increased mortality and morbidity, including end-stage renal disease. Given the limited number of pediatric TMA cases secondary to Onasemnogene abeparvovec reported in the literature, this case highlights the importance of monitoring for early complications and timely intervention to improve outcomes. Additionally, our patient responded well to the Eculizumab infusion making this case exceptional.

1465 - P1.209

SPONTANEUS COMPLETE REMISSION OF INFANTILE NEPHROTIC SYNDROME

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Aims: We report spontaneous remission in an infant with nephrotic syndrome.

Methods: Case report.

Results: A four-month-old boy presented with eyelid and foot edema, hypoalbuminemia 17 g/L (28-47) and proteinuria with u-albumin/creatinine ratio 2323 g/mol (< 3.0). Microscopic hematuria was present as well. The patient was hypertensive 117/67 mmHg (> 95th percentile). Creatinine was 11 µmol/L (14-42). Mild glanular hypospadia was found but no dysmorphic features. Enlarged kidneys with hyperechogenic cortex and decreased corticomedullary differentiation was detected by ultrasound. Serological tests for toxoplasma, rubella, syphilis, CMV and herpes simplex virus were negative. IgM for parvovirus B19 was marginally elevated, however PCR was negative. Hepatitis B and C were ruled out. Immunological workup for antineutrophil antibodies, antineutrophil cytoplasmic antibodies, complement C3, C4 were unremarkable. Kidney biopsy was performed percutaneously ten days after presentation. Light microscopy showed 36 normal glomeruli. No immune deposits were detected by immunofluorescence investigation. Electron microscopy revealed severe podocyte foot process effacement. Genetic testing was negative (Blueprint genetics Nephrotic syndrome panel (version 3 2018), 35 genes: ACTN4*, ADCK4, ANLN, ARHGAP24, ARHGDIA, CD2AP, COL4A3, COL4A4, COL4A5, COQ2, CRB2, DGKE, EMP2, FAN1, FN1, INF2, ITGA3, LAMB2, LMX1B, MAFB, MAGI2, MYH9, MYO1E, NPHS1, NPHS2, NUP107, PLCE1, PTPRO, SCARB2, SGPL1, SMARCAL1, TRPC6, TTC21B, WDR73 and WT1). The patient received treatment with angiotensin-converting enzyme inhibitor captopril and coenzyme Q10. Albumin infusions and diuretics were not prescribed. Dalteparin was administered for five days. The patient's condition improved, and immunosuppressive treatment was not initiated. Proteinuria resolved within three weeks. Captopril treatment was continued for five months due to hyperfiltration. Corrective surgery for hypospadia was performed at age of 2.5 years. During a five-year follow-up period, no relapse occurred, and kidney function remained normal.

Conclusion: Most patients with infantile nephrotic syndrome have a genetic basis for the kidney disease and poor outcomes. However, minimal change disease has been reported in some infants. For these cases, treatment with corticosteroids is recommended, following the same approach as for older children. We report spontaneous remission in an infant with minimal change disease in order to raise awareness of a subgroup of patients with good prognosis, advocating for initial expectancy for immunosuppressive treatment.

POSTE SESSION 2

57 - P2.001

DERMATOLOGICAL MANIFESTATIONS IN PEDIATRIC CHRONIC KIDNEY DISEASE PATIENTS

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Aims/Purpose:

This study aimed primarily to screen the different dermatological manifestations in pediatric patients with CKD, in addition to studying the relationship of dermatological manifestations with the CKD stage, types of dialysis, various clinical and metabolic parameters, based on the fact of chronic kidney disease (CKD), regardless of its cause, may be accompanied by various skin lesions. Data on different skin lesions in children with CKD is very limited; only few reports have been published discussing xerosis in pediatric patients and most studies were conducted on a small number of patients who needed renal replacement therapy.

Methods: This was a cross sectional study conducted on 70 patients were enrolled in our study being divided into two groups: group 1 including CKD patients stages (2-4) and group 2 including CKD patients with stage 5 on regular hemodialysis. Detailed dermatological & nail examination were conducted. Xerosis severity was assessed using a four-point xerosis assessment scale (0, normal skin, without any xerosis; 1, mild xerosis; 2, moderately dry skin with minimal flaking; 3, severe xerosis, heavy scaling visible), whereas pruritus was assessed using a visual analogue scale (VAS) on a scale of 1 (no itch) to 10 (worst possible itch). Laboratory data were withdrawn at the time of examination to correlate with different dermatological manifestation.

Results: In our study, xerosis was the most frequent dermatological manifestation (78.6%) following it pruritus (62.9%) then pallor (35.7%), hyperpigmentation (20%), hypertrichosis (10 %), nail and hair abnormalities (8.5%) & post inflammatory hyperpigmentation (4.3%). The prevalence of xerosis was not affected by clinico-demographic data, CKD duration & stage, type and duration of dialysis, the only significant relation was between efficacy of dialysis (Kt/V) and incidence of xerosis, where the higher dialysis efficacy rates were associated with low incidence rates of xerosis, in which effective hemodialysis contributes to better removal of uremic toxins, & hence decrease the xerosis. Leukocytosis was noticed in xerotic & pruritic patients, where xerosis & impaired skin barrier in children with CKD pose a risk for different cutaneous infections & inflammation, and hence pruritis.

Conclusion: Xerosis and pruritis are not uncommon dermatological manifestations among pediatric patients with chronic kidney disease, meanwhile the age of the patients and the underlying CKD etiology had no direct effect on skin changes. The most determinant factor affecting the xerosis was the hemodialysis efficacy, where higher efficacy was associated with less xerosis, meanwhile leukocytosis was associated with higher xerosis and pruritis.

62 - P2.002

THE INTERPLAY OF SERUM TRACE ELEMENT AND CARDIOVASCULAR STATUS IN PEDITARIC CHRONIC KIDNEY DISEASE PATIENTS

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Aims/Purpose: Trace elements blood levels are very important in cardiovascular structure & function, based on this knowledge, we studied trace elements blood levels & cardiovascular events which was identified as systolic, diastolic blood, hypertension (controlled or uncontrolled), echocardiographic findings (presence of left ventricular dysfunction & ejection fraction % {EF %})

Methods: This was a cross sectional study, that was conducted on 60 pediatric CKD5d patients, with similar number of age & gender matched controls, where serum Zn, Cu, Pb, cadmium, & Mn were measured and correlated with blood pressure & echocardiographic findings (Left ventricular dysfunction, & ejection fraction % {EF%})

Results: There was significant decrease in serum Cu and Pb levels in CKD5d patients (t = 3.066, 4.282, p =0.003, < 0.001 respectively) than controls. The mean EF % (± SD) was 10.22 (± 60.36) %, where 8 patients (13.3%) had left ventricular systolic dysfunction. Serum Cu level was associated with higher diastolic BP & lower EF% (r = 0.303, -0.281, p =0.019, 0.030). Regarding blood cadmium levels, albeit normal, a negative correlation with EF% was found, & was confirmed in a multiple regression model of analysis (B = - 17.85, p =0.01). Serum zinc was positively correlated with EF % (B = 0.305, p =0.022).

Conclusion: CKD patients have an imbalanced trace elements status & abnormal cardiac status. Serum Zn, Cu & cadmium had significant effects on cardiac status in our CKD5d patients.

63 - P2.003

IGG4 RELATED DISEASE AND RENAL DILEMMA

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Aims/Purpose: IgG4-related disease (IgG4-RD) is a multisystemic disease that is characterized by lymphoplasmacytic infiltrate, fibrosis, obliterative phlebitis, and increased IgG4+ plasma cells, and occasional higher serum level of IgG4. Any organ can be affected; however, pancreas, kidneys, orbit, salivary glands, and retroperitoneum are the most frequently affected. Hereby we report a girl who was diagnosed as an idiopathic chronic pancreatitis, which developed a renal impaired during her follow up which proved to be due to obstructive uropathy and retroperitoneal fibrosis (RPF), where surgical decompression was done, and the mass biopsy was heavily infiltrated with inflammatory cells including plasma cell that was positive for IgG4, which was highly elevated in serum level.

Methods: A 9-year-old girl, presented with recurrent attacks of epigastric pain, jaundice & low-grade fever, with increased pancreatic & liver enzymes. CT abdomen showed diffuse enlargement of pancreas, with local swelling at head of pancreas. MRCP showed segmentally narrowed pancreatic duct, with no obstruction. Investigations revealed high pancreatic enzyme & impaired renal functions, where the diagnosis of uremic pancreatitis was proposed. Abdominal U/S showed right sided hydronephrosis, a poorly marginated, periaortic mass, where CT with contrast revealed a confluent mass encasing sides of the Aorta, compressing IVC & mid-ureter with right sided hydronephrosis, dilated upper ureter with medial deviation of proximal ureter.

Results: Surgical removal of the mass with decompression of ureters and IVC, with insertion of indwelling ureteral stent was done, where the mass was histopathological examined & there were infiltrates with macrophages, plasma cells, B and T lymphocytes, where most plasma cells were positive for immunoglobulin G4 (IgG4). Serum level of igG4 was positive, where the diagnosis of igG4 related disease was confirmed, thereby therapy was stated with steroid with marked resolution of abdominal pain and fever, 1 month follow up, the patient had attack of fever and pancreatitis, and RPF increased, upon which Mycophenolate Mofetil was added that improved the disease activity, with no flare ups over 3 years follow up.

Conclusion: IgG4 RD should be considered in any patient with chronic pancreatitis, especially if was associated with other multisystem affection, especially RPF. Early diagnosis and prompt management is necessary for prevention of morbidity and mortality.

80 - P2.004

ROLE OF URINARY NGAL AS A MARKER OF NEPHROTOXICITY IN CHILDREN UNDERGOING CHEMOTHERAPY

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Aims/Purpose: To elucidate the role of urinary NGAL (Neutrophil gelatinase- associated lipocalin) as an early marker of acute kidney injury in cancer children undergoing chemotherapy

Methods: 40 children, a total of 116 chemotherapy cycles, were studied, with urinary NGAL levels measured before and 12 hours after the end of therapy. FEFi (fractionated phosphate excretion) was also studied as a marker for the occurrence of tubular damage resulting from nephrotoxicity, as well as 30 children who finished their treatment more than a year ago, for chronic kidney disease

Results: A statistically significant difference was observed in NGAL levels before and at the 12th hour after a chemotherapy cycle in patients who have completed or undergone their second (Z = -2.908, p =0.004) and third cycle (Z = -2.737, p =0.006), as well as in those with more than 4 chemotherapy cycles completed (Z = -2.678, p =0.007). However, NGAL levels remained within their reference ranges. Statistically significant lower levels of NGAL were observed at 12th hour after more than 3 chemotherapy cycles, particularly with the use of drugs with higher toxicity (U = 110.5, p =0.024). A statistically significant increase in the fractional excretion of phosphates at the 12th hour was also found, both after a single cycle and after more than one chemotherapy cycle. In the children who finished their chemotherapy more than one year ago, the stage of CKD (chronic kidney disease) by the generally accepted criteria of KDIGO - eGFR (glomerular filtration rate) and proteinuria was found in 11 of 30 children (36%), while elevated NGAL values in only two of them (6.6%).

Conclusion: NGAL, as a marker of nephrotoxicity, is nonspecific and unreliable, both for the onset of acute kidney injury and as a marker for the onset of chronic kidney disease. Fractional phosphate excretion, as a marker of established tubular injury, is highly specific for acute kidney injury, including subclinical injury caused by nephrotoxic drug therapy. It is suggested that Fractional Phosphate Excretion should be included in the routine follow-up for the occurrence of acute kidney injury, including subclinical injury, in all patients undergoing chemotherapy with nephrotoxic drugs.

82 - P2.005

THE NEED FOR SERVICE EVALUATION FOR YOUNG PEOPLE WITH CHRONIC KIDNEY DISEASE (CKD)

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Understanding social and clinical networks and commissioning for young people with CKD is paramount. This article provides a descriptive summary on the need for service evaluation for young people with Chronic Kidney Disease (CKD). Treatment costs for young people with CKD are not a trivial matter and service evaluation of the costs in an economic evaluation may provide the most efficient use of scarce healthcare resources. Having a better understanding of social and clinical care networks between health sectors will allow better integration of services so that providers and decision-makers know how best to allocate funding and practice for young people. Because social media, mobile and device technology are prevalent, healthcare professionals also need to consider the merits of engaging with young people to help advance renal services. Certainly, more qualitative data is needed to reflect real perspectives of young people with CKD and inform where investments should be made. Keywords: Paediatrics, Nephrology, Service Evaluation, CKD, Networks, Commissioning

87 - P2.006

ASSOCIATION OF ISCHEMIA-MODIFIED ALBUMIN IN SALIVA, SERUM, AND URINE WITH DIAGNOSIS OF CHRONIC KIDNEY DISEASE IN CHILDREN

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Aims/Purpose: Ischemia-modified albumin (IMA) is a secreted biomarker for ischemic oxidative stress. This case-control study aimed to evaluate the association of ischemia-modified albumin (IMA) in saliva, serum, and urine with diagnosis of chronic kidney disease (CKD) in 24 children.

Methods: The study involved 24 children with CKD. CKD was defined according to the Kidney Disease Improving Global Outcomes (KDIGO) diagnostic criteria. The control group consisted of 24 healthy children who were matched for age and gender to the experimental group. The concentration of IMA was determined by the colorimet ric method in non-stimulated whole saliva (NWS), stimulated whole saliva (SWS), serum, and urine of children with CKD. The Mann-Whitney U test was used for inter-group comparisons.

Results: IMA levels were significantly higher in NWS (P =0.0082) and SWS (P =0.0014) of children with CKD than in the control group. The concentration of IMA in NWS was correlated with standard indicators of kidney function, including the estimated glomerular filtration rate (r = -0.798, P£0.0001), stage of CKD (r = 0.814, P£0.0001), and serum creatinine (r = 0.711, P£0.0001) and urea levels (r = 0.738, P£0.0001).

Conclusion: Salivary IMA concentration depends on renal function in children. Salivary IMA discriminates children with end stage kidney disease from children with mild and moderate CKD and healthy children with high sensitivity and specificity. Further research is required, including assessment of the diagnostic usefulness and validation of the biomarker in a clinical diagnostic study.

89 - P2.007

OXIDATIVE STRESS IN PAEDIATRIC PATIENTS WITH CHRONIC KIDNEY DISEASE OR HYPERTENSION - SUPEROXIDE DISMUTASE AND INTERLEUKIN-2 RECEPTOR

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Aims/Purpose: Oxidative stress and systemic inflammation play an important role in the pathogenesis and progression of cardiovascular disease, with some evidence of deleterious effects on vascular involvement and atherosclerosis early in life. Oxidative stress indicators and elevated levels of inflammatory mediators are more often present in patients with known cardiovascular risk factors. The aim of our study was to determine the levels of superoxide dismutase and interleukine-2 receptor levels, serving as potential early markers of oxidative stress/inflammation of cardiovascular damage in children at risk.

Methods: 50 paediatric patients with hypertension, 46 paediatric patients with chronic kidney disease and 33 healthy controls were included in the study. In all, anthropometric measurements, body composition, liver damage and kidney function tests along with superoxide dismutase and interleukine-2 receptor levels were determined.

Results: Superoxide dismutase levels did not differ among groups, however, interleukin-2 receptor levels were significantly lower in patients with hypertension ($p < 0.001$) and with overweight/obesity presence ($p < 0.001$). Interleukin-2 receptor levels also significantly correlated with several anthropometric measurements and body composition parameters as well as with liver damage and kidney function tests, which was not confirmed for superoxide dismutase.

Conclusion: Interleukin-2 receptor levels were significantly lower in children with hypertension or obesity, which was not found for children with chronic kidney disease.

109 - P2.008

HYPERECHOGENIC KIDNEY IN A CHILD WITH PROLONGED DIRECT HYPERBILIRUBINEMIA CASE REPORT

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Aims/Purpose: Highlight the importance of monitoring renal function in children with liver diseases, particularly those with prolonged direct hyperbilirubinemia, since prolonged exposure to high levels of direct bilirubin or bile acids in infants with liver diseases can lead to renal diseases.

Methods: A case presentation of an 8-month-old baby boy with prolonged direct hyperbilirubinemia and intense itching, and was found to have hyperechogenic kidneys on ultrasound. Evaluation of the persistent hyperbilirubinemia revealed high levels of bile acids (> 350 µmol/L), suggesting an impairment in bile flow or metabolism. This finding raised suspicion of a cholestatic liver disorder, warranting further investigation into potential genetic causes, including Progressive Familial Intrahepatic Cholestasis (PFIC), which was eventually confirmed by Whole Exome Sequencing showing a homozygous mutation in the gene transcript ATP8B1 (c.3673del, p.Arg1225Alafs*64).

Results: Reviewing this case unveiled a potential connection between cholestasis and kidney injury, and specifically that prolonged exposure to high levels of direct bilirubin or/and bile acids in infants with liver diseases can cause kidney injury that may lead to chronic kidney disease. Relevant literature was reviewed to explore potential underlying mechanisms behind it.

Conclusion: The unexpected discovery of dysplastic kidneys in this case highlights the importance of monitoring renal function in children with liver diseases, particularly those with prolonged direct hyperbilirubinemia. The treatment of bile cast nephropathy is based on the management of hyperbilirubinemia to avoid kidney damage. Delayed management is associated with more extensive damage.

138 - P2.009

ASSESSING THE PERFORMANCE OF CONICAL CUFFS FOR BLOOD PRESSURE MEASUREMENT IN OBESE CHILDREN AND ADOLESCENTS

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Aims/Purpose: Findings from adult studies suggest that tronco-conical cuffs should be used for accurate blood pressure (BP) measurement in obese individuals with large arm circumference (AC). The aim of the present study was to examine differences in office blood pressure (BP) levels using conical cuffs compared to standard-shaped cylindrical cuffs in obese children and adolescents.

Methods: We performed an observational study enrolling 37 obese children and adolescents consequently recruited from the outpatient clinics of the Obesity Unit at General University Hospital Consortium of Valencia. The device used for the office BP measurements was OMRON HBP-1320 (HBP-1320-E). Middle AC was measured in all participants and the appropriate cuff size was selected among five sizes of conical and three sizes of regular cylindrical cuffs.

Results: Mean participants' age was 11.82.5 years, mean BMI was 28.83.4 kg/m2, BMI z-score was 2.120.32, and mean AC was 30.03.6 cm. There was no statistical significance in BP levels measured by cylindrical compared to conical cuffs (mean difference cylindrical-conical cuff was -0.226.55 mmHg for systolic blood pressure (SBP), -0.020.81 for SBP z-score, -0.704.95 mmHg for diastolic blood pressure (DBP), and -0.060.44 for DBP z-score). The analysis was repeated after excluding participants aged < 9 years old, retrieving similar results. A significant positive association was found between the measurements obtained by cylindrical and conical cuffs in both mean and z-score SBP and DBP values ($p < 0.001$). Bland-Altman analysis showed good agreement, with 94.6% of the values for all BP parameters, lying between the limits of agreement. No proportional bias was detected ($p > 0.05$).

Conclusion: The use of conical cuffs resulted in similar office BP levels in obese children and adolescents suggesting no advantage in enhancing tolerability and accuracy of office BP measurement in these patients. Although conical cuffs may be considered an alternative for office BP measurements in obese children, their reliability should be confirmed in larger populations and different settings.

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158 - P2.010

PREVALENCE OF SLEEP DISORDERED BREATHING IN CHILDREN WTIH CHRONIC KIDNEY DISEASE

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Background: Sleep disordered breathing (SDB) is reported in nearly 62% children with chronic kidney disease (CKD).We report the prevalence and severity of SDB in children with CKD stages 2-5T using polysomnography (PSG).

Methods and Materials: This observational, case control study was conducted in the Paediatric Nephrology outpatient clinic and Sleep medicine lab at a tertiary care centre in South India from March to December 2023.Children aged 5-18 years,with CKD stage ≥3, dialysis dependent and 3 months post renal transplantation formed the study group, with 1:1 CKD stage 2 patients acting as controls. After reporting the Epworth Sleepiness Scale questionnaire for Children and Adolescents (ESS-CHAD), patients underwent PSG, as per standard protocols. Age specific values of apnoea hypopnoea index (AHI) were used to diagnose and measure obstructive sleep apnoea (OSA) and SDB.

Results: Amongst the 36 patients (75% males) with CKD enrolled, even though only 2 (6%) clinically reported SDB as per ESS-CHAD, an overall prevalence of 72% of OSA was observed. Though increasing prevalence and severity was found with increasing stages of CKD, a significant proportion of patients with CKD 2 (78%) had OSA.

Conclusion: SDB is prevalent in all stages of CKD in children, with greater severity in higher stages of CKD.

199 - P2.012

PROPHYLAXIS OPTIONS IN CHILDREN WITH A HISTORY OF RECURRENT EPISODES OF RECURRENT URINARY TRACT INFECTIONS: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Aims/Purpose: The prevention of urinary tract infection recurrence (UTI) in children has been a challenge yet to be solved for the pediatric nephrology community. Current practice in children with recurrent episodes of UTI suggests that antibiotic prophylaxis may prevent further episodes of UTI and future complications. This is the first systematic review and network meta-analysis of the currently available randomized controlled trials (RCTs) comparing different prophylaxis options for the prevention of UTI and kidney scarring in children with a history of UTI recurrence.

Methods: We conducted a systematic literature search through major electronic databases (PubMed/MEDLINE, Scopus and Cochrane Library) until November 26th, 2023. Mean Difference and Standard Deviation were used for continuous outcomes and odds ratio for dichotomous outcomes. Our meta-analysis included 3,370 participants from 24 studies. The primary outcome was the effect of the different antibiotic and non-antibiotic prophylaxis options on the incidence of symptomatic UTI in children with recurrent episodes of UTI during prophylactic treatment.

Results: Cranberry products and nitrofurantoin lead to lower odds of symptomatic UTI episodes during prophylaxis compared to the control group and control/trimethoprim-sulfamethoxazole/trimethoprim groups accordingly. Nitrofurantoin may be the best option for UTI incidence reduction compared to all available documented interventions. No prophylaxis option has been shown to reduce kidney scarring.

Conclusion: Nitrofurantoin and cranberry products may decrease the incidence of symptomatic UTI episodes in pediatric patients with a history of UTI recurrence. Future RCTs studying non-antibiotic prophylaxis options, focusing on children with UTI recurrence and the risk for kidney scarring are needed to draw further conclusions.

221 - P2.013

PAIN INDUCED HYPERTENSION OR SOMETHING MORE?

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Aims/Purpose: Episodes of acute pain activate the sympathetic and neuroendocrine system, thus, causing an increase in peripheral resistance, heart rate and stroke volume. Hypertension caused by chronic pain is still debatable, especially in paroxysmal extreme pain disorder (PEPD) and inherited erythromelalgia (IEM). SCN9A gene mutation of NaV1.7 channels manifests as pain in the facial and anorectal area in PEPD, or in the distal parts of extremities in IEM. It is often triggered by micturation, defecation, physical activity or heat, and alleviated by cooling with possible immersion injury. Hypertension has been reported among complications, but it is questionable whether it is only pain induced, as in our patient with PEPD and IEM in whom hypertension was reported after successful treatment of cellulitis.

Methods: We retrospectively analyzed the medical records.

Results: A nine-year-old boy has been given multidisciplinary care since birth due to PEPD and IEM. During few pain episodes, hypertension has been reported, and attributed to pain stimuli. Due to cellulitis of the left leg and toxic shock syndrome caused by group A -hemolytic streptococcus and Staphylococcus aureus, he was admitted to the intensive care unit at the age of nine years and treated with antibiotics, immunoglobulins, potassium and albumin correction. He experienced daily pain episodes despite his regular therapy (carbamazepine, oxcarbazepine), and hypertension was reported (>95th percentile). Complete blood count, electrolytes, kidney, thyroid and adrenal function, lipidogram, cortisol, and aldosterone levels were normal, as well as fundoscopic exam, kidneys ultrasound, and Doppler ultrasound of the renal arteries. Echocardiography showed mild mitral insufficiency. ECG was normal. In 24-hour blood pressure monitoring (ABPM), systolic-diastolic hypertension was recorded (average pressure > 95th percentile). Doxazosin 1 mg per day was administered. Three months into treatment, the patient had normal blood pressure values in 24-hour ABPM.

Conclusion: Autonomic neuropathy, resistance vessels' vasocontriction, dysfunction of endothelial nitrous oxide, autoimmune and inflammatory etiology are some of the suggested theories of hypertension in PEPD and IEM. Research on pathogenesis and treatment is complicated due to a small number of patients. Nitroprusside, nifedipine, mexiletine, angiotensin-converting enzyme inhibitors, nitroglycerin, and calcium channel blocker therapy has been reported.

237 - P2.014

NORMATIVE URINARY MOLAR CREATININE RATIOS FOR SUBSTANCES OF THE GLYOXYLATE METABOLISM

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Aims/Purpose: Patients with primary hyperoxaluria (PH) are very often only diagnosed late. However, repeated spot urine or 24 h urine analysis for all parameters of the glyoxylate metabolism can help in distinguishing either PH type. As there are no normal values available for some of these parameters, we examined repeated spot urine samples in non-PH newborns less than 6 weeks of age.

Methods: Spot urine samples were analyzed from a group of newborns included into a newborn screening program for PH types 1 and 3 recently performed in Germany. We analyzed urine samples from 233 newborns heterozygous for the c.508G > A variant in the AGXT gene, (PH type 1) as well as from 251 newborns heterozygous for the c.700+5G > T variant of the HOGA1 gene (PH type 3), as well as from 24 unaffected babies as controls. At least three urine samples were collected per newborn and analyzed for oxalate (Uox), glycolate (Uglyc), glyceric acid (Uglycacid), hydroxy-oxo-glutarate (Uhog), dihydroxy-oxo-glutarate (Udhg) and 4-hydroxy-glutamate (U4ohglu). Values are depicted in molar creatinine ratios and compared to current normative data.

Results:

Table 1. Controls (n = 24; 105 samples), Uglycerate acid was not detected

	Uox	Uglyc	Uhog	Udhg	U4ohglu	Ucit
	mmol/mol	mmol/mol	mmol/mol	mmol/mol	mmol/mol	mol/mol
Mean	186.8	35.1	0	0	2.98	1.08
SD	101.2	38.9	0	0	5.14	0.49
Published normal	< 360	< 425	< 2.5	n.a.	n.a.	> 0.25

Table 2. *AGXT* Heterozygotes (n = 233; 985 samples), Uglycerate acid was not detected

	Uox	Uglyc	Uhog	Udhg	U4ohglu	Ucit
	mmol/mol	mmol/mol	mmol/mol	mmol/mol	mmol/mol	mol/mol
Mean	183.1	25.2	0	30.10	1.8	1.19
SD	87.5	35	0	1.20	4.1	0.56

Table 3. *HOGA1* heterozygotes (n = 251, 1133 samples); Uglycerate acid was not detected

	Uox	Uglyc	Uhog	Udhg	U4ohglu	Ucit
	mmol/mol	mmol/mol	mmol/mol	mmol/mol	mmol/mol	mol/mol
Mean	192.3	22.9	0.14	1.09	4.32	1.16
SD	87.8	38.6	3.02	3.67	6.51	0.74

Conclusion: Molar urinary oxalate and glycolate were within the published normative data. Uhog was only found in heterozygous HOGA1 newborns, which were mostly in normal range. Udhg was found in AGXT and HOGA1 newborns with significantly higher ratios in the HOGA1 group, as compared to the other two groups. U4ohglu was found in comparable ranges in controls, as well as in newborns with heterozygous AGXT or HOGA1 mutations, although significantly different for every group. We use the values detected for DHG (not detectable) and 4OHGlu (< 3 mmol/mol) now as our new normative data.

238 - P2.015

GLYCOLATE AND CITRATE EXCRETION IN PATIENTS WITH PRIMARY HYPEROXALURIA TYPE 1 TREATED WITH NEDOSIRAN (RIVFLOZA)

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Aims/Purpose: Primary hyperoxaluria (PH) is a family of three ultra-rare autosomal recessive inherited disorders of hepatic glyoxylate metabolism characterized by oxalate overproduction. Nedosiran is an RNA interference (RNAi) agent that inhibits hepatic lactate dehydrogenase, the enzyme responsible for the final step of oxalate production in all three genetic subtypes of PH. In a single-ascending-dose phase 1 study (PHYOX1) the safety, pharmacokinetics, pharmacodynamics, and exposure-response of subcutaneous nedosiran in healthy participants and in patients with PH types 1 and 2 were examined and published (1). In PH type 1 patients treated with lumasiran, another RNAi medication targeting glycolate oxidase, increases of already elevated urinary glycolate excretions and reduced citrate excretions were recently reported (2). To evaluate glycolate and citrate excretions under nedosiran medication, we retrospectively analyzed the urine samples available from six German PH 1 patients included into the PHYOX1 study.

Methods: We examined the 24 h urines of 6 PH 1 patients (age 14-26 years, 2 female) at screen 1, screen 2 and at days 8, 15, 29, 43, 57 and day 71 after dosing. Patients had received one single dose open-label nedosiran of 1.5, 3.0, or 6.0 mg/kg, respectively. Urines were analyzed for oxalate, glycolate and citrate via ion-chromatography/mass spectrometry.

Results:

		Screen 1	Screen 2	Day 8	Day 15	Day 29	Day 43	Day 57	Day 71
Glycolate (mmol/1.73m2/24h)	Median	1.49	1.47	1.75	1.45	1.35	1.69	1.51	1.73
	Max	5.79	3.58	6.89	3.47	3.88	4.29	3.21	3.75
	Min	0.99	0.83	1.6	0.95	1.03	0.62	0.9	0.8
Citrate (mmol/1.73m2/24h)	Median	2.46	2.39	2.79	2.77	2.98	2.9	2.59	2.76
	Max	3.8	4.14	3.25	3.47	3.71	3.71	3.36	3.57
	Min	1.92	1.27	2.66	1.44	2.41	1.53	1.7	1.64
Oxalate (mmol/1.73m2/24h)	Median	1.06	1.07	0.96	0.80	0.67	0.83	0.53	0.75
	Max	2.18	2.1	2.19	1.43	1.58	1.35	0.88	0.93
	Min	1.01	0.86	0.75	0.5	0.61	0.55	0.47	0.45

After one single dose of nedosiran, median glycolate excretion remained elevated but no substantial increase as compared to the range of the pre dosing values was visible. Urinary citrate also remained stable over time. Urinary oxalate nicely declined to a near normal level at day 57 post dosing and increased again thereafter. No dose related effect was visible.

Conclusion: There are no negative derangements in urinary glycolate or citrate excretion under nedosiran medication.

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245 - P2.016

EXPLORING POTENTIAL BIOMARKERS FOR DIAGNOSING CHILDHOOD-ONSET TAKAYASU ARTERITIS

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Aims/Purpose: Takayasu arteritis (TA) is a rare granulomatous inflammatory vasculitis that primarily affects the aorta and its major branches. This inflammation, if unrecognized, can lead to segmental stenosis, occlusion, dilatation, and/or aneurysms of the affected arteries, resulting in a broad range of clinical symptoms. Unfortunately, limited data exist on childhood-onset TA due to low patient numbers and absence of a uniform approach. Our objective was to identify and classify potential biomarkers for diagnosing TA in children, as reported in the literature. Additionally, we aim to provide practical guidance for clinicians confronted with childhood-onset TA in their daily practice.

Methods: We conducted a systematic search of MEDLINE, EMBASE, Wiley Cochrane Library, ClinicalTrias.gov, and WHO ICTRP. We identified all articles related to TA but restricted our search to pediatric age (0 to 18 years) and publications between January 2000 and August 2023. We extracted data on demographics, clinical features, laboratory measurements, and diagnostic imaging.

Results: Our literature search identified 2026 potential articles, of which 52 studies met our inclusion criteria. Descriptive analysis was performed on 42 case series, including 1067 pediatric patients. Our systematic review confirms the heterogeneous clinical spectrum of childhood-onset TA, predominantly presenting with cardiovascular, constitutional, and neurological symptoms. Laboratory parameters appear to lack sensitivity and specificity. Imaging predominantly reveals subdiaphragmatic affected vessels, with the abdominal aorta (54%, n = 712) and renal arteries (44%, n = 712) most frequently involved. Conventional angiography remains the most frequently used imaging modality in childhood-onset TA, although we propose MRA as preferred imaging modality, as recommended by EULAR guidelines.

Conclusion: Timely diagnosis of childhood-onset TA remains challenging due to its diverse and atypical presentation. To the best of our knowledge, this is the first systematic review to collect and review all existing data on diagnosing childhood-onset TA. Future multicentric collaborative efforts will be necessary to enhance understanding of the natural course of this rare disease and to identify sensitive and specific biomarkers for diagnosis and disease activity, ultimately improving the disease outcome.

267 - P2.017

END-STAGE-RENAL DISEASE IN CHILDREN: ASSESSMENT OF THE QUALITY OF LIFE OF THE CHILD AND HIS PARENTS

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Aim: End-stage renal disease in children is a major public health problem that impacts the psychosocial status of the child and his parents. These aspects related to quality of life have not been studied in Tunisia. The objective of our work was to evaluate the quality of life of children with end-stage renal disease and to describe the impact on the quality of life of their parents.

Methods: We conducted a quantitative descriptive observational study in the pediatric department of Charles Nicolle Hospital. Children and adolescents aged 4 to 20 years on dialysis who presented to the hospital from January to June 2021 were included. Univariate analyses were performed looking for an association between scores measured using the End Stage Renal Disease and Family Impact modules of the PedsQL™ and sample characteristics. A p-value < 0,05 at a confidence interval > 95% is considered statistically significant.

Results: A total of 54 patients were included in the study, 24 boys and 30 girls. The mean age was 14 ± 4.55 years (4-20). Scores were 50.95 for the child report and 49.62 for the parent report of the End Stage Renal Disease module and 52.49 in the Family Impact module. The reliability of the PedsQL™ was good with Cronbach's alpha coefficients greater than 0.7. Parent total scores were slightly higher than child total scores between ages 4 and 12 and slightly lower between ages 13 and 20. This difference was statically significant in the 4-7 and 13-18 age groups with p =0.025 and < 0.001 respectively. In the End Stage Renal Disease module, the scores reported by the parents were higher in the privileged socio-professional category group compared to the disadvantaged socio-professional group with 46.8 vs 56.34 p =0.037. In the Family Impact module, scores were 49.82, 50.33 and 62.47 respectively for the socio-professional levels 1, 2 and 3 groups with p =0.042. Children on Peritoneal Dialysis reported higher scores in the End Stage Renal Disease module with p =0.037 and 0.043 in child and parent reports respectively and lower in the Family Impact module with p =0.026.

Conclusion: Our results show that medical management is not sufficient for our patients and that we must focus our efforts on improving the quality of life of these children and their family to optimize patient care.

300 - P2.018

IMPACT OF INTENSIVE BLOOD PRESSURE CONTROL ON DIASTOLIC FUNCTION IN CHILDREN WITH CHRONIC KIDNEY DISEASE IN THE HOT-KID RCT

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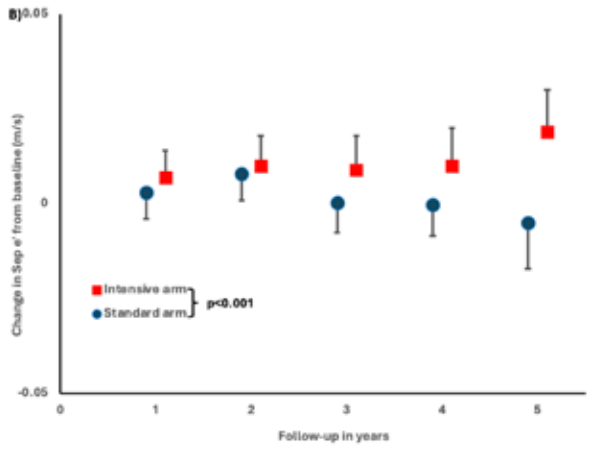
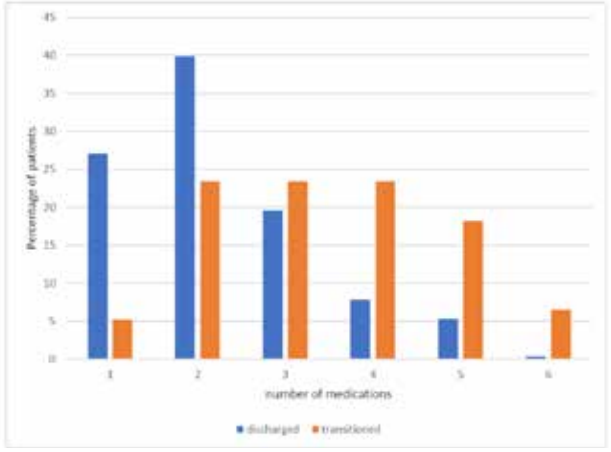
Aims/Purpose: Relationship between blood pressure (BP) control and left ventricular (LV) diastolic function in children with chronic kidney disease (CKD) is uncertain. The aim is to investigate whether achieving lower BP control yields a favourable impact on diastolic function by performing a secondary analysis utilising data from the HOT-KID randomised controlled trial (RCT) in children with CKD (ISRCTN25006406).

Methods: 124 children were randomised to standard (50th-75th percentile) or intensive (< 40th percentile) systolic blood pressure using office BP targets. Echocardiograms were performed at baseline and at follow-up visits. Diastolic function was assessed from echocardiographic measures of mitral inflow E/A ratio, Tissue Doppler imaging e', a', E/e' and e'/a' ratio, and left atrial volume index (LAVi) by a blinded observer.

Results: At baseline, there was no significant difference of E/A, e', a', E/e' and e'/a' between standard and intensive treatment groups. There was significant average annual rate of change in E/A ratio (difference in means -0.07 per year, 95% CI: -0.14 to -0.01, P =0.034), septal e' (difference in means -0.003 m/s per year, 95% CI -0.005 to 0.001, P =0.007), and LAVi (difference in means 0.82 ml/m2 per year, 95% CI 0.22 to 1.42, P =0.007) in the intensive compared to the standard treatment arm (figure 1). However, the average annual changes in all other diastolic function measures were similar between standard and intensive treatment groups.

Conclusion: Achieving lower blood pressure control has a favourable impact on LV diastolic function as measured by E/A ratio, septal e' and LAVi in children with CKD.





Figure

317 - P2.019

A DIFFICULT DIAGNOSTIC CHALLENGE. TAKAYASU ARTERITIS IN CHILDHOOD

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Aims/Purpose: Describe clinical presentation of Takayasu arteritis which is a chronic granulomatous vasculitis that affects large blood vessels, particularly aorta and its branches, producing progressive narrowing of arteries, compromising blood flow, raising blood pressure and causing organic ischemia. It presents non-specific symptoms, making early detection difficult, with hypertension being a key clinical finding.

Methods: We present two pediatric cases of Takayasu arteritis in childhood.

Results: Case 1. 13-year-old woman, with hypertension and overweight. Body mass index 26.5. BPP > 99 Laboratory tests show creatinine 0.62 mg/dL, estimated glomerular filtration rate 109.2 cc/min, hypokalemic metabolic alkalosis, marked elevation of renin and angiotensin; Increase in C-reactive Protein, Interleukin 6 and weak positivity for c-ANCA. Abdominal ultrasound shows atrophic left kidney. Abdominal vascular CT scan with left renal atrophy secondary to injury to the abdominal aorta that causes practically complete occlusion of the left renal artery. Aortitis. She needed hypotensive treatment (enalapril, losartan, amlodipine, hydralazine), systemic corticosteroid, tocilizumab and mycophenolate mofetil until left nephrectomy.

Case 2. A 5-year-old woman presents with poor general condition, drowsiness, stupor, syncope, prolonged fever, and elevated C-reactive protein; BPP > 99. Acute hemiparesis due to chronic infarction of the right middle cerebral artery and small hypodense left frontal cortico-subcortical lesion, reduction in the caliber of the left carotid artery with a beaded appearance.Treatment was started with high-dose corticosteroids, methotrexate, hydralazine, amlodipine, enalapril and furosemide. After 11 years of evolution, she requires methotrexate and tocilizumab. No antihypertensive treatment is required and normal kidney function is maintained.

Conclusión: Takayasu disease is a very rare and serious cause of secondary arterial hypertension, of a chronic nature and evolution in outbreaks. It is the third cause of vasculitis in children.

323 - P2.020

THE ROLE OF URINARY CHLORIDE CONCENTRATIONS IN THE DETERMINATION OF KIDNEY INJURY IN CHILDREN

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Aims/Purpose: Early stages of chronic kidney disease (CKD) are usually asymptomatic, but kidney damage that starts in childhood may persist until adulthood and can lead to serious morbidity and mortality in the following years. Therefore, preventive practices that can slow the progression of kidney damage in the pediatric period are strongly needed. In this study, we evaluated the relationship of urinary chloride concentrations with proteinuria and/or decreased kidney functions.

Methods: This study is a retrospective descriptive study. Between January 2020 and March 2021, patients aged between 2 and 18 years with available urine chloride studies during their follow-up and treatment in the pediatric nephrology department were included in the study. Patients were divided into subgroups based on two different eGFR threshold values (60 ml/min/1.73m2 and 45 ml/min/1.73m2), and proteinuria status. It was investigated whether there was a difference between the groups in terms of urine chloride levels.

Results: Urinary chloride concentrations were lower in pediatric patients with proteinuria (102.4 ± 73.7 mEq/L vs 158.8 ± 81.1 mEq/L, p =0.002). Similarly, urinary chloride levels were lower in those with low eGFR and the values deepened parallel to the decrease in the eGFR (46.4 ± 28.0 mEq/L for eGFR < 45 ml/min/1.73m2 and 69.4 ± 49.7 mEq/L for eGFR 60 ml/min/1.73m2). Besides, the lowest urinary chloride concentrations were found in patients with proteinuria and low eGFR (65.4 ± 49.9 mEq/L).

Conclusion: Strategies towards increasing the urinary chloride excretion may help to slow the progression of CKD by providing a renoprotective effect via tubuloglomerular feedback, which inhibits the increase in glomerular pressure.

774 - P2.021

ESTIMATED GLOMERULAR FILTRATION RATE (EGFR) USING CYSTATIN C (CYSC) VERSUS CREATININE AND ASSOCIATIONS WITH BLOOD PRESSURE IN PRETERM CHILDREN

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Aims/Purpose: Prematurity has been associated with the development of hypertension and chronic kidney disease during childhood and adulthood. The aims of the study were to evaluate the utility of estimated glomerular filtration rate (eGFR) based on cystatin C (Cys C) compared to creatinine upon their associations with office blood pressure (BP) and central systolic BP (cSBP).

Methods: This case-control study included children born prematurely (ex-preterms) and children born at full term (controls). The participants underwent office blood pressure (BP), ambulatory BP and central systolic BP measurement and assessment of serum creatinine and Cystatic C (CysC) values. The eGFR was calculated based on cystatin C and creatinine equations separately.

Results: 52 ex-preterms and 26 controls were included with a mean age of 10.74 ± 3.55 years. No significant differences were observed in BP levels, CysC values, eGFR(creatinine) and eGFR(CysC) between ex-preterm and control group. eGFR(CysC) presented positive association with office DBP ($r = -0.37$, $p = 0.006$, Spearman test) and cSBP z score ($r = -0.32$, $p = 0.022$, Spearman test) in the ex-preterm group, but not in the control group (figure). eGFR(creatinine) did not associate with any of the BP parameters. eGFR(creatinine) overestimated eGFR levels in ex-preterm group (mean difference 20.56 ± 22.66, $p < 0.001$). Two (3%) and 17(32.6%) ex preterm children had GFR < 90 ml/min/1.73m2 by creatinine-based eGFR compared by eGFR(CysC).

Conclusion: eGFR(CysC) presents a positive association with cSBP and thus, may better classify future CVD risk in ex-preterm children. cSBP elevation and its association with CysC maybe a target for future studies to elucidate the role of central hemodynamic alterations in the development of HTN and CVD disease in the ex-preterm individuals.

422 - P2.022

THE ONGOING PHASE 3 COMMUTE-A AND -P TRIALS OF CROVALIMAB IN ACUTE HAEMOLYTIC URAEMIC SYNDROME AND PATIENT PREFERENCE FOR CROVALIMAB VS ECULIZUMAB IN THE PHASE 3 COMMODORE 1 AND 2 TRIALS

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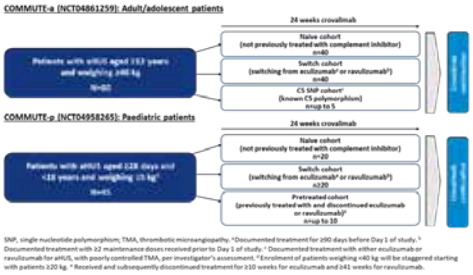
Aims/Purpose: We describe the currently enrolling Phase 3 single-arm COMMUTE-a (NCT04861259) and COMMUTE-p (NCT04958265) trials evaluating crovalimab (crova), a novel C5 inhibitor (C5i), in acute haemolytic uraemic syndrome (aHUS). Crova, with subcutaneous (SC) administration every 4 weeks (Q4W) (or every 2 weeks [Q2W] in patients [pts] < 20 kg with aHUS), and the potential for self-administration, could reduce treatment burden vs other C5is in aHUS. Pt preference data from the global, randomised, Phase 3 COMMODORE 1 (NCT04432584) and 2 (NCT04434092) trials (Röth EHA 2023, Scheinberg EHA 2023) evaluating crova in pts with paroxysmal nocturnal haemoglobinuria (PNH), another complement-mediated disorder, are reported.

Methods: COMMODORE 1 and 2 enrolled C5i-experienced and C5i-naive pts with PNH, respectively. Pts were randomised to receive crova (weight-based tiered dosing regimen: loading doses and SC Q4W maintenance) or eculizumab (ecu; 900 mg IV Q2W) over 24 weeks. All pts then received crova if continuing on trial. Treatment preference was assessed in adult pts using the validated Patient Preference Questionnaire (PPQ) after 17 weeks of crova treatment in C5i-experienced pts randomised to crova in COMMODORE 1 and in pts initially randomised to ecu who switched to crova at Week (W)25 in COMMODORE 1 and 2. COMMUTE-a is enrolling pts with aHUS aged ≥12 years [y] (N≈80) and COMMUTE-p is enrolling pts with aHUS aged ≥28 days to < 18 y (N≈45), both in 3 cohorts (Figure 1): (1) Naive, (2) Switch, (3) C5 polymorphism (SNP) cohort in COMMUTE-a: pts with known C5 SNPs; pretreated cohort in COMMUTE-p: pts previously treated with and discontinued ecu or ravu (with or without known C5 SNPs). In both COMMUTE studies, pts receive weight-based tiered crova dosing: IV and SC loading doses, and SC Q4W maintenance (or Q2W if < 20 kg). The primary efficacy objective of both studies is to assess the proportion of C5i-naive pts with complete thrombotic microangiopathy response from baseline to W25. Secondary efficacy endpoints include change from baseline in dialysis requirement status and estimated glomerular filtration rate. Treatment preference will be assessed using the PPQ in pts aged ≥12 y and in caregivers of pts < 12 y.

Results: In COMMODORE 1, 33 (85%) of 39 pts randomised to crova preferred crova over ecu at W17. Of pts randomised to ecu who switched to crova after W25, 27 (96%) of 28 pts in COMMODORE 1 and 32 (84%) of 38 in COMMODORE 2 preferred crova (Figure 2). Top reasons for crova preference over ecu were: fewer hospital visits required, easier administration, less time needed to administer and better quality of life. COMMUTE-a and COMMUTE-p are recruiting in 19 and 14 countries, respectively.

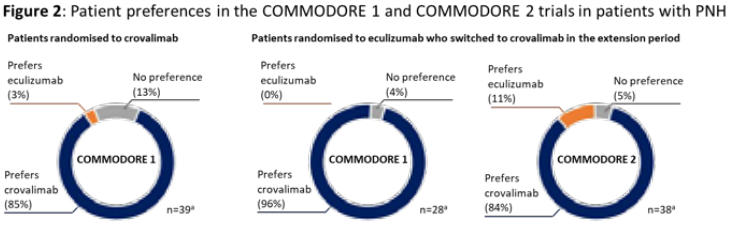
Conclusion: Most pts with PNH in COMMODORE 1 and 2 preferred crova to ecu, largely due to faster, easier administration. COMMUTE trials are currently enrolling pts with aHUS.

Figure 1: COMMUTE-a and COMMUTE-p study schema in patients with aHUS



SNP, single nucleotide polymorphism; TMA, thrombotic microangiopathy. [a]Documented treatment for ≥90 days before Day 1 of study. [b]Documented treatment with ≥2 maintenance doses received prior to Day 1 of study. [c]Documented treatment with either eculizumab or ravulizumab for aHUS, with poorly controlled TMA, per investigator's assessment. [d]Enrolment of patients weighing <40 kg will be staggered starting with patients ≥20 kg. [e]Received and subsequently discontinued treatment for ≥10 weeks for eculizumab and ≥41 weeks for ravulizumab.

Figure 2: Patient preferences in the COMMODORE 1 and COMMODORE 2 trials in patients with PNH



Patients were assessed after 17 weeks of crovalimab. [a] Only patients with available data (having completed the questionnaire) were included in the calculations of percentages. Kulasekararaj ASH 2023; #5628.

This abstract was previously submitted to ERA 2024.

449 - P2.023

EXTRACELLULAR DNA IN CHILDREN WITH CHRONIC KIDNEY DISEASE

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Aims/Purpose: Chronic kidney disease (CKD) is associated with chronic low-grade inflammation but the main factors triggering this inflammation remain to be elucidated. Extracellular or cell-free DNA (exDNA) originates from virtually all tissues as it is released during cell death. It is also a damage-associated molecular pattern and so, it stimulates the innate immune system. The present study was set out to analyze associations between exDNA, inflammatory markers and markers of cardiovascular health in children with CKD.

Methods: This observational cross-sectional cohort study included children with CKD, either non-dialysis CKD stage 2-5 patients (25 children) or kidney transplant recipients (CKD-T, 40 children), as well as 10 healthy controls. Total, nuclear and mitochondrial exDNA was analyzed in plasma by fluorometry and real-time PCR and correlated with clinical data, inflammatory markers in plasma, as well as blood pressure, standard and tissue-doppler echocardiography.

Results: Children with CKD, mainly children after kidney transplantation, had higher concentrations of exDNA in plasma, specifically nuclear DNA. Interleukin-6, antimicrobial peptide cathelicidin (LL-37), soluble vascular cell adhesion molecule-1 as well as several cardiovascular markers positively correlated with exDNA concentrations. However, multivariate analysis revealed left ventricular mass index as the only independent variable associated with high plasma exDNA.

Conclusion: We show for the first time that children with CKD have high exDNA in plasma. ExDNA positively correlated with certain markers of inflammation and cardiovascular dysfunction. We believe that our results bring new insights in the pathogenesis of CKD and its complications and may lead to identification of new therapeutic targets. Experiments have already suggested a potential systemic use of DNA-cleaving enzymes in animal model of sepsis or hepatorenal disease.

465 - P2.024

SEVERE ACUTE KIDNEY INJURY IN A PANCYTOPENIC INFANT. MYCOPLASMA OR HAEMOPHAGOCITYC LYMPHOHISTIOCYTOSIS, THE PERFECT INMUNOLOGICAL STORM

Yarima López Espinoza[1], Victor Lopez-Baez[1], Ana Cristina Aguilar[1], Marta Jimenez1, Yolanda Calzada Baños[1], Pedro Arango Sancho[1], Alvaro Madrid Aris[1]

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Aims/Purpose: Mycoplasma extrapulmonary involvement is rare and can affect different organs,including kidney and blood.Renal involvement may be directly or indirectly mediated by the disproportionate inflammatory response of the host and/or by endothelial involvement leading to microvaso-occlusion phenomena. On the other hand,haemophagocytic lymphohistiocytosis(HLH) disease can be the result of various aetiological processes including autoimmune,infectious,toxic and neoplastic,or a combination of these,and 16% of patients present with renal damage. In HLH,acute kidney injury(AKI) is the result of cytotoxic and haemodynamic damage to tubules and interstitium. Acute tubular necrosis is most common, occasionally infiltrative damage. Up to50% require dialysis and confer worse prognosis. The purpose of this paper is to present a case of a previously healthy 2-year-old girl with a rare form of anuric acute kidney injury,pancytopenia and hyperinflammatory state requiring dialysis therapy.

Patient Methods & Results: Patient with fever and respiratory symptoms accompanied the last 5 days by vomiting, diarrhoea and decreased diuresis. Initially treated with NSAIDs without improvement. She was febrile with mild to moderate dehydratio,haemodynamically stable,without neurological compromise,without adenopathies or hepatosplenomegaly. Initially, she presented leucopenia, thrombocytopenia, anaemia, creatinine(8.8 mg/dl), urea(359 mg/dl), hyperkalaemia(6.5mml/L) and was admitted to ICU for suspected thrombotic microangiopathy. The extended study showed normal ADAMTS13 activity with incipient data of haemolysis (schistocytes 3/field, LDH(3416UI/L). In contra position, normal Haptoglobin 4489 mg/L, reticulocytes 0.3%, weak positive direct coombs and total Bilirubin 0.3 mg/dl. Additionally, data of systemic inflammatory response CRP(180 mg/L), PCT(55ng/ml), Ferritin(4567ug/L), triglycerides(662 mg/dl), D-Dimer (31.8 mg/L). Microbiologically, Mycoplasma pneumoniae was identified. Bone marrow aspirate showed no malignancy, with some isolated images of haemophagocytosis. Renal biopsy showed extensive acute tubular necrosis, with focal cortical necrosis, associated non-granulomatous lymphohistiocytic tubulointerstitial nephritis.

Conclusion: The characteristic feature of the present case was marked AKI in a patient with Mycoplasma infection and suggestive, but not conclusive data of HLH. Heterogeneous mechanisms of renal injury have been described in the literature in both situations. In this case, the aetiology is probably multifactorial, including Mycoplasma infection, data suggestive of HLH and use of NSAIDs, which may also have a direct effect on renal damage in our patient.

480 - P2.025

RADIATION-INDUCED RENAL ARTERIAL STENOSIS IN CHILD

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Aims/Purpose: Radiation-induced renal arterial stenosis (RIRAS) is a rare late complication of cancer treatment.

Case: 9 year-age girl presented with symptomatic arterial hypertension stage 2 (BP 180/120 mm Hg). She had "Neuroblastoma with intraspinal extensions at the level Th10-L2, stage IV' and had received chemotherapy NB-2004, radiation treatment (36 Gy), tumorectomy and left nephrectomy (due to postoperative kidney arterial thrombosis, kidney infarction) 7 years earlier. There were no hypertension and vascular anomalies after 5 years of therapy according to clinical data and control MRI. The girl had eGFR (CKiDU25 CysC/Cr) 84 ml/min/1.73m2, normal renin (4.98 ng/ml; N = 3.2-52), aldosterone (155.4 pg/ml; N = 30-300), NSE (12 ng/l; N = 0-16.3) in blood and urine metanephrine (12 µg/day; N = 18-144), normetanephrine (85 µg/day; N = 29-145). US doppler demonstrated renal arterial resistive index 0.52 (suspicious for stenosis); renal arteriography showed right renal artery and celiac stenosis. Percutaneous transluminal balloon angioplasty of the renal artery was complicated by recurrent thrombosis and infarction of the right kidney. After 6 mo of peritoneal dialysis, cadaveric kidney transplant was performed.

Conclusion: Patients who received abdominal radiotherapy should be screened for arterial hypertension and in case of high blood pressure should be investigated for renal artery stenosis. The method of revascularization should be discussed by a multidisciplinary team given the risk of developing atypical procedure complications in patients with RIRAS.

482 - P2.026

HOW WE DETERMINE EGFR IN PRACTICE: A SURVAY OF PEDIATRIC NEPHROLOGISTS

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Aims/Purpose: Estimation of glomerular filtration rate (eGFR) is a key tool for determining the degree of chronic kidney disease and making clinically important decisions. The aim was to establish which formulas of eGFR are used in CKD children by pediatric nephrologists in Russia.

Methods: The information about eGFR formulas used (Schwartz equation, Schwartz- Lyon, Smeets equation, CKiDU25, Flanders metadata, FAS, EKFC, CKD-EPI) and factors influencing the choice of formulas (method of blood creatinine measurement, age of the child (< 1 month, 1 month-2 years, ≥2 years, adolescents-young adults), features of kidney disease, comorbidity) and availability of blood cystatin C measurement was obtained from a cross-sectional survey of 180 pediatric nephrologists.

Results: Sixty three % of respondents work in hospitals and routinely calculate GFR. Fifty two % of doctors believe that not have sufficient information to select eGFR formula due to the lack of clear guidelines. Respondents usually use the Schwartz bedside (63-77%) and Schwartz-Lyon formulas (18-24%) in children 0-15 years old (regardless of patients age, kidney disease, comorbidity, laboratory method for measuring creatinine); CKD-EPI (52%) and Schwartz bedside equations (32%) are used in adolescents and young adults. Cystatin C measurement is available in 58% of cases, including 38% in commercial laboratories. As confirmatory tests in doubtful cases doctors use: creatinine clearance (53%), calculation of GFR by cystatin (28%) or cystatin and creatinine (21%), radioisotope methods (17,5%).

Conclusion: Physicians are not sufficiently aware of the limitations of creatinine based eGFR formulas. The cystatin C is not available in routine practice, limiting its use for calculating GFR. Clearer recommendations for calculating GFR according to age, CKD stage, and patient status are needed.

568 - P2.028

PERFORMANCE OF CREATININE BASED-EQUATIONS IN AFRICAN CHILDREN WITH SICKLE CELL ANEMIA

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Aims/Purpose: Serum creatinine (SCr)-based equations are commonly used to evaluate glomerular filtration rate (GFR) in sickle cell anemia (SCA) patients. However, these equations may overestimate the GFR values due to the increased tubular creatinine secretion seen in these patients. In addition, none of these equations has been formally validated in this population. The present study aimed to evaluate the performance of commonly used SCr-based equations in African SCA children.

Methods: In this cross-sectional study, 109 steady-state SCA children aged 3-18 years were recruited in Kinshasa, the Democratic Republic of Congo. Measured GFR (mgFR) was obtained using iohexol plasma clearance, as the gold standard method. Serum creatinine (Scr) was determined by both the Jaffe and IDMS-traceable enzymatic methods. Estimated GFR (eGFR) was calculated using commonly used SCr-based equations in children. Correlations between mgFR and eGFR equations were tested by Pearson's correlation. The performance of these equations was evaluated by calculating the bias, precision and accuracy within 10% (P10) and 30% (P30) of mgFR.

Results: Mean mgFR was 149.1 ± 42.8 mL/min/1.73 m^2 and 65/109 (59.6%) participants were in the hyperfiltrating range (mgFR > 135 mL/min/1.73 m^2). No age and no sex dependency were observed with the mgFR. The bias, precision, correlation coefficient and accuracy of different eGFR equations compared to mgFR are shown in Table 1. Correlation coefficients between mgFR and the different eGFR-equations were relatively poor. Of the equations studied, the FAS-Age had the lowest bias (0.89). However, the 95% limit of agreement was very wide (-80.3 to +81.6) like all other equations. On the other hand, the bedside-Schwartz had the highest correlation (0.360) and P30 (78.9).

Table 1. Performance of different eGFR equations

eGFR equations	R	Bias (95% CI)	P10 (95% CI)	P30 (95% CI)
FAS-Age	0.291	0.89 (-10.0; 8.2)	27.5 (19.0; 36.0)	71.6 (63.0; 80.2)
FAS-Height	0.266	-8.7 (-14.7; 3.7)	24.8 (16.5; 33.0)	71.6 (63.0; 80.2)
EKFC	0.344	-24.9 (-33.3; -17.0)	22.0 (14.1; 29.9)	71.6 (63.0; 80.2)
Schwartz-old (Jaffe SCr)	-0.177	29.2 (9.9; 51.4)	22.0 (14.1; 29.9)	45.0 (35.5; 54.4)
Bedside-Schwartz	0.360	-2.7 (-7.5; 10.1)	37.6 (28.4; 46.9)	78.9 (71.1; 86.7)
CKiDU25	0.265	-12.2 (-19.2; -0.2)	29.4 (20.7; 38.0)	70.6 (62.0; 79.3)
Schwartz-Lyon	0.307	-13.9 (-19.2; -5.2)	33.9 (24.9; 43.0)	76.2 (68.0; 84.3)
LMR18	0.341	-26.0 (-36.1; -17.6)	19.3 (11.7; 26.8)	67.0 (58.0; 75.9)
CKDEPI40	0.354	-26.3 (-35.0; -17.7)	21.1 (13.3; 28.9)	66.1 (57.0; 75.1)

Conclusion: Accurate assessment of GFR remains challenging in SCA children. Our data showed that SCr-based equations should be used with caution in African SCA children. However, the bedside Schwartz and FAS-Age seem to be the most appropriate despite their imprecision. These results highlight the urgent need to develop more precise eGFR equations validated in SCA children.

596 - P2.029

HEMOLYTIC UREMIC SYNDROME IN THE LAST 20 YEARS IN A COHORT OF SPANISH CHILDREN: FROM OUR PERSPECTIVE

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Aims/Purpose: Hemolytic uremic syndrome (HUS) is a rare but clinically significant condition in pediatric patients. Research on this disease has expanded knowledge regarding its epidemiology in different geographical areas. This study aims to analyze all patients treated at a referral hospital from our setting over the last 20 years.

Methods: A retrospective analysis was conducted on all pediatric patients (up to 15 years old) who were diagnosed with HUS and admitted to our hospital from 2003 to 2023. Variables including both qualitative and quantitative aspects specific to each patient and their medical history, as well as clinical, diagnostic, and therapeutic processes, were included. Data was processed using IBM SPSS Statistics software.

Results: A total of 19 medical records (15 males and 3 females) which met the inclusion criteria were analyzed. All patients exhibited clinical and/or analytical data of microangiopathic anemia and renal insufficiency at the time of hospital admission. The annual incidence calculated for the population treated at our hospital was 0.4 episodes of HUS per 100,000 children under 15 years old. Thirteen patients (68%) were admitted at the age of 3 years or younger. Eighteen patients had a recent infectious history and 15 consisted of symptoms compatible with gastroenteritis (diarrhea, vomiting), which were the main reason for consultation (on average 3 days after onset of symptoms). Oliguria was recorded in 15 patients and hypertension in 18, with furosemide being the most commonly used treatment. 9 patients needed renal sustitution therapy. The diagnoses and summarized characteristics by subgroups are detailed in the following table.

Diagnosis	Cases (n)	Mean age at admission and range	Renal sustitution therapy	Complement inhibitors	Relapse
STEC-HUS	7	5,9 (R 9,2)	PD (2, both 1 y.o.) HD (1, 10 y.o)	1 (eculizumab during episode)	0
aHUS – St. pneumoniae	2	1,2 (R 1,8)	PD (2, 3 months and 2 y.o.)	1 (eculizumab during episode, exitus)	0
aHUS- genetic mutations	2	2,2 (R 2,2)	PD (1, 1 y.o, DGKE mutation, parental consanguinity)	0	1 (MCP mutation)
aHUS – other	8	4,6 (R 13,3)	PD (1, 2 y.o.)	HD (2, 3 and 13 y.o.) 2*	2*

STEC-HUS: Shiga toxin-producing Escherichia coli-associated hemolytic uremic syndrome. aHUS: atypical hemolytic uremic syndrome. R: range. PD: peritoneal dialysis, HD: hemodialysis. y.o.: years old.*Both eculizumab+ravulizumab, relapse while stopped treatment.

Conclusion: Hemolytic uremic syndrome is a heterogeneous condition both in its etiopathogenesis and management. Despite significant outbreaks not occurring in our setting, cases caused by infectious pathology account for almost half of the total. We emphasize the 8 cases where a clear etiology couldn't be established, which hinders comparison between subgroups. A better understanding of genetic involvement will benefit those patients in the future.

647 - P2.030

ASSESMENT OF KIDNEY FUNCTION IN CHILDREN WITH TYPE 1 DIABETES MELLITUS (DM1)

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Purpose: To conduct a comparative assessment of kidney function according to the calculated formulas of GFR in children with DM1.

Methods: Total 59 children with DM1 were examined in endocrinology department of Voronezh regional children's hospital at the age of 4 to 17 years. Among the patients there were 34 (65.4%) boys and 17 (34.6%) girls. Nobody had ketoacidosis, albuminuria or arterial hypertension. During the first 2 years of DM1 it was examined 23 patients, > 2 to 5 years – 17 children, > 5 years of the disease we investigated 19 children. GFR was calculated using Creatinine-based (Cr) formulas: Schwartz «bedside» (2009), Schwartz–Lyon (2012), CKiDU25; using Cystatin Cbased (CysC) formulas: FAS cysC, CAPA, Schwarts CysC; CKiDU25cysC; and also Schwartz combi formular. GFR data are presented as Me [Q1; Q3] ml/min/1.73m^2.

Results: The level of GFR when using Cr formulas was: Schwartz «bedside» (2009) - 77.21 [63.99; 89.27], Schwartz–Lyon (2012) – 71.30 [60.24; 83.58], CKiDU25 – 71.2 [61.85; 88.35] ml/min/1.73m^2; GFR when using CysC formulas was: FAScysC – 108.4 [66.05; 143.05], CAPA – 113.5 [66.56; 163.25], Schwarts cysC – 85.92 [54.08; 110.68], CKiDU25cysC- 99.6 [64.40; 129.20] ml/min/1.73m^2. According to Schwartz combi formular GFR = 80.6 [63.64; 100.44] ml/min/1.73m^2. The level of GFR was significantly lower when using creatinine – based formulas. It was a slight increase in serum Creatinine and Cystatin C level with an increase of duration of diabetes: for the first 2 years – 67.71 [57.69; 82.5] mcmol/l and 0.72 [0.63; 1.35] mg/l accordingly, for > 2 till 5 years – 76.16 [61.31; 83.58] mcmol/l and 0.84 [0.56; 1.23] mg/l, for > 5 years – 77.18 [62.39; 85.12] mcmol/l and 0.91 [0.57; 1.24] mg/l.

Conclusion: Differences in GFR level were revealed when using formulas based on Creatinine and Cystatin C. In our opinion Creatinine - based formulas may underestimate the actual values of kidney function. The data obtained indicate the need to continue searching for the optimal formula for calculating GFR in children with DM1. Serum CysC, independent of height and weight of children, may reflect impaired renal function.

679 - P2.031

RENAL INVOLVEMENT IN PATIENTS WITH MITOCHONDRIAL DISORDERS

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Aims/Purpose: Mitochondrial disorders are a heterogeneous group of diseases with multi-systemic involvement. The most susceptible tissues are those dependent on the oxidative system, including the kidney.

Material and Methods: Retrospective, observational study of patients with mitochondrial disorders under follow-up in a tertiary hospital born between 1999-2022, regarding glomerular and tubular function parameters at diagnosis and at their last follow-up.

Results: A total of 88 cases (48/88 males) genetically confirmed in 81/88 and with a mean age at onset of 4.7+/-4.5 years were revised. The mitochondrial diseases were: Leigh syndrome (14.8%), MELAS (10.2%), PDH deficiency (10.2%), lactic acidosis (4.5%), Leber optic neuropathy (4.5%) and others (55.8%). At diagnosis, blood tests were performed in all patients, 69/88 had a urinary sediment, and during follow-up complete urinary biochemistry was performed in 39/88. At diagnosis: (A) Hydro electrolytic disorders: hypercalcemia (in 32/76), hyperuricemia (11/36), metabolic acidosis (16/25). (B) Renal biochemistry: proteinuria (4/33), haematuria (4/72), decreased glomerular filtration rate (7/88). Regarding tubular disorders: elevated 2-microglobulin (7/14), increased fractional excretion of sodium (6/17) and potassium (7/18), decreased tubular phosphate reabsorption (1/12), hypercalciuria (1/18), aminoaciduria (7/21) and glycosuria (5/69). In the last follow-up (a total of 76 cases with a mean age of 8.68 +/- 4.99 years): (A) No notable electrolyte abnormalities in blood (B) Renal biochemistry: Normal glomerular function, except for proteinuria (6/15) and haematuria (2/45), decreased glomerular filtration rate (3/56). Regarding tubular function, elevated 2-microglobulin (3/6), increased fractional excretion of sodium and potassium (2/15), decreased tubular phosphate reabsorption (2/13), hypercalciuria (3/20), aminoaciduria (5/20) and glycosuria (3/49).

Conclusions: A complete glomerular and tubular renal study was not performed in most patients, but in those who was performed, tubular damage was more prevalent. Regarding glomerular manifestations, proteinuria (12%) predominates over haematuria (5%), with < 10% of patients presenting a decreased glomerular filtration rate. Regarding the tubular function, B2 microglobulin was found to be altered in 50% of the patients in whom it was requested, with aminoaciduria being the second most frequent finding (33%).

680 - P2.032

CHILDHOOD CKD EPIDEMIOLOGY AND TRAJECTORIES IN ISRAEL: A POPULATION-BASED STUDY

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Aims/Purpose: To perform a population-based assessment of chronic kidney disease (CKD) rates, characteristics and outcomes in Israeli children.

Methods: Based on Israel's largest health care maintenance organization electronic database for the years 2008-2020, we included all children aged 2-18 years with at least two serum creatinine levels taken 3-12 months apart. "Ever CKD"(e-CKD) was defined as two subsequent eGFR measurements < 75 ml/min/1.7m2. We defined children with recorded normal eGFR results before the first CKD as "Incident" CKD. We examined long-term patient outcomes, including progression or reversal of ("aborted") CKD, mortality, and the necessity for kidney replacement therapy. For individuals with numerous eGFR measurements, we employed time-to-event Cox regression analysis to assess the impact of various demographic and clinical factors on CKD reversal, defined as the event of interest.

Results: Out of 324,093 eligible children, 3,729 (1.1%) had e-CKD along the study period, 33.2% of them with stage 3 or higher, diagnosed at a mean age of 10.2 ± 5.5 years, 53.9% of them were male. More e-CKD children belonged to the higher socioeconomic status groups in comparison to non-CKD ($p < 0.001$). After a mean follow-up of 6 ± 3.7 years, 0.38% of the e-CKD group died ($p < 0.001$ Vs. non-CKD) and 4.4% needed kidney replacement therapy. Incident CKD was found in 1,282 children (34.4%) who had an originally normal eGFR. Contrary to that, 2,176 eCKD children (58.4%) improved their eGFR to > 75 ml/min/1.73m2, thus considered as aborted CKD. Time-to-event Cox regression analysis for aborted CKD showed it was independently associated with younger age, male sex, a milder CKD stage, and the absence of congenital anomalies of kidneys and urinary tract. The point prevalence (with 95% CI) of pediatric CKD in Israel on December 31, 2020 was 692 (647, 739) per million. Median (IQR) annual incidence was 257 (204-269) new cases/million/year.

Conclusions: In this population-based study, CKD incidence and prevalence rates are much higher than previous reports of hospital based, overt CKD. The over-representation of children of higher socioeconomic status in the CKD group, and the absence of albuminuria-based CKD diagnosis in this study hint for much higher rates if these tests are applied for population screening. A significant proportion of children defined as CKD by eGFR measurements (most of them at stage 2) normalized their eGFR. Still, being defined as e-CKD was associated with increased morbidity and mortality.

738 - P2.033

AUTOMATED PAEDIATRIC EGFR ACROSS A CHILDREN'S HOSPITAL

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Aims/Purpose: Creatinine needs transforming into estimated glomerular filtration rate (eGFR) to be useful: for medication adjustments, to monitoring acute kidney injury, and to communicate severity of kidney disease to families. This is standard practice in adult medicine. In 2019 our children's hospital adopted electronic patient records (EPR). Where a height is available within the last 6 months, eGFR is automatic generated using the Bedside Schwartz 2009 formula which is internationally the most recognised and accepted for paediatric use. The result appears as a valve in an adjacent row to creatinine. We studied its utility.

Methods: Observational EPR study of eGFR measurements at our hospital of children 12 months and < 16 years between January 2022 and May 2023. Low eGFR was defined as < 90 ml/1.73m2/min. To ascertain clinician response to low eGFR, a subset of patients with 1-2 eGFR measures were reviewed, with 6 months follow up.

Results: Over 17 months 41,286 creatinines were measured. Height was available for 28,215 (68%) creatinines so auto-generating eGFR for 5,264 children. 58% were during 4,309 in-patient episodes, remainder in out-patients. 59%, 24%, 9% and 9% of children had one, 2-4, 5-9 or 10 eGFR results respectively. 23% of eGFR measures were low with 13% 60-89, 6% 30-59 and 5% < 30 ml/1.73m2/min. Low eGFR were most prevalent in nephrology (77%), intensive care (19%), cardiology/cardiac surgery (17%) and surgery (9%) samples. Analysis of 1463 children with 3 eGFR measures showed substantial eGFR changes between best and worse valves during study period. Of 1313 children with best eGFR 90 ml/1.73m2/min, 21% had worse eGFR 60-89 and 8% < 60. Of 88 children with best eGFR 60-89 ml/1.73m2/min, 41% had worse eGFR < 60. We gauged clinician response to low eGFR using a subset of patients with 1-2 measures. Of 46/514 (9%) with eGFR < 90, at follow up of six months 12 (26%) did not have eGFR repeated: in 8 creatinine value was within range for age, 2 were adult sized adolescents, and no reason given in 2 which when later recalled returned normal eGFR. A survey of parents and non-nephrology healthcare staff found high acceptability and preference of eGFR over creatinine.

Conclusion: With EPR it is feasible and welcomed to auto-generate paediatric eGFR for all specialties. As many children had substantial changes in eGFR the next step will be to study its utility to detect acute kidney injury or to aid medication renal dose adjustments. We recommend all hospitals with EPR incorporate paediatric eGFR for all subspecialities, like in adult practice.

747 - P2.034

KIDNEY LENGTH AND VOLUME IN OVERWEIGHT AND OBESE CHILDREN

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Aims/Purpose: Kidney size including kidney length (KL) and kidney volume (KV) assessment is of particular interest in early detection and monitoring of chronic conditions such as polycystic kidney disease. The recently published KL and KV normative values for pediatric patients aged 0-19 years may not be adequate in overweight and obese children due to higher body surface area (BSA). The aim of the study was to assess KL and KV, anthropometric parameters and kidney function in the group of overweight (≥85th body mass index - BMI percentile) and obese (≥95th BMI percentile) children from obesity treatment outpatient clinic.

Methods: KL and KV calculated from ultrasound-based kidney dimensions were collected in 130 overweight/obese Polish children aged 14.19 ± 2.18 years. In addition, anthropometric measurements, and biochemical parameters (including serum creatinine level, estimated glomerular filtration rate - GFR and urine protein/creatinin ratio) were obtained. KL and KV were correlated with age, height, waist circumference, BMI and BSA.

Results: The mean +- SD KL and KV z-scores were significantly higher at 0.81 ± 1.11 and 1.81 ± 1.31 (both $p < 0.001$), in comparison to median KL and KV height-related normative values). Notably, in 13.8% and 43% of the patients, KL and KV exceeded the 97.5th percentile. Out of anthropometric parameters the highest coefficient correlation with KL and KV was observed for BSA ($r = 0.59$; $r = 0.62$), followed by height ($r = 0.57$; $r = 0.59$), waist circumference ($r = 0.44$; $r = 0.48$), age ($r = 0.42$; $r = 0.4$), and BMI ($r = 0.36$; $r = 0.37$; $p < 0.001$ for all). We found no significant correlation between kidney size parameters (KL and KV) and eGFR and protein/creatinin ratio.

Conclusion: Overweight and obese children have increased KL and KV, though this is not associated with abnormal kidney function or proteinuria. Our findings suggest the necessity to establish separate normative kidney size values for this population of children.

755 - P2.035

ASSOCIATIONS BETWEEN PREMATURITY, BIRTH WEIGHT AND ADOLESCENCE BLOOD PRESSURE IN A NATIONWIDE COHORT

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Aims: Prematurity is associated with incomplete nephrogenesis and an increased incidence of acute kidney injury [1]. These factors may increase the risk of future kidney disease, including hypertension, proteinuria and reduced glomerular filtration rate [2]. The aim of this study is to evaluate the risk of hypertension or proteinuria in adolescents born prematurely or small for gestational age, in a nationwide cohort.

Methods: Study cohort included potential recruits examined in the Israel Defence Forces (IDF) medical facilities, between November 2005 and October 2018. Clinical and anthropometric data, including birth weight and blood pressure (BP) measurement, were retrieved from the IDF medical files. Out of the study cohort, adolescents born between January 1993 to December 2000 had data regarding gestational age at birth, retrieved from the Israeli Ministry of Health database.

Results: Study cohort included 513,802 participants, aged 17.3 ± 0.9 years, of whom 48,994 had gestational age data. Adolescents born as very- and extremely preterm infants and those born with very- or extremely low birth weights had higher incidence of hypertensive-range BP (55%, 47%, 19% and 12% respectively). No significant association between birth weight adjusted to gestational age and hypertension was found. Within the overweight and obese adolescents, those born as very low- and extremely low birth weights, had further increased hypertensive-range BP rate (Figure 1). Proteinuria was diagnosed in 0.33% of study cohort, with no significant difference between birth weight or gestational age categories.

Conclusions: A birth history of very low birth weight or of significant prematurity is associated with adolescence high blood pressure, in our study. These adolescents should be monitored for the development of hypertension and its potential complications.

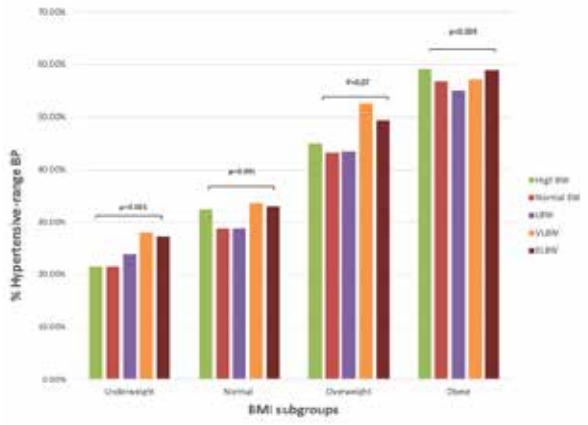

Figure 1: Prevalence of hypertensive-range BP in different birth weight groups (normal, LBW, VLBW, ELBW, high birth weight) according to BMI subgroups (underweight, normal, overweight and obese). [Abbreviations: BMI- body mass index, BW- birth weight, LBW- low birth weight, VLBW- very low birth weight, ELBW- extremely low birth weight]

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767 - P2.036

UNRAVELING THE PROGNOSTIC FACTORS IN CHRONIC KIDNEY DISEASE: SEEKING CLUES FOR IMPROVED OUTCOMES

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Aims/Purpose: Numerous factors play a role in the etiology and progression of chronic kidney disease (CKD) in children. Supportive therapies and renal replacement therapies increase the survival time and quality of life of the patients. In this study, we aimed to investigate unraveling the prognostic factors in chronic kidney disease.

Methods: A total of 187 patients who were followed up with a diagnosis of CKD in Çukurova University Faculty of Medicine, Department of Pediatric Nephrology between 2019 and 2023 were included in the study. The primary diagnosis of the patients, physical examination, clinical and laboratory findings at all visits during follow-up were evaluated.

Results: Of the patients included in the study, 102 (54.5%) were male and 85 (45.5%) were female. The median age at diagnosis was 108 (9-212) months. The most common diagnoses in the etiology of CKD were CAKUT in 34.8%, glomerular diseases in 17.6%, unknown cause in 10.2%, ciliopathies in 8%, tubulopathies in 7.5% and neurogenic bladder in 7.5%. The median age at diagnosis of patients with CAKUT was 76 months and they were diagnosed earlier than the patients in the other group (p =0.005). The mean height SDS of the patients was -1.78 ± 1.82 at the time of diagnosis and -2.68 ± -2.18 at the last visit (p < 0.001). Patients with a primary diagnosis of tubular disease had significantly lower height SDS at the time of diagnosis compared to the other groups (p =0.019). There was a positive correlation between the age at diagnosis and the final height SDS of the patients (p < 0.001, r = 0.259). Hypertension was present in 36.9% of the patients at the time of diagnosis. According to CKD stages, the frequency of hypertension increased after stage 3a, but there was no significant difference between the stages. The annual median GFR decline rate from the time of diagnosis to the last follow-up was found to be -3.18 ml/min/1.73m2 in those who received only supportive treatment. Age at diagnosis (p =0.006) influenced the rate of decline in GFR, while anemia (p =0.148), hypertension (p =0.872), hypoalbuminemia (p =0.333) and diagnostic groups (p =0.069) had no effect. When patients with CKD stage 5 at 5-year follow-up were analyzed for progression, early age at diagnosis, hyperphosphatemia, and high degree of proteinuria at diagnosis were found to be risk factors. In addition, anemia, hypoalbuminemia, metabolic acidosis, hypertension, and hyperphosphatemia were more common in patients with KRT.

Conclusion: When factors influencing prognosis in pediatric chronic kidney disease are identified and managed, the likelihood of progressing to end-stage renal disease diminishes.

785 - P2.037

NEUTROPHIL GELATINASE ASSOCIATED LIPOCALIN (NGAL) LEVELS ARE ASSOCIATED WITH ABNORMAL BLOOD PRESSURE PHENOTYPES IN PRETERM CHILDREN

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Aims/Purpose: Prematurity is considered as a risk factor for the development of hypertension (HTN) and other cardiovascular diseases during childhood and adulthood. The aims of the study were the evaluation of blood pressure (BP), serum biomarkers and the associations of the biomarkers with different BP phenotypes in ex-preterm children.

Methods: The present case-control study included children and adolescents born prematurely (ex-preterms) and children born at full term (controls). The participants underwent office and ambulatory BP monitoring and assessment of serum biomarkers, including NGAL, matrix metalloproteinase-2, -9 (MMP-2, -9), and Cystatin C (CysC) using enzyme-linked immunosorbent assay.

Results: 52 ex-preterms and 26 controls participated in the study with mean age of 10.74 ± 3.55 years. 17% of the ex-preterms and none of the controls had ambulatory HTN. 31% of the ex-preterm children and 23% of the controls had white-coat HTN. Serum biomarkers did not differ between BP phenotypes in the study population. Among ex-preterms, NGAL levels were found higher in children with WCH compared to children with normal BP [57.89 (IQR 50.79) versus 34.58 (IQR 46.22)], p =0.018). Receiver operator curve analysis showed that NGAL could be a significant predictor of WCH in the ex-preterm group with area under the curve (AUC) of 0.718 (95% CI 0.56-0.87, p =0.005) (figure).

Conclusion: HTN and WCH are common in ex-preterm children and adolescents, suggesting the importance of regular BP measurement in children with history of prematurity. The association of WCH with higher levels of NGAL in the ex-preterm children shows that more and larger studies are needed to examine the role of NGAL on BP phenotypes.

810 - P2.038

ACEI/ARB USAGE IN PAEDIATRIC CKD IN A NATIONAL CENTRE: ROOM FOR IMPROVEMENT?

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Aims/Purpose: The use of angiotensin converting enzyme inhibition or angiotensin receptor blockade (ACEi/ARB) to reduce proteinuria in patients with chronic kidney disease (CKD) has proven efficacy in adults in reducing progression to kidney failure(1). The impact of ACEi/ARB in pediatric ckd is similar, corroborated by large cohorts (2,3). Despite this, ongoing registry data and baseline data in studies suggests there is a reluctance to start these medications. We audited our CKD population over a decade, to determine the proportion on ACEi/ARB or intolerance. A secondary outcome was the rate of estimated GFR(eGFR) decline for those on and off ACEi/ARB.

Methods: All patients with eGFR < 60ml/min/1.73m2 on 2 occasions at least 3 months apart were identified using a database from 01/2013 to 03/2024. Data were collected on ACEi/ARB starting and stopping, reason for discontinuation, median protein:creatinine ratio (PCR) 6 monthly, eGFR 6 monthly. Data were collected until patients transplanted or the end of the collection period.

Results: From 276 patients, 181 were excluded leaving 76 eligible patients, 32 (42%) were on an ACEi/ARB at the time of data collection. 37 (49%) never received an ACEi/ARB. 7 discontinued ACEi/ARB: 2 due to hypotension, 1 due to hyperkalaemia, 1 due to rise in creatinine, 1 was deemed to no longer require it due to low proteinuria and adequate blood pressure, and 2 had no reason documented. Average PCR for patients on ACEi/ARB was 90 mg/mmol creatinine and 122 in patients not on. Average rate of GFR decline was 0.5ml/min/1.73m2/year for patients on ACEi/ARB and 1.1 for patients not on.

Conclusion: Despite evidence of potential benefit, nearly half of CKD patients in our institution were not on ACEi/ARB. Though reasons for discontinuing ACEi/ARB were often given, rationale for not starting was poorly documented.

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841 - P2.039

THE EFFECTS OF CICLOSPORIN AND METHOTREXATE ON KIDNEY FUNCTION IN THE TREATMENT OF SEVERE ATOPIC DERMATITIS IN CHILDREN - RESULTS FROM THE TREAT TRIAL

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Aims/Purpose: The TREatment of severe Atopic Eczema (TREAT) trial evaluated the impact of ciclosporin (CyA) versus methotrexate (MTX) on severe atopic dermatitis in 103 children and young people over 60 weeks. CyA and MTX can both affect kidney function and renal profile is routinely monitored alongside treatment. These tests are, however, not sensitive, as creatinine may change late in acute kidney injury (AKI). The present study comprehensively assesses the impact of CyA versus MTX on AKI through evaluation of functional (serum creatinine, symmetric dimethylarginine (SDMA), cystatin-C (CysC)) and kidney injury (urinary N-acetyl-beta-D-glucosaminidase (UNAG)) markers. No trial has yet assessed these biomarkers in the context of MTX and CyA.

Methods: All markers were measured at baseline, weeks 2, 12, 36, and 60. Treatment was randomised, 52 to CyA (4 mg/kg/day) and 51 to MTX (0.4 mg/kg/week). The difference at each time point was assessed using linear mixed models, including a random intercept for within-participant correlations across visits. The covariates in the models were the baseline value and an interaction between treatment group and visit in order to estimate the treatment effect at each time point.

The number of potentially relevant decreases in eGFR were collected, defined as a drop in eGFR > 20% from baseline (eGFR = height (cm) x 40 / creatinine).

Results: At baseline, demographics, clinical characteristics and renal markers were balanced between groups. Median values for markers remained stable within normal ranges in each arm, and were comparable between treatment groups at all time points (see figure 1). Using estimated difference in means between treatment groups at each time point demonstrated no statistically significant differences. 17 events affecting 14 (26.9%) participants in the CyA arm and 14 events affecting 8 (15.7%) participants in the MTX arm demonstrated a 20% decrease in eGFR. In every event the eGFR reverted to baseline when participants hydrated prior to a repeat test. No patients needed to stop treatment due to renal impairment.

Conclusion: CyA was not associated with decreased renal function or with worse renal outcomes than MTX over a 36-week treatment period. This provides reassurance to clinicians that both drugs can be used in severe atopic dermatitis, especially where access to newer biological agents is limited. Our data suggests no benefit to more frequent tests, and we suggest monitoring six-monthly on a stable regimen. To avoid potentially spurious drops in eGFR, children should be encouraged to maintain hydration when MTX or CyA is prescribed.

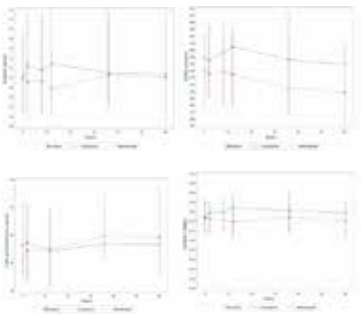

Fig 1. Median (interquartile range) profile plots for Creatinine, U NAG, SDMA and Cys-C s. Normal ranges: Creatinine: SDMA: < 533nmol/L, UNAG: < 56.0 PNP/h/mmol Creatinine: 1 month to 4 years: 13–39 µmol/l, 5-11 years 29–53 µmol/l, 12 years+ 40–90 µmol/l (micromoles/litre), Cystatin C: 0.5-1.27 mg/L (milligrams)

853 - P2.040

SPONTANEOUS VARIABILITY OF UREMIC TOXIN CONCENTRATIONS IN CHILDREN WITH CKD CANNOT BE EXPLAINED BY DIETARY DIFFERENCES

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Aims/Purpose: Within- and inter-patient variability of uremic toxins affect sample size calculation and study design, which underpins its understanding.

Methods: In this study, the within- and inter-patient variability of a selection of uremic toxins in a longitudinal cohort of children diagnosed with chronic kidney disease was assessed, using intraclass correlation coefficient (ICC) and the within-patient coefficient of variation (CV). Subsequently, the impact of anthropometry, estimated glomerular filtration rate (eGFR), dietary fiber and protein, and use of antibiotics on uremic toxin variability was evaluated, by comparing these adjusted models with an empty model with likelihood ratio test and by estimating the proportion of explained variability.

Results: Based on 403 observations from 62 children (9.4 ± 5.3years; 68% males; eGFR 38.5[23.1;64.0] mL/min/1.73m2), we found that that the within-patient variability is high for espe-cially PBUTs (ICC < 0.7; within-patient CV 37-67%). Moreover, eGFR was identified as predominant contributor of the inter- and within-patient variability for the majority of solutes, while no/minimal impact of the child's anthropometry, fiber and protein intake, and antibiotics on the variability of uremic toxin concentrations is found.

Conclusion: In conclusion, within-patient of especially protein-bound uremic toxins should be considered in future trial design and eGFR is a predominant factor driving inter/within patient variability.

856 - P2.041

ASSESSMENT OF BRAIN- DERIVED NEUROTROPHIC FACTOR AND IRISIN CONCENTRATION IN CHILDREN WITH CHRONIC KIDNEY DISEASE

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Aims/Purpose: The need to discover novel markers of chronic kidney disease, enabling improved classification of disease progression, encouraged us to evaluate the levels of selected myokines in the urine and serum of pediatric patients suffering from chronic kidney disease. In our study, we investigated the potential role of brain-derived neurotrophic factor (BDNF) and irisin (Ir) as markers of chronic kidney disease (CKD).

Methods: The study group included patients with a diagnosis of chronic kidney disease (n = 28) in stage 2-5, excluding dialysis patients. The control group (n = 44) was represented by children admitted for one-day surgery and with monosymptomatic nocturnal enuresis. BDNF serum and urine levels were estimated by the Cloud-Clone (USA)—Human BDNF kit. Irisin serum and urine concentrations were assessed using ELISA technique with Bio-Vendor (Czech Republic)- Human IRISIN ELISA nr RAG018R kit. OLA and OLAF trials for population of polish children was used to plot weight, height and BMI for age and sex on percentile charts.

Results: Serum levels of BDNF and irisin were reduced in CKD patients, while urine concentrations were increased for BDNF and decreased for irisin, compared to healthy controls. Positive correlations were found between anthropometric measures and urine BDNF concentration, as well as anthropometric measures and both serum and urine irisin levels in the study group. However, no dependence of the tested markers on the stage of chronic kidney disease was observed. According to ROC curve, both BDNF and Ir meet the requirements for a good disease marker, regarding sensitivity and specificity.

Conclusion: Our findings suggest that both BDNF and irisin could potentially serve as markers for chronic kidney disease. However, CKD is often accompanied by numerous complications, including malnutrition, which should be taken into consideration when drawing such conclusions. Since we did not find correlations between the levels of the studied markers and creatinine, urea, or eGFR values, but obtained associations with anthropometric parameters, it raises the question of whether they could serve also as markers for the risk of malnutrition. However, this will require further research.

879 - P2.042

COMPARISON OF IN-OFFICE BLOOD PRESSURE MEASUREMENT AND AMBULATORY BLOOD PRESSURE MONITORING IN ADOLESCENTS: DATA FROM A BIRTH COHORT IN A LOW-INCOME COUNTRY

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Aims / Purpose: The global prevalence of hypertension is on the rise, underscoring the importance of timely detection, thorough evaluation, and effective management of hypertension in children and adolescents. The aim of this study was to describe and to compare the prevalence of high blood pressure by in-office blood pressure measurement (ioBP) and ambulatory blood pressure monitoring (ABPM) in adolescents (11-13 years) from a birth cohort in a developing country.

Methods: Cross-sectional analysis of data from a birth cohort, assessing ioBP (n = 3254) and ABPM (n = 1067) from adolescents born in 2010-2011 (39.3% of the birth cohort), for the diagnosis of high blood pressure and its phenotypes. ioBP was measured using appropriate techniques in all participants, and the average of three consecutive measurements was used. Elevated BP (eBP) was defined as systolic (SBP) or diastolic (DBP) BP by ioBP between the 90th and the 95th percentiles, while hypertension (HTN) was defined as SBP or DBP by ioBP above the 95th percentile for age, sex, and height, based on the Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents, from the American Academy of Pediatrics (2017). ABPM was conducted using age-appropriate devices and was considered altered when the mean ambulatory SBP or DBP was above the 95th percentile, and/or if SBP or DBP load was above 25%.

Results: The participants' mean age was 12.3 [± 0.5] years and 52% were males. The proportions for prematurity (< 34 weeks), low birth weight, and intrauterine growth restriction were 2.5%, 1.3%, and 3.9%, respectively. The prevalences of overweight and obesity were 23.0% and 19.5%, respectively. By ioPB, HTN was diagnosed in 137 (4.20%), eBP in 175 (5.12%), summing an altered 9.34%. ABPM was inconclusive in 57 (5.3%) and altered in 308 (30.5%) participants. Comparing ABPM with ioBP measurements, 688 adolescents (68.1%) were classified as normal, 24 (2.4%) as having true HTN, 14 (1.4%) as having white coat HTN, and 284 (28.1%) as masked HTN.

Conclusions: Our study revealed a discrepancy between the diagnosis of hypertension using in-office blood pressure measurement (ioBP) and ambulatory blood pressure monitoring (ABPM), with prevalences of HTN of 4.20% and 30.49%, respectively, indicating a high prevalence of masked HTN. Further evaluation of these patients' profiles, along with potential associated risk factors, is warranted.

892 - P2.043

CAN ACUTE KIDNEY DISEASE PROGRESS TO CHRONIC KIDNEY DISEASE IN CHILDREN?

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Aims/Purpose: The aim of our study is to evaluate if children with a steady state renal function are at higher risk of developing chronic kidney disease (CKD) following a prolonged acute kidney injury (AKI).

Methods: We retrospectively analysed all patients admitted in a tertiary hospital from Romania, between 2014 and 2022. The inclusion criteria were: patients over 2 years old, recorded AKI episode, follow-up longer than three months and at least one serum creatinine measurement in the first 7 days following the AKI episode. The exclusion criteria was pre-existent CKD.

Results: The final cohort was represented of 313 patients with a mean age of 10 years (IQR 4.8-14), 52.1% males, and 52.1% from urban areas. The follow-up after AKI was 22.6 months (IQR 11-41). 66 out of 313 (21.1%) children progressed to acute kidney disease (AKD) after an AKI episode. 6.4% of the children progressed to CKD, 4% from the non-AKD group and 15.1% from the AKD group respectively. AKD increased the risk of CKD in both crude (OR = 7, 95%CI 2.3-21.4, p =0.0005) and adjusted analysis (OR = 4.1, 95CI 1.7-10, p =0.0015) for age, sex, environment, subsequent AKI, AKI severity and AKI causes. AKI and AKD severity had no influence on the risk of new-onset CKD.

Conclusion: AKD is an independent risk factor for CKD development following an AKI episode in children. Screening for CKD should be performed at 3 months after an AKI episode.

926 - P2.044

THE DIAGNOSTIC PROCESS FOR PEDIATRIC HYPERTENSION: IS IT ALL NECESSARY?

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Aims/Purpose: The diagnostic workup for pediatric hypertension includes a wide screening to exclude all the causes determining secondary hypertension. The objectives of this study were i) to evaluate the causes of hypertension in a population of hypertensive children and the costs of the diagnostic investigations, ii) to determine how many of these tests were actually contributory to obtain a diagnosis.

Methods: This was a single-center, retrospective cohort study of 70 patients aged 1–26 years referred between 2007 and 2024, to our pediatric nephrology center. The number of tests completed, their costs and diagnostic findings were determined. As per our clinical practice, patients underwent to the following investigations: serum creatinine, electrolytes, bicarbonates, lipid profile, thyroid hormones, renin, aldosterone, cortisol, adrenocorticotropic hormone (ACTH), dehydroepiandrosterone sulfate (DHEAS); urinalysis, proteinuria, creatininuria, microalbuminuria, beta2 microglobulin, urine metanephrines, normetanephrines, catecholamines, homovanillic acid; kidney ultrasound (US), doppler US of the renal arteries. Moreover, low-dose ACTH stimulation test and dexamethasone suppression test were performed when appropriate.

Results: Among the 70 hypertensive patients, obesity was found in 22 patients (31.4%), solitary kidney in 7 (10%), chronic kidney disease (CKD) in 6 (8.6%), kidney hypoplasia in 4 (5.7%), other congenital anomalies of the kidney and urinary tract (CAKUT) in 4 (5.7%); polycystic kidney disease (PKD) in 3 (4.3%), renal artery stenosis in 2 (2.9%); endocrine causes in 2 (2.9%); syndromes in 1 patient (1.4%). No cause was identified in 19 (27.1%) patients. We found that the extended protocol of tests was indeed useful in defining the cause of hypertension in cases of solitary kidney, CKD, kidney hypoplasia, other CAKUT, PKD, renal artery stenosis, endocrine causes, syndromes, for a total of 28 out of 70 patients. Kidney US had the highest yield of diagnostic results (36.2%). However, a reduced protocol consisting of serum creatinine, sodium, potassium, bicarbonates, urinalysis, kidney US and doppler US of the renal arteries was also effective in diagnosing a cause of hypertension or in identifying a patient with a suspect of secondary form of hypertension in 28/28 patients (100%) with a cause identified by the extended protocol. For the screening of the 70 enrolled patients, a total of 13.541,50 euro were spent (193,45 euro for each patient). However, applying the reduced protocol a total of 6.247,50 euro could have been spent (89,25 euro for each patient) with an economic save of 54%.

Conclusions: A simplified hypertension workup should be considered for the most cost-effective management. Further testing could be considered based on results of initial investigations.

945 - P2.045

HAEMOGLOBIN INTERFERENCE IN DRIED BLOODSPOT PROTEOMICS

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Aims/Purpose: The use of dried blood spots is an exciting prospect for longitudinal and at home sampling of paediatric kidney patients. This has the potential to avoid children missing school and reduce costs associated with attending medical appointments, whilst providing high quality samples for biomarker discovery and screening. Proteomics allows characterisation of the blood proteome using mass spectrometry. However, the presence of high abundance proteins, such as haemoglobin, can mask low abundance proteins making biomarker discovery less likely. By establishing methods to eliminate haemoglobin from reconstituted dried blood spots, other key proteins can be identified in CKD patients.

Methods: Initially, the best reconstitution for method for dried bloodspots was tested. A comparison was then undertaken between the three primary dried bloodspot devices: Capitainer qDBS, Neoteryx VAMS Mitra, and Whatman903. Once this was optimised the samples underwent haemoglobin depletion using Biotech Support Group's HemogloBind, NuGel HemogloBind and HemoVoid depletion kits. Protein components of these samples were then analysed by liquid-chromatography (LC)-tandem mass spectrometry (MS/MS) following digestion with trypsin. This was all done with healthy controls (n = 5).

Results: There was minimal difference in the proteins identified using different devices, although the Capitainer qDBS has been shown to have the highest success rate for patient sampling. The greatest number of proteins with the most consistency was extracted using 200 µL ammonium bicarbonate. Use of HemogloBind resulted in 21% of the haemoglobin remaining in the sample, NuGel 37% and HemoVoid resulted in only 6% of the haemoglobin remaining in the sample, compared to the untreated controls. Protein identifications increased from 578 in the untreated condition, to 703, 620 and 845 respectively.

Conclusion: The quantity of haemoglobin removed from the sample directly correlated with the number of proteins identified. Use of the HemoVoid resulted in the least amount of haemoglobin remaining in the sample, and consequently the highest number of protein identifications. This optimised workflow for robust blood spot proteomics may enhance the discovery of novel protein biomarkers for paediatric CKD, whilst allowing samples to be collected longitudinally from home to better understand the pathophysiology of CKD development and evolution.

960 - P2.046

DEPRESSIVE DISORDERS IN CHILDREN WITH CHRONIC KIDNEY DISEASE TREATED CONSERVATIVELY

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Backround: Chronic illness may contribute to the development of emotional and cognitive disorders. It is estimated that depressive disorders affect from 7 to 35% of pediatric patients with chronic kidney disease (CKD).

Objectives: The aim of the study was to analyze the incidence and characteristics of depression and depressive symptoms in children and adolescents with CKD treated conservatively.

Material and Methods: A cross-sectional, multicenter study was conducted, which included 73 children with CKD aged 8 to 18 years and 92 of their parents. The CDI2 (Kovacs Children's Depression Inventory 2) questionnaire was used, respectively CDI2: Self-Report and CDI2: Parent Form.

Results: Most children with CKD had average CDI2 scores. 11% of the respondents showed symptoms suggesting depressive disorders, and 8.2% of them met the criteria for depression. Significant relationships were found between age and the occurrence of interpersonal problems, age at the time of diagnosis of CKD and the total test result indicating the level of depressive disorders and also perceived lack of effectiveness in action and emotional problems. Depression symptoms depended on the stage of CKD and differed significantly between stages III and IV. We noticed a difference of opinion between children and parents regarding the reported symptoms of depression. Parents perceived their children's mental health as worse than themselves.

Conclusions: Depressive disorders occur in children with CKD treated conservatively. The main factors predisposing to their development seem to be age at the diagnosis of the chronic disease, its duration and the progression of CKD from stage III to IV. Discrepancies between depressive symptoms reported by children with CKD and their parents' assessment require further analysis. However, they already indicate that the final diagnosis of depressive disorders should be based on a multidimensional assessment of the patient's situation.

971 - P2.047

MEASURED GLOMERULAR FILTRATION RATE WITH IOHEXOL COMPARED TO FORMULAS IN CHILDREN WITH MILD CHRONIC KIDNEY DISEASE

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Aims/Purpose: Estimated glomerular filtration rate (eGFR) with different formulas are commonly used as a bedside tool to access kidney function in children and young adults. The aim of this study was to make a measurement of glomerular filtration rate (mgFR) in children with CKD and compare it to standard eGFR formulas.

Methods: 50 children with mild stages of CKD were measured with iohexol clearance measurement at 5 points and compared to standard eGFR equations for children. Estimated GFR was calculated by various standard formulas to try and find the best fit, using updated bedside Schwartz and CKID 2012 formula, which uses urea, creatinine and cystatin C values; as well as bedside Schwartz formula using cystatin C, Zapitelli et al., and Filler et al., both using cystatin C for bedside formulas. Measured GFR was compared to GFR measurement using creatinine clearance using plasma and 24-hour urine.

Results: There were a statistically significant correlations between all equations. The most correlating eGFR formula was the CKID 2012 formula, with the statistically significant correlation of 0.588 (95% CI 0.72 – 0.87), very good correlation was also found for bedside Schwartz formula, with correlation of 0.523 ($p < 0,001$, 95%CI 0.28 – 0.70). Cystatin C using formulas have a good correlation, while creatinine clearance did not correlate statistically significantly, probably due to problem with compliance when collecting the urine.

Conclusion: Glomerular filtration rate measured with iohexol showed good correlation with CKID 2012 formula in children. However, using it requires a significant amount of additional information, making bedside Schwartz equation more appropriate in terms of simplicity of use, since a very good correlation with this equation was also demonstrated.

980 - P2.048

MEASURING SERUM CREATININE ALONE RISKS MISSING RENAL FAILURE IN PAEDIATRIC PATIENTS WITH SHORT STATURE

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Aims: Serum creatinine is a widely used marker of kidney function. We observed discrepancy between a clinically normal serum creatinine concentration and a low estimated glomerular filtration rate (eGFR) in a patient with extremely short stature. This raised a concern that, in some patient groups, creatinine concentration might falsely reassure normal kidney function. Our aim was to investigate the risk of missing deteriorating kidney function when relying on serum creatinine concentration at a single paediatric tertiary centre. We hypothesised an increased chance of discrepancy between creatinine and eGFR in patients with short stature.

Methods: Retrospective analysis of electronic patient records for patients that attended outpatient clinic from 19/12/2023 to 29/02/2024 with a measured: height Z-score, urea, and creatinine. If measured, cystatin C results were collected. eGFR was calculated using Schwartz formula (ml/min/1.73m2) = 36.5 x (height (cm)/creatinine (µmol/L)). A discrepancy between creatinine and eGFR was defined as: eGFR < 80 when creatinine within the reference range or within 10% of the upper limit of normal of serum creatinine (ULN).

Results: Data from 4655 patients were analysed. Overall, 3370/4655 (72.4%) had a creatinine within the reference range or within 10% of the ULN; and 639/4655 (13.7%) had an eGFR < 80. There was discrepancy between creatinine and eGFR in 200/4655 (4.3%) patients across 21 subspecialties (most commonly nephrology in 58/200, 29%). Discrepant creatinine and eGFR were found in 29/317 (9.1%), 37/500 (7.4%) and 56/777 (7.2%) patients with height Z-score < -2, < -2.5, and < -3, respectively. Of patients with discrepant creatinine and eGFR, 142/200 (71%), 56/200 (28%), 37/200 (18.5%), and 29/200 (14.5%) had height Z-score ≥-2.0, < -2, < -2.5, and < -3, respectively. Of patients with discrepant creatinine and eGFR, and cystatin C measured, 18/22 (81.8%) had an abnormal cystatin C; and, of these patients, 9/18 (50%) had height Z-score < -2.

Conclusions: These results raise a concern that clinically significant reduced kidney function can be missed across paediatric sub-specialities when reliant on creatinine alone. In 4.3% of patients, creatinine concentration did not reflect the clinically significant low eGFR. Although a higher proportion of patients with short stature had a discrepancy between creatinine and eGFR, most patients with a discrepancy had a normal height; and, therefore, the results of this study highlight the potential for adverse outcomes, especially in patients whose renal monitoring heavily relies on serial creatinine measurements alone. Cystatin C is a biochemical marker of renal function that is less influenced by muscle mass, age, and gender; therefore, is clinically advantageous as compared to creatinine. Cystatin C could be routinely measured in certain patient groups to decrease the risk of overestimating kidney function.

999 - P2.049

EVALUATION OF EPICARDIAL ADIPOSE TISSUE AND INFLAMMATION INDICATORS IN CHILDREN WITH CHRONIC KIDNEY DISEASE

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Aim: Increased inflammation and atherosclerosis are observed in chronic kidney diseases (CKD). This study aims to evaluate and determine the effects of other inflammatory substances as well as epicardial adipose tissue (EAT), which plays an active role in the development of cardiovascular disease and atherosclerosis by secreting inflammatory substances in patients with CKD.

Materials and Methods: The study was conducted with the inclusion of pediatric patients aged 0-18 years with CKD who were followed up in the Pediatric Nephrology Outpatient Clinic of SBU Tepecik Training and Research Hospital. 59 CKD patients were examined retrospectively. The age at diagnosis, weight, height, BMI, laboratory parameters, EAT, and echocardiography (ECHO) findings were examined and recorded from the file data of these patients.

Results: When patients are evaluated in terms of ECHO findings, left ventricular mass index (LVmass), EAT1, and EAT2 (when viewed from the right ventricle and when viewed from the parasternal short screen in the parasternal long axis) measurements; It was observed to have a positive correlation with neutrophil/lymphocyte ratio (NLR) and parathormone (PTH) and a negative correlation with vitamin D level (Table 1).

Conclusion: Cardiovascular morbidity and mortality are high in CKD all over the world, and early diagnosis of cardiovascular diseases is important in this group of patients. Measurement and follow-up of EAT, especially showing its correlation with other inflammatory markers, can give us information in this sense as a non-invasive parameter.

Table 1. Correlation of inflammation markers and ECHO findings (r values)

	EAT1	EAT2	LVmass
NLR	0.682	0.717	0.828
PTH	0.764	0.837	0.751
Vitamin D	-0.914	-0.810	-0.870

1002 - P2.050

BILATERAL RENAL VEIN THROMBOSIS AS A RARE CAUSE OF NEONATAL ACUTE KIDNEY INJURY

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Aims/Purpose: Renal vein thrombosis (RVT) is a rare cause of acute kidney injury (AKI) in children. 70% of RVT occur in newborns with an incidence of 2.2 - 2.6 /100,000 live births. The typical triad consists of macrohematuria, thrombocytopenia and renal enlargement. In 35-40% of cases, RVT is bilateral. In these cases, thrombolysis and therapeutic anticoagulation are recommended, taking into account the contraindications (e.g., prematurity, perinatal asphyxia) and the overall risk of major bleeding of 15-21%.

Methods: We report the case of a male term newborn presented on day 2 of life with macrohematuria, thrombocytopenia (min. 55 G/l) and AKI pRIFLE stage 3 (creatinine 2.6 mg/dl, cystatin C 3.76 mg/l, eGFR 10 ml/min). Gestational diabetes had been present during pregnancy. The birth had taken place by emergency caesarean section due to a pathological CTG. Postnatally there were signs of perinatal asphyxia. In ultrasound, both kidneys were enlarged and there was intermittent end-diastolic zero flow over the renal arteries. The D-dimers were significantly elevated (> 35 ug/ml, N < 0.6). Due to perinatal asphyxia therapeutic anticoagulation (UFH 100 IU/kg/d, then switched to enoxaparin 8 mg/kg/d on day 3 of life) was initially performed without thrombolysis despite bilateral renal vein thrombosis with AKI. On day 4 of life, thrombolysis with rtPA 0.05 mg/kg/h was started because of oliguria and further declining kidney function. UFH was given additionally. Due to mild bleeding signs, thrombolysis was terminated after 24 hours. D-dimers had risen from 17.5 to > 35 ug/ml postulating efficacy of lysis. Diuresis resumed one day after lysis. On the 6th day of life, heparinization was switched to LMWH and continued for a total of 6 months. Despite lysis and anticoagulation, serum creatinine continued to rise until the 11th day of life (max. creatinine 8.1 mg/dl, cystatin C 3.87 mg/l, urea 110 mg/dl) and then fell continuously.

Results: One year later, renal function is still impaired (eGFR 65 ml/min, cystatin C-GFR 35 ml/min). However, the boy thrives and develops very well. Apart from antihypertensive therapy, he is not receiving any other medication.

Conclusion: Bilateral renal vein thrombosis in newborns is associated with a high risk of kidney failure. In bilateral renal vein thrombosis, thrombolysis with rtPA and anticoagulation should be performed at an early stage. However, contraindications of lysis need to be considered and critically discussed.

1012 - P2.051

ASSESSEMENT OF LIFESTYLE HABITS OF MEDITERRANEAN DIET AND PHYSICAL LITERACY IN CHILDREN WITH EARLY STAGES OF CHRONIC KIDNEY DISEASE

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Aims/Purpose: Chronic kidney disease (CKD) is a major cause of morbidity and mortality worldwide in adults as well as in pediatric population. Children with early CKD stages have no major medical lifestyle restrictions. However, in early CKD stages lifestyle interventions to slow down disease course may be more beneficial. Purpose of the present study is to investigate: a) whether pediatric patients with early stages of CKD follow the Mediterranean diet patterns as well as their level of physical literacy, b) the relationship between renal function of patients with early stages of CKD with adherence to the Mediterranean diet and their physical literacy.

Methods: A total of 25 children aged 7-18 years who attended at the outpatient clinic of the Pediatric Nephrology Unit of the Hippocration General Hospital, were investigated. Patients' renal function was assessed by eGFR using the Schwartz equation. Nutrition was assessed by the KIDMED questionnaire, which has been weighted for the Greek population. Physical literacy was assessed by the HALO CAPL-2 questionnaire and the areas of exercise motivation and self-confidence as well as knowledge and understanding were assessed around physical activity. Finally, a comparison was made between renal function and individual categories of adherence to the Mediterranean diet and physical literacy using univariate analysis of variance (SPSS 27).

Results: From the statistical analysis of the results, a low rate of adherence to the Mediterranean diet was observed as 20% of the participants showed a KIDMED Score ≥ 8), which seems to agree with similar studies in the Greek territory regarding young adults. In terms of physical literacy, 50% of the respondents were observed to be in the highest level of the questionnaire ("excelling") in relation to motivation and self-confidence for exercise and in the second highest level ("progressing") in relation to knowledge and understanding about physical activity. No statistical significant difference was observed between respondents' kidney function and adherence to the Mediterranean diet or individual domains of physical literacy.

Conclusion: Dietary habits of the pediatric population with early stages of CKD show a departure from Mediterranean diet patterns. This happens possibly due to the fact that patients with early stages of CKD had no major medical diet restrictions. However, satisfactory results are observed in the areas of motivation and understanding of physical activity and physical literacy. Diet and increased physical activity seem to play an important role in the progression of CKD and the occurrence of its complications. We should encourage families and children to follow healthy dietary habits even from early stages of CKD. Future research in the areas of nutrition and physical activity in these patients is necessary in order to design strategies suitable for improving their quality of life.

1020 - P2.052

KIDNEY DISEASE IS A FREQUENT FINDING IN PATIENTS WITH METHIONINE SYNTHASE DEFICIENCY

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Background: Methionine synthase deficiency (MSd) is a rare metabolic disorder affecting the intracellular cobalamin-processing pathway leading to elevated plasma homocysteine and low plasma methionine levels. Few reports exists regarding glomerulopathy in MSd (1, 2).

Methods: This retrospective observational study involve individuals diagnosed with MSd at Oslo University Hospital. The study evaluates Glomerular Filtration Rate using iohexol plasma clearance (iGFR), kidney biopsy findings and proteinuria and haematuria. Additionally, the study aims to identify the use of proper blood pressure lowering agents in cases of hypertension with or without proteinuria.

Results: From 1988 to 2024, we genetically identified nine patients with CblG disease. The first patient died at age 15 with unknown kidney status. For the remaining eight patients, the mean age at genetic diagnosis was 12.9 years (range 3.1 to 24.1 years), and the mean age at last follow up was 18.6 years (range 11.3 to 31.5 years). Mean age at biopsy was 9.2 years (range 6.8 to 14.0 years). Four of the eight patients (50%) had decreased iGFR, three had glomerulopathy and four patients used ACEi or CCBs (Table 1).

Table 1

P.nr	iGFR	Biopsy	Hematuria	Protein-creatinine ratio	ACEi or CCB
0	ND	ND	ND	ND	ND
1	14	÷	ND	ND	CCB
2	137	TMA in repair	+	136	ACEi
3	62	MPGN	+	222	ACEi
4	31	Chronic TMA	÷	52	ACEi
5	81	÷	+	ND	÷
6	121	÷	÷	4	÷
7	131	÷	ND	ND	÷
8	132	No	ND	ND	No

Abbreviations: ND: no data, TMA: thrombotic microangiopathy, MPGN: membranoproliferative glomerulonephritis, ACEi: angiotensin-converting enzyme inhibitor, CCB: calcium-channel blockers.

Conclusion: Chronic kidney disease and glomerulopathy were frequent findings in our cohort. We suggest surveillance for proteinuria in MSd. Further studies are necessary to establish pathogenesis, mainly if an association between MSd and alterations in the complement system exists.

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1021 - P2.053

HEIGHT AND BODY MASS INDEX IN ADOLESCENTS WITH CHRONIC KIDNEY DISEASE AT THEIR TIME OF TRANSITION TO ADULT HEALTHCARE: A CROSS-SECTIONAL STUDY OF THE REGIONAL REGISTRY FROM 2013-2022

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Aims/Purpose: The aim of this study was to describe the height and body mass index (BMI) distributions of 17-year-old adolescents with chronic kidney disease (CKD) at their time of transition to adult healthcare and to identify the relationships between these characteristics and clinical data.

Methods: This was a cross-sectional study based on a 10-year regional registry containing data on 17-year-old adolescents with CKD hospitalized at Voronezh Regional Children's Clinical Hospital from 2013 to 2022. Short stature was defined as the height SDS < −2, while tall stature was defined as the height SDS > 2. Underweight, overweight and obesity were defined as BMI-for-age SDS < −2, > 1, and > 2, respectively. Standard deviation scores (SDS) were calculated according to the WHO reference. The results are presented as the median and first and third quartiles [Q1;Q3]. Statistical significance was defined as a p value < 0.05.

Results: The registry contained data on 415 17-year-old adolescents with CKD. The majority of the patients had non-glomerular CKD (81%; 336/415). The median GFR based on the CKiDbed, CKiDU25, EKFC, and CKD-EPI equations were 81 [72; 94], 92.9 [79.9; 106], 92.1 [79.5;105.7], and 118 [100;130] mL/min/1.73 m2, respectively. By the time they turned 17, the boys had reached a median height of 178 cm [172;183] and the girls 164 cm [160;168]. Overall, the median height SDS was 0.23 [-0.46;0.86] (min:-5.74; max:3.31) and the median BMI SDS was 0.02 [-0.87;0.75] (min:-4.05; max:5.73). Short stature in patients with CKD was observed in 3.6% (15/415) of patients and tall stature in 4.1% (17/415). Most patients had a normal weight (78.8%; 327/415), followed by overweight and obesity (16.4%; 68/415) and underweight (4.8%; 20/415). There were significantly more adolescents with obesity and ones that were overweight in 2018-2022 than in 2013-2017. Underweight was more common in boys (p =0.043). Compared to normal weight adolescents, overweight and obese adolescents had higher creatinine levels (p =0.013) and lower GFR. Compared to patients with a normal height, patients with a short stature more often had a solitary or solitary functioning or transplanted kidney (p =0.01), lower GFR based on the CKiDbed (p =0.009) and CKiDU25 (p =0.008), and higher potassium (p =0.032) and urea (< 0.001) levels. However, there were no differences in the creatinine levels (p =0.457) and GFR based on the EKFC (p =0.333) and CKD-EPI (p =0.273) equations. Among the tall stature group, 47% (8/17) had obstructive uropathy, which was significantly greater than in normal height patients with CKD (19.3%; 74/383) (p =0.006).

Conclusion: The use of height-independent GFR equations in patients with a short stature results in overestimation of the GFR and underestimation of the severity of CKD in such patients. It should be considered at the time of transition to adult healthcare. Tall stature should be investigated as a risk factor for CKD.

1034 - P2.054

EFFICACY OF USING ANGIOTENSIN-CONVERTING ENZYME INHIBITORS VERSUS ANGIOTENSIN II RECEPTOR ANTAGONISTS AS ANTIPROTEINURIC TREATMENT IN CHILDREN AND TEENAGERS WITH DIABETES

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Introduction: Diabetic nephropathy is the world's leading cause of chronic kidney disease and is related to high morbidity and mortality. Persistent microalbuminuria is a marker of incipient nephropathy, progression of kidney damage and cardiovascular risk, so its control is essential. There is little evidence on which antiproteinuric drug is the most effective in this population.

Aims/Purpose: To evaluate the efficacy of angiotensin-converting enzyme inhibitors (ACE inhibitors) versus angiotensin II receptor antagonists (ARBs) in the control of microalbuminuria during a one-year follow-up.

Methods: Retrospective descriptive study of patients < 18 years of age affected by diabetic nephropathy with follow-up in our center in the last 10 years.

Results: 18 patients were analyzed, 11 received enalapril and 7 received candesartan. 50% were women and the median age was 12.5 years (range 7 – 16). Antiproteinuric treatment reduced albuminuria by 70% at 12 months. By treatment groups, enalapril obtained the greatest reduction (68.7 versus 55.6%). In patients with normal weight for their age, the decrease in albuminuria was greater in both groups, also in favor of enalapril (93% versus 80.1%). In contrast, in overweight/obese patients, candesartan obtained the best results (55.5% versus 9.2%). 5 patients (28%) were hypertensive. In patients with normotension, the reduction in albuminuria remained stable in the candesartan group, but increased in the enalapril group (53.1% and 84.5%, respectively). Systolic blood pressure showed a slight and similar decrease in both groups (14.5% enalapril and 10% candesartan). Diastolic pressure and glomerular filtration rate (-3.4 ml/min/1.73m2 enalapril and -4.8 ml/min/1.73m2 candesartan) remained stable. Only 2 subjects (11.1%) had mild side effects, both have received enalapril.

Conclusions: ACEIs and ARBs are effective and safe antiproteinuric drugs in pediatric diabetic patients. Enalapril showed a greater reduction in albuminuria after 12 months of treatment although it presented more side effects. This difference in favor of enalapril was maintained in patients with normal weight and was greater in normotensive patients. In overweight/obese patients, candesartan showed better results. No differences were observed in the reduction of blood pressure or glomerular filtration rate. Prospective studies are necessary to confirm these findings.

1064 - P2.055

HYPOTHYROIDISM: AN IMPORTANT REVERSIBLE CAUSE OF PEDIATRIC ACUTE KIDNEY INJURY

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Aims: Hypothyroidism is an uncommon but important reversible cause of acute kidney injury (AKI), especially in the pediatric population. Early identification of AKI can offer appropriate management, which may prevent the progression to chronic kidney disease (CKD). We aim to describe two cases of hypothyroidism-induced AKI, and to assess special characteristics of these patients.

Methods: Data were retrieved from medical records of Schneider Children's Medical Center, a tertiary, university affiliated, pediatric medical center in Israel.

Results (Cases description):

CASE 1: A 16-year-old girl presented with general weakness, fatigue and abdominal pain. Her past medical history was unremarkable, except for overweight. Her physical examination was normal with a blood pressure around 50th percentile. Her laboratory evaluation included: a normal complete blood count, a blood urea nitrogen (BUN) of 32 mg/dl, elevated serum creatinine of 1.34 mg/dl (her past creatinine two years prior was 0.49 mg/dl), mildly elevated liver enzymes, and creatine phosphokinase (CPK) of 108 U/L (normal range: 20-200). She was admitted for further investigation for AKI assessment, and a biopsy appointment was held in advance. Later, a hypothyroidism diagnosis was made with an elevated thyroid stimulating hormone (TSH) of 211.6 mIU/ml (0.48-4.1), and low free thyroxine T4 of 2.57 pmol/L (10.7-18.4). Anti-thyroid peroxidase (TPO) was extremely elevated > 1300 IU/ml. After 2 months of thyroid replacement therapy, her clinical symptoms resolved, and her blood creatinine level improved significantly to 0.91 mg/dl. Her TSH level was 46.8 mIU/ml and T4- 10.64 pmol/L.
CASE 2: A 17-year-old boy was admitted in a general pediatric ward due to AKI with a creatinine level of 1.75 mg/dl. His past medical history was notable for trisomy 21, an atrial septal defect, asthma, and obesity. He underwent a partial thyroidectomy one year ago due to thyroid adenoma. During the last 6 months, he gained 20kg in weight and suffered from fatigue and weakness. A physical examination revealed mild hypotonia and known dysmorphic features. His workup included a normal renal and bladder ultrasound, normal blood electrolytes, slightly elevated liver enzymes, and TSH levels above 150 mIU/ml with T4 < 3.3 pmol/L. CPK level was markedly high- 1808 U/L. He was diagnosed with severe hypothyroidism. After 6 months of thyroid replacement treatment, renal function tests were normal with a serum creatinine of 0.9 mg/dl, TSH of 23.7 mIU/ml and T4 of 17.7 pmol/L.

Conclusion: Although rare, hypothyroidism is an important reversible cause of AKI. We suggest assessing thyroid function and CPK in any unexplained AKI condition, as treatment can improve kidney function and prevent unnecessary invasive procedures. We assume an early diagnosis can decrease complications and progression to CKD, and probably improve long-term renal prognosis.

1084 - P2.056

COPEPTIN AS A POTENTIAL BIOMARKER OF CHRONIC KIDNEY DISEASE TO PREDICT THE DISEASE PROGRESSION IN CHILDREN WITH CHRONIC KIDNEY DISEASE

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Aims/Purpose: Biomarkers to predict the onset and progression of chronic kidney disease (CKD) in children are lacking, and no such definite biomarkers have been implicated in the diagnosis of CKD. Copeptin, a surrogate marker of arginine vasopressin (AVP), is partially cleared by the kidneys. In CKD or end-stage kidney disease patients, a positive association of copeptin with a decline in kidney function has been observed, and the level of copeptin was elevated compared to those with normal kidney function. We conducted this study to evaluate copeptin as a CKD marker and predict the disease progression by estimating the copeptin levels at baseline and 12 months follow-up in children with CKD stage 2 and above.

Methods: This prospective single-centre cohort study was conducted in children under 14 years with CKD stages 2-4. Healthy children attending vaccination clinics or siblings of patients served as control groups. Blood and urine samples were collected at enrollment and one-year follow-up for routine investigations, as well as serum copeptin, cystatin C, and uNGAL estimation. The estimated glomerular filtration rate (eGFR) was calculated using the Bedside Schwartz formula from the CKiD study. CKiD equation was used to calculate eGFRCr and eGFRCys.

Results: A total of 110 children (60 cases and 50 controls) were enrolled in the study. The male-to-female ratio in cases and controls was 57:3 and 33:17, respectively. The median age for cases and controls was 84 (IQR: 46.7-132) and 77.5 (IQR: 43.5-101.5) months. The diagnosis of CKD was congenital anomalies of the kidney and urinary tract (CAKUT) in all cases. Among the cases, 34 (57%) had stage 2 CKD, 21 (35%) had stage 3 CKD, and only 5 (8%) had stage 4 CKD. The mean eGFR of cases was 58.3 ± 18.7 ml/min/1.73m2. Serum creatinine-based renal clearance decreased from median eGFR 85 (59 to 155) to 63 (39 to 81) ml/min/1.73m2 at the end of 12 months follow-up. Although this difference was statistically insignificant (p =0.97). Among the cases, there was a significant rise in the serum copeptin levels from baseline 483.08 ± 319.2 pg/ml to follow-up at one year, i.e. 1046.82 ± 823.53 pg/ml ($p < 0.0001$). A significant difference was noted in the baseline values of serum cystatin C, i.e. 1512.98 ± 643.77ng/ml and 719.68 ± 106.96 ng/ml ($p < 0.0001$), and urine NGAL, i.e 13.53 ± 11.72 & 1.76 ± 2.37 ng/ml ($p < 0.0001$) between the cases and controls. There was no significant correlation (correlation coefficient = 0.10) between change in eGFR and copeptin levels during 12 months of follow-up in children with CKD stages 2, 3, and 4.

Conclusion: No significant correlation was found between the change in eGFR and copeptin levels during 12 months of follow-up. This can be due to the slow deterioration of renal functions, as most of the cases had underlying CAKUT, which is known to have a slow progression of CKD and a small sample size.

Keywords: Biomarkers, children, chronic kidney disease, copeptin.

1108 - P2.057

ESTIMATED GFR IN CHILDREN: THE NEPHROLOGIST IN THE MIST

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Aims: Glomerular filtration rate is essential for daily practice in pediatric nephrology. Being essential for a correct identification, classification and management of chronic kidney disease as well as progression, dosing of nephrotoxic drugs or those that require adjustment an accurate and precise GFR in needed. There are several formula for estimate GFR based on creatinine and/or cystatin C. However, the reliability of these equations remains a matter of debate. In adults, the error of formulas estimating renal function has been extensively studied, alowing that is large, frequent and random. Similar information in Pediatrics is lacking.

Purpose: To analyze the agreement between GFR equations with measured GFR.

Methods: We measured GFR by the clearance of iohexol-DBS (dried blood spot) in a group of children. Simultaneously were measured serum creatinine, urea and cystatin C for estimate GFR by 40 formulas. After de injection of iohexol, capillary blood is taken by finger prick and deposital onto filter paper (https://lfr.ecihucan.es/). This procedure is particulary useful in children. The agreement between estimated and measured GFR was assessed by specific statistics for continuous data, including the concordance correlation coefficient (CCC), total deviation index (TDI),coverage probability (CP).

Results: 184 children were studied (CAKUT 33%, glomerulopathy 7%, hypertension-obesity 27%, oncology 24%, other 8%) . The error was wide, as reflected by an average TDI of the formulas was 48% (45% Gao13, 55% FAScrea). The average CCC was 0.69 (Berg 0.73, FAS cr 0.64) y CP was 0.30 (Gao 0.32, Chechade 0.28). They were provide 10 examples of the error to help understanding of the reader (table 1).

Conclusion: The error of the formulas is wide, frequent and random, which limits its usefulness in the clinic.

Table 1.

Case	mgFR ml/in/1,73m2	Schwartz 09	FAS Cr	Gao 13	CAPA	Berg	FASCis C	FAScomb	Chechade 14
1	66	107	86	102	98	81	80	82	89
2	103	78	74	85	99	103	98	82	84
3	123	79	78	87	85	88	85	81	83
4	102	72	73	81	79	83	81	76	79
5	88	61	55	69	75	78	77	64	69
6	75	86	85	89	97	102	97	91	86
7	59	70	70	78	83	87	85	76	77
8	80	106	104	107	50	51	54	70	90
9	91	70	73	79	77	81	80	75	77
10	38	54	63	57	47	48	52	57	53

1121 - P2.058

MIND THE GAP: IMPROVING TRANSITION USING AN INTEGRATED CARE PATHWAY FOR YOUNG PEOPLE WITH CHRONIC KIDNEY DISEASE

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Purpose: Transitioning from paediatric to adult services increases morbidity and mortality risk. Over half of young people (YP) with chronic kidney disease (CKD) and parents experience a sense of being unprepared and anxious regarding this transition (Crawford et al. 2020). They express feeling powerless, have insufficient time to adequately prepare and lack control over decisions on timing of transfer and who care is transferred to. They also report a lack of clarity regarding the transfer plan and distrust in the adult team. These challenges result in adverse outcomes such as non-adherence to medical recommendations, low attendance at clinics and decisional conflict. Empowering YP and parents to be involved in care decisions is vital for successful transition, leading to improved patient experience, treatment adherence, knowledge, and trust in the adult team. To address this, we (Ready Steady Go-TIER Collaborative (www.readysteadygo.net)) developed a programme, 'Moving on Up Together: 16+ pathway', designed to be used 12-24 months before YP transfer to adult services. The pathway discusses the options, records decisions made, notes action plans and collects feedback from YP and parents. It ensures an acute focus on shared decision making, empowering patients to be active contributors in their care.

Aim: To assess the effectiveness of the 'Moving on Up Together: 16+ pathway' in improving the transition from paediatric to adult services.

Methods: As part of the pathway, at age 16 YP with CKD (stage 1-5) were informed:
- that their care will be transferred to adult services in 12-24 months
- they need to be involved in decisions surrounding who, where and when their care will transfer, e.g. how many joint adult-paediatric appointments there will be and where these will be held
- of the options and why some options were not appropriate, e.g. sole reliance on primary care for a kidney transplant

A feedback survey 'Making a Decision Together (SDMQ9+1)' was then completed by YP and parents to see how involved they felt in decision-making regarding the transition to adult services.

Results: From 2021 - 2023 100 responses were received (YP =51; parent = 42; YP + parent = 7). 96% of YP and parents felt involved in the decision making on where, when and to whom their care would be transferred to in adult services. 92% were aware of the transition plan put in place and 90% found this information useful. Overall, YP and parents felt reassured about the move to adult services and trusted the adult team; "I have been thinking about the future of my care for a long time ... this has completely put my mind at ease :)" (Young person, 2023).

Conclusion: Through its inclusive approach, the 'Moving on Up Together: 16+ pathway' ensures active participation of YP and parents and provides clarity and support, resulting in an improved transition to adult services and positive healthcare experience. Further work is needed regarding long term outcomes.

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1145 - P2.059

RENOVASCULAR HYPERTENSION REFRACTORY TO TREATMENT, A CASE REPORT

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Aims/Purpose: Describe a patient with renovascular hypertension refractory to treatment

Methods: Clinical case report

Results: Renovascular disease is a relatively rare but important cause of hypertension in children. It is responsible for 5 to 25% of hypertension in this population. Causes of vascular hypertension include narrowing of the renal arteries, mid-aortic syndrome, coarctation of the aorta, aneurysmal disease, and vasculitis. It can often be treated with angioplasty or surgery.

Clinical case: 13-year-old female patient being followed up by pediatric nephrology for renovascular arterial hypertension diagnosed at 3 years of age. CT angiography reported stenotic right renal artery, two right polar arteries with proximal stenosis. In the left kidney, hypoplastic main renal artery with severe stenosis and very hypoplastic superior polar artery. Hypoplastic left kidney. Stenosis in the superior mesenteric artery. Captopril test with elevated renin and aldosterone dosage (differential renins (350 vs 334 mIU/ml). Aldosterone greater than 100 ng/dL (orthostatism normal value 3.5 - 30). She has had multiple catheterizations for therapeutic purposes and stent placement on several occasions, with numerous complications. In 2021, immunological study was repeated (previously normal), showing positive anti-MPO ANCA and positive ANA. With suspicion of vasculitis, a renal biopsy was performed, which reported mesangial glomerulonephritis with deposits of IgM and IgG, and immunosuppressive treatment was initiated with corticosteroids and mycophenolate mofetil without obtaining a response. The last tomographic study was worse compared to previous ones, reporting proximal stenosis of the stent in the right inferior polar artery, stenosis at the origin of the celiac trunk and at the origin of the superior mesenteric artery. Currently, she persists with hypertension (mean 140/80 mmHg; 95th percentile of blood pressure: 114/76 mmHg) with multiple hypotensive therapy (amlodipine, labetalol, clonidine and hydralazine) at maximum doses, and spironolactone at 3 mg/kg/day. She presents stage two chronic kidney disease and mild proteinuria.

Conclusion: Renovascular hypertension is an important cause of hypertension in pediatrics. Endovascular treatment is usually successful. In this case, we describe a patient with persistent renovascular arterial hypertension despite established endovascular and pharmacological treatments at maximum doses with probably bad prognosis.

1148 - P2.060

CHILDREN FACING GLOBAL CHANGES - DIAGNOSIS OF CHRONIC KIDNEY DISEASE IN PANDEMIC AND MIGRATORY CONDITIONS

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Aims/Purpose: The clinically silent course of chronic kidney disease (CKD) at its early stages impedes prompt detection, especially under unfavorable social and healthcare conditions like COVID-19 pandemia or migratory processes. Pediatric CKD is mainly caused by congenital anomalies of the kidney and urinary tract (CAKUT), which should be diagnosed early enough to slow down the CKD progression and delay the onset of complications. Thus, the knowledge about actual etiology and clinical picture of CKD among pediatric patients is of paramount importance. The aim of this study was to evaluate the clinical data of children with CKD diagnosed at the Department of Pediatric Nephrology, Wrocław Medical University, Poland, in the last 10 years.

Methods: The clinical data of 175 CKD pediatric patients were assessed retrospectively. The etiology, stage of CKD at diagnosis, and occurrence of anemia, were analyzed in relation to the patients' age (subgroups: < 2 years of age, between 2 and 10 years, and > 10 years). Kidney function was assessed by the serum creatinine concentration in patients < 2y, eGFR values served for CKD stage classification in children > 2y. The comparative analysis concerned two five-year intervals: 2014-2018 and 2019-2023.

Results: The number of children diagnosed with CKD in 2014-2018 was 39% higher than in the following 2019-2023 period and this disproportion was most evident in the 2-10y age group (72%). CAKUT were the most frequent causative factors of CKD in all age groups, with the highest impact among patients < 2y (66% in 2014-2018 period, 40% in years 2019-2023). Meanwhile, the increasing share of genetic disorders in CKD etiology was noted, with the most clear progress among children < 2y (23% in 2014-2018, 36% in 2019-2023). The participation of unknown causes of CKD increased with the patients' age, irrespective of the time period, and reached 22% (2014-2018) to 24% (2019-2023) in patients > 10y. Among children < 2y, 13% (2014-2018) to 23% (2019-2023) presented with advanced CKD and anemia at diagnosis. In children 2-10y the proportions between time intervals looked less favorable: 58% vs. 39% of children with CKD stages 3-5, 61% vs. 43% of patients with anemia. The most alarming trend was revealed among those > 10y: 45% (2014-2018) and 75% (2019-2023) were diagnosed with advanced CKD, whereas the occurrence of anemia at diagnosis increased from 33% (2014-2018) to 64% (2019-2023).

Conclusions: The modern diagnostic tools secure identification of genetic diseases as a significant causative factor of CKD in children. The pandemic and migratory conditions may restrict admissions to pediatric nephrology departments in due time, thus delaying the diagnosis of CKD. The latter could add to the relatively high participation of unknown causes of CKD, identifying adolescents as a group most susceptible to late CKD diagnosis.

1165 - P2.061

MULTIPLE OFFICE BLOOD PRESSURE MEASUREMENT FOR THE DIAGNOSIS OF HYPERTENSION IN CHILDREN

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Aims/Purpose: Blood pressure (BP) measurement (M) in children may be challenging. Current international guidelines suggest measuring BP three times. However, in a previous study, we reported that both systolic (S) and diastolic (D) BP values of the first three readings are unreliable. At our Centre, multiple Office BP Measurement (mOBPM) has been introduced as standard practice for hypertension diagnosis in children since 2010. mOBPM consists of 10 serial BP readings taken at 3-minute intervals using a validated automated oscillometric device. After discarding outlier readings (< 5th and > 95th centile of the recorded values), the coefficient of variation (CV) and the remaining SBP and DBP mean values are calculated by a software. This contribution is aimed at testing mOBPM in a cohort of children to confirm our previous observations, and to bolster its use as an effective and practical tool to assess BP in children.

Methods: School children underwent mOBPM at baseline and after 12 months. After excluding M series with a CV > 15%, the mean SBP and DBP values obtained by mOBPM were compared with the 1st, 2nd, 3rd and 4th M (t test for paired data). The number of children with BP > 90th centile within the aforementioned M was also determined.

Results: One hundred and seventy-five children (93 females, 53.1%) with a mean age of 8.6 ± 0.3 and a mean BMI of 17.5 ± 2.9 (BMI > 20, n = 34; 19.4%) were enrolled. Thirteen mOBPM were excluded for a CV > 15% in either SBP or DBP. As represented in Figure 1, the remaining 328 mOBPM showed that the mean of the first three SBP and DBP values were higher ($p < 0.001$) than those obtained with mOBPM. The same held true for the mean of the 2nd and 3rd M, whereas the 4th M was the first one not significantly different from mOBPM. The number of children with BP > 90th centile by each reading and by mOBPM is also provided in Figure 1.

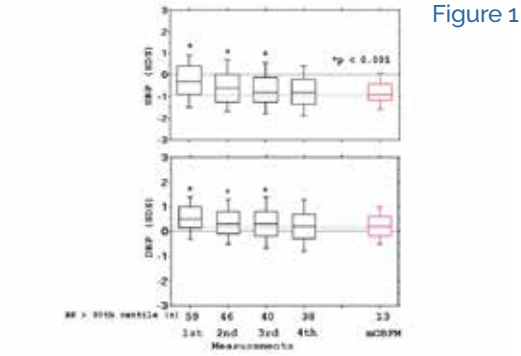

Figure 1

Conclusion: These findings confirm that relying solely on the first three BP measurements overestimates the number of hypertensive subjects, prompting unnecessary and burdensome diagnostic and therapeutic pathways. The 4th reading is more reliable but mOBPM provides a better evaluation of BP particularly when initial readings show higher than normal BP values.

1170 - P2.062

MULTIPLE OFFICE BLOOD MEASUREMENT, A PRACTICAL APPLICATION FOR THE DIAGNOSIS OF HYPERTENSION IN CHILDREN

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Aims/Purpose: In children office blood pressure (BP) measurement (M) may yield unreliable results. Using the mean value of the 2nd and 3rd M, as suggested by international guidelines, might be more accurate, yet it was shown to overestimate the actual number of hypertensive subjects. Multiple office BP measurement (mOBPM) represents the standard practice for diagnosing hypertension in children at our Centre. It consists in taking 10 serial readings on the non-dominant arm at 3-minute intervals by mean of a validated automated oscillometric device, discarding outlier values (< 5th and > 95th centile of the recorded values), and calculating the coefficient of variation (CV) and the mean of the remaining systolic (S) and diastolic (D) BP values through a software. In a previous study, we reported that the first 3 readings are significantly higher than the mOBPM mean, whereas, starting from the 4th one, we found no significant difference. The mOBPM identified a smaller number of subjects with abnormal BP values. The present study is aimed at testing mOBPM as part of a simple yet effective approach to reliably screen children for hypertension.

Methods: As suggested by Int'l. guidelines, we determined the number of school children with BP > 90th centile considering the first three readings and the mean of the 2nd and 3rd M. Among these, we identified children presenting a pathological BP at a 4th M and, subsequently, at mOBPM. Hence, we compared this result with the number of truly hypertensive children confirmed at the mOBPM repeated at 12 months.

Results: One hundred and seventy-five children (93 females, 53.1%) with a mean age of 8.6 ± 0.3 and a mean BMI of 17.5 ± 2.9 (BMI > 20, n = 34) were enrolled. Thirteen children were excluded for a CV > 15% in either SBP or DBP. Figure 1 represents the results. The mean of the 2nd and 3rd M identified 14 children with BP > 90th centile, but the 4th M showed a further reduction of the number of falsely hypertensive subjects and remains a more practical approach. None of the children with a normal BP value at 4th reading showed a pathological mOBPM result.

Conclusion: Although current guidelines recommend 3 BP readings, our findings suggest that, if the first 3 readings indicate elevated BP values, measuring a 4th BP value could be beneficial, as a normal value would unmask falsely hypertensive subjects. If, instead, the 4th BP reading is found abnormal, we advise to obtain a complete mOBPM to accurately identify truly hypertensive children.

1178 - P2.63

MALNUTRITION INFLAMMATION SCORE IN CHILDREN WITH CHRONIC KIDNEY DISEASE: RISK FACTORS AND CLINICAL OUTCOMES

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Aims/Purpose: The aim of this study is to develop the malnutrition-inflammation score (MIS) in children with chronic kidney disease (CKD), to assess its association with protein-energy wasting (PEW), systemic inflammation, risk of mortality and hospitalization and to investigate possible biomarkers.

Methods: The MIS was calculated in 53 CKD stage 3-5D patients, followed-up for an average period of 16.2 months. Decreased appetite and fatigue were each scored as 1 point. The duration of dialysis was scored as 1 point or 2 points if it exceeded 1 year or 4 years respectively. Body mass index (BMI) and lean tissue index (LTI) were each scored as 1 point or 2 points if they were less than 10th percentile (perc) or 5th perc for height-age and sex. Fat tissue index was scored as 1 or 2 points if it was less than 10th perc or 5th perc for age and sex. Height was scored as 1 point or 2 points if it was less than 5th or 3rd perc for age and sex. Both lean and fat tissue indexes were measured by bioimpedance spectroscopy. Additionally, serum albumin levels less than 4 g/dl or 3.5 g/dl were scored as 1 or 2 points respectively. Total iron binding capacity levels less than 300 μg/dl or 250 μg/dl were scored as 1 or 2 points respectively. PEW was defined as the presence of 3 of the following criteria: low BMI, low LTI, low height, reduced appetite, serum albumin ≤ 3.8 g/dl. Serum adipokines, myokines, mineral bone profile and IL-6, hemoglobin (Hb) and iron status were measured.

Results: MIS (median score 6,5, range: 0-13) was higher in CKD 5D patients ($p < 0.001$), was associated with PEW (8 patients) ($p < 0.001$) and correlated to lnIL-6 ($rs = 0.446$, $p < 0.001$). MIS better predicted hospitalization risk (6 patients) compared to PEW in CKD 5D patients (AUC 0.848 and 0.742 respectively) and was significantly higher in the 2 patients who deceased during the follow-up period ($p = 0.015$). In spearman correlation analysis adjusted to CKD stage and lnIL-6 level, lnFGF23 ($rs = 0.404$, $p = 0.003$), adiponectin ($rs = 0.618$, $p < 0.001$), resistin ($rs = 0.294$, $p = 0.036$), follistatin ($rs = 0.300$, $p = 0.033$), Hb ($rs = -0.514$, $p < 0.001$) and serum iron ($rs = -0.498$, $p < 0.001$), were correlated to MIS.

Conclusion: MIS is a better prognostic tool compared to PEW in predicting hospitalization in children with CKD. Anemia and iron deficiency are possible risk factors and parameters FGF23, adiponectin and follistatin potential biomarkers.

1179 - P2.064

LONG-TERM FOLLOW UP AFTER DIALYSIS FOR ACUTE KIDNEY INJURY IN PEDIATRIC INTENSIVE CARE UNIT

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Background and aims: Acute kidney injury (AKI) is frequent in pediatric intensive care unit, and in some cases continuous renal replacement therapy (CRRT) is essential to supplement the renal function. In certain cohorts of patients in pediatric intensive care units, CRRT is required in about 5%, and the mortality rate of these patients is about 60%. In addition, occurrence of AKI could have long-term consequences as developing chronic kidney disease. This study aimed to describe the prevalence of chronic kidney disease after dialysis for AKI in pediatric intensive care units.

Methods: We performed a monocentric retrospective study. We included patients from birth to 18 years old, admitted into intensive care unit at hospital Necker between 2014 and 2023, and who developed acute kidney injury requiring CRRT. The main exclusion criteria was preexisting renal disease. The occurrence of chronic kidney disease, defined by a creatininebased estimated glomerular filtration (eGFR) rate lower than 90 mL/min/1.73m2 or proteinuria at least more than 3 months after the end of CRRT, was the main outcome.

Results: Among 129 patients included in the study, 85 (66%) died in ICU, 44 (34%) were still alive at more than 6 months after developing AKI. The median age at CRRT was 3,1 (0,3-12,5) years old. The leading cause of developing AKI was acute tubular necrosis for 70% of patients. Oligo-anuria, hydroelectrolytic disorders and overload were the main indications for initiate CRRT. Survivors had a median length of CRRT of 8 (3-13) days. Among survivors, the median eGFR was 122 (92-146) mL/min/1,73m2. Height (18%) of survivors developed chronic kidney disease and 5 (11%) proteinuria. The median duration of follow-up of the renal function was 1.9 (1,0-3,7) years. No children had chronic renal replacement therapy or underwent kidney transplantation.

Conclusion: This study confirms that CRRT represents a huge severity factor with a high mortality rate for children with AKI in intensive care unit. Among the survivors almost 20% developed CKD at 2 years after the initiation of CRRT. These children should be followed by nephrologist to prevent the decrease of renal function.

1183 - P2.064

RISK FACTORS AND HEALTH CARE MODALITIES OF PATIENTS AFFECTED BY HINMAN SYNDROME. A MONOCENTRIC COHORT STUDY

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Introduction: Hinman syndrome (HS) or non-neurogenic neurogenic bladder is a voiding dysfunction of the bladder of neuropsychological origin, characterized by functional bladder outlet obstruction in the absence of neurologic deficits. The initial diagnosis approach is often challenging, with the necessity of ruling out organic abnormalities, in parallel to the psychological evaluation. The aim of this study was to analyse a cohort of patients with suspected diagnosis of HS, describe their health care modalities and their clinical course.

Method: Medical files of all patients referred to a pediatric nephrologist or urologist with a suspected diagnosis of HS between 2000 and 2023 were retrospectively analysed.

Results: 10 patients (70% girls) fulfilled diagnosis criteria of HS, i.e. clinical symptoms (urinary leakage, dysuria…), radiological hydronephrosis, but normal neurological clinical examination and normal medullar MRI. Median age at first consultation for clinical symptoms was 6 [5.6-6.6] years, but median age at definitive diagnosis was 10.6 [8.6-11.8] years, given a median delay of 3.9 years between first consultation and diagnosis of HS. Clinical symptoms were mostly urinary leakage (70%), dysuria (50%) and urinary tract infection (40%). Psycho-social disorders were present in 60% of patients. Urodynamic evaluation found detrusor sphincter dyssynergia in 40% of patients, and vesico-ureteral reflux and hypertrophic bladder in 40% of patients on cystography. Medium glomerular filtration rate (GFR) at diagnosis was 91 [70-109] ml/min/1.73m^2. Median follow-up after definitive diagnosis was 1.9 [0.9-3.3] years. All of the patients had at least one pyelonephritis during follow-up. 90% of patients needed intermittent catheterisation, and discontinuation was possible only in one patient. One patient had augmentation enterocystoplasty. At last follow-up, two patients had a decrease of GFR below 60 mL/min/1.73m^2.

Conclusion: Hinman syndrome is a severe voiding dysfunction, characterized by a long diagnostic delay, and most of the time chronicity of the symptoms, with need for intermittent catheterisation and sometimes urological surgery. Urinary tract infections are very frequent and there is a significant risk of chronic renal failure (CRF). Early recognition of this disease may help preventing CRF.

1232 - P2.066

ESTIMATED GFR WITH CREATININE AND CYSTATIN C IN CLINICAL PRACTICE: A SINGLE CENTRE STUDY

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Aims/Purpose: Accurate estimation of glomerular filtration rate (eGFR) in children is important both for use in clinical practice and as a reliable measure of kidney function for clinical trials. Serum creatinine is widely used as a filtration marker, however, it can be influenced by age, sex, pubertal status and muscle mass [1]. Cystatin C-based measurements are thought to improve the accuracy of creatinine-based GFR estimates however modified CKiDU25 formula has demonstrated strong performance [2]. This study aimed to examine the relationship between different measurements of GFR in a real-world setting.

Methods: This study was a retrospective, single-centre, cross-sectional study that took place at Alder Hey Children's Hospital, Liverpool from January 2019 to October 2023. Children aged 1-18 years who had Cystatin C measurements obtained for clinical purposes were included. Demographic data and values obtained on corresponding creatinine, height and formal GFR values. Comparisons were made between creatinine-based GFR and cystatin C-based GFR estimates.

Results: A total of 254 (Male 193, 76%) patients with median age 10 (IQR6;15) were identified. Creatinine-based GFR estimates were calculated in 187/254 patients and cystatin C-based GFR estimates were calculated in 247/254 patients. 11/254 patients had formal GFR measurements recorded. For the overall cohort (n = 187), Spearman's rank correlation showed good association between creatinine-based GFR and cystatin C-based GFR estimates ($r = 0.73$, $p < 0.001$). The association was strongest in the age groups < 2 years (n = 14) ($r = 0.86$, $p < 0.001$) compared to age groups 2-11 years (n = 91) ($r = 0.68$, $p < 0.001$) and age groups > 11 years (n = 82) ($r = 0.65$, $P =< 0.001$). A good association was also demonstrated between formal GFR measurements and cystatin C-based GFR estimates ($r = 0.70$, $p =0.002$). In comparison, relationship between formal GFR measurements and creatinine-based GFR estimates was not significant ($r = 0.11$, $p =0.750$). Formal GFR had a better association with average GFR estimates between creatinine and cystatin C measurements ($r = 0.77$, $p =0.005$).

Conclusion: There was a strong correlation between the estimated GFR using cystatin C and creatinine based CKiDU25 formula that did not differ according to age. The use of creatinine based CKiDU25 estimates appear to be reliable and likely to be the most suitable for everyday use. Cystatin C-based GFR estimate is superior for children with low muscle mass.

1234 - P2.067

BLAU SYNDROME - A RARE CAUSE OF CHRONIC KIDNEY DISEASE

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Purpose: Blau syndrome, a rare autosomal dominant autoinflammatory disorder mediated by NFkB, usually presents with a classical triad of granulomatous polyarthritis, dermatitis, and uveitis. Visceral organ involvement is rare. We present a case of a female adolescent with Blau syndrome complicated by chronic kidney disease (CKD). We aim to highlight the diagnostic and therapeutic challenges in this case.

Case Description: A 15-year-old female was referred to our hospital at the age of 13 from her homeland, Cape Verde, with a history of recurrent early-onset episodes of polyarthritis, which would last 3 to 6 days and were associated with camptodactyly, erythematous-desquamative papular exanthema, and uveitis. Additionally, she had developed CKD (stage 4), secondary hypertension, left ventricular hypertrophy, and dyslipidemia. As the hypothesis of an autoinflammatory syndrome was considered, treatment with steroids was continued, and methotrexate was added. A renal biopsy showed 19 globally sclerotic glomeruli, interstitial fibrosis with mononuclear cells infiltrate and tubular atrophy involving 90% of the cortex. Immunofluorescence and Congo red stain for amyloid were negative. Genetic testing showed a c.1001G > A (p.Arg334Gln) heterozygous mutation in NOD2 gene (R334Q), confirming the diagnosis of Blau Syndrome. With methotrexate, systemic complaints improved, but renal function deteriorated rapidly despite dose adjustments to eGFR and drug level monitoring, prompting a switch to adalimumab to mitigate nephrotoxicity. Renal function recovered to baseline over the following months. One year later, adalimumab was changed to infliximab due to hypercalcemia. Anti-TNF therapy doses and frequency of administrations were guided by clinical response, recommended adjustments to eGFR, and drug levels. Increasing doses or frequency were associated with improved systemic control of the disease and renal function deterioration. At present, the patient is being treated with infliximab every six weeks, alongside pharmacological therapy for CKD. Systemic complaints and ocular disease are relatively well controlled despite persisting refractory knee arthritis, and eGFR has remained stable at 20 mL/min/1.73 m2. The patient is being prepared for renal transplantation.

Conclusions: Blau syndrome represents a clinical and diagnostic challenge due to its rarity and heterogeneous presentation. Characterised by the classical triad of polyarthritis, dermatitis, and uveitis, this autoinflammatory disease can affect multiple organ systems, including the kidneys. Definitive diagnosis of Blau syndrome often relies on genetic testing for NOD2 gene pathogenic mutations. Finding the best therapeutic regimen to balance disease control without accelerating the decline in renal function due to nephrotoxicity is challenging.

1238 - P2.068

IFOSFAMIDE-INDUCED FANCONI SYNDROME IN PAEDIATRICS: A REVIEW OF CASES IN A TERTIARY HOSPITAL

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Purpose: Ifosfamide (IFO)-induced renal toxicity often presents as Fanconi syndrome (FS) and/or reduction in glomerular filtration rate (GFR). While most cases resolve after completion of chemotherapy (CTX), FS may be detected several months after exposure. If left untreated, metabolic bone disease may develop. We present 3 cases of FS secondary to IFO.

Methods: We collected data from patients over the last ten years who presented with ifosfamide-induced Fanconi Syndrome at our hospital.

Results: Case 1: A 2-year-old boy with Burkitt lymphoma and GFR of 60 mL/min/1.73m2 was treated with vincristine (VCR), cyclophosphamide, doxorubicin, and prednisone. He relapsed 3 months later, which prompted a salvage regimen with rituximab, IFO, carboplatin and etoposide, followed by allogeneic stem cell transplantation. During relapse treatment, downward crossing of weight and height centiles, metabolic acidosis and electrolyte disturbances were noted. FS was diagnosed and adequate supplementation was initiated with improvement of the patient's condition. Treatment was stopped 5 years later. Case 2: A 17-month-old boy with bladder rhabdomyosarcoma causing bilateral obstructive kidney disease underwent decompressive percutaneous nephrostomy and 4 cycles of IFO, VCR, actinomycin and doxorrubicin. GFR before CTX initiation was 75 mL/min/1.73m2. Following treatment, tumor enlargement occurred. Biochemical disturbances consistent with FS were noted and the patient started oral supplementation. A second CTX protocol with VCR, irinotectan and temozolamide was performed. To date, the patient maintains osteopenia, supplemented with vitamin D and phosphorus. Case 3: A 6-year-old boy with anaplastic nephroblastoma and preserved renal function underwent nephroureterectomy and CTX protocol with VCR, dactinomycin, and doxorubicin. After one year, he relapsed and was treated with 6 rounds of IFO, carboplatin and etoposide. One year after finishing CTX he reported general malaise, and biochemical workup was consistent with FS, with plasma phosphate of < 0,7 mg/dL. However, the patient lost follow up. At 15 years of age, he presented multiple pathologic fractures and weight and height at -6,2 and -7,6 SDS, respectively. Rickets secondary to previous FS was assumed, currently with normal plasma phosphate. The patient was started on vitamin D and zoledronic acid.

Conclusions: These cases illustrate the importance of close monitoring to identify renal toxicity of IFO as early as possible to allow adequate supplementation. Follow up must include detailed CTX protocols, growth, blood pressure evaluation, and laboratorial surveillance of kidney function and signs of tubulopathy.

1239 - P2.069

EVALUATION OF CASES WITH URINARY STONE DISEASE: SINGLE-CENTER EXPERIENCE

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Aims/Purpose: Urinary system stones in childhood can be idiopathic or may develop due to metabolic disorders, urinary anomalies, infections, environmental factors, and nutrition.1,2 Delayed diagnosis and inadequate treatment in patients with urinary system stones can lead to recurrent urinary system infections and kidney failure.3 This study aimed to evaluate the clinical, demographic, radiological characteristics, and treatment modalities of cases followed up with urinary system stones in childhood, as well as to determine metabolic and risk factors.

Methods: Epidemiological, clinical, and laboratory values, imaging results, treatment, and responses of 139 patients diagnosed with urinary system stones between 2018 and 2023 were retrospectively evaluated. Urine metabolite excretions that could pose a risk to patients were examined, and treatments and prognoses were compared.

Results: Of the patients, 77 (55.4%) were male and 62 (44.6%) were female. The mean age was 61.64 months. Urinary system infection was present in 62 (44.6%) patients, and structural anomalies were present in 9 (6.5%) patients. A history of stones was observed in 59 patients' families. Hypercalciuria was found in 34.5% of patients, hyperuricosuria in 18.7%, hypocitraturia in 14.3%, hyperoxaluria in 13.6%, and cystinuria in 8.6% of patients. There was no significant difference in urine metabolites compared to nutritional parameters. Urinary uric acid excretion was significantly increased in patients over 12 years old ($p < 0.05$). When patients receiving only alkalinization therapy were compared, it was observed that the response to treatment was significantly decreased in patients with a family history of urinary system stones compared to those without a family history ($p < 0.05$).

Conclusion: Urinary system stone disease requires careful follow-up of patients presenting for early diagnosis, prevention, and treatment. Metabolic causes that increase the risk of urinary system stone formation should be investigated for appropriate treatment selection and prevention of recurrences. Preventive measures such as increasing fluid intake and reducing salt intake should be taken, and patients should be regularly monitored.

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1249 - P2.070

BROWN TUMOR IN PEDIATRIC PATIENTS WITH CHRONIC KIDNEY DISEASE: TWO CASES OF A RARE CONDITION

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Aims/Purpose: Brown tumor (BT), characterized by excessive osteoclastic activity, is an uncommon manifestation of secondary hyperparathyroidism frequently observed in the jaw and long bones. While secondary hyperparathyroidism is a well-recognized complication of chronic kidney disease (CKD), BTs within this population, particularly among pediatric patients, are exceedingly rare. We aim to report two cases of BT identified in pediatric CKD patients undergoing hemodialysis at our center.

Methods: Patients were retrospectively analyzed in terms of clinical history, physical examination findings, laboratory investigations, imaging studies, and management strategies.

Results: Patient one, diagnosed with CKD secondary to Frasier Syndrome and undergoing hemodialysis for five years, presented with jaw swelling and left leg pain. Computed tomography (CT) revealed lytic lesions in the proximal femur, proximal right tibia, and left distal femur. Magnetic resonance imaging (MRI) detected calcified lesions in the right maxillary sinus and right mandibular corpus ramus junction. Laboratory results showed hypercalcemia, hyperphosphatemia, elevated serum alkaline phosphatase, and parathyroid hormone levels. A biopsy of the tibial lesion confirmed the BT diagnosis.Patient two, an 11-year-old child with CKD due to podocin mutation, who has been on hemodialysis for the last two years following four years of peritoneal dialysis, presented with jaw swelling and leg pain. CT imaging revealed a large lytic lesion in the mandibular corpus, and MRI showed a possible BT distal to the tibia. Laboratory revealed hypercalcemia, hyperphosphatemia, elevated serum alkaline phosphatase, and parathyroid hormone levels. Ultrasound and scintigraphy of the parathyroid gland indicated hyperplasia. A biopsy of the mandibular lesion confirmed the BT diagnosis. Dialysis prescriptions were reassessed for dialysis efficacy and treatment for renal osteodystrophy was optimized. A multidisciplinary approach helped symptomatic improvement and partial regression of CTs during close follow-up.

Conclusion: This report underscores the rarity of BT in pediatric CKD patients and emphasizes the importance of vigilant clinical assessment and multidisciplinary management for this rare complication. Further research and long-term follow-up studies are warranted to elucidate optimal management strategies and outcomes in patients with BT.

1274 - P2.071

CORRELATION OF EGFR USING TEN PEDIATRIC GFR EQUATIONS WITH IGFR MEASURED BY IOHEXOL CLEARANCE

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Aims/Purpose: The accuracy of equation-based estimations of glomerular filtration rate (GFR) in children is variable when correlated with GFR measured by a reference technique. Considering the strengths and limitations of the different equations is essential in clinical practice.

Methods: Iohexol clearance (iGFR) was measured in a cohort of 214 patients aged 2-20 years and compared by linear regression to the estimated glomerular clearance using ten different equations (eGFR). We included two creatinine-based equations (Bedside Schwartz 2009, CKiD-U25 Creat), four Cystatin-C-based equations (Filler, Zappitelli Cys, Schwartz Cys, CKD-U25 Cys), and four combined equations (Zappitelli CreaCys, Quadratic Chehade, Revised Schwartz full model 2012, CKiD-U25 average).

Results: Cystatin-based and combined equations performed generally better than creatinine-based equations. Creatinine-based equations had a significantly higher relative error and underestimated GFR in children under 15 y.o. CKiD-U25 (R2 = 0.57) performed slightly better than Schwartz 2009 (R2 = 0.53), especially in children under 10 y.o. and older than 15y.o. Cystatin-based equations tend to overestimate the GFR, with CKiD-U25 Cys (R2 = 0.72) presenting the strongest correlation. Filler and Zappitelli performed at least as well as CKiD-U25 Cys in children under 10y.o. Finally, all combined equations showed a strong correlation with the iGFR. The revised Schwartz full model (R2 = 0.71) slightly overestimated the GFR. CKiD-U25-average (R2 = 0.71) showed the strongest correlation and a low relative error among all patient's age compared to iGFR; allowing the best differentiation of CKD patients according to the KDIGO classification. All equations performed poorly in patients with an iGFR > 60ml/min/1.73m2 (R2 < 0.3 for KDIGO G1-G2); discrimination improved from KDIGO G3 onwards. The number of patients in KDIGO G4-5 was too small to draw any conclusion.

Conclusion: Cystatin-based or combined equations remain the most accurate for eGFR assessment. CKiD-U25 equations, designed for patients between the age of 1 and 25 years, outperformed other equations across all age groups and should be preferred in clinical practice. Unfortunately, all equations were suboptimal for estimating GFR in individuals with iGFR > 60 ml/min/1.73m2. Therefore, we encourage the development of novel equations and new biomarkers to improve GFR estimation.

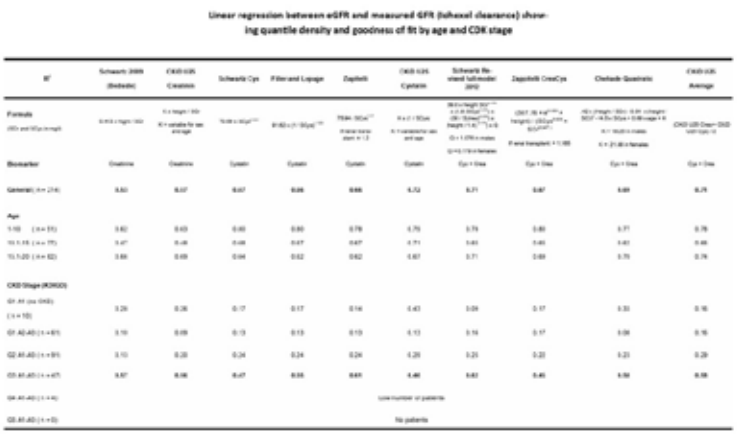

Table 1: Comparison of the goodness of fit (R2) of the linear regression between eGFR of the different equations and measured iGFR by Iohexol clearance. p-values were not shown, as they were all significant (< 0.001).

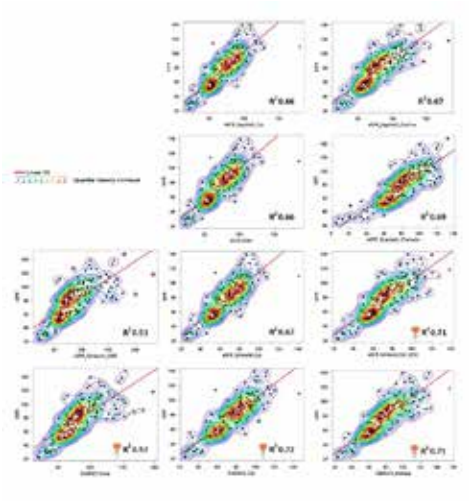

Figure 1. Linear regression between iGFR and eGFR of different equations with density clouds and goodness of fit (R2).

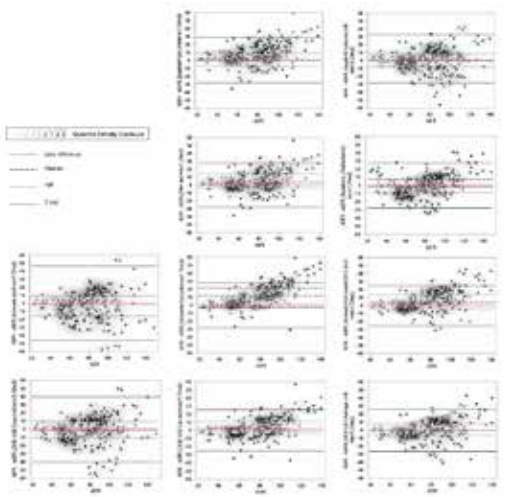

Figure 2. Relative error between iGFR and eGFR with density clouds

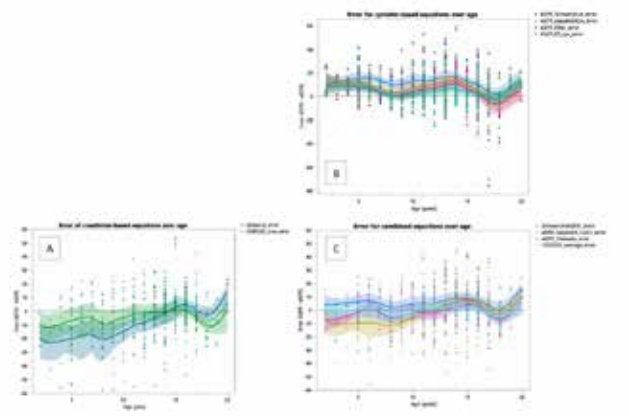

Figure 3. Relative error between iGFR and eGFR of different equations (A) Creatinine-based-, (B) Cystatin-based-, and (C) combined equations, along with patient's age.

1308 - P2.072

ASSOCIATION OF PROBLEMS, COPING STYLES, AND PREFERRED ONLINE ACTIVITY WITH DEPRESSION, ANXIETY, AND OTHER PSYCHOLOGICAL DISORDERS IN TURKISH ADOLESCENTS DIAGNOSED WITH CHRONIC KIDNEY DISEASE

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Aims/Purpose: To assess depression, anxiety, and other psychological disorders in chronic kidney disease (CKD)-diagnosed adolescents and their association with prominent issues, online activities, and problem-coping styles.

Methods: The study is conducted as a cross-sectional study with 84 adolescents with CKD and 68 healthy controls. The participants completed the Revised Child Anxiety and Depression Scale (RCADS). We recorded their age, gender, the most problematic issue (reported by the patient), coping methods with problems, and online applications they prefer in their leisure time.

Results: High-risk rates (scores > 70) of separation anxiety, panic disorder, obsession, depression, total anxiety, and total depression scales were statistically higher in the CKD group than in the control group. Separation anxiety, panic disorder, obsession, total anxiety, and total depression scales were higher in girls, and panic disorder, obsession, depression, total anxiety, and total depression scores were higher in younger ages in multivariate analysis. Among the CKD group, family issues/problems increased panic disorder, obsession, depression, total anxiety, and total depression scales. Crying in tears/yelling response against a problem was associated with increased separation anxiety. Also, social media-preferred patients were less likely to have separation anxiety.

Conclusion: Adolescents diagnosed with CKD are at risk for depression, anxiety, obsession, and panic disorders. Also, crying in tears/yelling responses are at greater risk for anxiety among CKD adolescents. Early psychiatric evaluation and routine psychiatric follow-ups initiated early may improve the mental health of this vulnerable population.

	Gender	Age	Problem	Coping type	Application preference
Separation Anxiety				Crying /yelling	Social media
Panic Disorder		Young	Family		
Obsession	Girls	Young	Young		
Depression		Young	Young		Social media
Total Anxiety	Girls	Young	Young		Social media
Total Depression		Young	Young		Social media

Red fonts describe increasing risk, and green fonts describe decreasing risk.

1311 - P2.073

COBALAMIN C DEFICIENCY MANIFESTING AS NEPHRITIC-NEPHROTIC SYNDROME IN LATE PUBERTY

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Background: Cobalamine C deficieny is a recognized cause of neonatal thrombotic microangiopathy (TMA) associated with high mortality. We describe a case of a 16-year old girl who presented with hypertension, kidney failure and a nephritic-nephrotic syndrome.

Case report:

Our patient presented with malaise, headache, stomach ache and mild facial swelling since 2 months. Apart from recurrent urinary tract infections, she had no relevant medical history. Neurocognitive development was normal. Physical examination revealed hypertension (165/110mmHg), urinalysis showed proteinuria (3+) and hematuria (2+). Laboratory results showed kidney failure: creatinine 246 µmol/L corresponding to an eGFR of 26 ml/min/1.73m2; albumin was 24 g/L. No hemolysis was seen. Kidney ultrasound and a comprehensive autoimmune panel including complement tests returned normal. Kidney biopsy showed mesangiocapillary glomerulonephritis with negative immunofluorescence for C3 and IgG. Marked chronic damage was seen with 25% sclerotic glomeruli and 20% interstitial fibrosis and tubular atrophy. Given the negative immunofluorescence, atypical TMA was suspected and genetic testing for complement-mediated TMA and metabolic screening were performed. Results revealed increased serum homocysteine (563 µmol/L) and methylmalonic acid (259 µmol/L) and a borderline low serum level of methionine (17 µmol/L). Vitamin B12 was normal (645 pmol/L). These results pointed towards a defect in the vitamin B12 metabolism. Two variants in the MMACHC gene [c.271dup (p.Arg91fs) and c.389A > G (p.Tyr130Cys)] were found. A late-onset Cobalamin-C deficiency diagnosis was established and therapy with betain, folinic acid and intramuscular hydroxocobalamin was started. Three weeks after diagnosis, serum levels of homocysteine and methylmalonic acid decreased significantly to 68 and 6 µmol/l respectively, but were still significantly elevated. Proteinuria decreased (1+) while kidney function remained poor. Cardiovascular and ocular screening showed no significant abnormalities.

Conclusion: While the c.271dup (p.Arg91fs) variant has been reported with the severe neonatal presentation of Cobalamin C deficiency with TMA and neurocognitive symptoms (mostly in homozygous cases), our patient presented with an isolated renal manifestation as a teenager. A mesangiocapillary glomerulonefritis with negative immunofluorescence and double contour formation should prompt measurement of homocysteine as a marker of Cobalamin-C deficiency.

1335 - P2.074

KIDNEY OUTCOME FOLLOWING 12 WEEKS OF ECULIZUMAB THERAPY FOR ATYPICAL HEMOLYTIC UREMIC SYNDROME. RESULTS OF A NATIONAL COHORT OF 98 CHILDREN DURING 2018-2023

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Aims/Purpose: Assessment of kidney outcome following eculizumab treatment for atypical HUS in a national cohort of 98 children from 9 pediatric nephrology centers.

Methods: The renal outcomes of all subjects < 18 years age who were enrolled and qualified to receive eculizumab for aHUS through a National Treatment Program were assessed. 98 subjects were identified from April 2018 till December 2023 and had been monitored at regular intervals through a National Health System platform. Estimated GFR (eGFR) was calculated by New Schwartz formula and reported in ml/min/1.73m2. eGFR values at entry into the program and values after 12 weeks of therapy were extracted and analyzed. Kidney outcome was classified as normal renal function (eGFR > 90ml/min/1.73m2), decreased eGFR (eGFR 89- 15ml/min/1.75m2) or dialysis dependence (eGFR < 15ml/min or on dialysis) or death.

Results: 86 children with aHUS initiated eculizumab therapy over the analyzed period of 68 months. 63 had received treatment for an initial acute episode of HUS, 21 following previous prophylactic plasma infusions/plasmapheresis and two during kidney Tx. 12 are awaiting therapy at relapse or kidney Tx. 54 subjects were girls and 44 boys. Median age at administration of eculisumab was 5 yrs (3months – 17 years). At initial evaluation 30% subjects demonstrated a eGFR < 15ml/min/1.73m2; 25% had eGFR between 15-29ml/min; 35% a eGFR between 30-59ml/min; 8% a eGFR between 60-89 ml/min and only 2% a eGFR > 90ml/min/1.73m2. Following 12 weeks therapy 74% had regained normal kidney function; 18% had eGFR between 60-89ml/min; 5% had values between 30-59 ml/min; 4% were still dialysis dependent and one child had died. Among the 63 children who initiated eculizumab therapy during an initial acute episode of aHUS, 53 (84%) had regained normal kidney function by 12 weeks from onset, one child had died (1,8% mortality rate).

Conclusion: eculizumab is an oustandingly efficacious therapy for treating acute episodes of aHUS. Survival is high (98,2%) and kidney outcome very good with the vast majority (84%) regaining a normal eGFR by 12 weeks from therapy onset.

1343 - P2.075

THE EFFECT OF BLOOD PRESSURE AND WEIGHT LOSS ON PULSE WAVE ANALYSIS IN OBESE PATIENTS

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Aims/Purpose: Central blood pressure (BP), Pulse wave velocity (PWV), and augmentation index (AIx) measurements are established markers of central hemodynamics and arterial stiffness and provide information regarding arterial health. The Mobil-O-Graph PWA monitor is a device that allows noninvasive measurement of BP, AIx, and PWV. In our study we aimed to evaluate whether PWV can be used as an early indicator of cardiac injury in obese children and whether weight loss has a restorative effect on this early injury.

Methods: Our study was prospective, single-center, analytical. Detailed anamnesis of the obese patients and the control group, whose informed consent forms were obtained, were recorded in their files for age, gender, physical examination findings and laboratory measurements. PWV analyses were performed before and after the appropriate diet and lifestyle changes, carotid intima and media thicknesses (CIMT) were measured, and ambulatory BP monitoring was performed.

Results: The female/male ratio of 45 obese patients participating in the study was 1.3/1, and 1/1 in the control group consisting of 83 patients. Systolic and diastolic BP values, stroke volume and cardiac output of the study group were significantly higher than the control group. The initial values of the study group were found to be higher than the 6th month control. During follow-up, it was seen that the augmentation index of the patients whose BMI did not change was lower than the patients whose BMI increased. It was observed that the initial systolic BP and cardiac output values of the patients whose BMI decreased during the follow-up decreased significantly after the weight loss. The baseline systolic BP and cardiac output of the non-dippers in the study group were significantly higher during the first visit than the control period. PWV of patients who are using metformin was found to be higher than the patients who didn't use the drug. There was a significant positive relationship between left CIMT and PWV.

Conclusion: In our study, it was observed that PWV increased significantly in obese patients and a significant improvement was achieved in those who managed to lose weight. Our study has shown that PWV analysis in the routine screening of obese patients will help in early detection of patients at risk of cardiovascular disease.

1346 - P2.076

VALIDATION STATUS OF BP DEVICES USED IN STUDIES ASSESSING ARTERIAL HYPERTENSION IN PAEDIATRIC POPULATION-A SYSTEMATIC REVIEW OF EVIDENCE

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Aims/Purpose: Until now, most of the validation protocols for BP devices are created based on data extrapolated mainly from adult studies. The accuracy of BP measuring validated devices in children remains unclear. We aimed to carry out a systematic review assessing the validations status, and the accuracy of BP measurement devices used in pediatric population.

Methods: A literature search of articles assessing Primary Hypertension and target organ damage was conducted in Medline, Web of Science and Cochrane databases.

Results: The search yielded a total of 1800 articles 57 of those underwent full-text review, and 28 reports were included. The majority of the reports had a cross-sectional design including 4,000 individuals with a maximum age of 16 years. For office BP measurements, 10 out 28 studies reported the device model used in their manuscript, while two of these studies used devices that have been validated. For Ambulatory BP measurement, nine out of eleven studies assessing ABPM reported the measurement device used while seven of these studies used ABPM devices that have been validated. Validation status could not be connected to higher accuracy in target organ damage detection due to lack of quantitative data.

Conclusion: There is a low report rate of BP measurement devices used in studies on paediatric arterial hypertension, while studies often use devices that has not yet been validated. Common devices that could pass validation protocols with reliable accuracy is needed in clinical and research settings.

Acknowledgments

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1366 - P2.077

TOTALITY OF THE EVIDENCE SUPPORTS EXTRAPOLATION OF ATYPICAL HEMOLYTIC UREMIC SYNDROME (AHUS) INDICATION FOR EPYSQLI (BIOSIMILAR TO REFERENCE ECULIZUMAB)

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Aims/Purpose: EPYSQLI (SB12), a biosimilar to eculizumab reference product (ECU-RP), was approved by the European Medicines Agency in May 2023 for the treatment of paroxysmal nocturnal hemoglobinuria (PNH), for which a confirmatory Phase III study was conducted. After demonstration of biosimilarity, extrapolation of data to other indications is possible based on the totality-of-the-evidence. In March 2024, the European Commission adopted also the indication of atypical hemolytic uremic syndrome (aHUS) by principle of extrapolation, supported by the totality-of-the-evidence discussed.

Methods: The biosimilar concept relies on the totality-of-the-evidence as much as the concept of 'extrapolation of biosimilarity' has been described as a logical consequence of the biosimilar concept (Blood. 2014 Nov 20;124(22):3191-6). Analytical comparability of SB12 to ECU-RP was assessed by more than 40 state-of-the-art assays, including biological activities associated with the mechanism of action (MoA) (BioDrugs. 2023 Jul;37(4):569-581). Pharmacokinetics (PK) equivalence and similarity in pharmacodynamics (PD), efficacy, safety, tolerability, and immunogenicity were assessed in clinical trials of healthy subjects (Phase I) and PNH patients (Phase III) (Int J Clin Pharmacol Ther. 2022 Jun;60(6):269-279; EJHaem. 2022 Dec 20;4(1):26-36). Complement inhibitor-naïve PNH patients were deemed the most sensitive population to assess potential differences in efficacy and risk of immunogenicity.

Results: The MoA of ECU-RP by terminal complement inhibition is consistent across its indications (EU Summary of Product Characteristics). Structural, physicochemical, and biological characterization results demonstrated that SB12 is highly similar to ECU-RP. MoA-related biological activities were similar in respect to overall critical and non-critical quality attributes (e.g., potency, binding activity). PK bioequivalence and similar PD, safety, and immunogenicity of SB12 and ECU-RP were demonstrated in healthy subjects. Equivalent clinical efficacy and comparable safety, PK, PD, and immunogenicity between SB12 and ECU-RP were confirmed in naïve PNH patients at ECU-RP approved dosage.

Conclusion: EPYSQLI (SB12) is a biosimilar to ECU-RP based on the totality-of-the-evidence, demonstrating their analytical, pharmacology and clinical comparability, and supporting its extrapolation to reference product indications, such as aHUS.

1371 - P2.078

AMYLOGENESIS IMPERFECTA AND RENAL FEATURES: WHICH ASSOCIATION IN CHILDREN?

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Aims/Purpose: Amelogenesis imperfecta (AI) is characterized by flaws in the formation of enamel. It may manifest on its own or in conjunction with other developmental abnormalities to form a syndrome. Our study's objective is to characterize the incidence of AI in relation to various renal diseases .

Methods: 7 cases of children affected by AI were collected and followed up at the Pediatric Department of Sahloul University Hospital in Sousse, Tunisia.

Results: The sex ratio was 3 boys to 4 girls. The average age at diagnosis was 12 years and 4 months [7 to 17 years old] Consanguinity was observed in all 6 cases. One patient's siblings had passed away as infants from acute dehydration and chronic renal failure of unknown etiology, while another had a history of nephrolithiasis . Clinical examination revealed discolored and malformed teeth with enamel defects ranging from mild striations to severe pitting and grooving, threatening hypertension in 2 patients and short stature and bone malformation (knee valgus) in 3 patient. Renal ultrasonography showed nephrocalcinosis in 2 patients and multiple renal stones in 4 patients. Biochemical blood investigations showed normal renal function in 2 patients and a high plasma creatinine level in 5 patients. Electrolyte and phosphocalcic disorders were noted in 2 patients. The diagnosis of Bartter syndrome was retained in one patient, chronic interstitial nephritis in another patient and proximal tubular disorders in 2 cases. During follow-up, one patient presented multiple episodes of urinary tract infection and recurrent renal colic, medically treated. 3 patients progressed to ESKD. All our patients patients received oro-dental care with symptomatic treatment of lithiasis, 2 patient underwent Renal replacement theray and one patient received a renal graft at the age of 8 years.

Conclusion: These 7 cases highlight the clinical diversity and complexity of amelogenesis imperfecta (AI) when associated with renal diseases in children. This work emphasizes the need for renal function screening as well as tubular assessment in cases of AI.

1382 - P2.079

EFFECTS OF GROWTH HORMONE TREATMENT IN CHILDREN WITH CHRONIC KIDNEY DISEASE

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Aims: Growth failure is common in children with chronic kidney disease (CKD). Research shows recombinant human growth hormone (rhGH)'s effectiveness in achieving target height. This study aims to characterize children with CKD who received rhGH treatment and to identify potential factors influencing height gain.

Methods: Retrospective study of children with CKD receiving rhGH treatment over the past 15 years at a tertiary portuguese center. We assessed the effect of rhGH on height and growth velocity at 1 (T1) and 2 years (T2) post-treatment initiation, comparing these outcomes with matched controls for age, CKD stage and CKD etiology. Univariate linear regression models were used to identify possible determinants of height gain in patients treated with rhGH.

Results: Thirteen patients received rhGH, 10(76.9%) were males. The majority of patients had stage 4 or 5 CKD (n = 9, 69.3%). The etiology of CKD was CAKUT (n = 9), glomerulopathies (n = 2) and tubulopathies (n = 2). The median age at the start of treatment was 63 months (P25-P75, 38-113.5; min-max 30-157). There were 16 controls, with 13 being males (81%) and the median age was 51 months (P25-P75, 44-99; min-max 29-155). At T1, compared with controls, patients treated with rhGH had a statistically significant lower height standard deviation score (SDS) (-1.95 vs. -0.95,$p < 0.001$), but showed statistically significant higher height SDS gain from baseline (0.78 vs.0.025,$p < 0.001$) and higher height velocity (9 vs 6,$p < 0.001$). No statiscally differences were found between groups at T2. In univariate linear regressions models, height SDS gain was positively associated with rhGH therapy duration (Beta(IC95%), 0.02 (0.01, 0.04),$p = 0.006$) and female gender(1.90 (0.20, 3.61),$p = 0.035$) and negatively with age at treatment initiation (-0.02 (-0.04, -0.01),$p = 0.034$), independently of CKD stage, target adjusted height SDS at the start of rhGH treatment and bone age retardation.

Conclusion: Our results are in line with previous studies which showed that rhGH treatment effectively addresses growth failure in CKD children, with significant improvements in height SDS and velocity within the first year. Our analysis confirmed that the duration of rhGH treatment, female gender and age at the start of treatment are predictors of growth response, independently of CKD stage. Further research with larger samples is needed to validate these findings, and explore the impact of acid-base balance and phosphocalcic homeostasis on rhGH treated patients.

1398 - P2.080

HIDDEN RISK IN OBESE CHILDREN WITH NORMAL BLOOD PRESSURE

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Aim / Purpose: Children with obesity are already known to be more prone to hypertension and physicians tend to feel safe when an obese child's office blood pressure (OBP) is normal. However, the prevalence of masked hypertension (MH) is higher in children with obesity and there is increasing evidence that MH contributes to long-term cardiovascular system damage. This study aimed to examine ambulatory blood pressure measurement (ABPM) results in children with obesity whose OBP were found to be normal.

Methods: Fifty-six children with obesity [Body Mass Index Standard Deviation Score (BMI-SDS) > 2] and normal OBP values were included in the study. Demographic characteristics of the patients, ABPM results, spot urine protein/creatinine ratios, transthoracic echocardiography (ECHO) and eye examination findings were retrospectively reviewed. MH was diagnosed when the patient's OBP measurements were below the 95th percentile, but the average blood pressure (BP) measurements obtained by ABPM over the 95th percentile. Children with average BP measurements at least 90th percentile, but less than 95th percentile are classified as having high-normal BP. Demographic and clinical data were evaluated. Mean, median, SD, and interquartile range (IQR) were calculated for numeric variables. Mann-Whitney U test (for continuous variables) and Chi-Square test (for categorical variables) were used.

Results: Among 56 patients who underwent ABPM, 22 (39.3%) were female and 34 (60.7%) male. The median age was 14.3 (IQR 11.6-16.5) years. The patients did not have any comorbidities apart from obesity. None of the patients were receiving antihypertensive treatment. Based on ABPM results, 27 (48.2%) patients had normal BP, 27 (48.2%) MH, and 2 (3.6%) high-normal BP. Among the 27 patients diagnosed with MH, target organ damage was detected in 11 (40.7%) as stage 1 hypertensive retinopathy (n = 5), left ventricular hypertrophy (n = 3), and ventricular septal hypertrophy (n = 3). None of the patients had microalbuminuria. There was no statistically significant difference between the patients with normal BP and MH in terms of gender and age (p =0.60, p =0.24, respectively). BMI values of the patients with MH were significantly higher than patients with normal BP (32.8 kg/m2 vs 28.8 kg/m2, p =0.01).

Conclusion: Children with obesity represent a risk group for cardiovascular complications. In our study we found that BMI was significantly higher in patients with MH compared to normotensive counterparts. In children with obesity the threshold for BP investigations should be kept low, and they should be thoroughly evaluated also for target organ damage even when OBP values are found to be normal.

1433 - P2.081

UNRAVELING GENOTYPE-PHENOTYPE LINKS TO REACH A DIAGNOSIS IN SEVERE EARLY-ONSET OF KIDNEY FAILURE

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Introduction: Chronic kidney disease (CKD) poses a significant challenge by impairing kidney function, which leads to several complications and developmental hurdles. Clinical presentation in early CKD is often subtle, underscoring the importance of remaining alert for particular signs on physical examination.

Case Report: An 18-month-old girl with a history of poor weight gain since 6 months of age and psychomotor development delay presented to the emergency department with profuse diarrhea, food refusal and prostration. There was no relevant medical or family history except for parental consanguinity. She exhibited severe dehydration, mucous membrane pallor and experienced a brief seizure episode. Her weight was 8kg and presented 75cm of height (both < 3rd WHO percentile). Blood analysis revealed metabolic acidosis (pH 7.04, HCO3- 4.9mEq/L, anion gap 27mEq/L), normocytic and normochromic anemia (hemoglobin 5.4g/dL) severe hyperkalemia (8.8mEq/L), hypocalcemia (ionized calcium 0.9 mmol/L), hyperphosphatemia (14.5 mg/dL) and elevated urea (441 mg/dl), creatinine (7.9 mg/dl) and parathormone levels (1546pg/mL). Due to severe, intractable metabolic acidosis and hyperkalemia, she was intubated and transferred to the intensive care unit, where kidney replacement therapy (KRT) was initiated. After 4 days of acute peritoneal dialysis, she transitioned to hemodialysis due to inadequate fluid management, which improved her hypervolemia, acidosis, hyperkalemia, and uremia. As kidney function did not recover KRT was continued and a diagnosis of CKD exacerbated by acute illness was established. Throughout hospitalization, she received treatment for CKD-related complications, including blood cell transfusions, erythropoietin and management of electrolyte imbalances. Genetic analysis revealed a VOUS in the INVS gene in homozygosity, which encodes nephrocystin-2, responsible for type 2 nephronophtysis, and a likely pathogenic variant in the ACE gene, in heterozygosity, associated with autosomal recessive renal tubular dysgenesis. Recognizing the importance of genetic testing to establish an etiological diagnosis and for reproductive options, a transcriptome analysis is ongoing. Presently, the patient exhibits refractory hypertension requiring three drugs for control, and undergoes regular hemodialysis and multidisciplinary follow-up, with plans for growth hormone therapy and kidney transplantation in the future.

Conclusion: This case highlights the complexity of diagnosing and managing pediatric CKD, emphasizing the importance of considering metabolic acidosis and/or kidney dysfunction in cases of developmental delay and poor weight gain. Early recognition, prompt intervention, and a multidisciplinary approach are essential for optimal outcomes, with genetic analysis playing a key role in understanding underlying causes, prognosis and counseling.

1443 - P2.082

DISTAL RENAL TUBULAR ACIDOSIS AS INITIAL MANIFESTATION OF PEDIATRIC SJÖGREN'S SYNDROME: A CASE REPORT

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Background: Distal renal tubular acidosis (RTA) in children is often hereditary, it can however be secondary to toxic or auto-immune causes, such as Sjögren's syndrome (SS). Renal involvement in SS commonly manifests as a tubulo-interstitial nephritis, which may lead to distal kidney tubular acidosis.

Objective: In this report, we describe a case of RTA secondary to SS in a child.

Observation: We report the case of an 11-year-old girl who was referred to our pediatric department for management and investigation of recurrent and refractory hypokalemia. Investigations revealed a one-year history of polyuric-polydipsic syndrome with no other relevant findings on clinical examination. Laboratory tests showed hypokalemia, metabolic acidosis with normal anion gap, hypercholremia, hypercalciuria associated with an alcaline urinary pH. Urine acidification test confirmed the diagnosis of distal renal tubular acidosis type I. Renal ultrasound revealed medullary nephrocalcinosis. Initial etiological investigations were negative. Audiogram was normal. The patient responded well to oral potassium and sodium bicarbonate supplementation. After 3 years of follow-up, the patient presented with polyarthralgia, asthenia, and parotid swelling. The diagnosis of Sjogren's syndrome was then, made based on a positive Schirmer test, abnormal tear film break-up time, and positive anti-SSA antibodies. Symptomatic treatment was initiated with good response.

Conclusion: Distal renal tubular acidosis may appear as the first manifestation of pediatric Sjögren's syndrome, emphasizing the importance of heightened awareness in cases of recurrent hypokalemia or nephrocalcinosis. Early diagnosis enables more effective management and prevention of disease complications.

808 - P2.083

NEUTROPHIL EXTRACELLULAR TRAPS AND THEIR INVOLVEMENT IN CRYSTAL-INDUCED CHRONIC KIDNEY DISEASE

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Aims: Neutrophil extracellular traps (NETs) are web-like structures of DNA coated with antimicrobial proteins including myeloperoxidase (MPO), neutrophil elastase (NE), gelatinase, etc. Beyond their front-line defense against pathogens, excessive formation of NETs is implicated in tissue damage, coagulation stimulation, and inflammation exacerbation. NETs play a pivotal role in various pathologies including CKD. However, whether the formation of NETs is involved in crystal-induced CKD is still unclear. Therefore, we aimed to determine whether mice deficient in peptidyl arginine deiminase type 4 (PAD4), an enzyme crucial for chromatin decondensation, will be protected from severe kidney damage in adenine-induced CKD.

Methods: 17 wild-type (WT) and 15 PAD4-deficient mice (PAD4−/− KO) were used in the study. CKD in mice was induced by intraperitoneal injection of adenine (100 mg/kg, Sigma Aldrich, Münich, Germany) for 2 weeks. Controls were injected with saline. Blood and urine were collected at the baseline, and after 7 and 14 days of adenine administration. Markers of NETs formation including extracellular DNA (ecDNA), and antimicrobial proteins were analyzed in plasma and urine. Concentrations of ecDNA were assessed using a fluorescent method (Qubit dsDNA HS Assay Kit, Invitrogen, Carlsbad, CA, USA). Concentrations of MPO, NE and NGAL were assessed using commercial kits (R&D Systems, Minneapolis, USA).

Results: Total plasma ecDNA was increased on day 7th by 88% and 250% in WT and PAD4−/− KO mice, respectively compared to corresponding control groups. Moreover, after 14 days plasma nucleosomes in mice injected with adenine were significantly higher compared to controls, regardless of the strain. Similarly, urinary ecDNA in WT and PAD−/− KO on day 7th was 4-times and 8-times higher compared to controls. Further, plasma concentrations of MPO, NE, and NGAL in WT and PAD4−/− KO mice were significantly increased on day 7th, together with their trend to increase in the urine. Moreover, there were positive mutual correlations between the main structural components of NETs – ecDNA and antimicrobial proteins in plasma and in urine.

Conclusion: Increased NET markers levels in mice with adenine-induced CKD suggest neutrophil activation with subsequent NETosis. However, PAD4−/− KO mice with diminished NETosis seem not to be protected from severe kidney damage which was confirmed by serum creatinine as well as by kidney histology. This suggests that either NETs formation is not directly involved in the adenine-induced CKD or PAD4 is not a unique enzyme crucial for histone citrullination and chromatin decondensation. Further studies should elucidate the role of other NETs inhibitors (chloramidine, disulfiram) in the pathomechanism of adenine-induced CKD.

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68 - P2.084

IDENTIFICATION OF A CANDIDATE LOCUS FOR AUTOSOMAL DOMINANT TUBULOINTERSTITIAL KIDNEY DISEASE

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Aims/Purpose: Autosomal dominant tubulointerstitial kidney disease (ADTKD) is a rare monogenic disease with high penetrance that presents with chronic kidney disease leading to end-stage kidney failure at the age of 30 to 60 years. Disease-causing variants are known to occur in five genes, namely UMOD, MUC1, HNF1ß, REN and SEC61A1, each of which is associated with certain unique clinical features. Diagnosis is important for potential future treatment. A family with positive family history and suspicion of ADTKD presented at our unit for genetic diagnostics. We obtained blood samples of 11 family members and one skin biopsy. Panel diagnostics of the five known disease-associated genes showed no pathological findings. We now aim to identify a new monogenic cause for ADTKD.

Methods: First, we conducted a linkage analysis on all 11 available family members. Genotyping was performed using Illumina's Infinium Global Screening Array-24. A LOD score was estimated across all chromosomal regions using the program MERLIN. Haplotyping, also available in MERLIN, will be used to further narrow down the linked region. In three affected family members genome sequencing was performed to cover coding as well as noncoding regions of linkage analysis derived candidate genes. Proteomic and transcriptomic data available through skin biopsy of an affected family member were processed using the programs OUTRIDER and FRASER to allow identification of significant aberrant expression of RNA and protein as well as aberrant RNA splice variants.

Results: We use a comprehensive molecular genetic approach to analyse the genome data of the family, consisting of linkage analysis, short read genome sequencing as well as transcriptomics and proteomics. Linkage analysis obtained a significant LOD score at two genomic regions, indicating linkage between these loci and the disease. We want to specify the linked regions further through haplotyping. We will look into the genome sequencing data to see whether there are variants in the candidate genes and regions identified by linkage analysis. Proteomic and transcriptomic data will provide additional evidence of the involvement of candidate genes.

Conclusion: Using linkage analysis together with multi-omics data including DNA, RNA and protein will likely lead us to the disease-associated gene in this family and to the identification of a novel gene associated with ADTKD.

181- P2.085

SCHIMKE SYNDROME: A RARE COMBINATION OF MALIGNANT HYPERTENSION IN THE ABSENCE OF NEPHROTIC SYNDROME

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Introduction: Schimke immuno-osseous dysplasia (SIOD) is an orphan monogenic disease. SIOD is inherited in an autosomal recessive manner caused by a mutation in the SMARCAL1 gene. SIOD is characterized by spondyloepiphyseal dysplasia, nephropathy and slowly progressive T-cell immunodeficiency.

Aims/Purpose: To draw attention to malignant hypertension in Schimke immuno-osseous dysplasia.

Methods: Clinical observation of patient with Schimke immuno-osseous dysplasia.

Results: A 2-year-old girl from the 5th pregnancy. The girl was delivered by caesarean section because of impaired fetoplacental circulation and fetal growth retardation at gestational age of 34-35 weeks. Low growth rates have been observed since birth, hip dysplasia was first diagnosed in 3 months, leukopenia has been first recorded in 4 months – 2.6x109/l. At the age of 1 year and 5 months there was a closed craniocerebral injury and fracture of the frontal bone caused by a fall. According to the radiography there was no osteoporosis. For the first time at the age of 1 year and 9 months, hypoplasia of both kidneys was detected on ultrasound. Isolated proteinuria was observed (protein – 0.75 g/l, microalbumin – 87 mg/l). During the second year of life, the girl developed malignant arterial hypertension (poorly controlled by drugs) with blood pressure rises up to 140-160/50-60 mmHg accompanied by the onset of seizure attack. Kidney function was stable, there was no nephrotic syndrome (total protein - 72 g/l, albumin - 38 g/l), urine contains sub-nephrotic proteinuria (protein-0.36 g/l), GFR is reduced - 84.3 ml/min (CKD stage 2). The child also had frequent diseases of the upper respiratory tract. Laboratory data of the patient: decrease in lymphocytes (CD3 – 0.266x109/l, CD3-4 – 0.136x109/L, CD19 – 0.336x109/l), IgG – 4.85 g/l. Because of the characteristic findings SIOD was considered and the patient was recommended to conduct a medical genetic study. The results revealed compound heterozygous mutations in the SMARCAL1 gene, which were confirmed by Sanger sequencing. As a result, the diagnosis of Schimke syndrome was confirmed.

Conclusion: The clinical case demonstrates that cardiovascular system damage in Schimke syndrome can also be caused by extrarenal causes, which necessitates further study of the pathogenesis of this syndrome. The multidisciplinary teams of doctors including immunologist, nephrologist and cardiologist should participate in the management of such patients.

231- P2.086

GENETIC ANALYSIS YIELD AND CLINICAL CHARACTERISTICS OF NEPHROLITHIASIS AND NEPHROCALCINOSIS IN CHILDREN: A SINGLE CENTRE RETROSPECTIVE STUDY

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Aims/Purpose: While nephrolithiasis (NL) and nephrocalcinosis (NC) are infrequent in the paediatric population, they impose a considerable disease burden, including an elevated risk of chronic kidney disease (CKD) and renal failure. NL/NC is linked to genotypes impacting various enzyme pathways, resulting in diverse phenotypes, and more importantly offering a possibility of therapeutic interventions.

Methods: A retrospective chart review of children diagnosed with NL and/or NC and performed genetic testing in the referral centre for paediatric nephrology of the Republic of Croatia from 2020 to 2023.

Results: Out of 9 included children (median age 2, range 0 – 14, 6 male), 7 were diagnosed with NL and 4 with NC. The most common laboratory abnormality was hypercalciuria detected in 6 children, followed by hyperuricemia in 4, hypocitraturia in 3, low serum bicarbonate in 2 and hypercalcemia, hyperoxaluria, elevated 25-vitamin D and hypomagnesemia present in 1 child each. Developmental delay and/or low stature was observed in 2 children, and dental and facial abnormalities in 1 child each. CKD was observed in 3 children. Stone composition analysis was performed in 3 children, revealing calcium phosphate in 2 and calcium oxalate stone in 1 child. Family history for urolithiasis was positive in 3 children. Commercially available gene panel testing was done in 7 children, while in 2 children, who developed NL/NC within the first six months of life and had concomitant malformations, whole exome sequencing (WES) was performed. The genetic testing was positive in 4 children, revealing Familial hypomagnesemia with hypercalciuria and nephrocalcinosis in 2 children, and Infantile hypercalcemia type 1 and Barter syndrome in 1 child each. Additionally, WES revealed a rare congenital malformation syndrome in 1 infant.

Conclusion: More than half of children in our cohort had a positive genetic finding for diseases with known or previously unknown association with NL/NC. The genetic cause was more frequent among children with laboratory and/or other clinical aberrations but was also identified in those with no apparent abnormalities. Finding the possible explanatory genetic variant in children with NL/NC at an early stage of the disease is of great importance since correct diagnosis changes the management. This includes not only tailored treatment, but also disease surveillance, as well as precise prognosis of the disease complications and CKD development. Moreover, expanding the testing to WES in children with concomitant malformations might reveal additional genetic burden. Therefore, genetic testing shows promise as a valuable tool for physicians, enhancing clinical practices for children affected by NL and/or NC.

232- P2.087

CO-OCCURRENCE OF NON-SENSE VARIANTS IN PKD2 AND WT1 GENES, ASSOCIATED WITH EARLY ONSET BILATERAL NEPHROBLASTOMA AND KIDNEY CYST IN AN INFANT

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Approximately 85% of patients with ADPKD have disease causing variants in the PKD1 gene, while 15% of patients have variants in the PKD2 gene on chromosome 4q21.2. Variants in the PKD2 gene are associated with a better prognosis, only 45% of patients developing renal failure at the age of 70. Missense and non-sense variants in WT1 gene result in early development of Wilms tumor, the most common primary renal tumor in children. Only approximately 10% of Wilms tumors occur bilaterally. However only approximately 20% of Wilms tumors have disease causing variants in WT1 gene. There are some reports illustrating genetic interaction with PKD1 proposing WT1 as potential modifier in ADPKD, hypothesing that the severe cystic phenotype could be due to the WT1 variant, enhancing pathogenicity of the "hypomorph" PKD1 allele.

Aim: To present a girl diagnosed at the age of 6 month with triphasic bilateral nephroblastoma medium risk who underwent surgical removal of tumors and right kidney, radiological treatment and chemotherapy. The patient's father was clinically diagnosed with polycystic kidney disease.

Results: Next generation sequencing kit Illuminia TruSight One testing for 4813 genes detected a pathogenic heterozygous stopgain variant NM_000297.4:c.916C > T in PKD2 gene and a likely pathogenic heterozygous frameshift deletion variant NM_024426.5:c.798del in WT1 gene. MRI and ultrasound confirmed the presence of milimetric cysts of the remaining left kidney.

Conclusions: We here report on an exceptional clinical presentation of a patient with non-sense variants of both PKD2 and WT1 genes. The clinical presentation suggests that the early appearance of kidney cysts could be due to the contribution of the additional WT1 variant alongside the PKD2 variant.

249 - P2.088

DO PEDIATRIC NEPHROLOGIST KNOW THEIR EDUCATIONAL COMPETENCIES?

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Aim: The competencies in the Medical Specialty Curriculum and Standards Development System (MSCSD) guides trainers in the preparation and execution of the training program and gives learners an idea about the state of mastery that they will reach by graduation. The aim of this study was to evaluate the knowledge of pediatric nephrologists about competencies in the field of specialization in Türkiye.

Methods: In the cross-sectional study conducted between January 2023 and 2024, the knowledge of pediatric nephrologists about specialty competencies was investigated with the two-round Delphi technique. Digital Delphi forms were sent to all pediatric nephrologists in Türkiye via email of the specialty society. In the Delphi form, all competency titles in the MSCSD v.2.3 curriculum were transformed into propositions that could be scored with a 5-point Likert scale. The frequency of 4-5, the difference between quartiles and the median were calculated for each of the statements. For participant consensus on the propositions, the median should be 4, the frequency of 4-5 should be above 70%, and the difference between quartiles should be 2.5 or less.

Results: Of the pediatric nephrologists in Türkiye, 59 responded to the first and 136 to the second round Delphi survey. In the first round, full consensus was found in the competency areas other than service delivery, while consensus was found in two of the 72 clinical competencies under the service delivery heading, namely systemic diseases and malignant diseases, and in two of the 26 interventional competencies (diversion and imaging). The analysis of the second round Delphi questionnaire based on this result showed full consensus on all competency headings. The variables of title, gender and training clinic made a difference in consensus.

Discussion and Conclusion: It was found that the level of knowledge of pediatric nephrologists about specialty competencies differed in terms of some variables and knowledge was more limited in young learners for whom competencies are legally binding. In conclusion, it is recommended that learners should be informed about the competencies at the beginning of specialty training and participate in updating the competency list.

280 - P2.089

THE RELATIONSHIPS BETWEEN URINARY ELECTROLYTES IN RECURRENT PEDIATRIC UROLITHIASIS: THE EXPERIENCE OF A PEDIATRIC CENTER

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Aims: Pediatric urolithiasis is a significant medical concern, necessitating a comprehensive understanding of associated risk factors. This study aims to investigate the correlation between calcium, magnesium, sodium, potassium, oxalate, and citrate in pediatric patients with recurrent renal calculi.

Methods: A total of 57 pediatric patients with recurrent renal calculi were included in the study. Data collection involved assessing demographic information, stone characteristics, urinary parameters, and family history. Statistical analysis was conducted to determine correlations between the Ca/Cr ratio and various urinary parameters, as well as their implications for lithogenic risk.

Results: Correlation analysis revealed a positive relationship between the Ca/Cr ratio and urinary parameters, including Ca/Citrate ($p < 0.001$), mg/Cr ($p = 0.002$), Na/K ($p = 0.001$), Oxalat/Cr ($p < 0.001$), and Citrat/Cr ($p = 0.005$). Furthermore, a positive correlation was found between the Ca/Cr ratio and the Na/K ratio ($p = 0.002$), highlighting the opposing roles of urinary sodium and potassium in the Ca/Cr ratio. The study also identified a significant positive correlation between the Ca/Cr ratio and Ca/Citrate ($p = 0.001$), emphasizing the importance of calcium and citrate in recurrent stone formation risk. Furthermore, the relationship between the Ca/Cr ratio and Oxalate/Creatinine was statistically significant ($p < 0.001$). Additionally, a positive relationship was found between mg and K ($p < 0.001$), while no significant correlation was observed between magnesium and citrate levels ($p = 0.123$).

Conclusion: These findings elucidate the intricate interplay between electrolytes in 24-hour urine and their implications in pediatric urolithiasis. The study underscores the importance of comprehensive risk assessment, including consideration of urinary electrolytes and their ratios, for effective management strategies in pediatric patients with recurrent renal calculi.

311 - P2.090

THE ROLE OF GENETIC TESTING IN THE DIAGNOSIS OF BRANCHIO-OTO-RENAL SYNDROME

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Aim: Branchio-Oto-Renal (BOR) syndrome is an autosomal dominant disorder, characterized by anomalies of branchial arches, ears and kidneys, it affects about 1 in 40 000 individuals. The diagnosis is based on the clinical criteria: in the absence of family history 3/5 major or 2/5 major and 2/5 minor criteria must be present, while individuals with an affected family member need to meet only one major criteria. Mutations in EYA1, SIX1, and SIX5 genes have been identified as causative factors in about 50% of BOR cases. This rare condition presents challenges in diagnosis due to its clinical and genetic heterogeneity. The aim of the study was to evaluate the need and role of genetic testing for our patients with suspected BOR syndrome.

Methods: Five patients with clinical symptoms consistent with BOR syndrome were identified at Vilnius University Hospital Santaros Klinikos in the last 25 years.

Results: presented in Table 1.

Table 1. Data of the patients.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Gender	Male	Female	Female	Female	Female
Year of birth	1990	2000	2011	2019	2023
Age at diagnosis	10 years	4 years	4 days	7 months	7 months
Major criteria	3	3	2	3	3
Minor criteria	1	1	1	1	2
Renal anomalies	Bilateral kidney hypoplasia	Left kidney hypoplasia	Bilateral kidney hypoplasia	Right kidney agenesis	Kidney cysts
Family history	Negative Positive*	Positive*	Positive**	Positive**	Negative
Genetic testing	Not performed	Not performed	Not performed	EYA1 gene mutation	No pathogenic variants in the EYA1, SIX5, SIX1 genes

*Patients 2 and 3 are sisters, their mother's sister was born with bilateral kidney agenesis, maternal grandfather was diagnosed with end-stage renal disease.
** The Patient's mother had fistuloplastic surgery, otherwise healthy.

Fifth patient had enough clinical criteria to be diagnosed with BOR syndrome, but had more symptoms, like: poor growth, cataract, labia majora hypoplasia, hydrocephalus.

Conclusions: Genetic testing plays an emerging role in diagnosis of BOR syndrome and might be important in genetic risk assessment, especially for patients with negative family history.

321 - P2.091

CYSTINOSIS AND ARTIFICIAL INTELLIGENCE: ANALYSIS OF CHATGPT IN DIFFERENT USERS, SOFTWARES, AND LANGUAGES

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Aims/Purpose: Artificial intelligence (AI) is a technology used to mimic human-like intelligence in computer systems. It has the potential to have a significant impact in many areas of the healthcare system. However, there is limited research focusing on the combination of rare diseases and AI applications. The aim of this study is to examine the usability of artificial intelligence applications in the management of cystinosis patients, and to evaluate if there is any difference in patient management among different users, softwares, and languages.

Methods: A and B users at Konya City Hospital were asked 13 questions about cystinosis. Questions were directed in English/Turkish language options through different versions such as Chat GPT 3.5/ Microsoft Copilot GPT 4.0. Responses were categorized by researchers as wrong, incomplete, correct, detailed, and scored between 0 and 3. Accuracy percentages were calculated with the total score obtained. Statistical analyses were performed using IBM SPSS 25.

Results: In the analysis using ChatGPT 3.5, it was observed that the accuracy percentages of responses given by the same user to questions directed in different languages were significantly higher in English compared to Turkish. In comparisons between ChatGPT 3.5 and 4.0, responses given by user B in Turkish in different softwares were more accurate in Microsoft Copilot GPT 4.0. There were important differences in responses given by both users in different softwares and languages, summarized in Table 1.

Conclusion: These findings indicate that the reliability of AI-based programs in medical information transfer, diagnosis, and treatment planning processes may vary. Particularly, in cases where subjects requiring medical expertise are addressed, accurate and reliable information transfer is crucial. However, as our study demonstrates, there are significant differences between language choices and versions of AI programs. Therefore, caution should be exercised in the use of these programs, and the reliability of responses in the preferred language and version should be evaluated.

Table 1. Comparison of accuracy percentages of responses received with different language and software versions by users

	User A	User B	p
ChatGPT 3.5			
Turkish	41	35.8	0.68
English	69.2	64.1	0.57
ChatGPT 4.0			
Turkish	58.9	64.1	0.53
English	69.2	82	0.23
	ChatGPT 3.5	ChatGPT 4.0	p
UserA			
Turkish	41	58.9	0.08
English	69.2	69.2	0.97
User B			
Turkish	35.8	64.1	< 0.01
English	64.1	82	0.05
	Turkish	English	p
User A			
ChatGPT 3.5	41	69.2	0.01
ChatGPT 4.0	58.9	69.2	0.34
User B			
ChatGPT 3.5	35.8	64.1	< 0.01
ChatGPT 4.0	64.1	82	0.5
	User A	User B	p
	ChatGPT3.5-Turkish	Microsoft Copilot GPT 4.0- Turkish	0.02
	ChatGPT3.5-Turkish	Microsoft Copilot GPT 4.0- English	< 0.01
	Microsoft Copilot GPT 4.0-English	ChatGPT3.5-Turkish	0.02
	Microsoft Copilot GPT 4.0-Turkish	ChatGPT3.5-Turkish	0.02

322 - P2092

RIVAROXABAN AS VENOUS THROMBOEMBOLISM TREATMENT IN NPHS1 CONGENITAL NEPHROTIC SYNDROME

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Purpose: Nephrotic syndrome (NS) is associated with a multifactorial hypercoagulable state. Congenital NS (CNS) exhibits a higher prevalence of thrombotic events compared to other types. Direct oral anticoagulants (DOAC) have been approved for paediatric acute venous thromboembolism. We present 2 CNS paediatric cases treated with rivaroxaban.

Methods: Rivaroxaban was used for treatment (Case 1) and prophylaxis (Case 2) of thrombotic events in CNS, in the absence of contraindications (antiphospholipid syndrome; risk of bleeding; liver dysfunction). Therapeutic doses were determined per the latest guidelines.

Results: Case 1: A 2-month-old male previously diagnosed with CNS with homozygous mutation in the NPHS1 gene, underwent central venous catheter (CVC) replacement during which multiple thrombi were seen. In the first 24 hours, the patient developed clinical signs compatible with pulmonary embolism (acute pallor, tachycardia, shortness of breath, hypoxemia, without fever). Chest radiograph showed a peripheral condensation on the left hemithorax. CT-angiography scan ruled out a major pulmonary embolism, with inconclusive result for peripheral embolism. Despite therapeutic doses of enoxaparin, adjustments were difficult with persistently low anti-Xa levels. The switch to rivaroxaban was performed after 11 days, and doses were regularly adjusted based on patient's weight. No adverse or other thrombotic events were reported, despite maintaining CVC. As expected, chronic kidney disease progressed (eGFR of 22 mL/min/1.73m2) at 19 months and rivaroxaban was suspended.

Case 2: A 8-month-old female with CNS and heterozygous mutations in the NHPS1 gene, underwent multiple CVC replacements due to recurrent obstruction despite regular heparinisation and alteplase administrations. Although there were no systemic thrombotic episodes, considering the high risk of thrombosis, prophylaxis with rivaroxaban was initiated. At the time, the patient presented an eGFR of 54 mL/min/1.73m2 (1-2 SD below expected eGFR). Weight-adjusted dose was prescribed. No severe adverse or thrombotic events reported until now, with 19 months. She still has a CVC with only one readmission due to its obstruction.

Conclusion: These cases suggest that the safety and efficacy profile of rivaroxaban may be encouraging for treating and preventing venous thromboembolism in CNS. However, additional studies are warranted to optimize DOAC use in children with complex conditions, such as CNS, allowing for more tailored management of anticoagulation in this high-risk population.

326 - P2.093

PRIMARY HYPEROXALURIA AND ARTIFICIAL INTELLIGENCE

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Aims/Purpose: Primary hyperoxaluria (PH) is a disorder of glyoxylate metabolism resulting in excessive oxalate production. It leads to nephrolithiasis, nephrocalcinosis, and renal failure and can pose serious health problems in advanced cases. ChatGPT, an artificial intelligence-powered chatbot developed by OpenAI, San Francisco, California, USA, has gained momentum in the medical field and is being used in various specialties. However, the potential utility of artificial intelligence in the diagnosis, treatment, and management of PH has not been previously investigated.

Methods: Using the local internet network of Konya City Hospital, 25 open-ended questions and 5 case scenarios related to PH were directed to ChatGPT 3.5 in English and Turkish languages. The accuracy of responses provided by artificial intelligence was evaluated by two researchers based on internationally recognized publications and guidelines.

Results: Inquiries directed in English yielded accurate responses regarding the definition of PH, epidemiological characteristics, and pathophysiological mechanisms of PH subtypes. Diagnostic methods were addressed, but current treatment options such as RNA interference therapies were not mentioned. Combined kidney-liver transplantation was elaborated on in detail, with prognosis focused solely on kidney survival. Inquiries directed in Turkish failed to obtain responses for PH type 3 due to insufficient information in practice. Unlike responses obtained in English, epidemiological data could not be accessed in the Turkish language, and treatment was limited to kidney transplantation without any mention of liver transplantation. In case scenarios, appropriate approaches were taken during the diagnostic process in both languages, but RNA interference therapies were not included in the treatment. Additionally, while liver transplantation was only recommended in cases of liver failure in English, there was no mention of liver transplantation in Turkish.

Conclusion: There are discrepancies in the information and guidance provided by ChatGPT in the field of PH, with certain points deviating from current approaches. Different responses can be obtained depending on the language used in the application. Further developments are needed for ChatGPT to become a valuable resource for the care and management of patients with PH.

335 - P2.094

HNF1B, SIZE DOES MATTER

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Aims/Purpose: Microdeletion 17q12 is the result of the partial deletion of the long arm of chromosome 17. It includes, among other genes, the morbid gene HNF1B and the LHX1 gene expressed in the brain and involved in the development of Purkinje cells in the cerebellum and in the migration of axons in the limbs. It is autosomal dominant and 75% of deletions are de novo. Manifestations include renal cystic disease, neurodevelopmental disorders and may be associated with juvenile-onset adult onset type 5 diabetes. The purpose is to present the case of a patient with CKD in the context of cystic kidney disease associated with neurodevelopmental disorders. Furthermore, to emphasise the importance of multidisciplinary work in the management of these patients.

Patient Methods & Results: A 10-year-old male, single right kidney and CKD 3aA1, with no history of interest, except for the father with 2 cysts in the right kidney with preserved renal function. Prenatal ultrasound showed increased bilateral renal echogenicity and renal asymmetry without cysts, but with intrauterine growth restriction. Delivery at 38+5 weeks with no perinatal incidents. At one week of life, these findings were confirmed with RD 52mm, marked decrease in corticomedullary differentiation without cysts. The IR was 40mm with the presence of multiple millimetric cysts, as well as a renal pelvis < 5mm without evidence of dilatation in other sections of the urinary tract. At 3 years of life, glomerular filtration rate of 82ml/min/1.73m2 and hypomagnesaemia. Subsequent controls showed persistent hypomagnesaemia 1.6 mg/dL (ref: 1.8-2.3 mg/dL) and associated elevated urates 5.8 mg/dL (ref: 1.5-5.5 mg/dL). A genetic study was performed which reported a de novo pathogenic mutation in HNF1B with complete deletion of the 9 exons of the gene in heterozygosis, by quantitative multiplex PCR of short fluorescent fragments (QMPSF). Global neurodevelopmental delay, learning disorders, tremor, ataxia and ADHD were observed from the age of 4 years, with good cognitive evolution. Genetic material analysis was requested by array CGH, which revealed a microdeletion of chromosome 17q12.

Conclusion: The multidisciplinary approach is essential for an accurate diagnosis and to optimise the follow-up of these patients. In our case, the detection of neurodevelopmental alterations was key to broadening the study, and knowledge of the different genetic study techniques is essential for a more precise diagnosis.

343 - P2.095

PHENOTYPIC DISCORDANCE IN SIBLINGS WITH IDENTICAL COMPOUND HETEROZYGOUS TTC21B MUTATIONS

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Aim: Nephronophthisis is a group of cystic nephropathies involving the tubulointerstitium with autosomal recessive inheritance. It is one of the most common hereditary diseases leading to end-stage kidney disease (ESKD) in children. Over 90 recessive single-gene causes have been identified. Biallelic pathogenic TTC21B variants are known to cause nephronophthisis-related ciliopathies. We report a novel case of two siblings with infantile-onset NPHP type 12 (NPHP12) demonstrating marked phenotypic variation despite harbouring identical compound heterozygous mutations in the TTC21B gene. A review of the literature comparing the clinical features of our case and potential hypothesis for genotype-phenotype correlation is provided.

Methods: We summarise the clinical and genetic findings of our case. Mutation analysis is performed using whole exome sequencing (WES). A systematic literature search for cases of NPHP12 caused by TTC21B mutation was performed in PubMed and Embase.

Results: Case: The index case was a 9 month old boy presenting with ESKD with bilateral renal dysplasia. Extrarenal manifestations included faltering growth, macrocephaly, brachydactyly, and liver enzyme abnormalities. He received a successful living donor renal transplant at age three. The proband's sister presented on day two of life with neonatal cholestasis, hypercalcaemia, and ESKD. Imaging revealed bilateral renal dysplasia, with hepatic fibrosis, portal hypertensive gastropathy and varices evolving in infancy. The proband was compound heterozygous for TTC21B variants, predicted to be pathogenic by AC mg criteria. WES revealed a maternally-inherited missense variant (p.Leu58Pro) in conjunction with a paternally-inherited deletion variant (c.796-5_865), resulting in exon skipping. Targeted testing in his sibling confirmed identical pathogenic variants. Literature review: 58 cases of NPHP12 associated with TTC21B mutations have been published. Extra-renal manifestations included hepatic (26%), skeletal (22%) and retinal involvement (12%). The widespread expression of the IFT139 protein in primary cilia explains the multisystem involvement. 57% were pathogenic heterozygous mutations, and 43% were compound heterozygous, with the latter affording an earlier onset of ESRD. Of the mutations, missense was the most common (77%), followed by frameshift (10%), splicing (8%) and nonsense (5%).

Conclusion: We present a case of identical biallelic pathogenic TTC21B variants in siblings, resulting in NPHP12 with distinct phenotypes. Current literature suggests TTC21B contributes both causal and modifying alleles across the ciliopathy spectrum. Compound heterozygous mutations in the TTC21B gene generate early-onset and more severe clinical symptoms with extrarenal manifestations. Despite more than 50 cases globally, to our knowledge, this is the first reporting this splicing mutation.

347 - P2.096

HYPOGAMMAGLOBULINEMIA AS POSSIBLE PREDICTOR OF TMA IN PATIENTS WITH CD46 GENE MUTATION

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One of the genes associated with atypical hemolytic uremic syndrome (aHUS) is CD46, which can be inherited in an autosomal dominant or autosomal recessive manner. The complement regulator CD46 is also known to be involved in the regulation of intestinal epithelial cell barrier function and can be connected with binding infections pathogens. The purpose is to describe the case of family hypogammaglobulinemia and dyspepsia as manifestations of pathogenic variants in the CD46 gene.

Methods: Two siblings (girl 9 y.o. and boy 6 y.o.) have dyspeptic symptoms (nausea, malabsorption, unstable stool) from birth. In both of them, from the age of 4 years, hypoproteinemia up to 48-50 g/l, hypoalbuminemia up to 26-18 g/l, IgG hypogammaglobulinemia 1.7-4 g/l and normal urine tests are detected consistently. High levels of stool alpha-1 antitrypsin are noted. Primary lymphangiectasia was excluded.

Results: The girl underwent whole exome sequencing, nucleotide variant CD46 hom c.848G > C, p.C283S was found. The same variant was found in the boy. Both children several times underwent pathology examination of an intestine biopsy; no signs of thrombotic microangiopathy (TMA) were found. One year later, against the background of high fever, the girl had signs of gross hematuria, petechial rash, and arterial hypertension up to 139/90 mmHg. Laboratory tests - proteinuria was 2.23 g/day, thrombocytopenia 14-12*10^9/l, anemia (Hb 77 g/l, RBC 2.72*10^12/l), schistocytes 2.3%, azotemia (creatinine 133-445 µmol/ l, urea 13-35.87 mmol/l), LDH up to 2849-3573 IU/l, hypoproteinemia 39 g/l, hypoalbuminemia 25-20 g/l, hypercholesterolemia 8.4 mmol/l. Decrease in C3 to 67.5 mg/dl, C4 14.4 mg/dl. Anti-CFH 683 units (reference is less than 1500). ADAMTS-13 activity was 82%. Plasma infusions N°2 were carried out. Taking into account previously identified variants in the CD46 gene, the aHUS diagnosis was clear, and the child was initiated on eculizumab therapy. During that, renal function was complete recovered, anemia, thrombocytopenia, and complaints of dyspepsia were relieved. All gastrointestinal symptoms, as well as persistent hypogammaglobulinemia, were consistently disappeared. The boy continues to suffer from dyspepsia, no episodes of TMA have been observed, and despite the presence of a pathogenic genetic variant no indications for the use of eculizumab have been identified.

Conclusion: Two siblings with the same clinical picture of the gastrointestinal tract have mutations associated with aHUS, however, one, due to the development of an episode of TMA, received specific therapy and relieved all complaints, while the other did not. Perhaps gastrointestinal problems and hypogammaglobulinemia should be taken into account as a predictor of the development of TMA in children with mutations in the CD46 gene.

356 - P2.097

GENETIC STUDY IN CHILDREN WITH PRIMARY GLOMERULOCYSTIC KIDNEY DISEASE

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Aims/Purpose: Glomerulocystic kidney disease, characterized by cystic dilation of Bowman's space, is a rare renal cystic disorder often associated with variants of UMOD and HNF1B genes, the latter linked to HNF1B-maturity-onset diabetes of the young (MODY), formerly known as MODY 5. This study aimed to conduct a genetic study in children exhibiting ultrasound features indicative of primary isolated glomerulocystic kidney disease.

Methods: Pediatric patients presenting with ultrasound evidence suggestive of isolated glomerulocystic kidney disease followed at the Pediatric Nephrology Outpatient Clinic, underwent whole exome sequencing (WES). WES was performed using Illumina DNA Prep Exome 2.0, Plus Enrichment, followed by sequencing on the Nextseq 1000 platform. Array–comparative genomic hybridization (CGH) was also performed in order to confirm copy number variants (CNVs).

Results: Four children (3 boys, 1 girl) aged 4.5 to 10 years, with longstanding ultrasound-confirmed glomerulocystic kidney disease were included. Ultrasound findings had consistently revealed normal kidney size, bilateral renal cortex cysts, increased echogenicity, and intact corticomedullary differentiation. Family history was unremarkable for cystic nephropathy or diabetes. All children had normal clinical examination, normal renal function, glucose metabolism, magnesium and transaminase levels and normal ultrasound of liver and pancreas. WES identified a heterozygous deletion at 17q12, spanning the HNF1B gene, in three children, indicative of autosomal dominant renal cysts and diabetes syndrome (OMIM: 137920). CNVs were also confirmed by CGH analysis. A deletion was not found in the fourth patient. However, the possibility of missing the disease-causing variant due to technical limitations or genetic heterogeneity occurrence cannot be excluded.

Conclusions: Genetic study is imperative for children with isolated primary glomerulocystic kidney disease, given the prevalence of HNF1B gene variants. WES in our patient group reached a diagnostic yield of 75%. Positive results necessitate long-term monitoring for renal function and potential HNF1B-MODY manifestations.

447 - P2.098

PATERNAL UNIPARENTAL ISODISOMY OF CHROMOSOME 1 LEADING TO STEROID-RESISTANT NEPHROTIC SYNDROME DUE TO NPHS2 VARIANT

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Aims/Purpose: Steroid-Resistant Nephrotic Syndrome (SRNS) due to pathogenic variants in the NPHS2 gene is an autosomal recessive disease caused by inheritance of biallelic variants. Segregation analysis will typically reveal that each parent is heterozygous for one of the two variants inherited by the child. Interestingly, we recently diagnosed a patient with NPHS2-related SRNS due to homozygous p.Glu233Argfs*34 variant caused by uniparental isodisomy. Here, we present this rare and unique case.

Methods: This patient was followed at Necker-Enfants Malades Hospital. Data regarding the patient were collected with consent from the parents. Genetic testing by Next-Generation Sequencing was performed in the patient and subsequent Sanger sequencing of the NPHS2 gene was performed in the parents. Polymorphic microsatellite markers were used to confirm this unusual mechanism.

Results: Our patient presented with SRNS with subsequent kidney failure at the age of 10 years and received a kidney transplant. Genetic testing revealed a homozygous frameshift variant (c.697_701delinsAGAAGA, p.Glu233Argfs*34) in the NPHS2 gene, explaining the SRNS. The father of the patient was heterozygous for this variant but surprisingly, the mother was not. First, to exclude an error in sampling, new samples were taken which confirmed the results obtained. We also repeated tests with a different primer to rule out the possibility of monoallelic amplification due to a single nucleotide polymorphism (SNP) affecting primer hybridization in the index case. Again, this confirmed our results. Finally, by segregation of Single Nucleotide Polymorphisms (SNP) and microsatellites markers within the NPHS2 locus, we established the monoparental (father) contribution to the genotype of the index case and confirmed the absence of maternal contribution to the NPHS2 locus. Segregation of polymorphic markers on the entire chromosome confirmed full paternal uniparental isodisomy. This is due to the rare event of fertilization of a monosomic paternal gamete with a nullisomic maternal gamete, leading to post-zygotic duplication of the chromosome (monosomy rescue).

Conclusion: Although rare, uniparental isodisomy may sometimes cause autosomal recessive disorders. It is important to identify these cases mostly because it will modify genetic counselling. In fact, the risk of recurrence for this couple is low, compared to the 25% risk of recurrence for autosomal recessive disorders. Detecting and describing these cases is therefore of the utmost importance.

484 - P2.099

ALKAPTONURIA AS A CAUSE OF DARK URINE IN A CHILD. CASE REPORT

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Aims/Purpose: Rare diseases are often underdiagnosed due to a lack of experience. Our aim is to implement knowledge about this infrequent disease.

Methods: We present a case of heavy proteinuria and dark urine due to an inborn error of metabolism. Additionally, we conducted a literature review of this entity.

Results: A 5-year-old boy, without previous clinical records, was referred due to asymptomatic dark urine. He has had dark urine since birth, which his mother described as having a terracotta colour. The boy also experienced his first episode of abdominal pain, accompanied by dark and profuse sweating. Initial examinations revealed the following. Kidney function appeared normal (eGFR 95 ml/min/1.73m2). No relevant data in blood tests. Spot urine analysis: No evidence of albuminuria or beta2 microglobulin. 24-Hour Urine Sample: Heavy proteinuria (65 mg/m2/h) was observed, but without albumin. The proteinogram was normal. Normal ion excretion, but notably low levels of creatinine (5 mg/kg/day) and uric acid (44 mg/1.73m2/day). Normal ultrasound. Further tests revealed significantly elevated levels of homogentisic acid in the urine (2021 mmol/mol). Genetic examination confirmed compound mutations in the HGD gene, which is associated with alkaptonuria. After diagnose protein dietary adjustment was made, with ameliorate of homogentisic acid in urine to 241 mmol/mol. However considerably high levels made us initiate nitisinone.

Conclusion: Alkaptonuria is an exceptionally rare disease, affecting approximately 1 in 250,000 to 1,000,000 individuals. It was the first inborn error of metabolism to be described. The disease results from pathogenic variants in the homogentisate 1,2-dioxygenase enzyme, leading to the accumulation of homogentisic acid in tissues. The three major symptoms of alkaptonuria include dark urine, ochronosis (dark staining of tissues), and early-onset severe arthropathy. While dark urine is often the only clinical feature in children, other manifestations typically appear around 30-40 years of age. From a kidney perspective, besides dark urine, the presence of kidney stones is not uncommon at any age. Some cases describe renal insufficiency, which can have worse systemic outcomes. Treatment aims to address specific symptoms. Nitisinone, originally used for treating tyrosinemia, has been postulated as a possible treatment. Although it lowers homogentisic acid levels, it does not significantly improve symptoms. Early intervention in paucisymptomatic patients could be beneficial. Rare diseases are been suspected when we have uncommon symptoms. Renal involvement in alkaptonuria is not well known. Low creatinine and uric acid levels are not been notified previously.

512 - P2.100

RENAL INVOLVEMENT IN MIRAGE SYNDROME: SINGLE-CENTRE EXPERIENCE

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Aims/Purpose: MIRAGE syndrome (MS) is a rare genetic disease characterized by myelodysplasia, infection, growth restriction, adrenal hypoplasia, genital abnormalities, and enteropathy, caused by a gain-of-function mutation in the SAMD9 gene. Very few cases of renal involvement have been reported to date. Renal complications including focal segmental glomerulosclerosis (FSGS), renal tubular acidosis, interstitial nephritis, renal hypoplasia and chronic kidney failure after bone marrow transplantation have been reported.

Methods: We describe two cases of genetically confirmed MS with renal involvement.

Results: Case report #1. Patient 1 was born at 32 weeks with a birth weight of 1125 g. He presented with adrenal insufficiency, genital ambiguities, myelodysplasia (monosomy 7), immune deficiency, and hypertension. At age 6 years, he developed glomerular proteinuria (UPCR 5.3 mg/ mg) without hypoalbuminemia. Kidney function was normal. The kidney biopsy showed FSGS, for which he received a course of steroid therapy that was unsuccessful in lowering proteinuria. Angiotensin converting enzyme inhibitor therapy allowed achieving complete remission of proteinuria. At age 11 he developed septic shock and acute kidney injury, from which he recovered, but retained moderate proteinuria. At age 11.5 he underwent hematopoietic stem cell transplantation from his phenoidentical HLA-matched mother. Cyclosporine was administered as part of the graft-versus-host disease prophylaxis, resulting in complete remission of proteinuria. After discontinuation of cyclosporine, the patient has limited residual proteinuria (UPCR 0.5-1 mg/ mg). Case report #2. Patient 2 was born at 37 weeks with a birth weight of 1450 g. He presented with adrenal insufficiency, myelodysplasia (monosomy 7), immunodeficiency, enteropathy with chronic diarrhea, and biliary cirrhosis. At the age of 5 year, he underwent liver transplantation, following which he showed a rise in creatinine, progressive metabolic acidosis with hypokalemia, and low-molecular-weight proteinuria without hypoalbuminemia. Biological signs of renal tubular damage seemed to worsen after starting tacrolimus therapy.

Conclusion: Patients with MS may have glomerular and tubular disorders. Impairment of the endolysosomal compartment in MS is likely to compromise normal podocyte and in tubular cell functioning, causing FSGS and/or tubular disorders.

535 - P2.101

CASE REPORT OF A 2-YEAR-OLD MALE WITH CKD STAGE 4, WITH A BACKGROUND OF AUTOSOMAL RECESSIVE RENAL TUBULAR DYSGENESIS

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Background: Autosomal-recessive renal tubular dysgenesis (AR-RTD) is a rare genetic disorder caused by defects in the renin-angiotensin system with most common outcome being foetal death or, neonatal death from renal failure, pulmonary hypoplasia, and/or refractory arterial hypotension. Several cases have been reported that describe survival past the neonatal period. We present a 2-year-old boy with RTD due to compound heterozygous ACE mutation, who has not required to date any form of renal replacement therapy.

Case Report: Born at 31 weeks gestation, by caesarean section due to oligohydramnios with reduced foetal movements. 26-week scan showed oligohydramnios and this was confirmed on antenatal MRI, reporting small lung volumes and small bladder with normal kidneys. He was born in poor condition, requiring intubation and ventilation for one day and a chest drain for pneumothorax. His creatinine on day 1 of life was 200 umol/L and he was oliguric. He had an ultrasound on day 2 and day 5 of life, which showed enlarged kidneys with increased cortical echogenicity, no hydronephrosis. Urine output and renal function improved with conservative management. He then had an episode of urosepsis and cardiac decompensation secondary to large patent ductus arteriosus, which required re-intubation, inotropes and diuretics. After discharge, his creatinine slowly improved (creatinine 28 umol/L at 3 months of age). Parents are non-consaguineous and there is a family history of a paternal 5-year-old sister with CKD on dialysis. Genetic analysis showed a 16p11.2 microduplication and compound heterozygosity for the ACE c47_70del p.(Leu16_Pro23del) pathogenic variant (father) and c.77 (6G > A p.(Arg259His) likely pathogenic variant (mother). He had several episodes of acute kidney injury requiring hospital admissions. At 14 months of age, fluodrocortisone was added, which has provided a period of stability. At the age of 2 years, he has good urine output, he is thriving, has mild proteinuria (urine protein:creatinine ratio 52 mg/mmol) and his creatinine clearance is 37 ml/min/1.73m2.

Conclusion: As the number of surviving cases increases, it should be emphasized that RTD may not be universally as fatal as previously reported. The type of mutation may have a prognostic significance and may help guide prognostication and medical decision-making.

538 - P2.102

PAST, PRESENT AND FUTURE IN HYPEROXALURIA TYPE 1 TREATMENT: A COMPARAISON OF RENAL OUTCOME IN TWO SIBLINGS

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Background and Aim of the Study: Primary hyperoxaluria type 1 (PH1) is a rare disease characterized by increased renal excretion of calcium oxalate, chronic renal failure secondary to recurrent urolithiasis, nephrocalcinosis, and systemic oxalosis. Until 2020, the mainstays of therapy have been dialysis and liver-kidney transplantation. Then, Lumasiran, a RNA interference molecule that reduces hepatic oxalate production by targeting glycolate oxidase, has been approved for the treatment of the disease.

The purpose of this paper is to compare the clinical course of PH1 in two siblings with the same mutation but different therapy in early life.

Methods: FS was born at term with a physiological neonatal course. At 2 months of age, he developed nephrocalcinosis and kidney failure. A compound heterozygous mutation of the AGXT gene, resistant to pyridoxine, was identified at genetic test, leading to PH1 diagnosis. He started treatment with potassium citrate and hyperhydration. MS, his younger sister, received a prenatal diagnosis of PH1 in 2020. She was born at 36 weeks and started Lumasiran for compassionate use on day 10th of life, in association with hyperhydration and potassium citrate.

Results: At 13 months of life, FS underwent isolated liver transplant, with CKD stage 3. and was performed. His GFR then showed a slow decrease during the following years, until he was started on hemodialysis at 8 yo. After 6 months he underwent kidney transplant from a living donor.

His sister developed nephrocalcinosis at 3 months of life and two unilateral kidney stones appeared at 9 months of life, but she didn't show a deterioration in kidney function. At 30 months, MS is growing according to her birth percentile with normal renal function, urinary and plasma oxalate values. Her last abdominal scan shows improvement in nephrocalcinosis, and kidney stones appear unmodified.

Conclusion: To date, early treatment of newborns with antenatal diagnosis of PH1 represents a therapeutic challenge for pediatric nephrologists. This report shows that Lumasiran, initiated early in life, can substantially affects the course of PH1. The use of Lumasiran appears to be safe in small infants.

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544 - P2.103

CLINICAL PHENOTYPE AND GENOTYPE OF RARE HEREDITARY TUBULOPATHIES WITH NEPHROCALCINOSIS IN CHILDREN

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Introduction: Nephrocalcinosis is a specific sign of rare hereditary tubulopathy (ORPHA) on primary hyperoxaluria (PH) types 1, 2, 3; familia hypomagnesemia with hypercalciuria and nephrocalcinosis (FHHNC); idiopathic infantile hypercalcemia 2 type (IIH 2 type), Bartter syndrome I type; Dent disease 2.

Material and Methods: We analyzed phenotype and genotype of genetic testing in 11 children aged 2–17 years with rare hereditary tubulopathies with nephrocalcinosis.

Results: Nephrocalcinosis (11), nephrolithiasis (2), metabolic acidosis (8), hypomagnesemia (3), hypermagnesuria (3), oxaluria (5), calciuria (5), metabolic alkalosis (2), hypercalcemia (2), CKD with normal GFR C1 (10) and decreased C4 (1) were diagnosed in 11 patients. PH was diagnosed in five children.The homozygous mutation c.508G > A, p.Gly170Arg AGXT gene was diagnosed in one patient with PH type 1. One patient at the age of 15 years old with PH type 1 had homozygous mutation c.33 dup, pLys12GlnfsTer156 in 1 exon of the gene AGXT. Heterozygous mutation c.370C > T, p.Arg124Cys in the GRHPR gene was identified in one proband with PH type 2. There were identified 2 heterozygous mutations in exon 6 of the gene HOGA1 c.763C > T; p.Arg255Ter and not previously described variant c.767T > G, p.Leu256Arg in one child with PH type 3. Homozygous mutation c.266G > A, p.Arg89His rs765160493 in exon 2 of the gene HOGA was identified in one proband with PH type 3. FHHNC was diagnosed in three children. The same heterozygous mutation c.217+5G > A p.Leu81Phe of the CLDN16 gene was found in two siblings with FHHNC. There were identified 2 heterozygous mutation c.414T > A p.Tyr138Ter (previously not described) in exon 4 and c.2125G > A in intron 2 of the CLDN16 gene in one girl 17 years old with FHHNC and CKD C4. The proband-boy with the IIH 2 type had heterozygous mutation c.464 T > C; p.Leu155Pro in 5 exon of the gene SLC34A1. Heterozygous mutation c.3287 C > T, p.Thr 1096Ile in 2 exon of the gene SLC12A1 was detected in boy 6 years old with Bartter syndrome I type. Deletion of the OCLR gene was identified in one proband-boy 11 years old with Dent disease 2 (XLR).

Conclusions: We described phenotype and genotype features of the rare hereditary tubulopathies with nephrocalcinosis in 11 children.

549 - P2.104

NOONAN SYNDROME-LIKE DISORDERS WITH RENAL TUBULAR ACIDOSIS: A NEW PHENOTYPE?

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Aims/Purpose: In renal tubular acidosis (RTA) renal bicarbonate reabsorption or hydrogen ions secretion are compromised causing in most children hyperchloremic metabolic acidosis, fatigue, failure to thrive, and osteopenia. We present two patients with Noonan syndrome-like (NSL) disorder and metabolic acidosis, without mutations in the classical RTA genes.

Methods: Clinical records were reviewed for clinical history, lab values, results of genetic tests and treatment.

Results: Patient #1 is a 9 years-old girl with failure to thrive who was admitted to the hospital at 4 months of age for severe diarrhea and dehydration. Physical examination showed frontal bossing and macrocephaly. Blood tests revealed severe hyperchloremic metabolic acidosis, urine pH was > 7. After IV rehydration with alkalizing solutions, she was maintained on oral sodium bicarbonate (> 5 mEq/Kg/day). Over the following months, metabolic acidosis was compensated and growth velocity improved. Alkali supplements were progressively reduced but complete discontinuation caused again metabolic acidosis. She progressively developed ichthyosis and sparse, loose and slow-growing hair. Genetic screening for distal RTA was negative. Exome sequencing showed a de novo heterozygous variant of the SHOC2 gene, associated with the NSL disorder with loose anagen hair. Patient #2 is a 30 months-old boy, born large for gestational age, who was admitted to the hospital short after birth for respiratory distress. Blood tests showed hyperchloremic metabolic acidosis requiring sodium bicarbonate IV infusion. At discharge oral sodium bicarbonate (2 mEq/Kg/day) was needed to maintain normal acid-base balance. Plasma levels of renin and aldosterone were high. At follow-up visits, growth velocity was poor despite adequate acid-base balance. Exome sequencing was negative for pseudohypoaldosteronism and distal RTA but revealed a de novo heterozygous variant of the CBL gene associated with the NSL disorder with or without juvenile myelomonocytic leukemia.

Conclusions: NSL are rare disorders caused by variants that deregulate RAS-mediated signal transduction pathways. Phenotypes vary significantly, including congenital heart defects, short stature, neurocognitive impairment, and distinctive craniofacial features. These two cases have different genetic variants and presented with different clinical features except for early-onset hyperchloremic metabolic acidosis. To our knowledge, similar cases have not been reported in the literature. Possibly, mild acidosis may be underdiagnosed in patients with NLS, in whom poor growth is often attributed to the underlying genetic defect.

555 - P2.105

STEROID SENSITIVE NEPHROTIC SYNDROME (SSNS) BY MUTATION NPH1, NUP93, NUP205, KANK2, COQ6, LAMB2 GENES IN CHILDREN

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Introduction: It is proved that mutations of genes encoding the main components of the glomerular basement membrane, slit diaphragm, structural and functional proteins of podocyte are responsible for the development of NS in children [R.Preston et al. (2019), O. Boyer et al. (2022)].

Aim: Describe the clinical phenotype and genotype of six children with SSNS.

Material and Methods: We analyzed clinical phenotype and genotype of genetic testing in six children with SSNS.

Results: The mutations NPHS1, NUP93, NUP205, KANK2, COQ6 genes were diagnosed in five patients with isolated childhood SSNS and normal GFR. Proband- boy 17 year-old with SSNS and minimal change (MC) is carrier of heterozygous mutation in exon 2 of the gene NPHS1 c.121_122 del, p. rs.386833873. The patient-boy 6 year-old with SSNS and MC had heterozygous mutation c.476C > T, p.Thr159Ile, rs:369482440 (not previously described) in 5 exon of the NUP93 gene. In a patient 15 year-old with heterozygous mutation c.2961C > G, p.lie987Met, rs:1756073 (not previously described) in 21 exon of the NUP205 manifestation of frequent relapsing SSNS and MC was at 4 year-old. SSNS without deafness was identified in one girl 5 year-old with heterozygous mutation c.451G > A, p.Ala152Thr (not previously described) in exon 4 of the COQ6 gene, the therapy with CoQ10 had a positive effect. Proband-boy 4 year-old with SSNS had heterozygous mutation c.2054A > G, p. His685Arg, rs:768034179 (not previously described) in 9 exon of the KANK2 gene. SSNS and normal GFR was diagnosed in child 15 year-old with Pierson syndrome with ocular abnormalities (refractive amblyopia and astigmatism) by mutation c4364 G > A, rs:764262021 in 18 exon of the gene LAMB2.

Conclusions: We demonstrate phenotype and genotype features of isolated and syndromic forms of Hereditary SSNS in six children.

563 - P2.106

LUMASIRAN IN CHILDREN WITH HYPEROXALURIA TYPE 1: REAL WORLD DATA FROM ITALIAN PEDIATRIC NEPHROLOGY UNITS

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Aims: PH1 is a genetic disease caused by increased renal excretion of calcium oxalate, chronic renal failure, urolithiasis, nephrocalcinosis and systemic oxalosis. Until 2020, dialysis and liver-kidney transplantation were the only treatment options. Then Lumasiran, an RNA interference molecule reducing hepatic oxalate production by targeting glycolate oxidase, has been approved for the treatment. The aim of this study was to evaluate the efficacy of Lumasiran in a cohort of pediatric patients.

Methods: Retrospective observational multicentric study. Inclusion criteria: pediatric patients with genetic diagnosis of PH1 treated with Lumasiran. The efficacy of Lumasiran was evaluated testing oxaluria, oxalemia, CKD stage and ultrasonographic (US) data every 6 months (M) (Tab. 1).

Results: 17 patients were enrolled [M:F 5:12; median age at diagnosis: 38 months (0-156; median age at Lumasiran initiation: 70 months (0-204)]. Median follow up (FU) was 18 months (6-36). All patients received supportive therapy (hydration, pyridoxine, urinary alkalinisation), 3 patients started dialysis before enrollment or during FU. At M6 oxaluria was reduced > 25% in all patients on conservative treatment; after M12, oxaluria was variable without symptoms in 5 patients. Oxalemia was below the limit of supersaturation during the whole FU. At M0, US showed urolithiasis or nephocalcinosis in 7 patients respectively, urolithiasis plus nephrocalcinosis in 1 patient and was normal in 2 patients (prenatal diagnosis). At last FU, US was unmodified in 16/17 patients: one patient developed nephrocalcinosis at M3 and nephrolithiasis at M12. CKD stage remained stable in 15/17 patients (in one case dialysis was started at M20 and in one CKD went from stage 2 to 3). No adverse effects were reported.

Conclusions: This study provides real-world evidence on the use of Lumasiran for PH1 treatment. Lumasiran is today the only therapeutic option with real impact on pediatric PH1 approved from birth and shows a good tolerability profile.

Table 1. Clinical data of 17 children treated with lumasiran

Patient n.	Age at Lumasiran start (months)	FU (months)	UOx/creat (mmol/mol)						Pox (mmol/l)						CKD	stage
			M0	M6	M12	M24	M30	M36	M0	M6	M12	M24	M30	M36	M0	Last FU
1	91	30	182	55	110	50	40	130	6	6	6,5	6	8	7	2	2
2	0,3	24	1200	495	90	90			68	10	10	10			1	1
3	14	18	214	50	30				13	5	5				1	1
4 *	190	24	143	72	24	94			75	NA	NA	34			4	5
5 °	27	36	#	#	#	#	#	#	116	79	90	171	104	103	5	5
6	13	30	500	243	245	83	90		96	16	18	NA	NA		2	3
7	124	24	135	66	54	NA			8	NA	2	NA			2	2
8	25	36	271	201	277	250	166	84	16	6	5	3	0,8	4	2	1
9	70	36	103	63	197	92	106	58	8	5	5	12	6	4	1	1
10	49	12	320	140	50				11	NA	NA				1	1
11	191	6	80	40					NA	NA					1	1
12	3	18	573	234	357				32	5	5				2	1
13	169	12	96	56	80				6	0,7	4				2	1
14	154	6	11	66					5	0,5					2	2
15	33	12	260	180	199				12	5	3				1	1
16	157	18	150	NA	60				0,8	NA	NA				1	1
17°	204	12	146	64	NA				65	50	NA				5	5

* Dialysis start post lumasiran, ° Dialysis start pre lumasiran, # anuric, NA not available

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594 - P2.107

ACTIVITIES OF FLAVONOID LUTEOLIN IN A MOUSE MODEL OF NEPHROPATHIC CYSTINOSIS

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Aims/Purpose: In Cystinosis, mutations in the CTNS gene lead to accumulation and crystallization of cystine in lysosomes, with progressive damage in most organs. Nephropathic cystinosis represents the most common and severe phenotype, characterized by early onset alteration of renal proximal tubular functions, that results in renal Fanconi syndrome. Cysteamine delays kidney damage, without preventing progression to end-stage kidney disease, suggesting that other pathways, unrelated to cystine accumulation, are involved in the pathogenesis of the disease. Aberrant autophagy, endo-lysosomal dysfunction, and apoptosis have been proposed as additional features that cause cellular and tissue damage and are emerging as new target for new therapies. Previously, we have identified with a cell-based high content drug-screening luteolin, a flavonoid compound that improves autophagy and other altered pathways in cell models and in a zebrafish model of cystinosis. In this study, we have investigated if luteolin prevents or ameliorates kidney dysfunction in a mouse model of nephropathic cystinosis.

Methods: We have fed 2 month-old Ctns-/- mice (n = 6 per group) with a standard diet or the same diet supplemented with 150 mg/kg/day of luteolin for 6 months.

Results: Our findings indicated that luteolin has a good safety profile, without compromising mice growth or causing hepatocellular toxicity. Tissue analyses after sacrifice confirmed that luteolin restores the defective endo-lysosomal compartment and improves autophagy and apoptosis. However, we did not observe a significant effect on the Fanconi syndrome.

Conclusion: These results question the contribution of abnormal autophagy and apoptosis to pathogenesis of cystinosis.

597 - P2.108

HNF1B MUTATIONS IN A COHORT OF SPANISH CHILDREN: RETROSPECTIVE STUDY FROM THE LAST 10 YEARS

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Aims/Purpose: Mutations in HNF1b (hepatocyte nuclear factor-1beta) are known for their variable expressivity, affecting the epithelial cells of different organs. In particular, renal cystic disease is one of the most prevalent manifestations in pediatric patients. With this study, we aim to analyze and show the characteristics of such patients in our setting.

Methods: A descriptive analysis was conducted on cases of patients of a referral hospital with mutations in the HNF1b gene, who maintained follow-up visits in Pediatric Nephrology and were genetically diagnosed in the last 10 years. The registered variables refer to the epidemiological characteristics specific to each patient, as well as clinical and analytical data related to their disease.

Results: Seven medical records of patients diagnosed between 2014 and 2024 have been analyzed, with relevant data summarized in the attached table. All patients were at term newborns, two of them with low birth weight. Renal parenchymal involvement was confirmed in prenatal ultrasounds in four of them, who were the only ones to initiate follow-up in Pediatric Nephrology during their first year of life. Six out of the seven genetic study results were obtained in the last 5 years, all corresponding to pediatric patients. Four patients showed microdeletions in 17q12 that included HNF1b, while the rest had point mutations in that gene. The latter group showed clearly decreased estimated glomerular filtration rate at the time of diagnosis (at different ages) and during follow-up. None of the patients developed arterial hypertension during follow-up. Only two patients with microdeletion had a normal renal ultrasound at diagnosis, the rest showed renal cysts and alterations in parenchymal echogenicity.

Patient nº	Sex	Age at diagnosis (genetic)	Genetic result	eGFR* at diagnosis	Comorbidities
1	Female	18	c.449T > C; p.(Leu150Pro) in HNF1b	58	Rokitansky syndrome, hypomagnesemia
2	Female	8	17q12 microdeletion	107	MODY 5, hypomagnesemia, ADHD
3	Female	14	17q12 microdeletion	85	MODY 5, hypomagnesemia, hyperuricemia, hypertransaminasemia bicornuate uterus
4	Female	5	c.827G > A; p.(Arg276Gln) in HNF1b	64	-
5	Male	1	c.454C > T; p.(Gln152*) in HNF1b	58	-
6	Female	12	17q12 microdeletion	133	Hypomagnesemia, hypertransaminasemia
7	Male	2	17q12 microdeletion	132	-

MODY: maturity onset diabetes of the young. ADHD: Attention deficit hiperactivity disorder. *eGFR (estimated glomerular filtration rate in ml/min/1,73m2) was determined by Schwartz 2009 or by CKiD U25 in patients > 18 years old.

Conclusion: Diagnosis of mutations in genes such as HNF1b has been facilitated in recent years by advances in genetic analysis. The analysis conducted in this study highlights the characteristics of patients in our setting, showing that those with microdeletions have more comorbidities compared to the rest of patients, who presented altered glomerular filtration.

608 - P2.109

REPLACEMENT OF RENAL BIOPSY THROUGH MOLECULAR STUDY IN PATIENTS SUSPECTED OF ALPORT SYNDROME

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Aims/Purpose: Sustain the replacement of renal biopsy through molecular study in patients with suspected Alport syndrome.

Methods: We describe the case of a male patient with persistent hematuria and proteinuria, with a family history of Alport Sýndrome

Results: Male patient aged 5 years, who started at 20 months with persistent microscopic hematuria of glomerular origin, mild isolated significant proteinuria, currently with normal renal function, without myopia or hearing loss . With a family history of maternal uncle with renal biopsy (unknown result) with chronic kidney disease stage 5 (CKD stage 5), hearing loss and myopia, deceased . Half-sister with renal biopsy (without electron microscopy), deceased uncles and cousins, mother with persistent microscopic hematuria. Renal biopsy is deferred and a molecular panel directed to Alport syndrome (CNVs and NGS) is performed . It reported an interstitial loss of approximately 298 kb in Xq 22.3, which includes the genes COL4A5 and IRS4. This result confirms the genetic diagnosis of Alport syndrome type 1, as well as hypothyroidism without goiter.

Conclusion: The diagnosis of Alport syndrome through genetic analysis has advantages over renal biopsy, such as avoiding complications in the surgical procedure, only being performed in atypical cases ; optimizing cost /benefit ; conducting complementary genetic panel and directed genetic counseling (risk of recurrence, kidney transplant donors, prenatal and preimplantation diagnosis); documenting digenic inheritance, which is sometimes associated with worse renal prognosis or contiguous gene syndromes

619 - P2.110

IS IT JUST NEPHRONOFTHISIS?

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Nephronophthisis is a rare genetic kidney disease characterized by cystic disease that causes chronic terminal renal failure in children.

It's divided into three clinical subtypes depending on the age of onset: neonatal, juvenile, late.

To date, mutations have been identified in 14 genes encoding ciliary proteins, including those of the NPHP3 gene that cause, in most cases, the late form.

We describe the case of a 4-year-old patient who came to our observation for terminal uremia and severe acute pancreatitis.

Phenotypically, the small presented lunar facies, olive complexion, saddle nose, slight macroglossia, malocclusion class 2 with increased overject associated with atypical swallowing, epicanth and onykodystropy.

Upon arrival, emergency hemodialysis started with CVVHDF technique, then shifted to chronic peritoneal dialysis.

After clinical stabilization, began clinical investigations aimed at identifying the syndromic picture.

Renal biopsy showed a non-specific diagnosis of chronic interstitial nephritis.

At the same time, started genetic investigation for cystic diseases with mutation in homozygous gene NPHP3, associated with nephrooptysis.

For the persistence of high levels of pancreatic enzymes, also performed genetics for cystic fibrosis which showed a genotype compatible with forms CFTR relate disorder (carrier of heterozygous for pathogenic variant F508 of the gene CFTR and polymorphism 5T;TG12).

At a distance of one year the patient had gynecomastia and bilateral galactorrhea associated with hyperprolactinemia with MRI of pineal gland cysts and failure to display the bright pituitary spot, currently still under diagnostic definition.

637 - P2.637

POLYURIA AND POLYDIPSIA AS EARLY MANIFESTATIONS OF NEPHRONOPHTHISIS IN AN ADOLESCENT

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Aims/Purpose: To present the features of clinical presentation of juvenile form of nephronophthisis in an adolescent girl due to non-specific symptoms such as polydipsia and polyuria. Nephronophthisis, type 1 (juvenile) is a rare ciliopathy with an autosomal recessive type of inheritance leading to the development of ESKD in children and young adults. This pathology is based on mutations in the NPHP1 gene responsible for the structure and function of the nephrocystin-1 protein in the primary cilia. Non-specific symptoms include polyuria, polydipsia, electrolyte disturbances (Fanconi syndrome) and the presence of cysts in the kidneys.

Methods: A 14-year-old girl with an unknown family history was examined (there are no data for pregnancy, childbirth and the neonatal period). She considered herself healthy until the age of 9 years. At the age of 9, complaints of polydipsia (3L/1.73m^2) and polyuria (3L/1.73m^2/24h) first appeared, renal function was not studied. At the age of 11, azotemia, hyperuricemia and elevated PTH were detected, and at the age of 13, diffuse changes in renal parenchyma were first detected.

Results: The girl was first examined in the Nephrology Department: physical development was average (25-50% of height; 75-90% of weight), polydipsia (more than 3L/1.73m^2/24h) and polyuria (2.3L/m^2/24h), no extrarenal manifestations. Laboratory examinations: hypokalemia (3.3 mMol/L), hyperuricemia (0.58 mMol/L) and hyperparathyroidism (263.6 pg/mL), no P-Ca abnormalities. Urinary syndrome presented with min low molecular weight proteinuria (-2- mg elevation), FE Na 2.04%; FE K 23.8%; FE mg 7.3%; Ca/Cr = 0.01; TmP/GFR 0.76). Signs of CKD G3A - eGFR - 37.9 mL/min/1.73m^2 (CKID U25). Ultrasound: V of kidneys > 97‰, parenchyma of increased echogenicity, cortico-medullary differentiation is disturbed, cysts (1.4x1.0 cm and 1.0x0.7 cm) in the medullary layer of both kidneys. According to 24-hour BPM data, stable systolo-diastolic arterial hypertension. X-ray - signs of osteoporosis. Taking into account the revealed changes, Autosomal dominant tubulointerstitial kidney disease (UMOD?) was suspected, and a genetic study was performed to exclude it. Full-exome sequencing revealed a homozygous deletion of a segment of chromosome 2, capturing the NPHP1 gene, which ruled out tubulointerstitial disease.

Conclusion: Nephronophthisis is an important cause of ESKD in children and young adults. Late diagnosis of the disease is often due to nonspecificity of the clinical presentation. Polyuria and polydipsia have been identified as initial symptoms of nephronophthisis, requiring timely evaluation of renal function. Early detection and genetic counseling of patients will help to initiate early nephroprotective therapy and reduce the progression of renal failure.

656 -P2.112

VALIDATION OF MULTIPLE OFFICE BLOOD PRESSURE MEASUREMENT. A NOVEL TOOL FOR EVALUATING BLOOD PRESSURE IN CHILDREN

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Aims/Purpose: Blood pressure measurement (BPM) is a common procedure in clinical practice, but it can be challenging to obtain reliable values in children. Casual office BPM (gold standard) is all but accurate and Ambulatory BPM (ABPM) may be difficult to perform or even misleading. Multiple Office Blood Pressure Measurement (mOBPM) was developed at our Center in 2010 for evaluating BP with serial and automated measurements (10 determinations in at least 30 minutes) using standard oscillometric devices. BP values were uploaded in a software and coefficient of variation (CV) was calculated after excluding outlier values (< 5th and > 95th centile of the recorded values).

Methods: The present study compares results obtained with mOBPM vs ABPM in children addressed to our center for suspected arterial hypertension (AH). Given that children develop myocardial hypertrophy soon after the development of AH, Cardiac Mass Index (CMI) was used as gold standard to categorize patients as hypertensive or normotensive.

Results: Forty-six children were enrolled. AH was confirmed by increased CMI in 16 (35%) of them. ABPM identified 26 (56%) hypertensive children vs 27 (59%) identified by mOBPM. Sensitivity and specificity were 75% and 53% using ABPM vs 81% and 53% using mOBPM. Positive Predictive Value (PPV) and Negative Predictive Value (PNV) were 46% and 80% vs 48% and 84%, respectively.

Conclusion: The present analysis shows that mOBPM provides similar results for the diagnosis of arterial hypertension compared with ABPM. In addition, mOBPM is less time consuming, available everywhere, cheaper, easier to repeat and less stressful. Thus, we recommend the routine use of mOBPM for measuring BP in children.

664 - P2.113

MORE RECENT PEDIATRIC KIDNEY STONES SHOW A TYPOLOGY SIMILAR TO ADULT ONES

Javier Lumbreras Fernández[1], María Dolores Rodrigo[1], Rafel María Prieto[2], Antònia Costa-Bauzà[2], Guillem Frontera Juan[3], Juan David González Rodríguez[4], Hector Rios Duro[5], Maria Isabel Luis Yanes[6], Montserrat Anton-Gamero[7], María del Mar Espino Hernández[8], Félix Grases[2], Iratxe Tapia[9], Jesús Ferrer[9], Group of Study Spanish Pediatric Kidney Stones Registry

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Aims/Purpose: Incidence of pediatric renal lithiasis has increased over last decades. Increasing knowledge about its ethiopatogenics offers an opportunity to improve its management. Our pediatric kidney stone registry provides information about local characteristics of patients and correlates their clinical, urinary and stone characteristics. Herein, changes in typology over the time are analyzed and correlated with patients' features.

Methods: A voluntary nationwide registry for patients under 18 years old with renal lithiasis was settled in 2015 in Spain sponsored by the National Pediatric Nephrology Society (AENP). Clinical, epidemiological, urine metabolic and stone data are collected. Stones have to be analyzed in a specialized laboratory for inclusion. In the present communication, findings described in patients included until Septembre 2018 (and previously communicated to IPNA 2019) are compared with those included between October 2018 and December 2023.

Results: A total of 146 stones from 125 patients were included for this study, 119 having reliable information about the date of diagnosis: 81 belong to the first period (including several stones retrospectively added as collected and analyzed by the same laboratory previously to 2015) and 38 to the second period. No statistically significant differences were found between both periods in terms of clinical variables (sex, gestational age at birth, family history of kidney stones, immobilization, related medications, diagnosis of genetically related conditions, clinical presentation and spontaneous or non-spontaneous resolution), nor in analytical variables (calcium, phosphate, citrate, oxalate and urate to creatinine ratio as well as proportion of patients diagnosed with hypercalciuria, hypocitraturia or hyperoxaluria). Only the proportion of stones whose patients had past history of urinary tract infection (UTI) was lower in the second period (26/55 vs 5/33, p =0.03), but the proportion of urinary tract abnormalities was not. The proportion of stones that could be related to UTI (struvite and hydroxiapatite) was also lower in the second period: struvite 13 (17%) vs 3 (8%), hydroxiapatite 12 (15%) vs 10 (10%); calcium oxalate dihydrate stones were more frequent: 26 (33%) vs 20 (51%), as well as those whose main component was calcium oxalate monohydrate not anchored to renal papilla: 8 (10%) vs 7 (18%).

Conclusion: Regarding typology, there is a significantly lower proportion of struvite and hydroxiapatite stones in the more recent period. In general, the pattern is similar to that described in adults. This finding is associated with a lower proportion of patients with past UTI history but no differences were found in metabolic urinary study nor in the prevalence of urinary tract abnormalities. This suggests a better management of patients in terms of preventing UTI or its related stones.

670 - P2.114

ADHERENCE TO DELAYED-RELEASE CYSTEAMINE IN NEPHROPATHIC CYSTINOSIS OVER TIME. A PROSPECTIVE COHORT STUDY: CRYSTOBS

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Introduction: Adherence to cysteamine in nephropathic cystinosis (NC) remains challenging, whilst poor adherence worsens progression of both renal and extra-renal long-term complications. We previously showed a better compliance with delayed-release (DR) cysteamine compared to short-acting (SA) cysteamine, with a median average number of hours of treatment per day at 22.5 (6.1–23.9) versus 14.9 (9.2–620.5) hours, and a better adherence score for delayed-release versus short-acting cysteamine (1.8 (0.1–62) versus 0.5 (0.3–1), PMID: 32901297). DR cysteamine is expensive when compared with SA cysteamine; DR cysteamine is available and fully reimbursed in France, but not worldwide, even in some European countries. In such cases, the main justification given by health authorities is the lack of sufficient evidence of improvement in the rendered medical service. Our aim here was to describe long-term compliance with DR cysteamine with 2-year follow-up.

Methods: Patients with confirmed NC, aged > 4 years and receiving DR cysteamine from 3 French reference centers were included (NCT02012114). Treatment adherence was mainly assessed using specific electronic caps (MEMs®). The percentage of days with good adherence has been previously described with an adherence score ranging from 0 (poor) to 2 (good). Leukocyte cystine and creatinine for estimating glomerular filtration rate (eGFR) were measured at each 3-month visit. Results are presented as median (range).

Results: Seventeen patients (10 girls), four receiving SA cysteamine (and switching to DR cysteamine after 26, 26, 29 and 91 days, respectively) and 13 receiving DR cysteamine at D1 and all receiving DR cysteamine since M3, were included, at a median age of 13.9 (5.4–33.0) years. Median ages at diagnosis and at initiation of cysteamine whatever the galenic form were 17 (3–77) months and 21 (16–116) months, respectively. The daily dose of cysteamine was 1.0 (0.6–1.4) g/m2/day at M3, and 0.9 (0.7–1.5) g/m2/day at M24. Median leukocyte cystine levels (nmol ½-cystine/ mg protein) were 0.8 (0.1–3.2) and below 1 for 52.9% of patients at M3 and 0.3 (0.1–3.1) and below 1 for 67% of patients at M24. The adherence score was 1.62 (0.03–1.98) over the entire 2-year follow-up period of DR cysteamine, with 64.5% of patients having good adherence (score 2) and 75.3% having partial or good adherence (score 1 or 2). There was no significant effect of time period (before or outside a consultation period) on adherence.

Conclusion: Our data describe a good long-term adherence to DR cysteamine, which is an additional argument in favor of its reimbursement.

678 - P2.115

CYSTINOSIS: THE VALUE OF FOCUS GROUPS IN BUILDING A NATIONAL ONLINE THERAPEUTIC EDUCATIONAL PROGRAM

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Objective: Identify the needs of cystinosis patients and their caregivers, in order to build a national online therapeutic educational program. Nephropathic cystinosis is an orphan autosomal recessive lysosomal storage disorder (OMIM #219800, 1/200000 live births) and the number of patients per center is very small, making face-to-face meetings impossible. The online mode was chosen in consultation with patient associations, based on existing programs for other rare diseases.

Methods: During a patient's day, we organised five focus groups including either cystinosis children, cystinosis adults, siblings or caregivers ran in parallel. The duration of each session was 1.5 hours; cystinosis patients/caregivers were asked to answer age-adapted « open questions » on their daily and quality of life. At the end, a global restitution was made. The needs identified were grouped and analysed, which allowed us to build the educational sessions.

Results: A total of 60 persons participated (17 patients with 7 children and 10 adults, 26 caregivers of children patients (parents and grandparents), 13 caregivers of adults patients (parents), and 4 siblings). Using the 5 groups' needs, 3 major themes emerged: « treatments », « daily life » and « informations ».

Conclusion: The study allowed us to identify the needs to build a national online therapeutic educational program for cystinosis patients and caregivers.

746 - P2.116

ENETIC VARIANT IN THE LAMA5 GENE WITH COMBINATION OF NEPHROTIC SYNDROME AND EXTRARENAL MANIFESTATION: A CASE REPORT

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Aims/Purpose: The LAMA5 gene encodes laminin-5, an essential component of the glomerular basement membrane. There have been reports of children with steroid-resistant nephrotic syndrome who carry the mutation. This specific gene has also been found in isolated manifestations of other systems. We present a rare syndrome of nephrotic syndrome in an infant in combination with congenital anomalies of the urogenital tract.

Results: It's a girl that was born with a C-section at 38 weeks. Birth weight 3170 gr. At birth she was diagnosed with rectal atresia, which was surgically corrected, high vaginal atresia with a hydrometrocolpos due to a fistula between the anterior wall of the vagina and the posterior wall of the proximal end of the urethra. She had right renal agenesia and vesicoureteral reflux on the left kidney. Other comorbidities include hypothyroidism, vocal cord membrane (Cohen type 1) and spinal cord lipoma. In the first month of life, she presented with reduced appetite and reduced urination as well as bloody feces and vomiting. Lab tests showed urinary tract infection and acute kidney injury. After an ultrasound was performed, pyometrocolpos was diagnosed which caused an obstruction in the ureter. Creatinine reached 1,6 mg/dl. A Petzer drainage tube was placed surgically. Up to this moment the infant doesn't have edema although she had severe albuminuria, hypoalbuminemia and microscopic hematuria. The renal function gradually improved, but the nephrotic-type proteinuria (Alb/Cr: 15) and the hypoalbuminemia still remained. With the diagnosis of congenital nephrotic syndrome a genetic test was sent. The genetic testing showed a possibly pathogenic heterozygous mutation in the LAMA5 variant c. 4565del (p. Leu1522fs) gene and the c.1240C > T(p.Arg414Cys) as variant of uncertain significance. The two mutations are in trans position meaning one of each parent. After 18 months of monitoring, the child is in good general condition with normal renal function, on maximized antiproteinuric treatment, initially captopril and later ramipril. Hypoalbuminemia and proteinuria are still present.

Conclusion: The LAMA5 mutation is known as the cause of congenital nephrotic syndrome. In our knowledge this is the first report of nephrotic syndrome in combination with extrarenal manifestations due to this gene.

753 - P2.117

THE FACTORS AFFECTING BLOOD PRESSURE PROFILE IN CHILDREN WITH DISTAL RENAL TUBULAR ACIDOSIS

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Aims/Purpose: Distal renal tubular acidosis (dRTA) is a disease characterized by hyperchloremic metabolic acidosis, reduced net acid excretion, and the inability to lower urinary pH to below 5.5 during acidemia or after an acid load. This study aims to evaluate the blood pressure profile in pediatric patients with dRTA.

Methods: A total of 40 pediatric patients diagnosed with dRTA were included in the study. Clinical findings, physical examination findings, laboratory results, genetic findings, and radiological imaging results were obtained from the patients' medical records. In addition, 15 of these patients underwent ambulatory blood pressure monitoring (ABPM) to assess blood pressure profile.

Results: Of the forty patients, 25 (62.5%) were male. The median age at diagnosis for our patients was 3.5 months. The follow-up period of all patients was 132.5 ± 70.3 months. According to office blood pressure (BP) measurements at the time of diagnosis, systolic blood pressure (SBP) was found to be normal in 95% of patients, elevated in 2.5% and stage 1 hypertension in 2.5%. In office BP measurements at the time of diagnosis, diastolic BP was normal in 60% of patients, elevated in 20% and 20% had stage 1 hypertension. When patients were evaluated based on SBP measurements at the last follow-up, 92.3% had normal BP, 2.6% had elevated BP, and 5.1% had stage 1 hypertension. When evaluated based on diastolic BP measurements at the last follow-up, 94.9% had normal BP, 5.1% had elevated BP. SBP measurements were significantly higher in patients with CKD stage 4 at the last follow-up (p =0.019). 24-hour ABPM was performed in 15 patients. Among them 10 patients (66.7%) had normal blood pressure, two (13.3%) had hypertension, and three (20%) had masked hypertension. Three patients with masked hypertension had CKD stage 1. 24-h SBP and DBP loads in ABPM were negatively correlated with the metabolic control percentages of the patients (Figure 1 and 2). There was an increasing trend in blood pressure load as the stage of CKD increased, but there was no significant difference in blood pressure load among the stages. As the stage of CKD increased, a tendency to increase in systolic and diastolic BP as well as mean arterial pressure SDS was observed in 24-hour and daytime BP measurements.

Conclusion: Hypertension in patients with dRTA is not typically observed as a symptom in the early stages before a decline in eGFR. A negative correlation was found between adequate metabolic control and blood pressure loads on ABPM, suggesting that adequate metabolic control results in lower blood pressure loads in patients with dRTA. However, the limited number of cases in this study may have prevented a comprehensive demonstration of the impact of tubular disorders on hypertension.

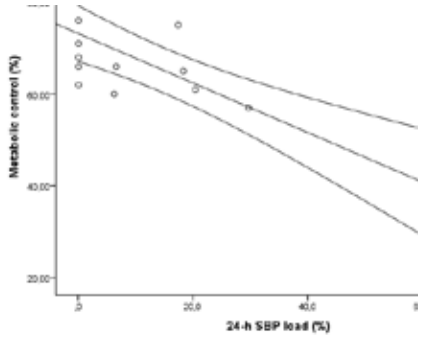

Figure 1. Plot of 24-h systolic blood pressure load vs. metabolic control percentage

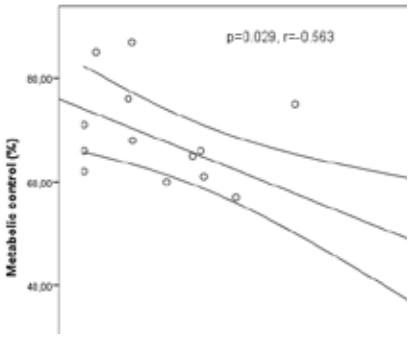

Figure 2. Plot of 24-h diastolic blood pressure load vs. metabolic control percentage

771 - P2.118

PEDIATRIC NEPHROLITHIASIS: A 14-YEAR SINGLE CENTER EXPERIENCE

Andria Panteli[1,2], Maria Mila[1], Argyroula Zampetoglou[1], Georgia Malakasioti[1], Evangelia Gkole[1], Varvara Askiti[1]

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Aims/Purpose: The incidence of nephrolithiasis in children is significantly increasing. The aim of this study was to evaluate the clinical features and risk factors of pediatric nephrolithiasis in a reference center.

Methods: A retrospective search was conducted to identify children managed with nephrolithiasis in our center from 2009 to 2023. Demographics along with clinical, laboratory, radiologic and genetic parameters were evaluated.

Results: A total of eighty-eight patients (45 male and 43 female) were identified. The mean age at diagnosis was 5.2 years (range 2 months-16 years). Thirty-nine out of 88 children (44.3%) were diagnosed during a hospital admission. The most common presenting symptoms on admission were flank pain and/or abdominal pain (41%), urinary tract infection (25.6%) and macroscopic hematuria (20.5%). The renal parenchyma was the main location of stones (88.6%). A positive family history of nephrolithiasis was recorded in 35.2% of children. An anatomic abnormality was detected in 10.2% of patients. Seventy patients had an underlying metabolic abnormality: 27 had hypercalciuria (38.6%) including 26 children with idiopathic hypercalciuria and 1 with Dent's disease, 18 children had hypocitraturia (25.7%), 6 had hyperoxaluria (8.6%), 4 had cystinuria (5.7%) and the rest of them had two coexistent metabolic abnormalities. The hyperoxaluria group included 4 patients with primary hyperoxaluria: three with type 1 and one with type 3. Genetic testing was performed only in 11 children, three had mutation in AGXT1 gene, one in HOGA1, one in HPRT1, one in SLC3A1 and one in CLCN5. Potassium citrate was given to all patients. In addition, patients with hypercalciuria received thiazide, children with cystinuria received tiopronin and those with hyperoxaluria type 1 were given lumasiran. Stones were passed spontaneously in 10% of the patients while lithotripsy was required in 12.5% of patients. An improvement in ultrasonography was noticed in 54.4% of the children during the follow-up period.

Conclusion: Although, the incidence of hypocitraturia has been increased in the general pediatric population, hypercalciuria was the most common cause of nephrolithiasis in this cohort. In conclusion, genetic testing has a crucial role in the early diagnosis and prompt treatment of serious genetic conditions which pose a high risk of chronic renal failure.

776 - P2.119

EIGHT PAEDIATRIC PATIENTS WITH BARTTER SYNDROME FROM THE CZECH REPUBLIC AND SLOVAKIA

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Aims/Purpose: Our aim was to collect and compare laboratory and clinical phenotype of paediatric patients with genetically confirmed Bartter syndrome from the Czech Republic and Slovakia.

Methods: We retrospectively analysed the clinical data and laboratory tests of 8 patients with Bartter syndrome who are being followed at 4 different centers. We compared the initial parameters at disease presentation with those at the latest outpatient visit in the context of the current treatment.

Results: In the cohort, we observed equal representation of both sexes, with patients ranging in age from 1.3 to 16 years old (average age 7.6 years). The majority (5 patients) presented with classic Bartter syndrome due to mutations in the CLCNKB gene, with the most common clinical manifestation being failure to thrive or growth failure. At the time of initial disease detection, the average age was 9.9 months. Antenatal Bartter syndrome was represented by 3 patients with mutations in the SLC12A1 (2 cases) and KCNJ1 (1 case) genes. These patients were diagnosed during the early neonatal period and exhibited clinical features such as polyhydramnios, prematurity, nephrocalcinosis, polyuria and polydipsia. In all patients, the characteristic laboratory finding of hypokalemic hypochloremic metabolic alkalosis and hyperreninemic hyperaldosteronism with normal systemic blood pressure was observed. Potassium supplementation, along with treatment with indomethacin and spironolactone led to an alleviation of clinical manifestations and normalization of laboratory parameters in all cases.

Conclusion: Bartter syndrome should be considered in the differential diagnosis in paediatric patients presenting with polyuria, polydipsia, failure to thrive, and characteristic laboratory abnormalities. Establishing registries, molecular-genetic diagnostics, and regular monitoring of patients are essential for the early detection of complications, improvement of management, and ultimately, the quality of life of patients with Bartter syndrome.

822 - P2.120

RENAL FUNCTION TRENDS IN PEDIATRIC AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE: A SINGLE CENTER EXPERIENCE

Samantha Innocenti[1,2], Andrea Latessa[1,2], Luigi Cirillo[1,2], Santina Petroccelli[1], Paola Romagnani[1,2], Francesca Becherucci[1,2]

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Aims/Purpose: Autosomal dominant polycystic kidney disease (ADPKD) is the most frequent genetic renal disease, characterized by progressive renal enlargement and function loss. Current management of pediatric patients focuses on addressing known risk factors for chronic kidney disease (CKD) progression such as hypertension and managing associated symptoms.

This study assesses renal function trends and related clinical-laboratory factors in pediatric ADPKD patients.

Methods: A retrospective study evaluated 93 ADPKD patients aged 1 to 19 years with a median age at enrollment of 9 years (IQR 4-12), from 2009 to 2023 at the AOU Meyer IRCCS Nephrology and Dialysis unit. Data were collected at different time points, first and last evaluation and two interim evaluations. We focused on blood pressure percentiles, renal function, abdominal ultrasound with kidney size, number and size of cysts. To estimate the glomerular filtration ratio (eGFR) the CKiDU25 equation was used. Blood pressure percentiles were based on 2017 American Pediatric Society charts and hypertension was set at 95° percentile for children and above 130/80 mmHg for adults. Kidney dimensions percentile were calculated with the Pediatric Kidney Length and Volume Calculator. Mann-Whitney U test was used to compare medians in quantitative variables, and simple linear regression was utilized to analyze relationships between quantitative variables. Statistical significance was set at $p < 0.05$.

Results: The median duration of follow-up was 4 years (IQR 2.75-6.25). At last follow-up, the median age was 14 years (IQR 9-18) and 86.2% of patients maintained an eGFR ≥ 90 ml/min/1.73m2, while 13.8% had an eGFR between 89-60 ml/min/1.73m2. No advanced chronic kidney disease was noted. The median eGFR slope was -2.52 ml/min/1.73m2 (IQR -0.52/-5.33). Larger kidney sizes at referral correlated with quicker function loss ($R = -0.07$; $R2 = 0.17$; $p < 0.001$) (Fig.1). Conversely, systolic and diastolic blood pressure values at referral showed no statistically significant association ($p = 0.72$ and 0.92, respectively).

Conclusion: The eGFR slope has been recently proposed as an outcome measure for CKD progression in adult patients. Our findings highlight its relevance in predicting renal outcomes in pediatric ADPKD, with larger initial kidney sizes indicating more rapid progression. These insights have potential practical implications for the clinical management of patients from the first nephrological evaluation.

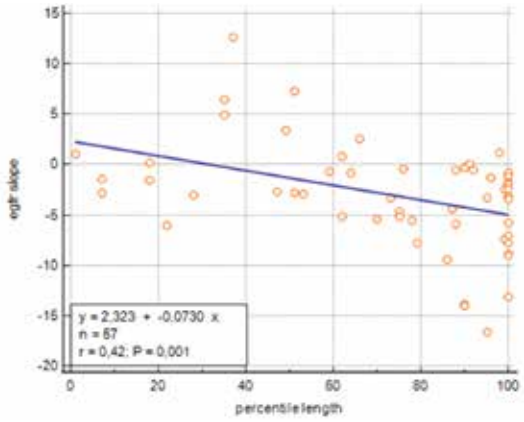

Figure 1. Linear regression between eGFR slope and percentile of kidney length at last follow-up

827 - P2.121

STEROID-RESISTANT NEPHROTIC SYNDROME DUE TO NPHS2 VARIANTS IS NOT ASSOCIATED WITH POSTTRANSPLANT RECURRENCE

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Aims/Purpose: Pathogenic variants in the NPHS2 gene cause Steroid-Resistant Nephrotic Syndrome (SRNS) which is not expected to recur after kidney transplantation. However, 9 cases of post-transplant recurrence in patients with NPHS2 pathogenic variants have been described, notably with the p.Arg138Gln variant which is more prevalent in Europe. The objective of this study was to assess the risk of recurrence in a large cohort of patients with NPHS2 biallelic variants.

Methods: Since January 2010, 117 patients identified at Necker Hospital (n = 61) and in the PodoNet Registry (n = 56) with NPHS2 variants causing SRNS were transplanted and were compared with 44 transplanted children with SRNS without an identified variant. We compared outcome between (1) patients carrying the NPHS2 p.Arg128Gln variant in trans to another pathogenic variant, (2) patients carrying other biallelic NPHS2 pathogenic variants and (3) patients with SRNS and no identified pathogenic variant on gene panel. Recurrence was defined as reappearance of nephrotic-range proteinuria after transplantation, with no other apparent cause. Follow-up period was until March 2019 for Necker Hospital patients and until February 2021 for PodoNet patients.

Results: Of the 117 patients, 23 carried the p.Arg138Gln variant in the homozygous state and 16 in the compound heterozygous state. The additional 78 patients carried other NPHS2 variants in the homozygous (n = 44) or compound heterozygous state. Familial forms were more represented in the group of patients with NPHS2 variants (30% versus 11%, p =0.005). Patients with NPHS2 variants had a lower age of onset of disease, as well as an earlier development of kidney failure and transplantation. Kidney biopsy at diagnosis revealed mainly focal and segmental glomerulosclerosis lesions in patients with NPHS2 variants whereas minimal change disease lesions were predominant in patients with no identified variant. Only one patient with NPHS2-related SRNS due to homozygous p.Leu347* variant experienced recurrence of nephrotic syndrome (NS) 7 days after transplantation. She responded well to immunosuppression, suggesting an immune-mediated etiology of post-transplant NS, likely unrelated to her hereditary podocytopathy. The other 116 patients with NPHS2 variants had no recurrence, whether on the short or long term (median follow-up 8.5 years [2.5-15]). Conversely, 7/44 patients without an identified variant recurred within 7 days after transplantation (median follow-up 8.9 years [0.6-13.9]).

Conclusion: In our cohort, when causal variants in the NPHS2 gene were identified, risk of post-transplant recurrence of NS was extremely low, whether with p.Arg138Gln or other variants. This is coherent with our knowledge of this genetic disease's pathophysiology. These data are reassuring and should be taken into account when counselling patients, making living kidney donors a safe choice.

844 - P2.122

46,XY DISORDER OF SEX DEVELOPMENT IN A GIRL WITH ASYMPTOMATIC PROTEINURIA

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Aims/Purpose: Proteinuria and nephrotic syndrome (NS) have a broad spectrum of differential diagnosis. Despite growing evidence pointing possible genetic causes of NS, genetic testing is still recommended only in infants and steroid resistant NS patients. Frasier syndrome (FS) is a rare disease caused by mutations in the donor splice site in intron 9 of WT1. Patients usually present with NS, 46,XY complete gonadal dysgenesis (CGD) and have increased risk for gonadoblastoma.

Methods: Case report.

Results: We present a 13-year-old girl referred at the age of 7 years due to asymptomatic isolated proteinuria. Standard workup showed normal kidney function with no structural abnormalities as well as negative immunological screening. Since proteinuria was persistent, kidney biopsy was performed revealing variations in glomerular basal membrane thickness, consistent with the diagnosis of Alport syndrome (AS). ACE-inhibitors and later on ARBs were introduced with limited effect on proteinuria that gradually worsened during follow-up. Since the course of disease was atypical for AS, we decided to preform genetic testing. Targeted sequencing of AS involved genes revealed variant of unknown significance in COL4A5 gene (c.3541A > G). Surprisingly, molecular testing also revealed hemizygosity for this X- linked gene, opting for additional workup. Additionally, she had short stature with no pubertal growth spurt, absent breast development, primary amenorrhea, and Tanner 3 pubic and axillary hair. Laboratory workup revealed high levels of gonadotrophins with unmeasurable low estradiol, while karyotype showed 46,XY. Based on the combination of glomerulopathy and 46, XY CGD we suspected a mutation in WT1 gene. Molecular testing revealed heterozygous pathogenic variant at splice donor site in intron 9 of WT1 gene – c.1432+4C > T confirming the diagnosis of FS. Prophylactic gonadectomy was performed and subsequently female hormonal replacement treatment was introduced. Rebiopsy was preformed, showing focal segmental glomerulosclerosis. Despite multiple drug adjustments and changes, proteinuria remained refractory to treatment.

Conclusion: Proteinuria and NS are still a diagnostic challenge for nephrologists. WT1 gene has multiple roles in kidney and gonad development, hence, WT1 impairment leads to complex phenotype such as FS. Detailed molecular testing is needed in patients with unexplained nephropathies, as well as girls with delayed puberty and 46, XY karyotype

868 - P2.123

REFRACTORY HYPERTENSION IN A CHILD WITH POLYCYSTIC KIDNEY DISEASE

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Aims/Purpose: High blood pressure is a growing health problem in children around the world. However, refractory hypertension, defined as uncontrolled blood pressure despite the administration of five or more antihypertensive medications, is very rare in children. Polycystic kidney disease (PKD) is responsible for causing hypertension, but refractory hypertension caused by PKD is very rare. Herein, we present a child with PKD and refractory hypertension.

Case: A 5-month-old male child was admitted to our clinic because of splenomegaly on physical examination and a cyst on renal ultrasound, which was performed because of a history of cyst in his sibling. His genetic screening was unremarkable for ADPKD, ARPKD and HNF1B related cystic disease At baseline, renal function was normal and ACE inhibitor was started because of high normal blood pressure. At follow-up, the ACE inhibitor was changed to a calcium channel blocker (CCB) because of increased creatinine and hyperkalemia. At the outpatient clinic visit at the age of two years, blood pressure was 180/100 mmHg, bilateral kidneys were palpable and splenomegaly was present. The patient was hospitalized in the ward because of elevated serum creatinine levels and very high blood pressure. Electrocardiography revealed marked left ventricular hypertrophy and short-acting CCB, beta blocker, alpha blocker, alpha methyl dopa and then ramipril were started in order to regulate blood pressure. Despite multiple antihypertensive treatments, blood pressure remained high and MR angiography performed to rule out renovascular hypertension was normal. Ramipril treatment was continued with potassium-lowering agents for hyperkalemia. The patient remained clinically asymptomatic throughout the follow-up and blood pressure reached the target level at week 3

Conclusion: The most important cause of hypertension in polycystic kidney disease is over activation of the renin-angiotensin-aldosterone system. Therefore, since hypertension may be severe and resistant in patients with PKD, these patients should be carefully monitored.

887 - P2.124

STEROID-RESISTANT NEPHROTIC SYNDROME CAUSED BY NUP93 PATHOGENIC VARIANTS

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Aims/Purpose: Although steroid therapy is a standard of care for nephrotic syndrome treatment, 15-20% of patients do not respond to it. Finding the genetic background is possible in > 10% of steroid-resistant nephrotic syndrome (SRNS) cases. Variants in genes encoding nuclear pore complex proteins are a novel cause of paediatric steroid-resistant nephrotic syndrome (SRNS). Recent studies suggest NUP93 variants to be a significant cause of paediatric onset SRNS. The clinical data on certain variants and disease history are still very limited.

Methods: We report the SRNS case of a 12-year-old boy with two detected NUP93 variants, which are pathogenic and possibly pathogenic.

Results: The onset of the disease was early and severe. The patient was admitted to the paediatric nephrology department due to nephrotic-range proteinuria and hypoalbuminemia with a long medical history of steroid and non-steroid immunosuppressive treatment. The genetic panel targeting 50 genes, clinically relevant for nephrotic syndrome, was performed. The only gene which was found to be affected by mutations, namely c.2326C > T and c.1162C > T, respectively, was NUP93. Conclusions: NUP93 variants are rarely identified as causes of SRNS. Clinical data are of utmost importance to establish the standard of care for SRNS patients suffering from this genetic disfunction.

Conclusion: This is the first case of a heterozygous patient with the c.2326C > T and c.1162C > T variants and confirmed clinical history of the SRNS described so far. Our data suggest the clinical relevance of the c.1162C > T variant.

912 - P2.125

CALL NEPHROLOGY; HYPOKALEMIC METABOLIC ALKALOSIS, AND HYPOCHLOREMIA. WHAT IS YOUR DIAGNOSIS?

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Aims/Purpose: Bartter syndrome is an autosomal recessive tubulopathy that presents with hyponatremic, hypokalemic, and hypochloremic metabolic alkalosis due to renal loss of these ions. In the absence of kidney involvement, we speak of Pseudo-Bartter syndrome. We present a case of a patient with metabolic alkalosis in whom renal tubulopathy was suspected, but other diagnostic options were sought.

Methods: A 9-month-old infant who consults due to decreased intake associates with mucus, weakness and quantitative weight loss. Not digestive symptoms are associated. Perinatal history: high risk in screening for unconfirmed chromosomopathies and polyhydramnios. Anthropometry at birth, Weight 2800gr (p32), Length 49cm (p57). Current weight 6.9 kg (< P1, -2.39DE) Size: 67 cm (< P1, -2.36DE) PC: 45 cm (P46, -0.09DE). The result of otoacoustic emissions and screening for inborn errors of metabolism, carried out on the 4th day of life, were negative. Admission after one month due to Klebsiella pneumonia urinary infection. Under follow-up due to failure to thrive since two months. In physical exam, the pediatric evaluation triangle appeared unstable; skin paleness and signs of severe dehydration.

Results: Laboratory test reflects hypochloremic and hypokalemic metabolic alkalosis with hyponatremic dehydration, and acute renal failure. Anion GAP normal, Schwartz eGFR > 90ml/min/1.73m2, EFNa: 0.5%, EFK: 5.5, GTTK: 5.9 EFCl : 0.35% so, ruling out other extrarenal causes, we think of Pseudo-Bartter syndrome secondary to cystic fibrosis (CF). Positive sweat chlorine determination (2) Genetic study: Heterozygous carrier of the F508 delta and R334W variants, diagnosis of Cystic Fibrosis.

Conclusion: Knowing the existence of Pseudo-Bartter syndrome and having a high index of suspicion favors the early diagnosis of pathologies such as CF.A negative neonatal screening does not exclude the diagnosis of cystic fibrosis.

929 - P2.126

AMBULATORY BLOOD PRESSURE STATUS OF CHILDREN WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

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Aims/Purpose: The aim of our study was to investigate the ambulatory blood pressure status of patients with autosomal dominant polycystic kidney disease.

Methods: This retrospective cross-sectional study enrolled children with autosomal dominant polycystic kidney disease who had performed an ambulatory blood pressure monitoring between January 2018 and March 2023. Ambulatory blood pressure monitoring was performed using the SpaceLabs Healthcare 90217 device.

Results: A total of 29 Caucasian patients with autosomal dominant polycystic kidney disease, aged 8 to 18 years, were included in the study. All 4 patients who were hypertensive on office blood pressure measurement had normal ambulatory blood pressure monitoring, i.e. white coat hypertension. Ambulatory blood pressure monitoring observed hypertension in 6 (20.7%) patients. All of them had nocturnal hypertension and 2 were hypertensive during the daytime. Of these 6 patients with hypertension on ambulatory blood pressure monitoring, 4 were on antihypertensive treatment (uncontrolled hypertension), while 2 had masked hypertension. Of 7 (24.1%) patients under antihypertensive treatment, 3 had good control of blood pressure. Angiotensin converting enzime inhibitors were prescribed in 7 patients and angiotensin II receptor inhibitor and beta blocker in one patient.

Conclusion: Hypertension in children with autosomal dominant polycystic kidney disease often requires ambulatory blood pressure monitoring for detection. Ambulatory blood pressure monitoring should be regulary perfrormed in children with autosomal dominant polycystic kidney disease.

934 - P2.127

RENAL INVOLVEMENT IN A PATIENT WITH DE NOVO CNOT3 MUTATION

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Aims/Purpose: To describe a patient with an extremely rare condition associated with a de novo CNOT3 gene mutation and renal involvement

Background: CNOT3 gene is encoding a component of the carbon catabolite repression 4-negative TATA-less (CCR4-NOT) protein complex known to be involved in early life neurodevelopment. To date, only 25 patients have been described worldwide with CNOT3 mutations with a very heterogeneous phenotype, most of them presenting with dysmorphic features and developmental disorders such as hypotonia, intellectual disability, speech delay and short stature.

Case Presentation: Our male patient was diagnosed antenatally with bilateral renal hydronephrosis. It was a twin pregnancy (twin sibling not affected) and he has born at 35+4 weeks of gestation with low birth weight of 1.8 kg. On examination after birth, he had dysmorphic features, hypospadias and bilateral fixed talipes. Brain MRI showed bilateral ventriculomegaly. His cardiological assessment showed PDA and VSD. His laboratory investigations showed impaired renal function with urea of 69 mg/dl and creatinine of 0.9 mg/dl. He had a renal USS that showed bilateral megaureters, bilateral hydronephrosis (left renal pelvis APD of 2.5 cm and right of 1.5 cm) and kidney size discrepancy (left 3.9 cm, right 6.6 cm). He had a cystoscopy that was negative for posterior urethral valves and MCUG that showed grade 5 VUR bilaterally. He underwent a MAG-3 at 3 months of life that showed reduced function of the left kidney (left 18%, right 82%) and delayed drainage bilaterally (T1/2 > 25 min bilaterally). He had a whole exome sequencing genetic testing that revealed a de novo CNOT3 mutation, c.169C > T (p.Arg57Trp). Currently, at the age of 2 years, he has severe developmental delay and chronic kidney disease stage 3 with an estimated GFR of 58 ml/min/1.73m2and cystatin C levels of 1.93 mg/L.

Conclusion: To the best of our knowledge this is the first report of renal dysplasia in a patient with CNOT3 mutation. Renal USS should be included in the diagnostic work-up of patients with this very rare condition in order to investigate for renal abnormalities.

990 - P2.128

A PHASE 3 STUDY TO ASSESS STIRIPENTOL EFFICACY AND SAFETY IN PATIENTS WITH PRIMARY HYPEROXALURIA

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Purpose: Primary hyperoxaluria (PH) is a family of rare genetic disorders leading to excessive oxalate production. Oxalate is produced in the liver from glyoxylate transformation by lactate dehydrogenase type 5 (LDH-5) isoenzyme and excreted in urine. Stiripentol, a drug currently marketed as an antiseizure medication in a rare type of refractory epilepsy, has been shown to inhibit LDH-5. As LDH-5 is the last step of hepatic oxalate production, stiripentol could thereby decrease urinary oxalate excretion in all three types of PH. A clinical trial, the CRYSTAL study, will be undertaken to confirm this assumption.

Methods: This randomized, double-blind, placebo-controlled phase 3 study will aim to demonstrate the clinical efficacy and safety of stiripentol in patients with primary hyperoxaluria (type 1, 2 or 3). This will be a multicenter and multinational trial, planned to be conducted in Belgium, France, Italy, and Morocco so far. Forty-two assessable patients are expected. Patients 6 years and older with a diagnosis of PH 1, 2 or 3, urinary oxalate excretion ≥ 0.70 mmol/24h/1.73m^2, and an estimated glomerular filtration rate ≥ 45 mL/min/1.73m2 will be invited to take part in the study. The randomization will be stratified by mean urinary oxalate excretion and by type of hyperoxaluria. Two periods are planned: a 6-month, 2:1 randomized, double blind, placebo-controlled period, followed by a 6-month open-label treatment period with blind maintained on previous treatment received. All patients who benefit from study treatment will then enter an open-label extension period of up to 60 months, that will evaluate the long-term safety and efficacy of stiripentol. The main study objective is to evaluate the efficacy of stiripentol in decreasing urinary oxalate excretion and the primary efficacy endpoint will be the percent change in 24-hour urinary oxalate excretion from baseline to month 6. Secondary efficacy objectives are the effect of stiripentol treatment on kidney function, the change in kidney stones, urinary parameters measured from urinary spot collections, together with the quality of life and the treatment satisfaction of patient, caregiver and investigator regarding the treatment.

Conclusions: Despite the recent approval of new treatments, there is still an unmet medical need in patients presenting with PH. Results of the CRYSTAL study will determine whether stiripentol could be a new treatment option in this severe life-threatening disorder.

998 - P2.129

MUTATION IN EXOSC5 GENE ENCODING SUBUNIT OF RNA EXOSOME: AS NOVEL CAUSE OF THROMBOTIC MICROANGIOPATHY?

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Aims/Purpose: Thrombotic microangiopathy (TMA) in association with RNA exosome encoding mutations has only recently been recognized. Mutations in genes encoding RNA exosome subunits and cofactors have been linked to neurodevelopmental and neurodegenerative diseases. However, little is known about the potential role of the RNA exosome in the pathogenesis of TMA. Here, we present a patient with an EXOSC5 mutation, associated with the clinical phenotype known as CABAC syndrome (cerebellar ataxia, brain abnormalities, and cardiac conduction defects), including pontocerebellar hypoplasia, who developed renal TMA at age of four months.

Methods: We describe an unique case of an infant with EXOSC5 mutation who developed renal TMA. Additionally, we provide a detailed description of the four additional cases described in literature of patients with EXOSC3 mutation who developed TMA.

Results: We describe a patient (female), who was born in our tertiary care center after complicated pregnancy by suspicion of cerebellar hypoplasia and severe intra-uterine growth restriction. Postpartum genetic diagnosis revealed homozygous mutation in the EXOSC5 gene (c.230_232del p.Glu77del) explanatory for the clinical features. Patient was severely affected with no signs of psychomotor development at age of three months in presence of frequent dysphoria, dystonic muscle tone and seizures poorly responding to anti-epileptic drugs. At the age of four months she presented with signs of septic illness after which she developed TMA. Stool culture showed rotavirus as potential trigger. Patient received eculizumab once, alongside supportive treatment, while awaiting diagnostic analysis of TMA including genetic complement analysis, all negative. Eculizumab was withdrawn and TMA recovered quickly. A review of the literature identified an additionally four patients, who developed TMA in the presence of mutations in EXOSC3. All patients had clinical phenotype of EXOSC3 mutation with neurological abnormalities. TMA occurred in all patients before the age of 9 months, triggered by viral infection. The recurrence of TMA in one of these patients with an EXOSC3 mutation while on eculizumab treatment underscores the apparent lack of responsiveness to C5 inhibition.

Conclusion: Mutations in genes influecing RNA exosome, like EXOSC3 and EXOSC5, characterized by neurodevelopment and neurodegenerative disorders, could potentially lead to TMA in absence of complement dysregulation. Hence, patients are likely non-responsive to eculizumab. Moreover, development of TMA already occurs during infancy. This is highly important for pediatricians to assure early detection of TMA in these patients and subsequent start of optimal supportive treatment.

1052 - P2.130

SCHIMKE IMMUNOOSSEOUS DYSPLASIA: A RUSSIAN COHORT STUDY

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One of the most unfavorable forms of hereditary steroid-resistant nephrotic syndrome is Schimke immunoosseous dysplasia (SIOD). A high risk of acute circulatory events and an extremely unfavorable course are some of the characteristics of SIOD. We observed 21 cases of SIOD at the Nephrology Department of the National Research Center of Children's Health.

Methods: We conduct a retrospective study to collect and systematize patients with SIOD. All children were investigated with a panel of 200 genes associated with kidney diseases or single gene sequencing using the next-generation sequencing (NGS) method.

Results: We found 21 unrelated children (12 of them were boys - 57%) with SIOD. Most of them were preterm delivered (94%), 25% of them had intrauterine growth retardation and 31% - hypotrophy. The median height at birth was -1,49 (-2,11; -0,83), median weight was -2,03 (-2,18; -1,62). The median age at diagnosis was 45 (35; 69) months, median proteinuria at that moment was 3,04 (1,43; 7,42). Among extrarenal signs there were osseous dysplasia (including body type disproportionality and flattering of the vertebrae) - in 20 (95%), multiple stigmas - in 17 (81%), leukopenia and agranulocytosis - in 16 (76%), vision impairment - in 10 (48%), hyperpigmented maculas - in 9 (43%), development delay - in 8 (38%), CACUT - in 7 (33%), anemia and congenital heart defects - 3 (14%) each, also there were microcephaly, congenital lung disease and thrombocytopenia - in 1 child each. Average age of CKD 5 was 62 (51; 79) months. 10 of them (50%) suffered a stroke during the observation period. The majority of patients with the performed molecular genetic study revealed the pathogenic variant c.2542G > T, p.E848* (in 14/21 patients - 67%), and in four (29%) - in the homozygous state. Five years survival rate turned out to be 87%. The average age of death was 80 months (6 years 8 months) ± 23 months. Median age of death - 88 (65; 99) months. Among the causes of death, acute cerebrovascular accidents (5/11 children - 45%), sepsis due to agranulocytosis (4/11 - 36%) were the most frequent. Kidney transplantation was performed in 3 children with a poor patient and graft survival. We conclude that SIOD is a disastrous congenital condition with still unfavorable prognosis.

1070 - P2.127

NUP85 NM_024844:C.1379G > A (P.ARG460GLN), A NOVEL VARIANT IN NEPHROTIC SYNDROME

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Aims/Purpose: NUP85 is a member of the nuclear pore complex family responsible for nucleocytoplasmic transport function. This study aimed to investigate the phenotypic association of a novel NUP85 homozygous variant, NM_024844: c.1379G > A (p.Arg460Gln), which was identified by whole-exome sequencing in a 15-year-old male patient during investigations for nephrotic syndrome resistant to steroids and other immunosuppressants.

Methods: The pedigree analysis of the index case and the family confirmed an autosomal recessive inheritance pattern. Segregation analysis was performed. Reads were mapped against the human reference genome assembly (NCBI NM_024844; ENSG00000125450). In silico predictions were made by Mutation Taster and PolyPhen2. Structure predictions were performed by ITASSER and AlphaFold2. The wild-type and the variant structures were then analyzed by molecular dynamics simulations. Lastly, the impact of p.Arg460Gln on the structural stability was calculated by four methods; namely FoldX, PremPS, DynaMut2 and INSP-3D.

Results: The NUP85 NM_024844: c.1379G > A (p.Arg460Gln) variant had a minor allele frequency of 0.000012 in GnomAD database, with no reported homozygosity before. Segregation analysis revealed heterozygosity in the parents and the unaffected sibling, confirming an autosomal recessive inheritance. The variant was found to be evolutionarily conserved. In silico analyses predicted the variant as possibly pathogenic. Both structure predictions by ITASSER and AlphaFold2 exhibited high similarity, showing Arg460 at the outer center of a 5-helix bundle. Simulations indicated a loosened 5-helix bundle in the variant structure, reflecting a possible destabilization of the NUP85 structure by the p.Arg460Gln mutation. Accordingly, all stability predictors consistently indicated that p.Arg460Gln destabilized the NUP85 structure extracted from trajectories (n = 12, FoldX = 1.74 ± 0.76, PremPS = 0.51 ± 0.18, DynaMut2 = 1.56 ± 0.11, INSP-3D = 1.29 ± 0.08).

Conclusion: NUP85 NM_024844: c.1379G > A (p.Arg460Gln) was considered pathogenic, representing a novel variant responsible for the phenotype in the patient. This study contributes to the understanding of the molecular basis of nephrotic syndrome, reflecting the importance of detailed genotype-phenotype correlations.

1101 - P2.132

RENAL INVOLVEMENT AND FUNCTIONAL IMPACT IN THE PEDIATRIC AGE OF A COHORT OF PATIENTS WITH TUBEROUS SCLEROSIS COMPLEX (TSC) AND CONTIGUOUS GENE SYNDROME (CGS)

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Aims/Purpose: TSC is a rare multisystem genetic disorder (1:6,000), autosomal dominant, due to mutations in TSC1(Cr9)/TSC2(Cr16), predisposing to tumor development by deregulation of the mTOR pathway. Premature deterioration of glomerular filtration rate (GFR) in adults (40%, without hemorrhages due to angiomyolipomas -AML-/interventions), suggesting the presence of intrinsic kidney disease. Cysts, associated or not with SGC (joint TSC2/PKD1 genes deletion), AML, arterial hypertension or the risk of nephrolithiasis (ketogenic diet or carbonic anhydrase inhibitors) are the other parameters to control. Our aim is to determine renal involvement and GFR affectation in a pediatric cohort of TSC and/or CGS followed in our service in the last decade (2013-2023)

Methods: Retrospective observational study of 116 patients (66 males, 50 females) diagnosed and/or in follow-up for TSC (111 patients/95.68%) or CGS (5 patients/4.32%) between 2013-2023. Patients with known renal damage unrelated to TSC/CGS were excluded. Data were collected on diagnosis/disease progression, ultrasound, abdominal MRI, serum and urinary tests, mTORi or other treatment and their responses after a variable follow-up period

Results: Mean age 13.39 years (SD 6.228). Kidney involvement 54.9% (67): AML 41.8% (mean 10.33mm/SD14.64), cysts 29.5% (mean 12.39 mm /SD 17.23. Patterns: multicystic 11.5%, polycystic 3.3%, cortical cystic 4.1%, cortical microcystic 9.8% and focal cystic 0.8%), 3 tumors of other type (1 hamartoma, 1 PEComa and 1 exophytic renal mass). HBP 4.1% (80% grade I/20% high BP), proteinuria 4.1% (median Pr/Cr 0.63 mg/ mg [0.28-59.32]. Median Alb/Cr 32.9 mg/mmol [6.1-75.1]. Only 2 CGS presented elevated B2 microglobulin) and 2 patients, both. Those who presented HBP and/or proteinuria were treated with ARB/ACE inhibitors and 2 of them with amlodipine. Only 1 patient with CGS presented CKD (stage IV) with the rest of the cohort having normal eGFR. 3 patients presented prelithiasis (1 hypocitraturia/microlithiasis ultrasound and 2 lithogenic risks: hypercalciuria/hypocitraturia and hypercalciuria/hyperuricosuria) in the context of ketogenic diet or topiramate use. 64% were taking mTORi (3 for renal indication/AML > 30mm). 1 patient presented hemorrhage treated with embolization. There was a statistically significant correlation (p =0.02) of renal implications with GCS, as well as between mTORi and control of AML/cyst size (p =0.03)

Conclusion: GFR impairment was exceptional, only in one patient with GCS, and LMA and renal cysts were the predominant conditions (41.8%/29.5%). early recognition (by MRI) and management of renal impairment, avoiding surgery and promoting the use of mTORi if indicated, are the fundamental factors for preserving renal function in these patients

1117 - P2.132

EVALUATION OF ISOLATED PROXIMAL RENAL TUBULAR ACIDOSIS CASES, TURKISH NATIONAL DATA

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Aim/Purpose: Na+/HCO3 cotransporter (NBCe1), located on the basolateral membrane in the proximal renal tubule, plays an important role in the absorption of bicarbonate. The NBCe1 protein gene (SLC4A4) is located on chromosome 4q21. In SLC4A4 mutation, problems occur in the absorption of 80-90% of the bicarbonate, and a clinical picture of renal tubular acidosis resulting in hyperchloremic metabolic acidosis is observed. In isolated proximal renal tubular acidosis (pRTA), metabolic acidosis, hypokalemia, short stature, eye pathologies (glaucoma, band keratopathy, cataract), dental enamel defects, mental retardation, calcification in the basal ganglia, hyperamylasemia and rarely hypothyroidism can be seen. Herein, we review the data of patients with this rare disease followed up in different centers in Turkey

Methods: In the study, it was planned to retrospectively evaluate patients with isolated pRTA who were followed up in pediatric nephrology centers in Turkey. The patients' sociodemographic characteristics, clinical and laboratory parameters at the time of diagnosis and at the last follow-up were noted from their files.

Results: Nine isolated pRTA patients from six pediatric nephrology centers were included in the study. The average age of the patients at diagnosis and last control were 26 ± 24.2 months and 11.7 ± 5.39 years, respectively. 77.7% of the patients were female and 66.6% had a history of consanguineous marriage. The mean body weight and height SDS of the patients at the last follow-up were -2.16 ± 1.85 and -2.27 ± 1.75, respectively. The oral bicarbonate requirement of the patients was 8.4 ± 4.36 mEq/kg/day. 77.7% of the patients had band keratopathy, 44.4% had cataracts and 88.8% had glaucoma. The age at which ocular pathology was detected was 71 ± 41.7 months and eye surgery were performed on 4 patients. Among the extrarenal involvement, 1 patient had pancreatitis attacks, 1 patient had an enamel maturation defect, and 3 patients had mental retardation.

Conclusion: Isolated pRTA patients, which are among the very rare causes of renal tubular acidosis, pose a challenge to us, pediatric nephrologists, in follow-up due to the need for high doses of oral bicarbonate. It should not be forgotten that, in addition to renal involvement, patients suffer from extrarenal involvement and that patients should be examined at regular intervals for these involvements.

1142 - P2.134

REFRACTORY ARTERIAL HYPERTENSION OF NEONATAL ONSET AND GENETIC CAUSE. DO WE THINK ABOUT IT?

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Aims/Purpose: Illustrate a clinical case of rare hereditary vascular condition with complex and torpid evolution

Methods: Generalized arterial calcification of infancy (GACI) is a very rare genetic vascular condition (300 cases) caused by mutations in ENPP1 and ABCC6 genes, which presents as extensive calcification and stenosis of medium-large caliber arteries with very varied vascular (heart failure, hypertension, respiratory distress) and extravascular (skin, retina, deafness, rickets, renal) manifestations

Results: 13-year-old boy, non-consanguineous parents, who from neonatal age presented hypertension in upper limbs and low blood pressure in lower limbs, requiring antihypertensive treatment with multiple drugs (captopril, nifedipine, furosemide, hydralazine, spironolactone, carvedilol) up to maximum doses to achieve partial improvement. After initially ruling out aortic coarctation, an etiological study was continued, showing left ventricular hypertrophy, together with normoaldosteronic hyperreninemia, hypothyroidism and images of peripheral thyroid calcification of probable vascular origin, as well as calcifications in multiple vascular territories (lower limbs, hepatic artery and both renal and interlobar arteries). In view of the suspicion of occlusive infantile arteriopathy, a genetic study was performed and started bisphosphonates + vitamin-D treatment. Finally, the genetic study showed 3 heterozygous mutations in ABCC6 gene (exons 24, 27 and 28), confirming GACI type II (father homozygosis carrier and mother heterozygosis carrier). During his evolution, he presented renal dysfunction secondary to captopril with complete normalization of renal function after its withdrawal. He has required multiple hospital admissions due to infectious and pulmonary processes and blood pressure decompensation with the addition of doxazosin and minoxidil to the treatment, achieving partial control of the hypertension. At 10 and 12 years of age he presented acute aortic syndrome, requiring urgent surgery in the first episode and intensification of the antihypertensive regimen (7 drugs) at full doses, achieving blood pressure stability until today. Intermittent proteinuria has been observed (currently iPr/Cr 0.28 mg/ mg, up to 3.25 mg/ mg levels) at the expense of albuminuria

Conclusion: Early clinical, histopathological and imaging diagnosis (prenatal) of GACI is vital for initiation therapy and multidisciplinary management, avoiding progression and preventing complications. Genetic confirmation is crucial in order to provide adequate genetic counseling. Although the prognosis is very poor and rarely survive the first 6 months (few can live to adolescence/early adulthood), the recent development of new therapies for the disease opens new pathways to change its poor prognosis

1152 - P2.135

DENYS-DRASH SYNDROME WITH CEREBRAL ATROPHY AND NEUROLOGICAL DEFICIT - A CASE REPORT

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We present a case of Denys-Drash syndrome complicated by cerebral atrophy and severe neurological deficit, not traditionally associated with the syndrome.

Patient presented as a female infant, born at 37 weeks gestation. Immediately after birth a low amount of urine was noted, as well as a reduced muscle tone. Neurosonography revealed slight hydrocephalus with no clinical signs of compression. She was discharged home, and presented at our tertiary centre at one month of age with severe generalised edema, hypertension, and anuria. Neurosonography was normal at this time. Peritoneal dialysis was initiated. Karyotype testing showed 46, XY. An oncogene panel revealed a pathogenic heterozygous variant of WT1 (NM_024426.6(WT1):c.[1316G > A];[1316 =]), confirming Denys-Drash syndrome. Abdominal and pelvic MRI showed no signs of nephroblastoma, and no gonadal tissue was identified. At two months of age, due to anuric ESRD and risk of malignancy, a double nephrectomy was performed. Nephrogenic foci were found in the histopathological study. Poor wound healing was noted, resulting in hernia at the incision site. In the following weeks the patient was increasingly irritable, had had worsening dysphagia. At 3 months focal seizures started to occur. Neurosonography and MRI showed severe cerebral atrophy, showing radiological signs of hypoglycaemic origin, however no hypoglycaemia episodes were registered. Full exome sequencing and metabolic testing revealed no additional inherited abnormalities.

At 6 months of age, due to progressive swallowing difficulties a gastrostomy was placed, again showing poor post-operative wound healing, which resulted in peritonitis one week after surgery. The healing process took 1 month, during which time parenteral feeding was utilised.

At 18 months of age the patient remains seizure-free with minimal doses of levetiracetam and phenobarbital, however MRI shows progressive cerebral atrophy, including atrophy of the optic nerves, resulting in blindness. Psychomotor development remains severely delayed.

The cerebral atrophy and neurological deficit were initially attributed to post-nephrectomy hypotension, however the patient's condition continued to deteriorate later in life with blood pressure well under control. Also, the patient did show some signs of neurological deficit (low muscle tone, dysphagia) before the nephrectomy was performed. The exact cause of the deficit remains unexplained at this time.

1163 - P2.136

EVALUATING THE UTILITY OF GENETIC TESTING AND GENETIC COUNSELLING AS PART OF A NATIONAL CYSTINOSIS SERVICE

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Aims/Purpose: The clinical utility of genomic testing extends beyond obtaining a diagnosis, with the potential to impact therapeutic management, surveillance, and discussions with patients about how a condition may affect them and their families. Incorporating genetic counselling into the multidisciplinary care approach for cystinosis has been advocated to enhance comprehension of reproductive health choices, family planning enabling patients and their caregivers to make well-informed decisions promptly.

Methods: Genetics was incorporated into an NHS England Paediatric Cystinosis clinic model to include diagnostics, disease-specific, reproductive and preconceptual planning for patients and their families. The clinician-reported genetic testing utility index (C-guide v1.2) was used to evaluate clinical utility and a survey conducted to assess patient and family perspectives.

Results: Genetic results were available for 11 patients aged between 8 months to 16 years. A complete genetic explanation was provided in all cases, reducing the likelihood of other potential differential diagnoses. Further testing to identify a genetic diagnosis could be avoided for those patients. Genetic confirmation allowed 9 patients to continue surveillance through the NHSE service, with 2 new referrals. All patients were evaluated by their clinicians to have had significant psychological benefit from receiving a genetic diagnosis. However, 3 families were perceived to have experienced stigmatisation within their cultural network. All families reported that receiving a genetic diagnosis with the associated counselling gave them new information. One family reported that all information was new. Five families were already aware of autosomal recessive inheritance and the implications for relatives but found going into further detail consolidated their knowledge and allowed them to ask more specific information. One family found value in understanding the specific familial genetic variant. Genetic counselling was rated as being beneficial by all families including those who had undergone diagnostic testing more than 10 years prior. Understanding how siblings may be affected, how genetic counselling can be accessed when older and planning of future pregnancies were some of the specific benefits noted.

Conclusions: Integrating genetics within a national cystinosis service model has shown clinical utility from a clinician as well as patient and family perspective. Benefits were gained whether diagnostic genetic testing was undertaken at the time or when historic results were re-explored. Patients and families expressed a need for on-going input from genetics to allow for elaboration of topics relevant to the age and circumstances of the patient and their family, including cultural and societal influences.

1167 - P2.137

BARTTER-TYPE TUBULOPATHY IN AN INFANT WITH CHLORIDE DIARRHEA: SLC26A3 MUTATION, A NOVEL CLINICAL PHENOTYPE

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Aims/Purpose: Illustrate a clinical case of a new clinical entity with similar characteristics to salt wasting tubulopathy.

Methods: Congenital chloride diarrhea is a rare autosomal recessive disorder (about 250 cases reported worldwide) due to mutations in the SLC26 family genes affecting intestinal chloride/bicarbonate transport, characterized by excessive chloride in the feces, hypochloremia, hypokalemia, hypokalemia, hyponatremia and metabolic alkalosis

Results: Three-year-old boy, son of consanguineous parents. Third gestation at 31+5 weeks of gestational age due to polyhydramnios. Since birth he presented severe polyuria, dehydration and dyselectrolytemias with need of sodium intake (up to 13 mEq/kg/day) because of persistent hyponatremia together with high limit potassium and hyperreninemia. In the following controls he presented hypochloremic metabolic alkalosis with persistent high borderline potassium, preserved renal function and tubular study with high % volume, low transtubular potassium gradient (TTKG) and increased fractional sodium excretion. Renal ultrasound with no signs of nephrocalcinosis. In view of these findings, a genetic study was performed, which was negative for salt loss syndromes, including classic and antenatal Bartter Syndromes, MAGED-2, Gitelman Syndrome, CasR gain mutations, pseudohypoaldosteronism and HELIX Syndrome. He was also followed up by gastroenterology for persistent diarrhea with normal upper and lower endoscopic studies. In view of the suspicion of congenital chloral diarrhea, a genetic study was extended and a homozygous mutation in the SLC26A3 gene causing congenital chloral diarrhea was detected. She has maintained normal calcemia levels at all times, as well as magnesium at the high limit of normality together with hypomagnesiuria. During her follow-up he has needed oral potassium and sodium intake, increasing markedly her requirements in case of hydroelectrolytic decompensations during intercurrent processes

Conclusion: Chloride diarrhea is a rare congenital disorder that requires a high clinical suspicion and regularly the need for genetic study for confirmation due to the high genotype-phenotype variability. Early diagnosis is essential for proper management, genetic counseling to the family and prevention of long-term complications, avoiding misdiagnosis in some patients who have similar clinical features since birth as in the case of some tubulopathies (Bartter syndrome, Gitelman, renal tubular acidosis) that today continue to be a challenge for the treating physician

1190 - P2.138

KIDNEY SURVIVAL IN BOYS WITH NEPHROTIC SYNDROME ASSOCIATED WITH COL4A5

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Aims/Purpose: Nephrotic syndrome (NS) is a late stage of kidney disease in patients with Alport syndrome. Its development is associated with FSGS. The aim of study was to evaluate the kidney survival in males with NS associated with variants in gene COL4A5.

Methods: In a single cohort study we evaluated 97 males with genetically confirmed X-linked Alport syndrome (XLAS). Clinical-laboratory data including variants in gene COL4A5, age of NS (blood albumin < 30 g/l, proteinuria ≥1 g/m2/day) and ESKD development, treatment with ACEi (age of start, doses according to ramipril, mg/m2/day) were obtained. Statistical analysis was performed using Statistics 10 software (StatSoft Inc., USA). All continuous data are expressed as median and interquartile range. Kaplan–Meier estimates were used to generate an overall survival curve for the development of ESKD after NS onset. The differences among groups with and without ACEi treatment were assessed by log-rank test. A value $p < 0.05$ was considered statistically significant.

Results: NS developed in 24 boys (q = 0,25) with XLAS at an average age 12,1 ± 3,9 years. ESKD was observed in 18 pts with NS and in 4 children without NS (0,75 vs 0,05, $p < 0,01$). There is no a statistically significant difference in the age of ESKD development between groups (17,5 ± 3,22 vs 18,3 ± 4,1 years, $p > 0,05$). Eighteen pts with NS (q = 0,75) received ACEi (start at age 8,2 ± 3,5 years, dose 4,6 ± 1,3 mg/m2/day). No remission of NS (partial or complete) was observed. All pts without treatment and 9 pts on treatment developed ESKD (1 vs 0,5, $p < 0,001$). At Kaplan-Meier analysis demonstrated that pts with NS had a 10-year kidney survival rate of 12%, without difference between groups of ACEi-treated and non treated pts (log-rank 0,54; p =0,59).

Conclusion: Kidney survival in males with XLAS and NS is poor and comparable to that of monogenic podocytopathies. ACEi treatment does not increase the likelihood of NS remission in XLAS.

1291 - P2.139

VARIABILITY OF CLINICAL MANIFESTATIONS OF BARTTER SYNDROME TYPE IVA

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Aims/Purpose: Bartter syndrome, type IVA (BSIVA; OMIM #602522) is a rare subtype of the disease associated with pathogenic variants in the BSND gene. The aim of the study was to present two cases with variable manifestation of BSIVA.

Results: Case 1. The boy was born prematurely after a pregnancy complicated by severe polyhydramnios. Soon after birth, the child developed respiratory failure, blood test revealed hyperkalemia and increased serum creatinine level. Hearing tests showed an absence of evoked response to stimulation. At the first admission in our center at the age of 8 years the boy had short stature, polyuria/polydipsia, hypokalemia, hyponatremia, hypochloremic metabolic alkalosis and hyperreninemia; increased calcium excretion, fractional excretion (FE) of potassium and sodium. His eGFR was 71.2 ml/min/1.73 m2. Kidney US showed NC grade 2. NGS revealed previously reported homozygous variant p.Gly47Arg (c.139G > A) in exon 1 in the BSND gene. The boy has been treated with Indomethacin 1.33 mg/kg/d, 4% KCl 3.6 mmol/kg/d and NaCl 10 mmol/kg/d. Ongoing therapy led to a correction of urine output, decreased the severity of metabolic alkalosis and hypokalemia. By the age of 12 years his eGFR was 94.3 ml/min/1.73 m2. Case 2. The boy was born prematurely after a pregnancy complicated by polyhydramnios. After birth he developed respiratory failure of the 3rd degree. Hearing tests showed an absence of evoked response to stimulation. Data on acid-base state, electrolytes and fluid balance were not available. At the first admission at the age of 19 month the boy had psychomotor development retardation, short stature, polyuria/polydipsia, hypokalemia, hyponatremia, hypochloremic metabolic alkalosis and increased renin activityhttps://healthmatters.io/understand-blood-test-results/renin-activity-plasma; hypercalciuria, elevated FE of potassium, eGFR was 58.8 ml/min/1.73 m2. Kidney US showed NC grade 2. NGS revealed previously reported compound heterozygous variants p.Gly47Arg (c.139G > A) in exon 1 and p.Pro151fs (c.452del) in exon 3 in the BSND gene. The boy has been treated with Indomethacin 1.68 mg/kg/d, 4% KCl 2.7 mmol/kg/d and NaCl 6 mmol/kg/d. Ongoing therapy led to normalization of urine output without reducing the severity of metabolic alkalosis and hypokalemia. By the age of 3 years his eGFR was 72.5 ml/min/1.73 m2.

Conclusion: These cases demonstrated a typical clinical picture of BSIVA with polyhydramnios, severe condition in the neonatal period, polyuria/polydipsia, hypokalemic hypochloremic metabolic alkalosis, sensorineural hearing loss. Stable kidney function and a partial response to therapy in these cases are not typical for BSIVA and might be explained by effect of the disease-causing p.Gly47Arg BSIVA variant on the protein synthesis that produces a mild renal phenotype.

1191 - P2.140

HEREDITARY RENAL HYPOURICEMIA IN TWO SIBLINGS

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Aims/Purpose: Hereditary renal hypouricemia (HRH) is a rare genetic disorder due to dysfunction of the tubular uric acid transporters, URAT1 and GLUT9, encoded by the genes SLC22A12 (Type 1) and SLC2A9 (Type 2) respectively. Most of the patients are asymptomatic and sometimes they can debut with complications such as nephrolithiasis, hematuria or acute kidney damage after intense physical exercise.

Methods: An 11-year-old boy, with history of prematurity (32 weeks), twin pregnancy (IVF) and ADHD under treatment. Weight and height in p10. Non-consanguineous parents with no known history. In a routine blood test, a serum uric acid level of 0.8 mg/dl is detected and confirmed. Renal function was studied.

Results: In an isolated urine sample without glycosuria, proteinuria, or hypercalciuria, the fractional excretion of uric acid being of 54%. Estimated GFR, acid-base balance, and renal ultrasound were normal. Family data are reviewed, the mother had normal uricemia figures. His sister shows sustained hypouricemia between 0.6-0.8 mg/dL with a fractional excretion of uric acid being of 40%. Weight and height in p25. Glycosuria, proteinuria, or hypercalciuria were not detected in an isolated urine sample. Estimated GFR, acid-base balance, and ultrasound were normal. Given the suspicion of renal hypouricemia, a genetic study of both siblings was carried out, and a homozygous variant in the SLC22A12 gene was detected. The mother presents the same variant in heterozygosity.

Conclusion: All hypouricemia below 2 mg/dl should be studied. Molecular analysis of the SLC22A12 and SLC2A9 genes is important to confirm the diagnosis of HRH. Prevention of its complications is the main treatment.

1200 - P2.141

ACUTE RENAL FAILURE IN AUTOINMUNE HEMOLYTIC ANEMIA

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Aims/Purpose: Autoimmune hemolytic anemia (AIHA) is a rare inmune disorder due to autoantibodies directed against erythrocytes, causing shortened erythrocyte survival, with or without complement activation. The disorders can appear as a primary disorder (idiopathic) or secondary to other autoimmune disorders, malignancies, or infections. Treatment involves immune modulation.

Methods: We report an 5-year-old girl who has presented fever, hyporexia and a cough in the last < 12 hours. In the emergency room, she had unstable pediatric assessment triangle (PAT) due to shock. She was transferred to PICU and started IV empiric antibiotics after blood extraction and urine cultures. In blood test, she presented leukocytosis with neutrophilia, CRP 182 mg/L, hemolytic anemia with normal platelets and acute kidney injury (creat 1.8 mg/dL, urea 153 mg/dL). Direct Coombs was positive (C3D+, with negative IgG, IgA, IgM and C3c). Chest X-ray revealed atelectasis of the right upper lobe. She had negative pneumococcal antigenuria, negative urine and blood cultures. After 48 hours, she had higher rate of creatinine and urea, the hemolytic anemia worsened and had significant thrombocytopenia. That required red blood cell transfusion and initiation of continuous hemodiafiltration, which was maintained for 3 days. Having differential diagnosis between autoimmune hemolytic anemia (AIHA) and atypical hemolytic uraemic syndrome (aHUS) due to pneumococcus without isolating the microorganism, we started corticosteroids at 2 mg/kg/day. After starting with the steroids, stabilization and decreased hemolysis at 72 hours, presenting worse renal function up to urea of 235 mg/dL with ions and controlled blood pressure. All that improved after 6 days, without requiring renal replacement therapy. At discharge, 21 days after admission, she presented normal glomerular filtration.

Results: Agglutinin test was negative on several occasions, until 14 days after admission to the Coombs reference center, direct positive for IgG and C3D was obtained, being compatible with AIHA IgG + complement by warm antibodies.

Conclusion: In hemolytic anemias with associated renal damage, we must establish differential diagnosis of thrombotic microangiopathy versus autoimmune hemolytic anemia. Given the suspicion of autoimmunity, early initiation of steroids is important to improve the kidney function prognosis. Immunosuppressive drugs may be indicated as second level treatment, once the diagnosis is established.

1220 - P2.142

GENETIC ANALYSIS AND PROGNOSIS IN PEDIATRIC PATIENTS WITH ALPORT SYNDROME

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Aims/Purpose: Alport Syndrome (AS) is an inherited progressive renal disease caused by mutations in COL4A3, COL4A4, and COL4A5 genes encoding 3, 4, 5 chains of type IV collagen. We aimed to investigate clinical and genetic characteristics, genotype–phenotype correlations and prognosis of AS in children.

Methods: A cohort of 54 (36 female, 18 male) patients with AS, all of whom had genetic analysis between the years of 2016 and 2022 were enrolled in our cross-sectional, retrospective study. Demographic, clinical, laboratory characteristics, renal biopsy and genetic test results, treatments and follow-up results were evaluated.

Results: The median age at first presentation was 6.2 (3.9-9) years and the mean follow up time was 7.8 ± 4.1 years. 24 patients (44.4%) had X-linked AS, 14 (26%) had autosomal recessive AS and 16 (29.6%) had autosomal dominant AS. Of 21 patients (38.9%) who had a renal biopsy, 4 (19%) revealed FSGS on light microscopy and 3 (75%) of them had CKD stage 5 in follow-up. Hypertension and proteinuria at first presentation, decline in eGFR, CKD stage 5 and renal transplantation were higher in patients with autosomal recessive AS ($p < 0.05$).

Conclusions: Genetic analysis is important to confirm the diagnosis and predict prognosis in patients with AS. Alport syndrome should be kept in mind in patients with FSGS on biopsy, and genetic analysis should be performed for diagnosis to avoid potentially toxic side effects of immunosuppressive therapies.

Keywords: Alport syndrome, focal segmental glomerulosclerosis, genetic analysis, prognosis

1227 - P2.143

KAT2B - A LIKELY PATHOGENIC VARIANT WITH FSGS, CATARACTS AND CARDIOMYOPATHY

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There are more than 60 known genes causing monogenic steroid resistant nephrotic syndrome (SRNS) with ongoing work to identify new candidate genes. The identification of novel causative mutations will help to elucidate the mechanisms of glomerular disease and podocyte function. Features that suggest monogenic cause of SRNS include positive family history or the presence of extra-renal manifestations.

Lysine acetyltransferase 2b (KAT2B) is a gene strongly expressed in murine cardiac and kidney tissue. It has not been associated with genetic disease apart from a single case report describing a family of three siblings with proteinuria and dilated cardiomyopathy. In another study, KAT2B was highlighted as a potential FSGS susceptibility gene by rare variant analysis in a cohort of patients with FSGS.

We describe a 14 year old boy who presented with ESKD and underwent living paternal donor kidney transplantation after genetic confirmation of homozygous variant of KAT2B. He presented with acute shortness of breath, ankle oedema and frothy urine for three months. There was severe renal impairment necessitating PICU care and urgent kidney replacement therapy for fluid overload and hyperkalaemia. He was hypertensive with BP readings above the 99th centile and eGFR of 4.7mL/min/1.73m2. There was nephrotic range proteinuria with urine protein:creatinine ratio of 5050 mg/mmol. He also had cardiomyopathy with significantly impaired biventricular function and elevated cardiac enzymes requiring inotropic support with milrinone. He had brief cardiorespiratory arrest while undergoing percutaneous renal biopsy and peritoneal catheter insertion

He is one of two sons born to consanguineous parents who are first cousins. Parents as well as younger sibling were healthy and there was no known family history of kidney or heart disease. There were no concerns in the antenatal period and he had a normal birth. However, he was found to have delayed milestones and was investigated for global developmental delay. He had bilateral cataracts and underwent cataract surgery at three years of age.

Histopathology showed extensive global sclerosis with one glomerulus showing focal and segmental glomerulosclerosis. There was also significant electron microscopy findings of prominent podocyte foot process effacement with villous transformation and no immune deposits seen.

He was not able to continue peritoneal dialysis due to poor catheter function and he was commenced on home haemodialysis. He responded well to home haemodialysis with gradual improvement of cardiac function and underwent living paternal donor kidney transplantation two years after presentation without complications. He currently has good renal allograft function with estimated glomerular filtration rate of 65mls/min/1.73m2.

This case report highlights a patient with a variant of unknown significance that is likely to be a true pathogenic gene

1251 - P2.144

CONGENITAL NEPHROTIC SYNDROME: A CLINICAL CASE WITH IDENTIFICATION OF COMPOUND HETEROZYGOUS MUTATIONS IN THE NPHS1 GENE

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Aims: Congenital nephrotic syndrome (CNS) comprises a heterogeneous group of diseases characterized by nephrotic-level proteinuria, hypoalbuminemia and edema which manifest in utero or in the first 3 months of life. The main cause of CNS is mutations in the genes of structural proteins that form the filtration barrier of the kidney. We present a clinical case of CNS diagnosed with the help of molecular-genetic testing.

Methods: Complete sequences of the NPHS1 and NPHS2 genes of a patient with CNS with hematuria and hypertension associated with hypothyroidism were obtained using NGS (Illumina).

Results: A boy from the 1st pregnancy and the 1st term birth with a complicated gynecological history (anemia, chronic feto-placental insufficiency, COVID-19, polyhydramnios, large placental mass). On the 3rd day after birth the child was diagnosed with testicular hydrocele, proteinuria (3.39 g/l), hypoalbuminemia (23 g/l). An increase in the level of thyroid-stimulating hormone was observed (11.37 mU/l). The parents don't present any symptoms of kidney disease. Based on the results of a molecular genetic study, 2 mutations were detected in the NPHS1 gene in a compound heterozygote. Both variants were found in the ClinVar database (Variation ID: 188734 and 2115119) and classified as pathogenic/likely pathogenic. NM_004646:exon18:c.2335-1G > A is a splice site mutation, it was previously discovered in patients with CNS in a heterozygous state. M_004646:exon8:c.C847T:p.Q283* leads to the formation of a stop codon, records about it date back to the 2022–2023, but don't contain information about the affected status of individuals, observed with the variant. In the present clinical case we have traced the origin of variants: the c.2335-1G > A was passed down from the father and the p.Q283* – from the mother; both parents were heterozygotes.

Conclusion: We identified a compound heterozygous variant in the NPHS1 gene. These variants are likely the cause of the Finnish congenital nephrotic syndrome which is known to have autosomal recessive inheritance.

1258 - P2.145

CAUSES AND FUNCTIONAL CHARACTERISTICS OF PEDIATRIC NEPHROCALCINOSIS. SINGLE CENTER STUDY

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Aims/Purpose: To study the data of children with nephrocalcinosis (NC) regarding the main monogenic causes, clinical symptoms and renal function.

Methods: Our research included 100 children younger than 18 years who were diagnosed with NC by ultrasonography in our Center in the period 2012-2024. Clinical features, etiology, estimated glomerular filtration rate (eGFR) were evaluated at presentation and at last follow-up. Genetic analysis included of target regions of 200 genes associated with hereditary kidney diseases or clinical exome sequencing and whole exome sequencing.

Results: Medullary NC was diagnosed at the median age of 17,2 [IQR 3,6–57,7] months, among whom 46 children were younger than 12 months. The most common initial symptoms were failure to thrive developmental delays at an early age (26%) and urinary tract infections (7%). The NC was incidentally detected in 51% case, during a routine ultrasound examination at the median age of 12 [IQR 2,2–58,6] months. At the first ultrasound examination, 57%, 40% and 3% of children were diagnosed with grades 1, 2 and 3 nephrocalcinosis, respectively. Kidney function was normal at first follow-up in 83% of children. Causative mutations were identified in 47 children in 14 genes: CLCN5(n = 9), AGXT(n = 8), CYP24A1(n = 7), HPRT1(n = 6), OCRL(n = 3), CTNS(n = 3), SLC4A1(n = 2), ATP6V1B1(n = 2), PHEX(n = 2), CLDN16(n = 1), CASR(n = 1), KSNJ1(n = 1), KSNJ5(n = 1), SLC5A1(n = 1). Also, 3 children had a 1.5- to 1.8- Mb deletion of chromosome 7q11.23. The etiological structure of other children (n = 50) included idiopathic hypercalciuria (n = 12), pharmacological causes (loop diuretics, vitamin D/calcium supplements, n = 6), unknown or no underlying disease (n = 32). In children with monogenic causes, the mean eGFR changed from 97,68 ± 27,77 ml/min/1.73m2 at the first follow-up to 89,18 ± 22,58 ml/min/1.73m2 at the 3-year follow-up, with statistically significant (p =0,03). In two cases (Familial hypomagnesemia with hypercalciuria and nephrocalcinosis; Lesch–Nyhan syndrome) eGFR changed to ≤60 ml/min/1.73m2 at the 3-year follow-up. In one child with primary hyperoxaluria type 1 (PH1) eGFR changed from 56 ml/min/1.73m2 at the first follow-up to 20 ml/min/1.73m2 at the 5-year follow-up. In two children with PH1 eGFR remained stable through month 24 during the course of lumasiran treatment.

Conclusion: Dent disease, primary hyperoxaluria and idiopathic infantile hypercalcemia and were the common monogenic causes of nephrocalcinosis in our patient population.

1268 - P2.146

SLC2A2 MUTATIONS ASSOCIATED WITH A MILD ATYPICAL PHENOTYPE OF FANCONI-BICKEL SYNDROME

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Fanconi-Bickel Syndrome (FBS) is a rare genetic disorder that causes glycogen accumulation in the liver and kidneys leading to hepatomegaly and severe dysfunction of the proximal renal tubule. It typically appears between 3-10 months of age with growth retardation and rickets and can have a severe course.

A 4-year-old female came to our attention due to the occasional finding of isolated glycosuria without hyperglycemia. She was in good clinical condition, with good growth in height and overweight. The acid-base balance, electrolytemia and calcium-phosphorus balance were normal. Hypouricemia and increased plasma renin were found, with normal aldosteronemia and blood pressure. Generalized aminoaciduria and a slight increase in urinary 2-microglobulin were found. Calciuria and tubular excretion fractions, except the uric acid excretion fraction, were normal. Abdominal ultrasound revealed hepatic and renal normal appearance.

The study of glucose metabolism revealed mild and non-specific alterations such as basal blood sugar levels and after 30 minutes from glucose load to slightly high, with normal insulin response and HbA1c.

Although the mild urinary alterations were compatible with the involvement of the proximal tubule, no therapy was needed and the patient was only monitored.

In the two years following, the patient continued to experience high levels of glycosuria and generalized aminoaciduria. Hypercalciuria with osteopenia on osteosonography showed up always with normal phosphorus and phosphaturia. Therefore, a genetic investigation was carried out and revealed a compound heterozygosity of the SLC2A2 gene. The maternal variant c.589G > A has been reported in a single case, in homozygosity, associated with a mild FBS phenotype, as well as being associated with diabetes; while the paternal variant c.963+1G > T has not been previously reported, however other variants affecting the same nucleotide associated with FBS have been described.

Currently, the little girl follows only a low galactose diet, has good growth and no signs of hepatomegaly.

This atypical, mild phenotype of FBS expands the spectrum of the disease suggesting that some characteristic clinical signs, such as hepatomegaly, rickets and short stature, may be absent. Therefore, GLUT2 mutations could be implicated in glycosuria even in the absence of other typical signs of FBS.

1270 - P2.147

A RARE CAUSE OF HYPERTENSION OF GENETIC ORIGIN

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Aims/Purpose: Rare causes of hypertension could be missed in spite of current recommended screening according to clinical guidelines. We present a patient affected by a rare condition responsible for arterial hypertension.

Clinical Case: A 12-year-old girl was referred due to an isolated elevation of normetanephrine in urine -5336 mcg/g Cr 24h (normal values 38-523) - in the investigation of arterial hypertension. Clinical symptoms reported include sweating over a year, accompanied by decreased appetite and weight loss (3 kg) in recent months, as well as occasional self-limiting frontal headaches. Upon admission physical exam was normal, but blood pressure (BP) readings were about the 95th percentile for sex and height (118/79 mmHg), without BP gradient, confirmed by 24h ambulatory blood pressure monitoring. Blood and urine tests revealed normal electrolytes, acid-balance and estimated glomerular filtration rates from serum creatinine and cystatin C (average CKiD U25 eGFR 129 mL/min/1.73m^2), and no associated proteinuria or hematuria. Abdominal ultrasound and kidney duplex were normal and no mass was observed. Target organ exams (echocardiogram and funduscopy) showed no abnormalities either. Repeated metanephrine collection confirmed increased levels (6869 mcg/g Cr 24h). A MIBG scan was performed, revealing a right paravertebral thoracic mass with increased catecholaminergic activity. Thoracic MRI confirmed those findings. Paraganglioma was suspected and doxazosin was initiated, with an increasing dose up to 4 mg per day, resulting in rapid cessation of associated symptoms. After blood pressure control and volume expansion with a diet rich in fluids and salt, propranolol was initiated, up to 30 mg/day. Afterwards, the patient underwent thoracoscopic surgery with complete mass removal, requiring hydrocortisone due to subsequent hypotension. She is currently asymptomatic, with blood pressure within normal range and without treatment. Lesion histology confirmed a paraganglioma with no vascular invasion or necrosis. ki67 index < 5%. Negative immunohistochemical expression of SDH-b. In the genetic study, a presumably suspected pathogenic variant in SDHB gen (c.723C > G) was detected.

Conclusion: This case report illustrates a child with a paraganglioma of genetic origin causing hypertension. Mutations in the succinate dehydrogenase (SDHx) genes are the most common cause of inherited paragangliomas, with a dominant transmission pattern. Patients are on risk of presenting associated tumors such as renal carcinomas, pituitary adenomas and gastrointestinal stromal tumors. Family screening is highly recommended.

1282 - P2.148

PLCE1-RELATED NEPHROTIC SYNDROME IN A POLYMALFORMATIVE DISEASE: IS THAT PART OF THE SAME STORY? A CASE REPORT

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Aims: We report the case of a 8-month-old baby girl with a steroid-resistant nephrotic syndrome (SRNS) in the context of a polymalformative syndrome characterized by involvement of transposition of the great arteries, closure defects of the atrial and ventricular septum, thinning of corpus callosum with delayed myelination, peripheral paresis of the right facial nerve, right microtia with severe ipsilateral hearing loss, retinal maturation defect, muscle asymmetry and delay in motor development. Nephrotic syndrome was associated with concomitant rapid decrease in renal function. We performed genetic testing with exome sequencing analysis from peripheral blood of the patient and from the father, while the maternal genetic contribution could not be analyzed as the baby was born from egg donation. Genetic test highlighted a compound heterozygosis in PLCE1 gene: mutation c.3391G > T have not been described in scientific literature nor in HGMD (The Human Gene Mutation Database). The second one, inherited from the father, was previously reported in literature as associated with nephrotic range proteinuria. Both were considered pathogenic according to HGMD.

Methods: We did a review of literature to identify possible extrarenal manifestations in patients suffering from PLCE1-related nephrotic syndrome. We also evaluated the protein expression in different tissues using Human-protein-Atlas (www.proteinatlas.org).

Results: With the exception of ocular involvement (glaucoma), no extra-renal manifestation was reported in patients with SRNS due to PLCE1 mutation (1). This gene encodes a phospholipase enzyme involved in intracellular signaling. According to protein-atlas, PLC is highly expressed in the brain, muscle and connective tissue, and it also has a role in heart development: these organs were affected in the clinical picture described.

Conclusion: Mutations in the PLCE1 gene are associated with Nephrotic syndrome type 3 with autosomal recessive inheritance, but not in association with extrarenal manifestations except for eye features. In this clinical case we reported a case of SRNS due to PLCE1 mutation, in the context of multi-organ involvement. The lack of additional variants supporting the extrarenal manifestation and the systemic expression of the protein, allowed us to hypothesize the possible link of the clinical features with the genetic background. Additional genotype phenotype correlations and functional studies are needed to confirm the hypothesis.

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1285 - P2.149

THE UTILITY OF GENETIC TESTS IN CHILDREN WITH VARIOUS KIDNEY DISEASES

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Aims: A substantial proportion of kidney diseases in children are monogenic. The aim of this study was to analyze the importance of genetic tests in children with various kidney diseases.

Methods: The genetic analysis of children with a suspicion of monogenic kidney disease between September 2022 and January 2024 were analyzed retrospectively. The disease-associated clinical exome tests of the patients were performed using the Sophia CES_V3.3 kit and run on the Illumina NextSeq 2000 device. The obtained data were analyzed with the Sophia DDM analysis platform. ClinVar, dbSNP, GnomAD, 1000 Genomes Project, VarSome, HPO, ClinGen, OMIM, GenCC data servers were used as reference in the analysis.

Results: Genetic analysis was performed in 140 children with kidney disease; 48 with nephrolithiasis, 26 proteinuria or nephrotic syndrome (NS), 22 tubulopathy, 14 chronic kidney disease with unknown etiology (uCKD), 13 hematuria, 11 renal cysts and 6 with hemolytic uremic syndrome (HUS). A causative mutation was found in 70 patients (50.0%). Positive test ratio was 86,4 % in tubulopathies, 85.7% in uCKD, 72,7% in cystic kidney diseases, 69,2% in hematuria, 35,4% in nephrolithiasis and 19.2% in proteinuria/NS, whereas no patient with HUS had any mutation. The most common mutations were SLC34A1 (n = 5) and ATP6V (n = 4) in tubulopathies, COL4A4 (n = 4) and COL4A5 (n = 4) in children with hematuria, PKD1 (n = 5) in cystic kidney diseases, mutations leading to Alport syndrome (n = 5; three COL4A3, one COL4A4 and one COL4A5) in uCKD, and mutations leading to cystinuria (n = 4, SLC3A1 and SLC7A9) and mutations in genes associated with renal phosphate wasting (n = 4, SLC34A1 and SLC34A3) in nephrolithiasis.

Conclusion: We found high positive genetic test results, especially in children with tubulopathy, cystic kidney disease, hematuria and chronic kidney disease with unknown etiology. We suggest to perform genetic tests in these group of patients.

1287 - P2.150

PROXIMAL RENAL TUBULAR DYSFUNCTION IN CHILDREN WITH DISTAL RENAL TUBULAR ACIDOSIS

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Aims/Purpose: Distal renal tubular acidosis (dRTA) is caused by a genetic defect (involved genes ATP6V0A4, ATP6V1B1, SLC4A1, FOXI1, or WDR72), which causes tubular transport defects characterized by an inability to appropriately acidify urine with resultant persistent hyperchloremic metabolic acidosis. Proximal renal tubular dysfunction has been described in some patients with dRTA. The aim of the study was to evaluate the frequency and severity of proximal renal tubular dysfunction and the response to alkaline treatment in children with dRTA.

Methods: We conducted retrospective longitudinal study of 12 children (6M/6F) with dRTA associated with variants in the following genes: SLC4A1 (n = 5), ATP6V1B1 (n = 5), ATP6V0A4 (n = 2) with a median follow-up of 35.0 (29.5; 67.0) months. The median age of patients at the first follow up was 41.7 (16.7; 70.1) months. At the first examination 3 children received alkaline therapy with correction of acidosis.

Results: Among patients with acidosis increased low-molecular-weight proteinuria (LMWP) was revealed in 8/8 (100%) of cases, decreased serum uric acid (UA) level due to loss of urine (increased FEUr) in 9/9 (100%), decreased TmP/GFR level in 5/9 (55.5%), hypophosphatemia in 2/9 (22.2%) patients, none of children had glucosuria. All patients have been treated with alkali (bicarbonate and/or citrate) at a dose of 3.3 (2.1; 3.5) mEq/kg/d. Acidosis was persisted in 3/12 (25%) children despite the treatment. During alkali therapy increased urinary excretion of LMWP was detected in 4/10 (40%) of cases (1/3 (33.3%) with acidosis), decreased serum UA level with increased FEUr in 4/12 (33.3%) children (2/3 (66.7%) with acidosis), decreased TmP/GFR level and hypophosphatemia in 1/12 (8.3%) (1/3 (33.3%) with acidosis) patients.

Conclusion: All children with acidosis due to dRTA presented with features of proximal tubular dysfunction various severity. The most prevalent features of proximal tubular dysfunction in our study were LMWP, decreased serum UA and phosphaturia. Proximal tubular dysfunction persists in a third of children with dRTA despite the correction of the acidosis.

1292 - P2.151

NUTRITIONAL MANAGEMENT AND RISK OF FEEDING DISORDERS IN PATIENTS WITH BARTTER SYNDROME

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Background: Bartter syndrome (BS) is a rare inherited salt-wasting tubulopathy, requiring daily needs for fluids and electrolyte supplementations, and often nonsteroidal anti-inflammatory drugs use. In case of severe neonatal forms, these supplementations can be huge, with higher risk of feeding disorder appearance (i.e. impairment of oral food intake, trouble accepting food textures, choking or vomiting when eating...). The aim of this study was to describe the nutritional management of children with BS, and evaluate the risk of feeding disorder.

Methods: Medical records from the cohort of incident patients with BS in the three paediatric nephrology centres in Paris in the last twenty years were retrospectively analysed, and surveys concerning feeding disorders were sent to the families.

Results: A total of 40 patients were included. Genetic screening showed 10 (25%) type 1 BS (SLC12A1 mutation), 5 (12.5%) type 2 BS (ROMK/KCNJ1 mutation), 22 (55%) type 3 BS (CLCNKB mutation), 1 type 4 (BSND mutation) and 1 transitory form with MAGED2 mutation. The median follow-up was 9 years. 20 (50%) of patients in the global cohort had a feeding disorder, mostly patients with type 1 BS (90% of them) and type 3 BS (36% of them). 18 (45%) children required enteral nutrition during management, initially with nasogastric tube. A gastrostomy (GS) was later inserted in 14 patients (35%), with a median (range) age at insertion of 1 [0,9;1,3] years. At last follow-up, 10 patients of 14 still had their GS, and 6 of them were still dependant on enteral nutrition. In the surveys, parents of patients with GS were highly satisfied, because it avoids oral electrolyte supplementations, which is often a struggle for the child and his parents, and which may induce feeding disorders.

At last follow-up, growth of children with type 1 BS was lower than in the other types: median weight -1 DS and a median height of –2 DS versus 0 DS and -0.2 DS in other BS patients respectively ($p < 0.05$).

Conclusion: In our cohort, half of the children treated for BS had feeding disorders. Patients with type 1 BS, with the highest needs for fluids and electrolyte supplementations, were the most frequently affected, possibly because of the amount of treatments they have to take from an early age. Early introduction of a gastrostomy for these patients may reduce feeding disorders and avoid growth failure.

1296 - P2.152

A CASE OF ATYPICAL NEPHROCALCINOSIS WITHOUT PHOSPHATURIA WITH SLC34A HOMOZYGOUS MUTATION

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A case of atypical nephrocalcinosis without phosphaturia with SLC34A homozygous mutation

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Introduction: Mutations in the SLC34A1 gene (called infantile hypercalcemia 2) cause hypophosphatemia by preventing NaPi-IIa channels from transporting phosphate. Too much active vitamin D into the bloodstream increases the absorption of both phosphate and calcium from the intestines, causing hypercalcemia in affected patients. Hypercalcemia causes high levels of calcium in the urine, causing calcium to accumulate in the kidney tissue and the formation of kidney stones.

Case: A 9-month-old boy was admitted to the hospital with suspicion of urinary tract infection after complaining of vomiting attacks lasting several weeks when he was 1.5 months old. The patient, who was diagnosed with hypercalcemia and nephrocalcinosis during his hospitalization. Renal ultrasound revealed medullary nephrocalcinosis in bilateral kidneys. İn the SLC34A1 gene in genetic analysis homozygous mutation was detected. Although our patient did not have phosphaturia or hypophosphatemia, a known homozygous mutation was found in the NaPi2a protein. In our patient, the phosphate level was found to be normal in the presence of low PTH level and inappropriately normal (141pg/ml) 1,25-dihydroxyvitamin D.

Conclusion: Deletions of the NaPi2a gene and mutations in the SLC34A gene should be considered in patients with atypical presentation, no phosphaturia, normal serum phosphate level, and medullary nephrocalcinosis.

Keywords: hypercalcemia, phosphaturia, nephrocalcinosis, SLC34A mutation, NaPi2A gene

1298 - P2.153

MATERNAL 17Q12 DELETION IS ASSOCIATED WITH A HIGH RISK OF NEUROPSYCHIATRIC INVOLVEMENT

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Aims/Purpose: 17q12 deletion is the most common cause of renal cysts and diabetes syndrome (RCAD, OMIM #137920), and is also associated with neuropsychiatric disorders. We aimed to explore the role of parental origin in the risk of neuropsychiatric involvement.

Methods: HNF1B deletion was screened by quantitative multiplex PCR of short fluorescent fragments (QMPSF) in eight of its nine exons. In case of de novo deletions, the parental origin was determined by maternal or paternal haplotype loss. The D17S1872, rs58553128, rs1405901686, D17S1867, rs5820230, rs58710993 and D17S1818 microsatellite markers were amplified by fluorophore-labeled primers for haplotyping. Neuropsychiatric involvement was determined retrospectively.

Results: Out of the 24 patients with 17q12 deletion, parental samples were available in fifteen to determine the parental origin. Ten deletions were present on the paternal allele (eight arised de novo), and five on the maternal allele (four de novo). While out of the ten patients with paternal deletion, only one adult was treated for anxiety, all five patients with maternal deletion were treated with either autism (n = 4), schizophrenia (n = 1), learning difficulty (n = 2) or behavorial problems (n = 1) (5/5 vs. 1/10, p =0.002).

Conclusion: The neuropsychiatric involvement associated to 17q12 deletion is suggested to be influenced by parental origin. These findings will need to be confirmed in a larger patient cohort.

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1299 - P2.154

JANSEN`S METAPHYSEAL CHONDRODYSPLASIA: A RARE CAUSE OF HYPERCALCEMIA AND NEPHROCALCINOSIS

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Aims/Purpose: Describe clinical manifestations, diagnosis and treatment of a patient affected by Jansen metaphyseal chondrodysplasia (CMJ) which constitutes a extremely rare disease. CMJ is a skeletal dysplasia caused by activating mutations of the parathyroid hormone/parathyroid hormone-related protein (PTH/PTHrp) receptor (PTH1R). It produces ligand-independent activation, like an hyperparathyroidism without elevation of PTH. It mainly presents deformity of long bones and sever short stature and a phenotype with hypertelorism, micrognathia and high-arched palate. It is associated with chronic asymptomatic hypercalcemia, hypophosphatemia, hypercalciuria and nephrocalcinosis.

Methods: Clinical description of a 15-month-old girl patient

Results: Case report: daughter of healthy, non-consanguineous parents, from Morocco. Mother with two spontaneous abortions. Prenatal diagnosis of polyhydramnios, retrognathia and curvature femurs. At birth choanal stenosis and facial, sphenoid and petrous hyperostosis (tomography scan). Incidentally, severe asymptomatic hypercalcemia is identified. Examination reveals hypertelorism, exophthalmos, retrognathia, varus deformity of both legs, height and weight delay (weight: 6kg, -4.0 SD, height 71cm, -2.55 SD) and psychomotor delay (no crawling or standing).
Supplementary tests:
- Laboratory results: hypercalcemia (14 mg/dl), hypophosphatemia (2.8 mg/dl), elevated alkaline phosphatase (499 mg/dl), inhibited PTH (PTHi pg/ml and PTHrp pmol/l < 1), elevated vitamin D (25- 0H 50.8ng/ml, 1.25 OH vit D 74pg/ml), hypercalciuria (Ca/Cr 2.32 mg/ mg), decreased tubular phosphate reabsorption (69%), polyuria (Vo/100FGRe 4.5%) and proteinuria (prot /Cr 0.5 mg/ mg).
- Abdominal ultrasound: bilateral nephrocalcinosis
- Bone series: extensive metaphyseal long bones involvement with marked irregularity and widening, femoral varus deformity, bell-shaped thorax

The genetic study confirms the disease with a mutation in the PTH1R gene (H223R variant). None of the treatments used to reduce hypercalcemia were effective. She currently receives treatment with biphosphonates (intravenous zoledronic acid) every three months to inhibit bone resorption, decrease hypercalcemia and to reduce pain and improve quality of life. She receives nutritional support and rehabilitation therapy too.

Conclusions:
- CMJ should be suspected in the presence of suppressed PTH and PTHrp along with the characteristic phenotype and radiological alterations.
- Persistent hypercalcemia is associated with increased cardiac risk and hypercalciuria and nephrocalcinosis with renal damage. The extensive metaphyseal involvement leads to limitation of mobility and chronic pain.
- The literature describes patients treated with bisphosphonates and hydrochlorothiazide, with different results. For the moment our patient seems to have less pain.

1301 - P2.155

AN UNUSUAL CASE OF NEPHROTIC SYNDROME

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Aims/Purpose: Alport Syndrome is a genetically heterogenous disorder resulting from variants in genes coding for alpha-3/4/5 chains of Collagen IV, resulting in defective basement membranes in the kidney, cochlea and eye. The syndrome has different inheritance patterns: X-Linked (COL4A5 mutation); Autosomal recessive (homozygous or compound heterozygous mutations in COL4A3 or COL4A4 genes); and Autosomal dominant (heterozygous mutations in COL4A3 or COL4A4 genes). Almost all males with X-Linked Alport Syndrome (XLAS) progress to end stage kidney disease.

Methods: We present the case of a fifteen year old female, with nephrotic range proteinuria, hypoalbuminaemia, hypertension and haematuria. The patient underwent a kidney biopsy, with findings in keeping with focal segmental glomerulosclerosis. The patient's condition was refractory to steroid therapy.

Results: Steroid resistant nephrotic syndrome genetic testing revealed a novel, likely pathogenic variant in the COL4A5 gene – c.3722G > A, p.(Gly1241Asp). This variant had not previously been reported in literature. The c.3722G > A sequence change is predicted to cause the substitution of a highly conserved glycine residue for an aspartic acid residue, at positon 1241. Other amino acid changes at the same position have been reported in literature, in association with XLAS. Parental genetics were performed, both of which were negative. This suggests this variant arose de novo in this patient, supporting its pathogenicity.

Conclusion: We present the first published case of XLAS from a novel, heterozygous, likely pathogenic variant in the COL4A5 gene – c.3722G > A, p.(Gly1241Asp). Heterozygous females with XLAS can develop chronic kidney disease and hearing loss. Female patients should be followed in the same way as their male counterparts, with urinalysis, blood pressure monitoing, audiological and ophthalmological assessments. Further study into X-chromosome inactivation in tissue samples for Alport Syndrome is warranted. Clinicians should be mindful when reviewing kidney histology to include Alport Syndrome as a differential for female patients. COL4A-3/4/5 genes should be included in steroid resistant nephrotic syndrome genetic panels.

1304 - P2.156

CASE REPORT: A MILD CASE OF HYPOPHOSPHOREMIC HYPERCALCIURIA DUE TO SLC34A3 HETEROZIGOSITY

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Purpose and Introduction: Hereditary hypophosphatemic rickets with hypercalciuria is a rare and complex metabolic disorder characterized by increased urinary calcium excretion and reduced blood phosphate levels. This condition is determined by an SLC34A3 gene mutation which encodes for sodium-phosphate cotransporter NPT2c, essential for phosphate reabsorption in the proximal tubule of the kidney. In homozygosity or compound heterozygosity, the pathological condition is characterized by bone pain and deformities, rickets, osteomalacia and myopathy, with variable renal involvement. In heterozygosity, on the other hand, the pathology is characterized by reduced phosphate reabsorption and modest hypophosphatemia, increased 1.25-OH vitamin D levels, hypercalciuria, nephrolithiasis (the only sign in 15% of cases), nephrocalcinosis, but no bone demineralization or rickets. We present the case of a patient with hypophosphoremic hypercalciuria due to compound heterozygosity in SLC34A3 gene.

Case Presentation: The patient came to our attention following an episode of renal colic in January 2023. Imaging exams showed dilatation of the calyceal-pelvic cavities and the right ureter, with the presence of a kidney stone. Subsequent ultrasound follow-up showed persistent mild hyperechogenicity of the renal medulla bilaterally without features compatible with lithiasis. Laboratory tests revealed hypercalciuria (urinary calcium/creatinine ratio 0.69, normal value < 0.21) and hyperoxaluria (urinary oxalate/creatinine ratio 0.13, normal value < 0.06), with low blood phosphate levels (3.3-3.2 mg/dl, normal value 3.8). To rule out type 1 hyperoxaluria, AGXT gene analysis was performed by NGS sequencing, which was negative. Subsequently, a genetic panel for renal stone diseases was performed, identifying three variants in the SLC34A3 gene, one known as pathogenic (c.1246_1247delCT; p.Leu417fs*175) and the other two (c.1415C > T; p.Pro472Leu and structural variant chr9:140130635-140130946) of uncertain significance. The presence of pathogenic mutations in the SLC34A3 gene is compatible with the clinical picture of hereditary hypophosphatemia with hypercalciuria. This diagnosis was further supported by the patient's good response to phosphate supplementation, resulting in the normalization of calcium and phosphate levels.

Conclusions: The diagnosis of hypophosphoremic hypercalciuria is complicated by our current incomplete knowledge of SLC34A3 gene variants and the associated phenotypic spectrum. Many questions remain regarding the treatment and long-term management of this condition, including the role of phosphate supplementation in preventing the formation of kidney stones and the progression of bone disease, especially in cases characterized by simple heterozygosity.

1309 - P2.157

A CASE OF POSTNATAL BARTTER SYNDROME TYPE I WITH HYPERTRIGLYCERIDEMIA

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We present the case of a girl born in October 2023 at the Women's and Children's Hospital of Verona with a postnatal diagnosis of Bartter syndrome and, at 4 months of age, the development of significant hypertriglyceridemia.

Female, born at 29+2 weeks of gestation. During hospitalization, hypokalemic alkalosis, stunted growth, and constipation were observed, which led to a genetic investigation that was positive for Bartter syndrome due to a mutation in the SLC12A1 gene in apparent homozygosity (c.1316G > A). Prenatal investigations did not show any anomalies, and the presence of polyhydramnios had never been reported. A general urine examination revealed altered excretion fractions with mild urinary potassium, calcium, and chloride loss. Oral supplementation with KCl was initiated due to hypokalemia. In February 2024, follow-up blood tests revealed hypertriglyceridemia (2457 mg/dL) and hypercalcemia (11.3 mg/dL) with low parathyroid hormone (0.9 pmol/L), prompting admission to the Pediatric Ward. Exclusive feeding with low-fat milk was initiated upon admission, resulting in a gradual reduction in triglyceride levels. An abdominal ultrasound was performed, showing small gallbladder infundibular calculi, and hyperechoic renal medullas with hypotonia of the calyx-pelvic cavities. The lipid profile of the parents was normal, and genetic testing using NGS for dyslipidemia in the child was negative. Therefore, therapy with Indomethacin was started, and oral KCl supplementation was continued. Subsequent nephrological evaluations confirmed alkalosis with hypokalemia, mild hypernatremia, mild hypercalcemia with hypercalciuria (Ca/Cr 1.7 mol/mol), modest polyuria (4.8 cc/kg/hour), and hypotension.

We chose this clinical case due to the association between Bartter syndrome and hypertriglyceridemia, both rare in pediatric age. To our knowledge, data from the literature regarding the association between these two conditions are limited. A similar case of a child with a prenatal diagnosis of Bartter syndrome and onset of hypertriglyceridemia was described in England at the Bristol Royal Hospital for Children. Genetic investigation revealed Bartter syndrome type one with heterozygosity for two frameshift mutations (c.471delG in exon 3 and c.1041delT in exon 8) in the SLC12A1 gene. Further studies are needed to clarify if there is an association between these two clinical conditions and any underlying pathogenetic mechanisms.

1310 - P2.158

CASE REPORT: RENAL CYSTIC DISEASE CAUSED TO HETEROZYGOUS NEK8 VARIANT IN PEDIATRIC PATIENT

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Aims/Purpose: Polycystic kidney diseases (PKDs) are the most prevalent inherited kidney disease1. They are caused by pathogenic variants in genes encoding for proteins with roles in the functioning of primary cilium. They are also classified as Ciliopathy and can occur with isolated renal involvement with/without systemic manifestations. As 1 of the family of "Never in Mitosis A–related kinases" (NEK), NEK8 is a regulator of Hippo pathway. Biallelic NEK8 mutations are reported as causing a syndromic ciliopathy with multiorgan developmental defects, referred to as renal-hepatic-pancreatic dysplasia1. A recent paper1 analyzed a total of 21 patients from 12 families with heterozygous NEK8 variants and cystic kidney disease and proposed a dominant negative effect for specific heterozygous variants in the NEK8 kinase domain as a new cause of PKD.

Methods: We describe a case of PKD associated with NEK8 heterozygous mutation.

Results: 8 years old female patient accessed to Emergency Department with first evidence of isolated macro-hematuria. Previous medical history was unremarkable. The girl was afebrile, in good clinical condition, with elevated blood pressure values (120/82 mmHg) at the physical examination. The laboratory tests showed normal blood count with hemoglobin 11.7 g/dl, serum creatinine 0.42 mg/dl, no inflammatory markers. Urinalysis revealed proteinuria (100 mg/dL), hemoglobinuria, active urinary sediment with microhematuria (3557 red blood cell/microliter) and leukocyturia (535 white blood cells/microliter). An abdominal ultrasound study observed kidneys of increased size (longitudinal diameter of approximately 14 cm) with presence of multiple cystic formations with a maximum diameter of 2 cm and lost cortico-medullary differentiation; other organs were normal. Ultrasound findings were confirmed with MRI. The macrohematuria resolved quickly, however we recorded the persistence of positive urinary sediment. No other concomitant clinical manifestations were recorded and the cardiological evaluation was normal. Suspecting a cystic renal disease, we proposed a genetic analysis by whole exome sequencing (WES): an heterozygous NEK8 variant (c.133C > T, p. Arg45Trp) was found.

Conclusion: The patient's clinical history and onset of disease agree with the data described in the literature for the NEK8 variant c.133C > T, p. Arg45Trp. In literature all patients had an early onset of PKD. Enlarged kidney were present in 79%, followed by hypertension in 67% of cases; no patients had liver involvement, as in our patient. Thus, it is suggested to include NEK8 in the genetic analysis when PKD is suspected.

References

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1315 - P2.159

A HETEROZYGOUS LAMA5 VARIANT - CAUSE OF RENAL DISEASE IN A 17 YEARS OLD PATIENT

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Aims/Purpose: The glomerular filter consists of podocytes, fenestrated endothelial cells, mesangial cells and the glomerular basement membrane(GBM). The LAMA5 gene encodes laminin 5, an indispensable component of GBM. A homozygous pathological variant in LAMA5 is known to cause a systemic developmental syndrome including glomerulopathy, frequently manifested as nephrotic syndrome with onset before 4 years of age. However, the role of heterozygous LAMA5 gene variants in human renal diseases have remained unclear, but several previous publications suggested a clear association with adult-onset autosomal dominant focal segmental glomerular sclerosis(FSGS). We aimed to study the correlation between heterozygous LAMA5 variant of uncertain significance(VUS) found in a 17 years old patient with proteinuria and patient's phenotype.

Methods: We examined a 17 years old male patient who presented to our Clinic for persistent proteinuria and microscopic hematuria with onset 3 months prior to the referral to our Clinic, with normal urinalysis one year ago. We performed extensive urine and blood tests (including 24h urine collection, viral/parasitic serologies and immunological tests), kidney ultrasound, but also genetic tests (nephrotic syndrome panel) and kidney biopsy.

Results: The patient has 2nd grade obesity, nephrotic range proteinuria without features of full blown nephrotic syndrome, microscopic hematuria, normal renal function and normal blood pressure. There is no known history of renal disease. Both kidneys have slightly hyperechoic cortical appearance and right kidney is smaller (50 percentile). Viral/parasitic serologies and all immunological tests are normal. Kidney biopsy revealed mild GBM structural defect (thinning and lamellation) in some of the glomeruli and FSGS, but with podocytes foot processes preserved in most of the glomeruli. Genetic test revealed a heterozygous mutation in LAMA5 c.6371G > C,p.(Cys2124Ser)–VUS.

Conclusion: We consider there is a correlation between heterozygous LAMA5 variant identified in our patient and his phenotype, explicitly the histopathological findings (mild structual defect of GBM, FSGS), although at this moment we do believe that lesions of sclerosis found on biopsy are mostly, but not only, due to secondary FSGS (obesity, smaller right kidney). We identify the need to follow the clinical evolution and histopathological findings in this case in order to identify if this particular heterozygous mutation in LAMA5 is actually associated with autosomal dominant FSGS.

1326 - P2.160

EVALUATION OF KIDNEY FUNCTIONS IN PATIENTS WITH CYSTINURIA: SINGLE CENTER EXPERIENCE

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Aims/Purpose: Cystine stones may form in patients with cystinuria due to the low solubility of cystine at normal urine pH. The overall prevalence of cystinuria worldwide is 1 in 7000. In the general population, cystine stones account for 0.9-2% of all urolithiasis cases. It has been reported that 7-17% of urinary system stones in Turkey are cystine stones.

Methods: 24 children aged 0-18 years who were followed up with cystinuria in our pediatric nephrology outpatient clinic between January 2000 and January 2024 were retrospectively reviewed. Cystinuria was diagnosed as follows: detection of cystine stones in stone analysis, or high cystine levels in 24-hour urine or spot urine compared to the age group, or detection of significant disease-compatible mutations in the SLC3A1 and SLC7A9 genes, or cystine crystals in direct urine microscopic examination in patients with kidney stone. The patients' demographic information, laboratory values, number of surgeries due to urinary stones, and lithotripsy sessions to break down kidney stones were evaluated.

Results: The median age at diagnosis of our 24 patients was 4.14 (IQR 7.44) years, and the median follow-up period was 45.6 (IQR 81.9) months. 45.8% (n = 11) of the patients were female and 54.2% (n = 13) were male. 41.7% of our patients had stones in both kidneys, 37.5% had multiple or staghorn stones in a single kidney. While 54.2% of the patients did not need lithotripsy, 21% of them underwent 3 or more lithotripsy sessions. Open surgical interventions were performed in 79.2% of the patients. The average size of the largest kidney stones was 9.9 ± 5.2mm. There was no significant difference between the median glomerular filtration rates (GFR) at their first admission and at last follow-up (161.83 ± 54.61 ml/m2/min and 152.9 ml/m2/min respectively) (p =0.7). A negative correlation was detected between the patients' GFR at their last follow-up with the size of their kidney stones, and the number of open surgeries, but it was not statistically significant. Proteinuria and hypertension were observed in only one of our patients. Scar formation was observed in 81.8% of our 11 patients who underwent DMSA scintigraphy. Urine alkalinization was applied to 91.7% of the patients during treatment. While 29.2% of the patients stated that they used tiopronin treatment regularly, 25% used it for a certain period of time, and 45.8% did not use it at all.

Conclusion: Although hereditary stone diseases are expected to be diagnosed in early childhood, they can also be diagnosed at older ages. Cystinuria should be considered in patients with stones in both kidneys, multiple stones, and staghorn stones.

1327 - P2.161

PRIMARY HYPEROXALURIA IN CHILDREN, CLINICAL, GENETIC FINDINGS AND LONG-TERM OUTCOME. A SINGLE-CENTER STUDY IN SAUDI ARABIA

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Aims/Purpose: To identify most common genetic mutation in PH in Saudi Children and it's correlation with clinical presentation (Phenotype).

Methods: This is a retrospective study conducted at the King Faisal Specialist Hospital and Research Centre in Riyadh, Saudi Arabia. The study included all patients below the age of 18 at the time of diagnosis of PH from January 2014 to September 2023, while patients with incomplete data were excluded.

Results: A total of 20 cases with PH were included; male to female ratio was 1:1with a median age of 36 months [IQR: 6-66] at the time of diagnosis. Consanguinity is common, and 80.0% of our patient population has family history renal Stones. Clinical features included kidney stones (70.0%), failure to thrive (40.0%), nephrocalcinosis (45.0%), CKD stage 5 (45.0%), and hematuria (35.0%). Treatment modalities varied, with 75.0% were on conservative management, (45.0%) received liver transplants, while (10.0%) received dual kidney and liver transplants and the overall mortality rate was (10.0%).

Conclusion: PH type I is the commonest form of hyperoxaluria affecting Saudi children. The most common and frequently observed AGXT gene variant in this study was c.33dup p.(Lys12Glnfs*156) in (30.0%). There was no clear correlation between the genotype and phenotype, and different members from the same family sharing same genotype found to have different age at presentation. Early liver transplant has been found to be effective in preventing advanced kidney disease and the development of systemic oxalosis. Family screening, early recognition and confirmation of the diagnosis would facilitate early management and improve outcome. The use of mRNAi therapy (Lumasiran/ Nedosiran) that has been approved as the preferred treatment for PH type I has been started recently in our affected population. Overall, these findings contribute to a better understanding of the clinical spectrum and genetic variability of PH in Saudi Arabia.

1333 - P2.162

EXPLORING NUCLEOPORIN 205 (NUP205) DYSFUNCTION IN PEDIATRIC RENAL PATHOLOGIES: A CASE REPORT AND GENETIC INSIGHT

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Introduction: Nucleoporins are essential components of the nuclear pore complex (NPC), with few disease linked to NPC dysfunction. Mutations in genes encoding nuclear pore proteins (NUPs) are associated with steroid-resistant nephrotic syndrome (SRNS) and focal and segmental glomerulosclerosis (FSGS). Additionally, studies are attempting to demonstrate the association of mutations in NUP genes with ciliary dysfunction. However, the mechanisms underlying NUP deficiency in podocyte dysfunction and failure of the kidney filtration barrier remain unclear. Notably, nucleoporin205 (NUP205), a main component of NPC, has been implicated in a distinct form of SRNS describes in the literature as NPHS13.

Case report: A 1-year and 7-month-old boy presented at 3 months of age with bilateral renal hypoplasia, hyperechogenic kidneys, hyperparathyroidism, and hypotonia. He was born naturally at 39 weeks gestation, weighing of 5200 g and measuring 56 cm in length. Following birth, he required 45 days stay in the intensive care unit due to respiratory insufficiency. Additionally he presented increased creatinine (1.8 mg/dl), low serum calcium (8 mg/dl). Delayed psychomotor development was observed. Family history revealed parental consanguinity, and the patient has a half-sister from the father's side with significant neurodevelopment delay. Laboratory investigations showed elevated intact parathyroid hormone (PTH) levels (900 -1000 pg/ml; normal range < 99 pg/ml), with low calcium, elevated phosphorus, alkaline phosphatasse levels and serum creatinine. Albumin, calcium and vitamin D levels were within normal limits. Subnephrotic range of proteinuria was detected. Abdominal ultrasound revealed bilateral hypoplasic kidneys with markedly echogenic cortices (Fig.1). Genetic testing through Whole Exome Plus sequencing (Blueprint Genetics - Finland) identified the patient as homozygous for the NUP205 variant c.3128G > C,p.(Gly1043Ala), categorized as a variant of uncertain significance. No other variants were reported. Over time, we observed slow improvements in the kidney function and iPTH levels and he achieved satisfactory motor skill development with good neurological progress.

Results: The patient has a homozygous variant in the NUP205 gene, typically associated with SRNS and FSGS, his proteinuria is around 1g/day, but he does not have edema, hypoalbumiemia or high cholesterol. However, the presence of small kidneys and chronic renal failure with protein loss associated with hypotonia and developmental delay raises consideration for a potential ciliary dysfunction.

Conclusion: Considering the limited literature on the consequences of homozygous mutations in the NUP205 gene, it is important to consider this possibility from early days of life but also to remain vigilant for potential late-onset manifestations in affected patients.

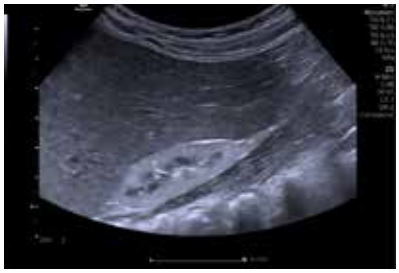

Fig. 1: Abdominal ultrasound

1342 - P2.163

RARE CASE REPORT: PATIENT WITH FANCONI SYNDROME, DISTAL RENAL TUBULAR ACIDOSIS AND AUTOIMMUNE HEPATITIS

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Aims/Purpose: Renal tubular dysfunction is definitely a rare disorder in pediatrics, but it is occurred commonly tubular isolated damage.

Methods: We presented a case with both proximal and distal renal tubular disfunctions and autoimmune hepatitis.

Results: A 14-year-old girl with incomplete Fanconi syndrome and liver abnormality with a history of salt appetite of childhood and growth retardation, genu valgus at 10-12-year-old was referred to our center. On admission, height -2.04 SDS, weight -2.09 SDS, polyuria and polydipsia, hepatosplenomegaly and elevated transaminases, alkaline phosphatase, gamma-glutamyl transferase test, mild anemia, level IgG 22.6 g/l, ESR 8 mm/h, eGFR 115 ml/min/1.73m2, hypophosphatemia (0.8 mmol/l) of renal origin (TmP/GFR 0.61), hypokalemia (2.2 mmol/l), non-anion gap hyperchloremic metabolic acidosis with alkaline urine, low molecular weight proteinuria, mild hypercalciuria, 2 stage nephrocalcinosis and medullary multiple cysts of kidney. No glycosuria, aminoaciduria, hyponatremia, hypouricemia were observed. Complementary tests no hepatitis C, B viruses, human immunodeficiency virus were observed. And no antinuclear antibodies, anti-SSA/SSB antibodies were observed. Slit-lamp examination of the cornea showed no cystine crystals. No history of nephrotoxicity drugs and herbals. Three time genetics testing detected no pathogenic variants. The patient was started on continuous replacement of substances lost in the urine and potassium citrate. In view of the autoimmune hepatitis, immunosuppressive treatment was initiated consisting of azathioprine (1.5 mg/kg/day) and prednisolone (1 mg/kg/day) with subsequent slow tapering to 0.12 mg/kg/day. After started azathioprine had been canceled due to vomiting. Follow-up after the first 6 months of treatments showed efficacy of liver but tubular dysfunction was no resolved, eGFR was normal.

Conclusion: We couldn't do kidney biopsy due to cysts and nephrocalcinosis. Monogenic disorders were excluded. Renal involved including Fanconi syndrome, distal renal tubular acidosis and autoimmune hepatitis may be manifestations of pediatric Sjögren's syndrome. But patient had laboratory test normal and was no developed sicca syndrome. Long-term follow-up is needed.

1357 - P2.164

FIVE CASES OF PERSISTENT PROTEINURIA DUE TO CUBN GENE MUTATION

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Aims/Purpose: To describe 5 cases of cubilin deficiency detected by our unit: 3 boys and 2 girls (two couples of them are siblings), all suffering from persistent proteinuria caused by a compound heterozygosity mutation in the CUBN gene encoding cubilin (chromosome 10). Cubilin is a transmembrane protein that mediates the reabsorption of ultrafiltered low-molecular-weight proteins into the proximal tubule. It facilitates the internalization of the intrinsic factor-vitamin B12 complex in the small intestine. Functional cubilin deficiency can cause isolated proteinuria or, if associated with megaloblastic anemia, the rare Imerslund-Grasbeck syndrome. No signs of progressive renal impairment are described. Our patients don't have B12 deficiency neither megaloblastic anaemia.

Methods Case Series: Results Nicolò, 4 years old, had an episode of macrohematuria diagnosed as post-infectious Glomerulonephritis due to SBEGA. Two months later, proteinuria and microhematuria were occasionally found also in his younger sister (23 months). During the follow-up of both patients, we noted significant glomerular proteinuria associated with normal renal function, C3 hypocomplementemia, mild von-Willebrand-factor deficiency. The little sister, who had more marked proteinuria, underwent kidney biopsy that showed "minimal interstitial fibrosis". Genetic analysis by NGS showed on both siblings a compound heterozygosity: variant p.Trp2120Ter (c.6359G > A), of paternal inheritance, already described in the literature as pathological, and variant p.Pro2822Leu (c.8465C > T), of maternal segregation, never described before.
Filippo, 8 years old, at the age of 3 months had an episode of UTI with the first finding of a mixed glomerular/tubular proteinuria confirmed at the follow-up for which ACE inhibitors and ARB therapy was started without results. Genetic analysis with NGS showed: compound heterozygosity of the variants c.9053A > C P.(Try3018Ser) and c.10102A > G p.(Met3368Val), both already reported in association with proteinuria.
Arianna, 2 years old, performed a urinalysis for stranguria and found proteinuria and microhematuria. During follow-up Arianna presented a significant glomerular proteinuria, associated with normal renal function. NGS genetic analysis revealed compound heterozygosity of the variants c.10397T > C and c10363-3A > G, classified as uncertain-meaning variants. However, they are similar variants of Cubilin classified as pathogenic.
The same variants was found in her older brother, Gerardo 7 y.o., that also presented proteinuria without any simptoms.
Conclusion: The presence of persistent proteinuria is not necessarily a pathological condition: in the specific case described, the clinical presentation seems to be a benign condition, not associated with renal damage that does not require specific therapy but deserves periodic follow-up.

1360 - P2.165

SEVERE AND RESISTANT HYPERNATREMIA IN A PREMATURE NEWBORN BABY

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Case Presentation: A 15-day-old male baby who was referred to our hospital due to resistant hypernatremia was admitted to the neonatal intensive care unit. From the patient's history, it was learned that he was 34 weeks premature, was born weighing 2610 grams via cesarean section, needed positive pressure ventilation and short-term intubation after birth, ampicillin and gentamicin treatments were started on the patient empirically due to high C-reactive protein level in the mother, and the patient also had a stage 1 intracranial hemorrhage and received dopamine infusion. It was noted that there was no consanguinity between the mother and father and the patient had a healthy 4-year-old sister. On physical examination, the patient's blood pressure was 85/50 mmHg, body temperature was 36.6˚C, peak heart rate was 130/min, he appeared slightly dehydrated, he was conscious and extubated. Other system examinations were normal. In biochemical examinations upon admission, serum urea value was 45 mg/dL, serum creatinine 0.60 mg/dL, sodium 169 mEq/L, potassium 4.5 mEq/L, albumin 4.4 g/dL. Hemogram, acute phase reactants, liver function tests, and thyroid function tests were normal. In blood gas, pH was 7.46, pCO2: 29.9, HCO3: 21. The patient was given intravenous fluid with a concentration of 1/5 saline of 180 cc/kg and sodium was monitored at 2-hour intervals. Despite fluid revisions, the patient's sodium level could not be reduced below 170 mEq/L in the follow-up. Due to the history of intracranial bleeding, the Pediatric Endocrinology department was consulted for central diabetes insipidus. A total of two doses of desmopressin 5 mcg were administered to the patient, but serum sodium levels did not change. The patient's serum osmolarity was 328 mOsm/kg (275-295), simultaneous urine osmolarity was 77 mOsm/kg, urine density was 1002-1003, and spot urine sodium was 15-30 mEq/L. Urine output was around 6.5-7 cc/kg/hr. Anti-diuretic hormone (ADH) level was found to be 21.47 pmol/L (< 13). Congenital nephrogenic diabetes insipidus was considered because the patient's existing hypernatremia did not improve with hydration, the patient was polyuric, his urine osmolarity was low, he was unresponsive to desmopressin, and his ADH level was high. The patient benefited significantly from hydrochlorothiazide, which was started at a dose of 5 mg/kg/day divided into two doses. Sodium levels gradually decreased to the normal range. The drug dose could be reduced during follow-up. Genetic analysis revealed a homozygous mutation in the AVPR2 (Exon3 c.856C > T) gene.

Conclusion: Congenital nephrogenic diabetes insipidus should be considered in cases of hypernatremia unresponsive to classical treatment approaches in newborns. ADH levels are usually normal or high. Sodium-restricted diet and diuretics such as hydrochlorothiazide are recommended to reduce the renal osmolar load.

1372 - P2.166

RENAL INVOLVEMENT IN TUBEROUS SCLEROSIS COMPLEX: RESULTS OF THE REGIONAL SURVEILLANCE PROTOCOL ALLOWED EARLY DIAGNOSIS OF RENAL ONCOCYTOMA IN AN 11 YEAR-OLD PATIENT

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Aims/Purpose: The study aims to establish renal involvement characteristics and evolution in patients affected by Tuberous Sclerosis. Furthermore, we evaluate systemic involvement and the effect of concomitant therapies on the clinical picture.

Methods: We started examining 10 affected patients, 3 males and 7 females, in January 2022. The patients underwent evaluation of renal function, blood pressure, renal sonography, brain and abdominal MRI. If necessary, additional tests were performed.

Results: Out of 10 patients (ages 10 to 17), 3 received prenatal diagnosis due to cardiac rhabdomyoma, 5 in the first year of life due to epilepsy, and 2 patients after the age of 10. These last carried the TSC1 mutation, the others were found to have TSC2 mutations in 6 cases, 1 had a contiguous TSC2/PKD1 gene syndrome, and another one had a still unidentified mutation. All patients showed multisystemic involvement with varying degrees of neurological impairment and mental retardation. Renal manifestations were detected in 9 out of 10 patients: AML 9/10 diameter < 3 cm, simple renal cysts 7/10, polycystosis 1/10, complex cyst 1/10, oncocytoma 1/10, hyperfiltration 9/10, hypertension 1/10, albuminuria 1/10, microhematuria 1/10. The age of onset of renal involvement cannot be determined since it was already present at the first evaluation. Notably, the only patient without lesions began therapy with Everolimus early for neurological indication. Renal function was normal in all patients, but hyperfiltration was present in 9 out of 10 cases, representing a risk factor for future kidney damage. During the re-evaluation conducted after one year, all patients showed a stable clinical picture, except for one patient who had a rapid growth of an oval renal lesion, which grew up to 78 mm. The patient underwent a lesional biopsy, which diagnosed the lesion as oncocytoma and required surgical treatment performed with robotics to spare the Kidney structure.

Conclusions: The management of these patients must necessarily be multidisciplinary. Renal disease, which is the main cause of morbidity and mortality in this pathology, must be evaluated and researched at the time of the first diagnosis. In pediatric patients, studies are necessary to assess the effectiveness of Everolimus therapy on renal lesions and the role of ultrasound surveillance in detecting neoplastic lesions.

1376 - P2.167

A CASE OF AUTOSOMAL-RECESSIVE RENAL TUBULAR DYSGENESIS SUCCESSFULLY SURVIVING WITH NEUROSENSORY HEARING LOSS DUE TO TWO DIFFERENT AND INDEPENDENT MUTATION

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Aims: We present a patient, female, 2 y.o., affected by Autosomal-recessive renal tubular dysgenesis (AR-RTD) associated with angiotensin-converting enzyme (ACE) mutations who is also affected by neurosensory hearing loss due to GJB2 gene mutation.

Method: She is a female firstborn by non-consanguineous parents without a family history of renal disease. The pregnancy was complicated by severe oligohydroamnios. After birth she required intubation, ventilation, endotracheal surfactant administration and inotropes support due to low blood pressures. Morover, she was treated with peritoneal dyalisis for 5 days. Increased serum renin levels (> 5500 mU/L) and low aldosterone values (< 3.7 ng/dL) were detected. Besides, sonography shows normal-size kidneys with poor corticomedullary differentiation. Genetic testing by Whole Exome Sequencing for nephropathies was performed and it revealed a homozygous mutation of the ACE gene (c.1831C > Tp Gln611er, chromosome 17) first time described. This lead as to the diagnosis of AR-RTD. After the neonatal unit discharge, she continued to experience frequent electrolyte fluctuations associated with low blood pressure. Therefore, in the sixth month of life, off-label therapy with mineralocorticoids (fludrocortisone) was started at a dosage of 0.05 mg/day. This maintained good blood pressure and electrolyte levels for a while and it improved Kidney function. However, our patient as a particularly fragile clinical balance, she seems to be extremely sensitive to minor changes such as mild infections, reduced water intake, or increased protein intake. Meanwhile, bilateral neurosensory hearing loss was discovered due to a pathogenic variant in heterozygosity of the GJB2 gene, it was treated with a right cochlear implant with good results.

Results: Actually, the little girl is currently on a low-protein diet, requires 0.1 mg of fludrocortisone per day and has recently started erythropoietin due to anaemia associated with renal failure. She has achieved good psychomotor development and has a normal facial appearance, with small stature and low weight.

Conclusion: AR-RTD is a rare genetic disorder caused by mutations in genes encoding the renin-angiotensin-system components: ACE, angiotensinogen, renin, and angiotensin II receptor type 1. The advancement of neonatal intensive care has allowed the survival of these patients. Up to now, the only drug effective in delay the onset of end-stage renal failure is fludrocortisone with low glucocorticoid effect and very high mineralocorticoid action.

1378 - P2.168

CRANIOECTODERMAL DYSPLASIA IS A RARE VARIANT OF CILIOPATHY. CLINICAL CASE

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Aims/Purpose: To present a rare clinical case of a patient with cystic renal dysplasia and an unusual phenotype.

Methods: Description of the clinical case.

Results: Cranioectodermal dysplasia (CED), OMIM 606045, is a very rare autosomal recessive disorder characterized by typical craniofacial features and skeletal anomalies, liver fibrosis, nephronophthisis and retinitis pigmentosa. Our patient, an 6-year-old boy, is the first child of healthy parents who were not related. He was born by planned CS at term (3.6 kg/50 cm). Dysmorphic signs noticed at birth comprised short limbs, dolichcephaly, high forehead, low-set prominent ears. He was observed by neurosurgeon and was underwent surgical treatment for craniosynostosis at 8 months. Signs of renal involvement were detected for the first time at the age of 5 years, when proteinuria appeared. A renal ultrasound showed enlarged kidneys with poor corticomedullary differentiation and multiple cysts up to 13 mm in diameter. Renal function was moderate reduced: creatinine IDMS - 60 µmol/l, urea - 6.6 mmol/l, cystatine C - 1.6 mg/l, eGFR «bedside» Schwartz - 73 mL/min/1.73 m^2, CKID U25 cysC - 49.4 mL/min/1.73 m^2, CKID U25 Cr+cysC - 57.6 mL/min/1.73 m^2; microalbuminuria (urinary albumin excretion per creatinine) - 40 mg/g. Arterial pressure was very high - up to 160/100 mm Hg (90 centile - 108/70 mm Hg), LVMI - 76,57 g/m^2,7 (90 centile - 40,18). No signs of renal anemia, CKD-MBD, hyrepuricemia, metabolic acidosis, congenital heart defects were found. Psychomotor development was normal and ophthalmological analysis revealed no evidence of retinal dystrophy, but showed mild myopia. Clinical examinations revealed hypotelorism, epicanthus, craniosynostosis, dolichocephaly, narrow thorax, brachydactyly, reduction of tooth enamel, microdontia, sparse hair. Antihypertensive and nephroprotective therapy was immediately started: enalapril 0.3 mg/kg/per day, then amlodipine 0.25 mg/kg/per day and carvedilol up to 0.2 mg/kg/per day were added). During the therapy, a significant improvement in well-being was noted. Blood pressure gradually decreased and after 6 months is 105-110/65-68 mm Hg, LVMI - 59,6 g/m^2,7. A search for pathogenic variants associated with ciliopathy was carried out. A previously undescribed pathogenic variant of the nucleotide sequence was identified in exon 30 of the IFT122 gene (chr3:129519662C > T) in a homozygous state, leading to missense replacement (NM_052985.4: p.(Pro1240Leu)).Pathogenicity prediction algorithms evaluate this variant as likely pathogenic. This variant (chr3:129519662C > T in the IFT122 gene) in a heterozygous state was detected in the proband parents and was confirmed by direct Sanger sequencing.

Conclusion: To identify a rare form of ciliopathy - CED - in patients with bilateral cystic renal dysplasia, it is important to take into consideration the characteristic phenotype.

1379 - P2.169

THE IMPORTANCE OF GENETIC TESTING IN CHILDREN FOR THE EARLY DIAGNOSIS OF ALPORT SYNDROME SECURING PROMPT TREATMENT INITIATION, BETTER PROGNOSIS, CASCADE SCREENING AND ACCURATE GENETIC COUNSELING

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Aims/Purpose: In this study we aimed to diagnose Alport Syndrome (AS) in children that fullfilled criteria of the disease using Next Generation Whole Exome Sequencing (WES). Alport Syndrome is a well described glomerulopathy that can lead to end stage renal disease. Genetic pathogenic variants in COL4A3, COL4A4 and COL4A5 consist the main genetic cause and produce phenotypes that vary from microscopic hematuria, microalbuminuria, significant proteinuria and chronic renal disease. Disease progression can be significantly delayed after prompt treatment with angiotensin converting enzyme (ACE) inhibitors in childhood.

Methods: Inclusion criteria were renal (hematuria, proteinuria, chronic renal disease) and/or extrarenal (neurosensory hearing loss, refractory visual impairment) manifestations of AS combined with positive family history. Families were referred to our clinic or came voluntarily seeking definitive diagnosis. After acquiring a thorough medical history and clinical examination we obtained consent for proceeding with Next Generation Whole Exome Sequencing using blood sample from patients.

Results: During the last 2 years we diagnosed 9 children with Alport Syndrome with pathogenic genetic variants in COL4A3, COL4A4 and COL4A5. In 3 cases the pathogenic variant was in COL4A5 generating diagnosis for Alport Syndrome 1, X- linked. In 4 cases the pathogenic variant was in COL4A3 generating diagnosis for Alport Syndrome 3, autosomal dominant. In 2 cases the pathogenic variant was in COL4A4. In 1 case the patient was compound heterozygote and was diagnosed with Alport syndrome. In 1 case the patient was carrying only 1 variant and was diagnosed with familial benign hematuria. Cascade testing was performed revealing further patients with Alport syndrome in 7 cases. Additionally, parents of patients from our cohort (3 cases) received a definitive diagnosis of Alport Syndrome, although they had a prior non- conclusive renal biopsy. Treatment with ACE inhibitors was initiated according to clinical indications. At the time of presentation all patients had microscopic hematuria. In 5 cases there was isolated microscopic hematuria.In 4 cases there was combined microscopic hematuria and proteinuria. In 4 families there was a positive family history of extrarenal manifestations. In 3 cases neurosensory hearing loss was present. In 1 case refractory visual impairment was present.

Conclusion: It is becoming increasingly established that genetic testing exceeds the need for renal biopsy for the definitive diagnosis of Alport Syndrome. Targeting these patients in early childhood secures prompt treatment initiation and improves prognosis. Furthermore, all family members at risk can benefit from a definitive diagnosis, genetic consultation and treatment.

1397 - P2.170

PEDIATRIC NEPHROLITHIASIS: CLINICAL MANIFESTATIONS AND METABOLIC CHARACTERISTICS, DATA FROM A DEDICATED CLINIC

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Purpose: The prevalence of nephrolithiasis in children has increased over the past two decades. Among children with nephrolithiasis, there is a high incidence of metabolic and genetic risk factors and thus recurrence of stone disease is common. Despite the relatively high incidence of metabolic and genetic risk factors, the detection rate of these underlying diagnoses remains variable. The aim of our study was to evaluate the incidence of metabolic abnormalities in pediatric patients followed in a multidisciplinary pediatric stone clinic.

Methods: Retrospective review of 164 patients who presented to our dedicated multidisciplinary nephrolithiasis clinic. To define or exclude a specific metabolic abnormality, at least 2 separate metabolic evaluations were done, including 24-hour urine collections or spot urine sample (the latter was primarily used in incontinent children.)

Results: The mean age at first stone presentation was 7.8 ± 5.6 years, 96/164 58.5% were boys, 44/164 (26.8%) had a family history of stone disease, 112/164 (68%) were symptomatic at presentation, and 55/164 (33.5%) had an anatomic abnormality. Full metabolic evaluation was completed in 139/164 (84.7%). At least one metabolic risk factor was identified in 110/139 (79.1%) including: hypercalciuria in 54/139 (38.8%); hypocitraturia in 60/139 (43.2%), hyperoxaluria in 25/139 (18%) and cystinuria in 4/139 (2.9%). Either a metabolic or anatomic abnormality were found in 121/139 patients (87%). Approximately half of the patients had stone available for analysis. Of these, the most common stone composition was calcium oxalate. An apparent monogenic abnormality was found in 18 patients including: primary hyperoxaluria (type 1 or 3) (n = 7), CYP24A1 mutation (n = 7), SLC3A1 mutation (n = 1), cystinuria (n = 4), distal renal tubular acidosis (n = 1) and autosomal dominant polycystic kidney disease (n = 3). Of the 139 patients who completed metabolic evaluation, 121/139 were recommended either specific dietary modifications and/or drug therapy, with around half of these patients receiving at least one prescribed medication (including Citrate supplementation, thiazide treatment and/or thiola).

Conclusion: With thorough investigation, a modifiable risk factor for nephrolithiasis can be found in a high percentage of pediatric patients, enabling tailored recommendations to reduce the recurrence or progression of stone disease.

1399 - P2.171

RENAL MANIFESTATIONS IN TUBEROUS SCLEROSIS COMPLEX AND MTOR INHIBITOR THERAPY: A RETROSPECTIVE COHORT

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Aims/Purpose: Tuberous sclerosis complex (TSC) is a genetic disorder where anomalous activity of the mammalian target of rapamycin leads to multiple organic features, including the kidneys. The most frequent renal manifestations are angiomyolipomas (AML), for which the mammalian target of rapamycin inhibitors (mTORi) has been a paradigm shifting therapeutic. Our aim was to analyze renal outcomes of patients with TSC with and without mTORi therapy.

Methods: Retrospective cohort study enrolling patients (children and adults) with TSC followed in a level III hospital, between 2016 and 2024. Sociodemographic, clinical and laboratorial data were analyzed. Baseline and last follow-up estimated glomerular filtration rate (eGFR) and CKD stage (based on eGFR) was compared between patients with and without mTORi therapy. AML's largest dimension was analyzed in patients under mTORi therapy (pre and post therapy).

Results: 46 patients were included, 30 (65.2%) were male. Mean age was 18.2 years (IQR 10.2-24.0) and mean time of follow-up was 6.1 years (IQR 1.2-11.9). Eleven (23.9%) patients had prenatal diagnosis. Regarding genetics, TSC2 mutation was present in 20 (68.9%) patients, TSC1 in 9 (19.6%) and TSC2/PKD in 3 (6.5%). Of all, 19 (41.3%) were submitted to mTORi (18 everolimus, 1 sirolimus) for a mean time of 30.2 months (IQR 25.9-57.8). At baseline follow-up, 8 patients had CKD stage ≥ 2 (KDIGO) and mean eGFR was similar between groups (mTORi 131 vs no mTORi 124 mL/min/1.73 m2, p =0.368). No patient was under dialysis. At last follow-up, mean eGFR remained without differences between groups (mTORi 129 vs no mTORi 132 mL/min/1.73 m2, p =0.961), and 8 (17.4%) patients with CKD (based on eGFR), where 1 (2.2%) patient showed CKD stage improvement and 3 (6.5%) revealing progression. Regarding other renal manifestations, 30 (65.2%) presented multiple kidney cysts, 26 (56.5%) had AML and 3 (6.5%) had polycystic kidney disease. Those with AML, 11 (23.9%) were under mTORi and 8 (17.4%) showed AML reduction: ≥ 50% reduction in 2 (4.4%), 30-49% reduction in 2 (4.4%) and ≤ 30% reduction in 7 (15.2%). Two patients under mTORi therapy revealed AML dimension increase between evaluations.

Conclusion: Therapy mTORi appeared to be effective and safe in reducing AML secondary to TSC, in line with recent evidence. Possible effect of mTORi in CKD progression shall be further investigated in long-term follow-up.

1434 - P2.172

UROTENSIN-II GENE POLYMORPHISM AND SERUM UROTENSIN-II LEVELS IN CHILDREN WITH BARTTER SYNDROME

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Aims / Purpose: Bartter syndrome is a rare hereditary renal tubular disorder characterized by hypokalemia, hypochloremia, metabolic alkalosis, and hyperreninemia. One of the most important findings is normal blood pressure despite high renin and aldosterone levels. Urotensin II is the most potent vasoconstrictor known. It also possesses vasodilator activity in certain vascular beds, and much is still to be learnt regarding its actions on vascular tone. No study has investigated the urotensin-II (U-II) gene sequence or level in children with Bartter syndrome. Considering U-II's renal synthesis and vasoactive role, this study aimed to examine the gene sequence of U-II in children with Bartter syndrome, measure its serum levels, and investigate its relationship with other clinical and laboratory findings.

Methods: The study included 46 patients under 18 years of age diagnosed with classical Bartter syndrome by clinical and/or genetic study and 41 healthy volunteer children. Genomic DNA isolation was performed using the spin column method with a commercial kit (Jena Bioscience). The gene containing four exon regions was amplified using PCR with appropriate primers designed for these regions (3Prime, Techne). Urotensin-II level was determined in serum samples by using the ELISA method. SPSS 23 IBM statistical package program was used for data evaluation

Results: The average age at diagnosis was 2.08 + 3.15 years, and 22 of 46 were male. The sequence analysis results performed in the four exon regions of the U-II gene revealed that single nucleotide polymorphisms, rs228648 in the 1st exon, rs228650 and rs228651 in the 2nd exon, were detected. The r228651 variant showed a significant difference between the control and patient groups (p =0.025), and the GG wild-type genotype was more common than the GA+AA genotypes in Bartter syndrome children. The blood pH level at diagnosis was higher in patients with the rs228648-CT genotype (p =0.045), and the creatinine value was higher in patients with the rs228650-CC genotype (p =0.035). The rs228651-GG genotype was found to be more common in the patient group (63% vs 39%, p =0.025), and the serum mg level at diagnosis was lower in patients with this genotype (p =0.032). The serum U-II level was higher in patients with the rs228651-GA genotype (p =0.043). No statistically significant relationship was observed between the clinical and laboratory parameters at the initial diagnosis and during the study and the serum U-II level. Serum U-II levels did not vary according to genotypes in the Bartter patients and controls.

Conclusion: The rs228648, rs228650, and rs228651 polymorphisms of the U-II gene may contribute to some laboratory variability in classical Bartter syndrome. However, more studies are needed to interpret its exact role in this disease.

1467 - P2.173

ALPORT SYNDROME IN ICELAND: EPIDEMIOLOGY AND OUTCOMES

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Aims/Purpose: Alport syndrome (AS) is caused by mutations in the collagen IV genes, COL4A3, COL4A4 and COL4A5. Three types of AS have been described: X-linked (XLAS) autosomal recessive AS (ARAS) and autosomal dominant AS (ADAS). The aim of this study was to examine the epidemiology and outcomes of AS syndrome in Iceland in the period 1968-2023.

Methods: Patients were identified by family tracing of index cases, and by retrospectively searching both the Icelandic Renal Registry and the national electronic health record systems for ICD-10 codes indicative of AS. Medical records were reviewed to confirm AS. Clinical characteristics, family history and genetic testing were used for the diagnosis of XLAS. Persistent hematuria in the index case where 1 or both parents were also affected was defined as ARAS, and the diagnosis of possible ARAS was made in an individual with isolated glomerular hematuria if neither parent had hematuria. End-stage kidney disease (ESKD) was defined as the need for kidney replacement therapy.

Results: We identified 76 individuals with AS, 52 with XLAS (13 males), 2 females with ADAS and 22 (8 males) with ARAS or suspected ARAS. Out of 52 XLAS cases 45 were confirmed with genetic testing. Both ADAS cases were confirmed with genetic testing but no ARAS case. The mean (± SD) age at the diagnosis of XLAS was 28.5 (± 22.3) years but 10.2 (± 9,8) years for ARAS and 2 sisters were diagnosed with ADAS at the age of 2 and 3 years. No ARAS patient had albuminuria at latest follow-up and all had normal kidney function. The prevalence of XLAS in January 2024 was 11.5 per 100,000 population. The average yearly incidence for XLAS in the last 10 years was 0.54 per 100,000 population. A total of 10 patients with XLAS developed ESKD, 7 men and 3 women, at the median age of 19 [16, 25] years for males and 60 [37, 69] years for females.

Conclusion: The prevalence and outcomes of XLAS in Icelandic the population are similar to other Western countries. A high proportion of men with XLAS develop ESKD. The outcome of ARAS and ADAS in our study population is excellent but longer follow-up is needed to determine outcomes.

985 - P2.174

INTERVENTIONS IN CHILDREN WITH RENOVASCULAR HYPERTENSION: A SINGLE-CENTER EXPERIENCE

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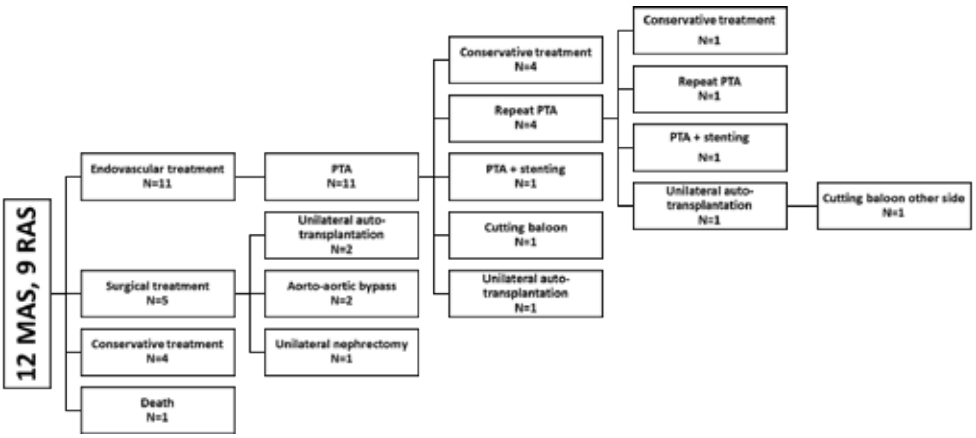
Aims/Purpose: Renovascular hypertension (RVH) is a rare cause of high blood pressure in children that is secondary to renal artery stenosis (RAS) and/or middle aortic syndrome (MAS). MAS is characterized by severe narrowing of the distal thoracic and abdominal aorta, frequently involving both visceral and renal arteries. When severe, RVH is usually poorly responsive to medical therapy including angiotensin-converting-enzyme inhibitors, beta-blockers and arterial vasodilators. In these cases, different procedures including percutaneous transluminal angioplasty (PTA), stent implantation, and surgery (vascular bypass, renal auto-transplantation) are used.

Methods: We retrospectively evaluated the clinical outcomes of 12 children with MAS and 9 patients with RAS admitted to the Bambino Gesù Children's Hospital in Rome from February 2006 to April 2023. All children were diagnosed by angiography. Data on initial presentation, treatment and follow-up were recorded.

Results: Blood pression (BP) at presentation was above the 99th centile for age, gender and height in all children. Median age at presentation was 6 years. Genetic conditions were present in 11 (55%) of patients. Neurofibromatosis type I (NF-1) was the most common syndrome. One patient with extended and extremely severe vascular narrowing died from multiple organ failure. During follow-up, several interventions were performed, as shown in Figure 1. Blood pressure control was achieved only with anti-hypertensive medications in 4/21 (19%) patients. Of the 11 patients who underwent primary endovascular treatments, 7/11 (63%) required repeat treatment that allowed in 6 patients reducing the dose and number of antihypertensive drugs. Of the 5 patients who underwent primary surgical treatment, early improvement of BP after surgery was observed in 4. Overall, 18/20 (90%) patients had normal kidney function at the last follow up.

Conclusion: Our results are in line with previous data from the literature showing better outcome in patients that have undergone surgery without attempting PTA before the surgical procedure. PTA alone does not achieve long-lasting improvement in most cases, especially in patients with MAS. Nonetheless, it helps delaying surgical revascularization until adolescence, when the surgical procedure can be optimally performed.



1328 - P2.175

SUCCESSFUL EMERGENCY KIDNEY AUTOTRANSPLANTATION IN A CHILD WITH RENOVASCULAR DISEASE

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Aim: Renal artery occlusion is a rare but potentially catastrophic complication of paediatric endovascular renal artery interventions. Emergency autotransplantation may be required to salvage the kidney, though to date this has only been described in adults. We report our experience of performing emergency kidney autotransplantation following acute renal artery thrombosis in a 20-month-old child undergoing redo renal artery angioplasty.

Method: Retrospective clinical case report describing with the surgical and medical management with 10-year follow-up in addition to a review of the current literature.

Results: 20-month old child presented with refractory hypertension and hypertensive cardiomyopathy secondary to multifocal fibromuscular dysplasia with a single functioning kidney. Acute thrombosis of the renal artery during redo-endovascular balloon angioplasty necessitated emergency renal autotransplantation. There was a functional warm ischaemia time of two hours intraoperatively. He had stable kidney function for 4 years following the auto transplant with no left ventricular hypertrophy on echocardiography. 9 years post-procedure he has an eGFR of 14.8ml/min/1.73m2 with a BP of 92/66mmHg on three antihypertensives.

Conclusions: Acute kidney injury sustained as a result of unintentional renal artery occlusion during endovascular intervention is potentially reversible with benefit to renal function in the short-term follow up. However, long-term optimal outcomes are not guaranteed in this disease especially in the context of extended functional warm ischaemia time. We recommend that high-risk patients undergoing renal artery intervention do so at centres with renal and vascular surgical backup on-site.

706 - P2.176

ANTI-CD19 CAR T-CELL THERAPY IN A HIGHLY SENSITIZED PATIENT AFTER FAILING A FIRST KIDNEY TRANSPLANTATION

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Aims/Purpose: To date, several desensitization protocols have been attempted in hyperimmune patients, with conflicting results. Recently, we have treated with autologous CD19 CAR T cells a highly sensitized 18-years-old woman who had failed a first kidney transplant at the age of 3½ years due to recurrence of focal and segmental glomerulosclerosis (FSGS). When she was listed for re-transplantation at age 14 years, panel reactive antibodies (PRA) showed 80% and 89% reactivity against class I and II HLA antigens, respectively. After several years on a national waiting list for hyperimmune patients, she was treated with anti-CD19 CAR T cells in the attempt to decrease her degree of sensitization.

Methods: CD19 CAR T cells were produced using a lentiviral second-generation CAR construct and an automated, Prodigy®-based manufacturing process. The patient received lymphodepletion with fludarabine 24 mg/sqm/day on day -5/-4/-3 and cyclophosphamide 250 mg/sqm/day on day -4/-3. Hemodialysis was performed daily, starting 12 hours after the end of chemotherapy, to avoid toxicity. CD19-CAR T cells were administered at a dose of 1 x 106 viable CAR+ cells/kg on day 0.

Results: CAR T-cell therapy was well tolerated, with only self-limited grade 1 cytokine release syndrome (CRS) and grade 1 immune effector cell-associated neurotoxicity syndrome (ICANS). Complete B-cell depletion in peripheral blood and in the bone marrow were rapidly achieved. At 6 months, the bone marrow showed no detectable short-and long-lived plasma cells. Antibodies against HLA antigens progressively decreased in the 6 months following CAR-T cell infusion. After 6 months, the PRA titers had decreased from 92% and 89% to 75% and 65% for class I and class II antigens, respectively. These changes are expected to increase the likelihood of finding a compatible cadaveric kidney by 2 to 3-fold in a "standard" waiting list, and considerably more if subjects have access to prioritized programs for hyperimmune patients. Unexpectedly, after 5½ months after CAR T-cells therapy, the patient was offered a fully compatible deceased-donor kidney, with 5/6 antigen match and a negative crossmatch performed with sera harvested before CAR T-cell therapy. She however, rapidly developed recurrence of FSGS. Treatment included plasmapheresis and two infusions of daratumumab (16 mg/Kg/dose), to which she has responded incompletely. Anti-nephrin antibody titers before and after transplantation were negative.

Conclusion: These results suggest that anti-CD19 CAR T cells can produce sustained reduction of anti-HLA antibodies in sensitized patients awaiting kidney transplantation. It also suggests that B cells may not be involved in post-transplant FSGS recurrence when patients have no circulating anti-nephrin antibodies.

691 - P2.177

PERCUTANEOUS BIOPSY UNDER DEEP INTRAVENOUS OR CONSCIOUS SEDATION: WHICH IS THE BEST OPTION FOR PEDIATRIC RENAL TRASPLANT RECIPIENTS?

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Aims/Purpose: Percutaneous renal allograft biopsy is a routine procedure in the diagnostic work up of kidney transplant recipients. As it is a minimally invasive procedure in transplant recipients, even in childhood and adolescence, it can be performed by administering conscious sedation or intravenous sedation, according to age and compliance. We examined differences in safety, efficacy and renal findings between biopsies performed under intravenous sedation and conscious sedation in paediatric and adolescent renal transplant recipients.

Methods: We retrospectively analysed all the percutaneous ultrasound-assisted biopsies performed at our Paediatric Transplant Centre from January 2014 to January 2024. Differences in length and composition (cortex/medulla) of the core, number of glomeruli, complications and achievement of a renal pathology diagnosis after percutaneous biopsy performed under conscious sedation or deep intravenous sedation were evaluated. Furthermore, indications for biopsy and complications of intravenous sedation were analysed. Biopsies performed under general anaesthesia (with intubation) were excluded.

Results: In the study period, 523 biopsies were performed in 167 patients (67% male and 33% female, median age at the time of biopsy 13 years). Median time between transplantation and biopsy was 2 years. Indication to biopsy was per protocol in 62% and per cause (allograft dysfunction, circulating donor specific antibodies, proteinuria) in 38% of cases. Biopsies performed under intravenous deep sedation (group 1) were 441 (84%) and those under conscious sedation (group 2) 82 (16%). Mean age of patients at the time of biopsy was 10 years in group 1 and 19 years in group 2. Difficult sampling was encountered in 21% of group 1 vs 10% of group 2. Mean length of cores was 1 cm (both first and second specimen) in group 1 and 1 cm (first specimen) and 0,3 cm (second specimen) in group 2. The second specimen was not collected in 19% of cases in group 1 and in 22% in group 2. Medulla was prominent (> 50% of the core) in 12% of samples in group 1 vs 15% of group 2. Mean number of glomeruli was 24 in group 1 and 13 in group 2. Samples were not adequate (according to Banff criteria) in 11% of cases in both groups. Complications of biopsy were observed in 10% of cases in group 1 vs 8% in group 2. Complications of deep sedation was observed in 4% of the procedures. The same data were collected in the subgroup of adolescents undergone to intravenous sedation (mean age 17 years) and compared with those of group 2 (mean age 19 years).

Conclusions: No significant differences between biopsies performed under deep sedation and conscious sedation were observed in terms of safety, efficacy and renal findings in paediatric and adolescent renal transplant recipients. Other factors (such as emotional aspects and economic issues) must be taken into account in preferring intravenous rather than conscious sedation.

642 - P2.178

ENDOTHELIN-1 TYPE-A RECEPTOR ANTIBODIES IN PEDIATRIC KIDNEY TRANSPLANTATION: SINGLE CENTER EXPERIENCE

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Aims/Purpose: HLA donor-specific antibodies (HLA DSA) are a significant risk factor for kidney transplant failure. However, recent studies have shown that non-HLA DSA, such as endothelin-1 type-A receptor antibodies (ETAR-Ab), might induce an antibody-mediated rejection. The interaction between ETAR and ETAR-Ab can cause vasoconstriction, cell proliferation, and inflammatory processes, leading to hypertension and graft failure.

Methods: We determined the presence of ETAR-Ab at 6 and 12 months from transplantation (times of protocol biopsies) or in the case of biopsies performed for clinical indications in 40 kidney transplanted patients at the Bambino Gesù Children's Hospital in Rome. In addition, we assessed at the same timepoint angiotensin II type-1 receptor antibodies (AT1R-Ab), HLA DSA, and the presence of antibody and T-cell mediated rejection.

Results: Results are shown in Table 1. ETAR-Ab positivity exists in half of the population, mainly in younger and male subjects, with no difference between living or deceased donors. We observed an ETAR-Ab / AT1R-Ab concordance in 92.5%, whereas no correlation was noticed between ETAR-Ab and HLA DSA or acute rejection episodes. No significant difference in the number of hypertensive patients or eGFR values was reported between ETAR-Ab positive and negative.

Conclusion: These preliminary data indicate that ETAR-Ab positivity occurs frequently in pediatric kidney transplants, particularly in young and male subjects, and is often associated with AT1R-Ab positivity. Conversely, little correlation between ETAR-Ab and HLA DSA was observed. Differently from what was reported in the literature, no increased risk of rejection emerged, possibly because of the small size of the sample and the short follow-up. In conclusion, ETAR-Ab and AT1R-Ab could have a synergistic and pathogenetic role in rejection HLA DSA negative, but further studies with prolonged follow-up are needed in pediatric kidney transplants.

Table 1. Population Characteristics (n = 40).

	ETAR-Ab + N= 21 (52%)	ETAR-Ab - N= 19 (48%)
Mean Age (years)	11.8	17.4
Gender M / F (%)	71 / 29	58 / 42
Donor L / D (%)	38 / 62	37 / 63
eGFR (ml/min/1.73 m2)	81	77
Proteinuria (UPCR> 0.2 mg/mg)	4	5
Hypertension (>95° for age/height)	15	11
ARB treatment (n)	11	3
Anti-AT1R + (n)	18	0
Anti-HLA DSA I class + (n)	2	1
Anti-HLA DSA II class + (n)	7	4
Protocol Biopsy at 6 months AMR (n)	0	0
Protocol Biopsy at 12 months AMR (n)	1	0
Protocol Biopsy at 6 months TCMR (n)	4	4
Protocol Biopsy at 12 months TCMR (n)	3	2
Indication Biopsy (n)	9	11
Indication Biopsy AMR (n)	2	2
Indication Biopsy TCMR (n)	3	5

ETAR: anti-endothelin subtype A receptor; L/D: living/deceased; UPCR: urinary protein creatinine ratio; ARB: angiotensin receptor blockers; AT1R: anti-angiotensin II type I receptor; HLA DSA: human leukocyte antigen donor-specific antibody; AMR: antibody-mediated rejection; TCMR: T-cell-mediated rejection.

580 - P2.179

IMPACT OF VIRAL INFECTIONS ON GRAFT FUNCTION AFTER PEDIATRIC KIDNEY TRANSPLANTATION: A RETROSPECTIVE MONO CENTRIC ANALYSIS

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Aim/Purpose: Infections and reactivations of CMV, EBV, BKV after kidney transplantation (KTx) are frequent complications especially in the first years posttransplant and may have an effect on graft function. The susceptibility, the duration of DNA prevalence, and the control of the infection seem to not only depend on immunosuppressive therapy and the virus status of donor and recipient before but also on the individual immune response after KTx. Different therapeutic concepts are favored. The influence of the outcome on graft function is unclear.

Methods: In this retrospective monocentric analysis, 95 of 258 children after KTx between 2004-2022 were included and a total of 139 CMV, BKV or EBV episodes occurred in the first 3 years after transplantation. The time, type, duration, their influence on estimated glomerular filtration rate (eGFR), and graft rejection rate during the infection period were analyzed. The results were correlated with the respective therapy.

Results: Mean age at KTx was 8.6 years with a follow-up of 29.5 (± 9.9) months. EBV was detected in 54%, BKV in 29%, and CMV in 17% of patients. EBV-infections occurred mainly in the 2nd and 3rd year after KTX. CMV-infections were evenly distributed over the three years while BKV infections predominately occurred in month 4-12 after KTx. The average time of detection in the blood-PCR was 4.3 (± 6.2) months for EBV, 4.1 (± 7.8) months for BKV and 2.7 (± 4.4) months for CMV, respectively. Treatment options were categorized into three groups, I) use of an antiviral agent, II) modification of immunosuppressant medication, and III) "watchful waiting". Antiviral therapy was used in 19% (n = 28). Immunosuppression was modified in 20% (n = 29). No specific therapy was administered in 61% (n = 91) of cases. The majority of immunosuppressive drugs were switched from a combination of calcineurin inhibitor and mTOR inhibitor to a monotherapy of mTOR inhibitor and prednisolone in 14% of cases. No significant difference regarding ΔeGFR before and after infection in the various treatment options was seen. Patient in most groups had a slight reduction of ΔeGFR (mean 3.63.6 ml/min/1.73m2), without statistical significance. The greatest decrease in ΔeGFR was shown in patients with EBV infection in group II (mean difference of ΔeGFR of 10.6 ml/min/1,73m^2 (p =0.13, N = 9). Patients with BKV infection (3 patients with biopsy-proven BK nephropathy) even had an improvement of ΔeGFR of 5.1 (p =0.553, N = 4) and 2.83 ml/min/1,73m2 (p =0.37, N = 16) in groups I and II. Rejections were found in two thirds of the indicated biopsies (N = 60) performed during the periods of infection. In most cases, borderline changes followed by acute cellular rejection were reasons for treatment; these occured predominant in the group with BKV infections.

Conclusion: This study showed that the eGFR remained stable despite infection with EBV, BKV and CMV after KTx, regardless of the type of treatment.

530 - P2.180

METABOLIC COMPLICATIONS FOLLOWING PEDIATRIC KIDNEY TRANSPLANTATION: TUNISIAN SERIES

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Aim: To study the main metabolic complications in pediatric post-kidney transplantation (KT).

Methods: This was a retrospective study conducted in the pediatric nephrology department of Charles Nicolle hospital, Tunis, Tunisia over a period of 34 years (from January 1, 1989, to December 31, 2022). Renal transplant patients under the age of 20 were included in our study.

Results: A total of 97 patients were included. We reported 9 cases (9.3%) of new-onset diabetes after transplantation (NODAT), of which 1 (11.1%) subsequently experienced rejection. This diabetes was transient in 2 cases. The median triglyceride level post-transplantation was 1.63 ± 0.75 mmol/l. Hypertriglyceridemia relative to age was found in 41 cases (42.3%), of which 13 (31.7%) subsequently experienced rejection. The mean uric acid level post-transplantation was 367.5 ± 107.6 µmol/l. Hyperuricemia was found in 29 cases (29.9%), of which 13 (44.8%) subsequently experienced rejection.

Conclusion: Metabolic complications occurring in pediatric post-renal transplantation are common. Close monitoring of the transplanted child is paramount.

523 - P2.181

CHARACTERISTICS OF REJECTION IN TUNISIAN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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Aims: Kidney transplantation (KT) is currently the preferred treatment for end-stage renal disease (ESRD) in children, enhancing both their survival rates and quality of life. Rejection poses as one of the potential complications that may compromise the survival of the transplant. The aim of our study was to investigate the characteristics of renal transplanted children who presented kidney rejection (KR).

Methods: This was a retrospective and descriptive study that included renal transplanted children followed in the Pediatric services of Charles Nicolle Hospital in Tunis over a period of 34 years (from January 1, 1989, to December 31, 2022). We included patients who underwent RT at an age younger than 20 years old. For patients who received more than one transplant, each transplantation was considered as an independent procedure.

Results: 97 patients were included in our study. There were 56 boys and 41 girls, with a male-to-female sex ratio of 1.4 [Rejection (+): M/F = 0.8 versus (VS) Rejection (-): M/F = 1.6]. The average age of recipients at the time of RT was 15.4 ± 3.2 years [Rejection (+): 15.4 ± 2.4 VS Rejection (-): 15.4 ± 3.5 years]. The median time between the onset of ESRD and RT was 23 months [15 – 43.6] [Rejection (+): 19.5 months [12.5 – 41.7] VS Rejection (-): 23.8 months [15.4 – 44]]. Twenty-two patients (22.7%) experienced at least one histologically proven humoral rejection. The median time from transplantation to rejection diagnosis was 62 months [23 – 102]. Rejection occurred early in 18.2% (n = 4) and late in 81.8% (n = 18) of cases. Clinical manifestations of rejection were predominantly gastrointestinal symptoms, such as diarrhea and/or vomiting, observed in 36.3% of cases. Proteinuria was present in 45.5% of cases. Acute rejection was present in 63.7% (n = 14) and chronic rejection in 36.3% (n = 8) of cases, resulting in an overall prevalence of 14.4% for acute humoral rejection and 8.2% for chronic humoral rejection. Humoral rejection was of the active humoral type in 50% of cases. Associated cellular rejection lesions were found in 13.6% of cases. The study of the complement fraction C4d was performed in 15 cases. Among the documented humoral rejections, C4d was negative in 9% of cases (n = 2).

Conclusions: The diagnosis of rejection must be early in order to improve prognosis.

395 - P2.182

KIDNEY TRANSPLANTATION IN CHILDREN WITH ANURIA OF GREATER THAN ONE YEAR

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Aims/Purpose: Retrospective review of kidney transplantation in children ≤ 5 years old who have been anuric for at least one year but have no lower urinary tract disease. There is currently little data for this group. We aim to use this information to help guide future practice and to help develop a national registry of such patients.

Methods: Questionnaire sent to all 13 UK Paediatric Nephrology centres. Data returned from 10 centres.

Inclusion criteria: Kidney transplants 01/01/06 to 31/12/21; Anuric for > 1 year (as disuse bladder atrophy is thought to develop over at least 12 months); ≤ 5 years of age at transplant; No lower urinary tract disease.

Results: 31 patients. Average age at follow up - 124 months (range 45 to 251), 19 female, 12 male. Diagnoses: 5 Denys Drash syndrome, 5 renal dysplasia, 4 congenital nephrotic syndrome, 3 autosomal recessive polycystic kidney disease, 3 focal segmental glomerulosclerosis, 3 cortical necrosis, 2 cystic kidney disease, 2 WT1 mutations, 1 atypical haemolytic uraemic syndrome, 1 NPHP1 mutation, 1 Wilm's tumour, 1 cystic nephroma. Anuric from average age of 15 months (range 0 to 41), 5 anuric from birth. Anuria for average of 26 months (range 12 to 49). Pre-transplant: Urinary tract infection (UTI) – 2 patients. Investigations: Videourodynamics (VUD) – 3. All had small bladder capacity, Micturating cystourethrogram (MCUG) - 1, Cystourethroscopy - 1. Expansion of bladder capacity – 2 (neither were in the group who had VUD). At transplant: Average age 41 months (range 25 to 59), 29 transplanted into native bladder, 9 Suprapubic/urethral catheters used to expand bladder, 1 Vesicostomy, 2 cutaneous ureterostomies (1 unplanned). Post transplant: Average follow up of 68 months (range 14 to 199), Daytime incontinence (over 5 yrs old) - 9, Enuresis (over 5 yrs old) - 18, Recurrent UTI – 14. Investigations: non-invasive bladder assessment - 7, VUD - 2, MCUG - 1, Nil other than ultrasound scan - 21, Graft loss 2, Rejection – 1, Chronic allograft nephropathy - 1.

Conclusion: This is the largest published cohort of kidney transplants in anuric children with no lower urinary tract disease. There is a marked variation in pre and post transplant investigations. The few who had pre-transplant VUD had small bladders. A very small number had pre-transplant bladder expansion. The majority had their transplant ureter inserted into their bladder. There were various strategies re post transplant catheterisation and expansion of the bladder. There were significant levels of urinary incontinence and recurrent urinary tract infection post transplant. Graft loss was not due to urological issues. Further work will help us better understand this group e.g. GFR and graft surivival compared to matched paediatric transplant recipients. A national registry of these patients will help us gather ongoing data with which to improve our understanding, and therefore treatment, of this group.

272 - P2.183

KIDNEY TRANSPLANT OUTCOMES IN COVID-19 POSITIVE RECIPIENTS DURING THE FIRST WAVE: FOCUS ON VASCULAR COMPLICATIONS IN A SINGLE-CENTER, 3-YEAR FOLLOW-UP STUDY

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Aims/Purpose: Our study aims to assess the three-year outcomes of pediatric kidney transplant recipients (pKTRs) who received kidneys from donors with pre-transplant positive SARS-CoV-2 serology or were SARS-CoV-2 positive themselves during the initial COVID-19 wave and presented with graft vascular stenosis.

Methods: All pKTRs (0-18 years old) transplanted in Hopital Necker Enfants Malades during the first pandemic wave (02/2020-07/2020). Clinical, laboratory, and imaging data were collected retrospectively. A systematic doppler exploration of the whole graft artery (from anastomosis to ileum) was performed. Arterial stenosis was evidenced by an increase in peak systolic velocity (PSV) ≥250 cm/sec.

Results: Nine children received a kidney transplant (KT) during the study period. Among them, graft vascular stenosis occurred in seven (77.8%), lymphocele requiring surgical intervention in five (55.6%), and moderate/severe hypertension in six (66.7%). None of the pKTRs exhibited multisystem inflammatory syndrome (MIC-S) or COVID-19 symptoms, despite positive antibodies against the SARS-CoV2 S2 subdomain detected via luciferase immunoprecipitation assay systems (LIPS) in six pKTRs and in two donors of LIPS-negative pKTRs. At the three-year follow-up, no occurrences of graft loss were observed, with all nine pKTRs presenting a median glomerular filtration rate of 71.0 (IQR 66.5-131.5) ml/min/m2. Two out of nine patients showed persistent mild acceleration of their renal arteries (PSVs 210 and 230 cm/s, respectively), raising suspicion of mild KT artery stenosis. Despite this, post-immune SARS-CoV-2 induced graft vascular stenosis was not observed. Additionally, persistent hypertension was noted in five patients overall, managed with 1-2 agents.

Conclusion: Despite initial post-COVID complications, pKTRs recovered well at three-year follow-up. However, uncertainties remain about variant risk, viral replication, and vaccination's long-term effects. Continuous outcome reporting and re-evaluating organ use from COVID-19 donors are crucial for future decisions in pediatric kidney transplantation, emphasizing ongoing monitoring in this population.

271 - P2.184

UROLOGICAL COMPLICATIONS IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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Aims/Purposes: Kidney transplantation is the best treatment for children with end-stage renal disease, but its outcome can be affected by urological complications, which have an incidence rate of 1%-27%. This study was aimed to analyze the occurrence and the management of the urological complications (in particular, ureterovesical reflux and ureteral obstructions) in pediatric renal transplant recipients.

Methods: Demographic and clinical data of children undergone to kidney transplantation between 2011 and 2023 were analyzed. Urological complications were categorized as early, intermediate or late, based on their onset. Complications occurring within 7 days after transplantation and undrained fluid collections were excluded.

Results: A total number of 178 children were enrolled into the study. 28 (15.7%) children experienced urological complications after transplantation. Most of these patients (61%) had a pre-existing anomaly of the urinary tract. Diagnosis was primarily ultrasound-based, with supplementary diagnostic techniques as needed. Early complications (7-30 days) were all obstructive: 5 cases of ureterovesical junction obstruction and 2 perirenal collections. Intermediate complications (1-3 months) comprised ureteral stenosis, symptomatic vesicoureteral reflux, and obstructive lymphocele. Late complications (> 3 months) included symptomatic vesicoureteral reflux and ureteral stenosis, with ureteral rupture in one case. The overall incidence of ureteral stenosis (7.3%) and symptomatic vesicoureteral reflux (6.7%) was consistent with the data from the literature. No correlations between patients' characteristics and the risk of urological complications did emerge. Most ureteral stenoses were treated with initial endoscopic stents, followed by surgery. Vesicoureteral reflux was treated by endoscopic correction, with a high success rate (75%).

Conclusions: Our findings emphasize the importance of a tailored post-transplant follow-up, especially for patients with pre-existing risk factors, to promptly recognize and manage urological complications in order to preserve long-term graft function.

799 - P2.185

SINGLE CENTRE EXPERIENCE OF SWITCHING FROM TACROLIMUS TO SIROLIMUS USE IN PAEDIATRIC RENAL TRANSPLANT PATIENTS

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Aims: Tacrolimus, a calcineurin inhibitor, is commonly used in paediatric renal transplantation with good immunosuppressive effect but side effects include nephrotoxicity, alopecia and tremors. Sirolimus, a mTOR inhibitor, has been used as an alternative agent but there are concerns of delayed wound healing, proteinuria, and increased episodes of acute rejection. Our aim was to review our experience of Sirolimus following paediatric renal transplant and its impact on graft function and frequency of adverse effects and acute rejection.

Methods: Paediatric renal transplant records at Birmingham Children's Hospital were retrospectively reviewed to identify all patients who were switched from Tacrolimus to Sirolimus over a 10-year period between 2014 and 2024. Patient notes were studied to identify indications for switch, timing of switch and renal function pre and post Sirolimus. Treatment duration on Sirolimus, adverse effects and acute rejection episodes on Sirolimus were recorded.

Results: 28 patients (mean age at switch 11 years; range 5-16) switched from Tacrolimus to Sirolimus. Indications included raised creatinine with biopsy findings of no acute rejection and/or chronic allograft nephropathy, significant tremor, significant hair loss, thrombotic microangiopathy and post-transplant haemolytic uraemic syndrome. On average patients switched 26.9 months after transplant (range 1-114) and mean eGFR 6, 12 and 24 months prior to the switch was 55, 57 and 63 ml/min/m2 respectively. Of the 28 patients who switched, 64% (18) had improvement in renal function, 29% (8) had no change in renal function and only 7% (2) had a further deterioration in renal function. Mean eGFR after switching to Sirolimus at 12, 24 and 36 months was 53, 50 and 52 ml/min/m2 respectively. 22/28 (79%) continued Sirolimus (mean duration 39 months; range 2 – 104) and 6/28 (21%) were switched back to Tacrolimus (3 with proteinuria, 1 with vascular rejection, 1 with persisting donor specific antibodies, 1 with severe mouth ulcers). 3/28 (11%) had biopsy proven episodes of acute rejection on Sirolimus (1 patient had 3 episodes, 1 patient had 2 episodes and 1 patient had 1 episode). The main adverse effect on initiation of Sirolimus was mouth ulcers in the initial period which occurred in 4/28 patients (14%). 3 patients continued Sirolimus with regular mouth care and 1 switched back to Tacrolimus after 2 months.

Conclusion: Sirolimus can be considered as an alternative immunosuppressant in patients with persistently raised creatinine and biopsy evidence of chronic allograft nephropathy without acute rejection; or those who experience other side effects of Tacrolimus. Our single centre experience suggests it stabilises renal function, is well tolerated in the medium term and has few cases of acute rejection.

817 - P2.186

CORRELATION OF INDIRECT CALORIMETRY AND PREDICTIVE EQUATIONS IN DETERMINING RESTING ENERGY EXPENDITURE IN YOUNG PEOPLE WITH END STAGE KIDNEY DISEASE

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Aims/Purpose: Kidney transplant is the therapy of choice in children approaching end-stage kidney disease (ESKD). Weight gain is expected after transplant; however this is often more rapid than anticipated for concomitant linear growth, resulting in overweight, obesity and metabolic complications. Indirect calorimetry (IC) is the gold standard method of measuring resting energy expenditure (REE) in the clinical setting, although is not readily available. There are no published studies to date reporting REE utilising IC in paediatric kidney transplant recipients (KTR), resulting in reliance on predictive equations. These are based on healthy populations and do not take into account physical activity, disease state or effect of dialysis exposure. This study aimed to explore the correlation of predictive equations with IC in estimating REE in the ESKD population.

Methods: All patients attending the kidney transplant clinic at a tertiary children's hospital were eligible for inclusion. REE was measured using the 'Q-NRG®' IC device at ≥1 of 4 time points: pre-transplant, < 1 month, 3-6 months, 9-12 months and > 12 months post-transplant. Anthropometric data was collected from the Electronic Medical Record and predicted REE was calculated using Schofield and Henry-Oxford equations at each time point. Twenty-seven children were assessed on 38 occasions. Correlations between REE measured by IC and predicted by Schofield and Henry-Oxford equations were analysed using Pearson's correlation co-efficient. A $p < 0.05$ was considered statistically significant.

Results: Twenty-seven patients including 18 (66.7%) males with a mean age at transplant of 10.57 ± 5.0 years were included. Six children (22%) had tube feeding at time of transplant (1 nasogastric, 6 gastrostomy). The mean body mass index (BMI) z-score was 0.55 ± 1.08, with 10/27 classified as overweight and 1/27 classified as obese. There was strong correlation between the IC and Schofield ($r = .883$; $p < 0.001$) and IC and Henry-Oxford ($r = .878$; $p < 0.001$) predictive equations, and between the Schofield and Henry-Oxford predictive equations ($r = .996$; $p < 0.001$).

Conclusion: The high correlation between predictive equations and IC data support confidence in continuing to use predictive equations in this patient group where IC is unavailable. However improvements in IC device portability and ease of use potentially means that IC can be readily utilised in children and young people with ESKD. Individualising the nutrition prescription in this way may be the first step to mitigating excessive weight gain peri-transplant. Further studies using IC to determine REE in a larger population of KTR are warranted, to track associations with growth post-transplant and explore relationships with body composition.

928 - P2.187

NON HUMAN LEUCOCYTE ANTIGEN ANTIBODIES IN CHILDREN AFTER KIDNEY TRANSPLANTATION

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Aims/Purpose: After pediatric kidney transplantation (KTx), antibody-mediated rejection (ABMR) remains a significant challenge, often resulting in a notable decline in graft survival. Its diagnosis typically involves biopsy confirmation and the identification of human leukocyte antigen (HLA)-donor-specific antibodies (DSA). However, ABMR histology can also manifest in patients lacking HLA-DSA. While certain non-HLA antibodies have been associated with ABMR histology, their exact contribution to kidney allograft injury remains unclear. We aimed to elucidate the role of 60 different non-HLA antibodies in 83 pediatric kidney transplant recipients.

Methods: We enrolled all patients who underwent KTx at a single centre from 2014 and had serum samples biobanked. We retrospectively assessed sera collected pre transplantation and one and two years post-transplantation (n = 249) for the presence of 60 different non-HLA antibodies using the LIFECODES Non-HLA Antibody kit (Immucor, Inc) based on Luminex technology. Assignment of non-HLA antibodies was based on the manufacturer's cut-off.

Results: In almost all patients non-HLA antibodies could be detected (pre KTx 82, 1 year after 81, 2 years after 81 of 83 patients). 77/83 patients showed kidney specific (shown in literature) non-HLA antibodies pre transplantation, 70/83 patients 1 year after KTx and 75/83 patients 2 years after KTx. N = 7 patients developed a ABMR during the two years of our study and 10 patients later on. Preliminary regression analysis showed a positive association of GDNF and PECR non-HLA antibodies with ABMR.

Conclusion: There is surprisingly a very high prevalence of non HLA DSAs in pediatric patients before and after KTx. Further regression analysis and finding of cohort specific cut off are further steps in our investigation.

947 - P2.188

FIRST CASE OF A SUCCESSFULLY TREATED ALK-1 NEGATIVE ANAPLASTIC LARGE CELL LYMPHOMA POST HLA INCOMPATIBLE KIDNEY TRANSPLANT

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Background: Post transplant lymphoproliferative disorders (PTLD) are lymphoid proliferations that occur after transplantation. The lifetime risk for post kidney transplant paediatric patients to develop lymphoma is 29 times higher compared to the general population. CD30 positive Anaplastic Large Cell Lymphoma (ALCL) is a Non-Hodgkin's lymphoma accounting for a small percentage of PTLD. ALCL is either ALK-1 protein positive or negative. ALK ALCL is extremely rare with reported 5 yr overall survival rate of 17- 49%

Case Report: We present the first reported case of post-transplant diagnosis of an ALK-1 negative, CD30 positive ALCL in a 17-year-old boy who underwent HLA incompatible (HLAi) second kidney transplant. Prior to transplant, the patient had history of transient mild splenomegaly and intermittent self-resolving episodes of fever and high c-reactive protein for which he was investigated extensively, and no cause was found. Induction immunosuppression for B-cell cross match positive HLAi kidney transplant, as part of desensitisation, included Alemtuzumab, three sessions of plasma apheresis and three doses of IVIG 2g/kg. Tacrolimus and mycophenolate mofetil were commenced one week prior to transplant. Three weeks after the transplant, the patient developed persistent fever with hepatosplenomegaly, lymphadenopathy, high ferritin and LDH. PET scan showed avid lymph nodes above and below diaphragm with pleural, peritoneal and cutaneous lesions. Immunophenotyping from total splenectomy showed monomorphic infiltrate that was CD 30 positive ALK negative and EBER was negative. Molecular genetic testing showed TP53 missense variant. Chemotherapy treatment included brentuximab vedotin, cyclophosphamide and doxorubicin with very good response. After fifth cycle of chemotherapy, patient developed intraocular lymphoma with reduced vison. His vision improved with intraocular methotrexate injection. Six months after the transplant, he continues treatment for lymphoma awaiting 6th chemotherapy cycle (last planned cycle) and has excellent allograft function with baseline serum creatinine of 90-110umol/L (and no evidence of acute rejection on allograft biopsy) and stable tumor markers (normal LDH and reduced ferritin). He continues to have high level of donor specific antibodies as expected after HLAi transplantation and is on maintenance tacrolimus and daily prednisolone as antiproliferative medication was stopped as part of management of lymphoma. This is the first known case of successfully managed aggressive ALK ALCL in a immunologically complex paediatric kidney transplant recipient.

970 - P2.189

PATHWAY ANALYSIS OF URINARY EXTRACELLULAR VESICLE PROTEOME FOR NOVEL BIOMARKER DISCOVERY FOLLOWING KIDNEY ALLOGRAFT REJECTION

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Aims/Purpose: Early detection of rejection following kidney transplantation is key to maintaining long-term graft function. The current diagnosis of allograft rejection mainly relies on clinical monitoring and a kidney biopsy, which is invasive and many times insufficiently informative for clinical decision-making. Thus, there is a need for a non-invasive diagnostic technique with good early predictive values to determine graft injury and to provide accuracy in titrating immunosuppression. In this study, we used a non-biased approach to discover novel biomarkers for rejection through analysis of urinary EV proteome of kidney transplant recipients to identify network-based markers for early detection of rejection.

Methods: Urine from pediatric and adult kidney transplant recipients at SCMCI and RMC and healthy controls was collected. Evs were extracted using an ultracentrifuge method and quantified using Nanoparticle tracking. Proteins were analyzed using LC/MS and compared between patients with acute rejection, stable allograft, chronic glomerulopathy, and healthy controls. Stable transplant was used as a baseline value and a fold change per protein expression was calculated for all the other groups: control samples, chronic rejection, and acute rejection. Protein level fold change was compared between the various allograft states. To identify biomarkers that can perfectly split the patients between acute and chronic kidney rejection we first found the genes and the expression threshold that splits the dataset most accurately. We then recursively applied the same algorithm to the split branches of the data, until all patients were accurately classified, thus constructing a decision tree that perfectly splits the patients between acute and chronic rejection. A small validation cohort was tested with the constructed decision tree. The study was approved by the local ethics committee.

Results: The cohort included 42 participants ages 3-70 years old, females (33%) were included. 7 (16%) healthy controls, 10 patients (23%) with chronic allograft glomerulopathy, 15 (35%) with stable allograft function, and 12 (28%) patients with acute rejection. 2747 proteins were identified in the cohort. EV proteome was analyzed to develop a gene formula to extract 4 biomarkers couples. The accuracy of these biomarkers was tested with 10 additional samples (5 stable allograft recipients, 2 chronic rejection, and 3 acute rejection) whose status was left unknown at the time of analysis. All samples were classified correctly but one. Enrichment analysis showed differential expression between acute vs chronic rejection in the complement activation pathway.

Conclusion: Propagation-based enrichment analysis showed a significant dysregulation in the complement activation pathway comparing chronic rejection and acute rejection in the urine EVs from kidney transplant patients.

983 - P2.189

KIDNEY TRANSPLANTATION IN CHILDREN AND ADOLESCENTS WITH C3 GLOMERULOPATHY OR MEMBRANOPROLIFERATIVE IMMUNE COMPLEX GLOMERULONEPHRITIS: AN INTERNATIONAL SURVEY OF CURRENT PRACTICE

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Introduction: C3 glomerulopathy (C3G) and primary membranoproliferative immune complex glomerulonephritis (IC-MPGN) are rare kidney diseases with an incidence of around 1-2 cases per million inhabitants. Complement-mediated C3G in particular has an uncertain prognosis: in adults, around 50% of affected patients will require dialysis within the first 10 years after the onset of the disease, as the immunosuppressive drugs currently available for this disease are only effective to a limited extent. Another problem is the high recurrence rate after kidney transplantation (NTx). There are currently no guidelines or recommendations for the indication of NTx or management after NTx.

Material and Methods: We therefore initiated an international online survey via Survey Monkey (https://www.surveymonkey.com) on C3G and IC-MPGN in children with CKD stage 5 before and after NTx. The survey consisted of 17 questions regarding listing for deceased donation, living donation and preemptive NTx as well as management of immunosuppressive therapy after NTx and in case of recurrence. All NTx centres of the European Society of Paediatric Nephrology (ESPN) were invited to participate in the survey, which was conducted from 23.08.2023 to 25.11.2023.

Results: 65 (63%) of the ESPN NTx centres surveyed (n = 103) took part in the survey. 12% of centres reported having made at least one decision against NTx for a child with C3G or IC-MPGN; 26% of centres had made at least one specific decision against living donation for such a child. The main reason for more than 80% of these decisions was predominantly concern about recurrence of the underlying disease in the transplant. The majority of centres (88%) indicated deceased donation as an option when living donation was not an option for a child with C3G or IC-MPGN at their discretion. With regard to decision-making on NTx in children with C3G or IC-MPGN, one third of the centres surveyed indicated the existence of a centre-specific guideline; none of the centres surveyed referred to the existence of a supra-regional guideline on management or decision-making regarding NTx. In the case of recurrence of the underlying disease in the transplant, a therapy trial with eculizumab was initiated in 60% of cases, in addition to other measures.

Discussion: There are currently no national or international guidelines for deciding in favour of or against NTx in children with C3G or IC-MPGN, nor for immunosuppressive therapy management after NTx or for the treatment of recurrences. The decision not to transplant an affected child with C3G or IC-MPGN in CKD stage 5 is predominantly based on the concern of a recurrence of the underlying disease in connection with the lack of reliable treatment options in such a case.

1059 - P2.191

RENAL TRANSPLANTATION IN PEDIATRIC PATIENTS WITH THROMBOTIC MICROANGIOPATHY: CASE SERIES

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Aims/Purpose: To analyze a pediatric cohort of patients with thrombotic microangiopathy (TMA) who underwent kidney transplantation.

Methods: This study provides a descriptive analysis of pediatric renal transplant recipients diagnosed with TMA at our institution between 2003 and 2023. Data encompassing the type of TMA, age at onset, complement-related mutations, age at transplantation, administration of complement blockade therapy, renal biopsy findings, presence of hypertension, levels of proteinuria, and estimated glomerular filtration rate (eGFR) according to Schwartz formula at the final of the follow-up period were compiled.

Results: Out of 268 renal transplants conducted during the specified timeframe, 7 (2.65%) were performed in patients with TMA (including 5 cases of atypical hemolytic uremic syndrome, 1 case associated with Shiga toxin-producing Escherichia coli, and 1 case linked to pneumococcal infection) The median age at TMA onset was 24 months (interquartile range: 7-41), with complement-related mutations identified in 5 patients. Two patients underwent preemptive kidney transplantation, and only one was from a living donor. The median age at transplantation was 6 years (interquartile range: 4-10 years), with 6 initial transplants conducted. Two patients received prophylactic Eculizumab post-transplant for 1 and 2 years, respectively. None of the patients exhibited evidence of hemolysis during the follow-up period. Three patients underwent renal biopsy due to graft dysfunction, revealing a mean eGFR of 54.46 ml/min/1.73m2 (standard deviation ± 10). Among them, one patient diagnosed with TMA recurrence restarted Eculizumab treatment. One biopsy demonstrated chronic graft glomerulopathy with moderate intimal hyperplasia and severe arteriolar hyalinosis, while the other displayed 80% global glomerulosclerosis and severe intimal hyperplasia. Both patients, currently experiencing graft loss, had graft durations of 6.7 and 18 years, respectively. Among the functioning grafts, with a median follow-up of 11.74 years (interquartile range: 3.9-12.5), 2 presented with microalbuminuria, 4 required antihypertensive medication, and the median eGFR was 72 ml/min/1.73m2 (interquartile range: 49.3-93).

Conclusion: Further research is imperative to elucidate the pathogenesis and tailor management strategies. Identification of TMA localized to the graft demands a heightened clinical suspicion and renal biopsy. Typically, findings unveil chronic TMA with predominant vascular involvement. This complexity poses challenges in both diagnosis and the implementation of appropriate treatment modalities, which may impede renal graft survival and function.

1061 - P2.192

KIDNEY TRANSPLANTATION IN CHILDREN WEIGHING 10 KG OR LESS: IS IT A CHALLANGE?

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Purpose: Kidney transplantation (tx), which is considered as the most appropriate treatment for children with end-stage kidney disease, is generally applied in children over 10 kg of body weight. Young children represent the vulnerable population in terms of post-transplant fluid-electrolyte and blood pressure management and immunosuppressive treatment. Infections are a significant risk in these patients and may affect graft survival. We aimed to evaluate the clinical outcomes of transplantation in young children, especially infants weighing less than 10 kg, by comparing them with older children.

Methods: Kidney transplant recipients less than 10 kg were included in this retrospective observational study. This patient group was matched with a pediatric control group in the recipient's sex and post-transplant follow-up by the nearest neighbor matching method. The primary endpoint was all-cause mortality and graft loss. The secondary endpoints were the occurrence of allograft rejection, Cytomegalovirus (CMV), BK virus (BKV), and Ebstein-Barr virus (EBV) infections.

Results: Thirty-four kidney transplant recipients were followed for a median of 36 months after transplantation. Although, there were no statistical differences in both groups in terms of BKV (5 vs. 7; p =0.134), CMV infections (8 vs. 11; p =0.166); EBV DNAemia (11 vs. 1; p < 0.001) were common in the patient group than the control group. EBV-related Post tx lymphoproliferative disease (PTLD) occurred in 2 children in the patient group.

Table 1. Demographic characteristics of the patients

	All patients (n=34)	Patient group (n=17)	Control group (n=17)	p value
Age (months, IQR 25-75)	73.5 (48.5-161.5)	49 (36.5-64)	158 (110.5-195.5)	<0.001
Height (cm, IQR 25-75)	90.3 (72.8-129.9)	73 (68-78.5)	129.9 (100-149)	<0.001
Weight (kg, IQR 25-75))	10.9 (8.8-26.1)	8.8 (7.7-9.45)	25.5 (17.8-51.4)	<0.001
Gender (n, %) Male	26 (76.5)	13 (76.5)	13 (76.5)	1
Recipient serology				
CMV Ig G negative	9 (26.5)	8 (47.1)	1 (5.9)	0.017
EBV Ig G negative	15 (44.1)	12 (70.6)	3 (17.6)	0.005

Table 2. Outcomes of the patients

	All patients (n=34)	Patient group	Control group	p value
Duration after transplantation (months, IQR 25-75)	36 (16.5-48.25)	36 (14.5-48)	36 (14-48.5)	0.972
Primary outcomes				
Death	1 (2.9)	1 (5.9)	0	1
Graft loss	0	0	0	-
Viral complications				
BK virus (n, %)	12 (37.6)	5 (29.4)	7 (46.6)	0.134
BK viruria	6 (18.8)	4 (23.5)	2 (13.3)	
BK viremia	6 (18.8)	1 (5.9)	5 (33.3)	
CMV DNAemia (n, %)	19 (59.4)	8 (47.1)	11 (73.3)	0.166
EBV DNAemia (n,%)	12 (37.5)	11 (64.7)	1 (6.7)	<0.001
Allograft rejection	1 (2.9)	0	1 (5.9)	1

Conclusion: The survival rates of infants less than 10 kg were %100 at a median three years follow-up. But the frequency of EBV DNAemia in these patients has increased compared to the other pediatric population. Therefore, close follow-up of these patients is required.

Keywords: kidney transplantation, infants, viral infections, graft-patient survival

1067 - P2.193

THE CLINICAL EFFICACY AND SAFETY OF RITUXIMAB IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS WITH REFRACTORY EPSTEIN-BARR VIRUS: A CASE CONTROL-CONTROL STUDY

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Purpose: Epstein-Barr virus (EBV) infection is a known risk factor for the development of post-transplant lymphoproliferative disease (PTLD), which occurs as a consequence of immunosuppression after kidney transplantation. Although reduction of immunosuppression (IS) and initiation of antiviral therapy are recommended in clinical practice, there are no guidelines for the preemptive use of rituximab to reduce the risk of PTLD in patients with refractory EBV viremia.

Methods: Total 112 children (median age 8.3 years (IQR: 4-13.3) who underwent kidney transplantation at Koç University Hospital between June 2018 and December 2023 were analysed retrospectively. Treatment for EBV viremia was initiated by starting valganciclovir at a threshold of greater than 150 copies/mL, concurrently with IS reduction. Patients with refractory EBV DNAemia at the end of the 3rd month of standard approach were treated with rituximab (Rituximab 375 mg/m2). The outcomes of EBV DNA clearance, graft function, allograft and patient survival for patients who received rituksimab and those who did not were compared statistically. The side effects of the rituksimab were also evaluated.

Results: Out of 112 patients who underwent kidney transplantation (median of follow-up 30 months (IQR: 17-47.25), 28 (25%) developed EBV DNAemia at a median of 269 days post-transplant (IQR: 36-4102). At the time of transplantation, 18 of these patients (64.3%) were EBV seronegative and 10 (35.7%) were seropositive. After the initiation of standard treatment, 10 of the 28 (35.7 %) respond to this strategy and cleared EBV while 18 patients (64.3 %) continued to have EBV DNAemia defined as 500 copies/mL for > 3 months. PTLD occurred in 3 of these 18 patients (10.7%) with persistent viremia, recovered with rituximab therapy and kidney function was preserved. Overall, 18 patients (64.3%) received 1-4 doses of Rituximab (375 mg/m2 weekly dose) due to persistent EBV-DNAemia. Complete resolution was achieved in 12/15 patients (80%) following the 2nd dose of rituximab. Rituximab treatment was related with temporary hypogammaglobulinemia in 7 patients and an allergic reactionin 1 patient. No child developed PTLD after rituximab, and there was no graft loss due to refractory EBV in the study group.

Conclusion: The best clinical practice recommendations for EBV viremia, a significant challenge in pediatric kidney transplantation, vary between centers. Standard approaches such as reduction of immunosuppression, IVIG, and/or Valganciclovir do not prevent the development of refractory EBV viremia in many cases. The results of our study show that preemptive Rituximab treatment is an effective and safe approach in ensuring viral clearance and preventing the development of PTLD in patients with persistant EBV DNAemia.

148 - P2.194

PREDICTIVE INDICATORS FOR GRAFT SURVIVAL IN PEDIATRIC KIDNEY TRANSPLANTATION: A COMPREHENSIVE ANALYSIS OVER TEN YEARS IN OUR SINGLE CENTER EXPERIENCE

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Aims/Purpose: Identifying predictive factors for pediatric kidney transplant survival informs tailored therapies, improves long-term outcomes, and refines recipient selection criteria.The aim of this study was to explore and analyze prognostic factors associated with 10-year allograft survival in pediatric kidney transplantation.

Methods: This retrospective study enrolled children who underwent kidney transplantation at our department, between 1993 and 2013. Participants were tracked until a follow-up duration of 10 years. Our endpoint was death-censored 10-year graft survival after excluding recipients whose grafts failed within one-year of transplant. A comparative analysis was conducted, evaluating demographic, clinical, immunological, and laboratory profiles of patients with functional grafts at 10 years post-kidney transplantation versus those with allograft failure at 10 years. Multivariate analysis was performed using Pearson Chi-Square tests and Logistic Regression model.

Results: The study cohort included 105 patients with a mean age of 12.5 ± 3.84 years. We identified 87 (82.6%) patients with a functional graft for 10 or more years after transplantation, with a mean graft survival of 18.9 ± 6.0 years. In the univariate analyses, higher donor age (p =0.03) was found to be a significant negative prognostic factor for graft survival - donors aged over 17 years approximately triple the risk for rejection at 10 years, as indicated by the odds ratio. In this study, factors that did not influence graft function over time were: gender of recipient (p =0.123) or donor (p =0.381), pre-emptive (p =0.45), time on waiting list (p =0.28), living donor (p =0.0175) versus deceased donor (p =0.017), number of previous transplants (p =0.27), presence of acute tubular necrosis (p =0.67), previous blood transfusions (p =0.12), donor or recipient of cytomegalovirus status (p =0.41 and p =0.89, respectively), ABO-identical matching (p =0.26) or use of Thymoglobuline versus non-use of Thymoglobuline (p =0.18). Regarding HLA-matching, HLA-A, HLA-B or HLA-DR mismatches were found not to be significant factors for graft survival status. (Table 1).

Conclusion: Understanding prognostic factors in pediatric kidney transplants is vital for optimal outcomes. This study identifies donor age as a negative predictor of long-term survival. Insights inform decision-making and underscore resource needs.

Table 1. Chi-Square Tests data

	Pearson Chi-Square Value	Asymptotic Significance (2-sided)
Gender Recipient	2.381	0.123
Gender Donor	1.122	0.381
Blood Transfusions	1.174	0.012
HLA-A	0.271	0.07
HLA-B	0.271	0.873
HLA-DR	1.683	0.431
Number of previous transplants	1.174	0.279
Acute Tubular Necrosis	0.179	0.672
Blood Group	1.276	0.528
Thymoglobuline Use	1.730	0.18

164 - P2.195

ARE INTRAVENOUS IMMUNOGLOBULINS EFFETIVE IN PREVENTING PRIMARY EBV INFECTION IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENT?

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Aims/Purposes: About half of < 5 year-old children are seronegative for Epstein-Barr virus (EBV) and are at risk of contracting primary EBV infection after transplantation, especially if the donor is EBV-seropositive. Posttransplantation lymphoproliferative disorder (PTLD) is the most harmful complication of EBV infection in transplant recipients. In the literature, there are no univocal recommendations on prevention of EBV primary infection in pediatric renal transplant recipients. EBV-seronegative (negative EBNA) kidney transplant-recipients (R-) of EBV-seropositive (positive EBNA) donors (D+) were serially administered intravenous immunoglobulins (IVIG) during the first six months after transplantation (PT), in order to evaluate if IVIG can prevent primary EBV infection and enhance protective immunity in short and long-term follow up.

Methods: IVIG (200 mg/kg/dose) were administered to 12 pediatric R- (M/F:7/5, average age 6 years) according the following schedule: day 0 (time of transplantation), day 1-7-14 and 21 PT. Then, every 3 weeks for 3 months, and then monthly until the sixth month PT. All children received basiliximab/thymoglobuline and steroids as induction, and then calcineurin inihibitor with mycophenolate mofetil/mTOR inhibitor and steroid. EBV-DNA and EBV antibodies (VCA, EA, EBNA) were regularly monitored and evaluated on month 6, 12, 24, 60 and 72 PT.

Results: EBV-DNA positivisation was observed during the first 6 months PT in 50% of patients who received IVIG. EBV-DNA remained positive in all follow up analysis in these patients. No one developed protective immunity against EBV (negative EBV-EBNA) by month 12 PT, but 50% of patients resulted EBV-EBNA positive by the end of follow up. In a group of 12 R- patients with the same clinical features, who did not receive IGIV, EBV-DNA positivization was observed in 25% of cases during the first 6 months PT and then EBV-DNA remained positive until the end of follow up. All patients of this group had developed EBV-EBNA by month 12 PT. The only patient who developed PTLD belonged to the IGIV group.

Conclusion: Despite the small number of patients, our data do not seem to support the use of IGIV as a tool to prevent EBV primary infection in pediatric R- who receive the graft from D+.

1087 - P2,196

COSTS OF HOSPITAL OUTPATIENT MEDICINES FOR PATIENTS PRE AND POST KIDNEY TRANSPLANT FOR 2006 - 2018

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Aims/Purpose: The NICE Health Technology Asssessment 'Immunosuppressive therapy for kidney transplantation in children and adolescents: systematic review and economic evaluation' published in 2016 found limited data for costs of medicines used to treat paediatric kidney transplant recipients. Electronic systems allow these data to be extracted relatively easily and on a regular basis.

Methods: Patients were identified who received a kidney transplant between 2005 and 2019 at a children's hospital. Data for pre- and post-transplant outpatient medicine costs, and tacrolimus levels were extracted from the hospital's electronic health records and uploaded into the hospital's digital research environment for manipulation.

Results: 370 patients (220 (59%) male) were identified. The number of patients per year varied from 43 to 181. Costs include both pre- and post-transplant outpatient costs for all patients. The tacrolimus levels included those taken in all settings (including as an inpatient). Tacrolimus preparations accounted for the highest cost during this period. This was matched by the combined costs of home haemodialysis and peritoneal dialysis (the majority being pre-transplant costs). The amount of tacrolimus prescribed as granules or as liquid (unlicensed) since 2014 has varied between 32% and 45%. The average cost/ mg tacrolimus per year was £2.04 (range £1.70 - £2.40). Tacrolimus levels measured were below 5ng/ ml on 37% of occasions over the 13 year period.

Conclusion: NHS Clinical Commissioning repatriated tacrolimus prescribing to hospitals in 2015 and therefore hospital costs increased. Some of the variation in cost can be attributed to the proportion of different formulations used in any year. With the increasing competition in the market the cost/ mg should decrease. This does rely on a willingness to 'switch' which requires effort by the clinical team to achieve it safely. Information derived from data such as these can help inform future decisions. In particular, providing local justification for the time (and possible costs) associated with a specific 'switch'. Association with outputs/outcomes may also be beneficial.

1103 - P2.197

PAEDIATRIC KIDNEY TRANSPLANTATION AND BIOPSY PROVEN ACUTE REJECTION: A 2 CENTRE, RETROSPECTIVE STUDY OF THE EFFECTS ON GRAFT OUTCOMES.

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Aims: To study the clinical features of kidney transplantation (KT) recipients who developed biopsy proven acute rejection (BPAR) in the first year following KT and the effect of this on their graft function.

Methods: A 2 centre, retrospective study of 130 children who underwent KT between 2015 and 2023 and were followed up for a minimum period of 12 months. Eighty-Two patients were initiated on early steroid withdrawal immunosuppression (IS) regimen and 79 had on-going steroid maintenance therapy.

Results: Of the 130 patients included in the study, 88 (67.7%) were from a living donor (LD) and 42 (32%) were from a deceased donor. Forty-eight (37%) underwent a graft biopsy within the first 12 months due to an acute rise in creatinine - 35 in the first 3 months, 6 in months 4-6 and 7 in months 7-12. The overall average time from transplant to biopsy was 10.8 weeks. Twenty-seven (20.8%) of all patients had evidence of BPAR and these were categorised based on histological Banff grading: 16 (59%) grade 1A, 7 (26%) grade 1B, 2 (7.4%) grade 2A, 1 (3.7%) grade 2B and 1 (3.7%) grade 3. DSA was positive within the first year in 5 (18.5%) BPAR patients and 8 (7.8%) non-BPAR patients. Seventeen (63%) BPAR episodes were from LD and 11 (40.7%) were on steroid free IS at time of rejection. The mean tacrolimus level at the time of biopsy was 7.8 (range 2-16-8) in those with BPAR, compared to 6.9 (range 1.2-17.9) in those without. At the time of biopsy, patients with BPAR had an estimated GFR (eGFR) of 46ml/min/1.73m2 (CI 39-52ml/min/1.73m2). Following treatment with 3-5 days of IV methylprednisolone, +/- increase in background IS, eGFR in this group was 76ml/min/1.73m2 (CI 67-85ml/min/1.73m2) at 1 month. Twelve children with BPAR underwent a repeat graft biopsy due to persistent poor graft function – 7 of these showed resolution and 5 showed ongoing rejection which required additional treatment. At 12 months; the mean eGFR of those with BPAR was 55ml/min/1.73m2 (CI 46-63ml/min/1.73m2) compared to 77ml/min/1.73m2 (CI 72-83ml/min/1.73m2) in those without. At the latest follow-up (mean 4.2 years, range 1-8.7 years), the mean eGFR in those with BPAR was 55ml/min/1.73m2 (CI 46-63ml/min/1.73m2) with 2 having an eGFR < 30ml/min/1.73m2, compared to a mean of 59ml/min/1.73m2 (CI 55-63ml/min/1.73m2), and 9 having an eGFR < 30ml/min/1.73m2, in those without.

At the latest follow-up 41 patients were hypertensive as defined by either > 95th centile or need for therapy; 10 BPAR (37%) (OR 1.36 CI 0.56-3.32) and 31 Non-BPAR (30%). Four patients experienced graft failure and returned to haemodialysis, 2 with BPAR at 4.5 and 6 years and 2 without BPAR at 4 and5 years following KT.

Conclusions: Over a quarter of children will have persistent graft dysfunction after treatment for BPAR and merit a further graft biopsy. Acute rejection in the first year following KT if identified and treated appropriately is associated with good medium term graft function.

1133 - P2.198

BIOLOGICAL MARKERS PREDICTIVE OF RENAL GRAFT SURVIVAL - EXPERIENCE OF A SINGLE CENTER

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Aims/Purpose: Kidney transplantation is the most appropriate treatment for end stage kidney disease. Early detection of the risk for post-transplant graft dysfunction is very important for the graft survival. The aim of this study is to analyze two predictive biological markers in comparison with serum creatinine for the evaluation of renal function.

Methods: 21 pediatric patients were included in the cohort study group, all of them were recipients of the first renal transplantation between January 2011- August 2021. The patients had a complete HLA typing and a negative cross-match. 17 patients with renal function within normal limits were enrolled as a control group.

Results: The average age of the patients was 11.36 years with a masculine predominance (M:F = 13:8). 13 patients (62%) were grafted from deceased donors and 4 patients (19%) benefit from a preemptive renal transplantation. We evaluated the use of NGAL and KIM1 in comparison with serum creatinine for the prediction of the renal graft. The mean value of the NGAL in the study group was 23.75 ± 308.42 vs 14.45 ± 187.88 in the control group, with p =0.03. KIM1 had a mean value of 13.56 ± 463.11 in the study group vs 18.10 ± 1249.93 with a p value > 0.05. There is a correlation between the serum creatinine and NGAL, with a R2 = 0.01.. The mean follow up period was 3.14 years, with two patients having graft dysfunction.

Conclusion: NGAL in addition with serum creatinine can predict the dysfunction of renal graft.

1166 - P2.199

IMMUNOSUPPRESSIVE THERAPY IN A LIVING DONOR KIDNEY TRANSPLANT PATIENT WITH PREVIOUS CARDIAC TRANSPLANT AND SEVERE OSTEOPOROSIS

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Aims/Purpose: Long-term use of glucocorticoids as part of a maintenance immunosuppressive regimen after kidney transplantation varies among transplant centers. Conflicting data are available on the risk of rejection associated with steroids withdrawal/avoidance. However, detrimental effects on bone mineralization are expected. We present the case of a living-donor kidney transplantation on a boy with a previous cardiac transplant and severe osteoporosis.

Methods: A 9-year-old boy was hospitalized for acute heart failure due to HHV6 viral myocarditis requiring ECMO and VAD implantation. The patient received a heart transplant and immunosuppression included steroids, tacrolimus and mycophenolate. The post-transplant period was complicated by rhabdomyolysis, severe hypercalcemia, and AKI requiring CKRT. The origin of hypercalcemia was multifactorial and mostly related to prolonged bed rest, use of steroids, supplementation with vitamin D analogs and genetic. The patient underwent a whole-body MRI that confirmed the picture of severe osteoporosis and multiple vertebral fractures. Genetic tests for osteoporosis, identified a heterozygous mutation in the LRP5 gene. Steroid therapy was suspended and bisphosphonate treatment started with radiological improvement but persistence of significant disability. Renal function did not recover and a renal biopsy revealed irreversible tubular damage and tubular obstruction (referable to myoglobinuria/rhabdomyolysis). The patient was started on chronic dialysis but peritoneal dialysis failed due to refractory pleural effusion and limited vascular accesses were available for hemodialysis. The work-up for a kidney transplant from a living donor was initiated.

Results: The boy received a successful kidney transplant from his mother. In the post-transplant, to balance severe bone status and the need for more steroids in case of rejection, we use 60 mg/mq/day of steroids in the very early phase with a prompt tapering of the dose to 7.5 mg/mq/day at month 6. The patient received 2 protocol renal biopsies at 6 and 12 months after transplantation, both negative for rejection. Endocrinologists, Orthopedics and Physiotherapists closely followed the patient and 12 months after transplantation he was able to walk again. Nineteen months after transplantation, he has optimal renal and cardiac function on immunosuppressive therapy with a minimal dose of steroids (5 mg) every other day, tacrolimus and everolimus.

Conclusions: Optimal immunosuppressive regimen after kidney transplantation is particularly challenging in patients with many comorbidities and should be tailored to the specific condition. A low-dose steroid regimen was successfully used in our patient balancing the pros and cons. The multidisciplinary and careful evaluation also allowed a good functional recovery and documented an improvement in bone mineralization.

1181 - P2.200

EXPERIENCE IN THE USE OF MELTDOSE TACROLIMUS IN PAEDIATRIC KIDNEY TRANSPLANTATION. SINGLE-CENTER RETROSPECTIVE STUDY

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Aims / Purpose: Tacrolimus (TAC) is the cornerstone of immunosuppressive therapy for kidney transplantation (KT) and its action is closely correlated with plasma levels. It has a narrow therapeutic range, poor bioavailability and high inter- and intra-individual variability. MeltDose formulation (LCP-TAC, Envarsus®) has demonstrated similar efficacy and safety compared to immediate-release tacrolimus (IR-TAC, Prograf®) and extended-release tacrolimus (ER-TAC, Advagraf®), greater bioavailability and better pharmacokinetics. Although the results seem to be extrapolated to children, we have few data in pediatrics. The aim of the study is to review our experience with the use of LCP-TAC in paediatric kidney transplantation.

Methods: A single-centre retrospective observational study is performed, that includes KT recipients whose immunosuppressive regimen is modified from IR-TAC or ER-TAC to LCP-TAC from January 2016 to December 2023. Patients older than 18 years old at the time of the conversion were excluded, and it was mandatory at least 12 months between kidney transplantation and the modification and a stable clinical situation. Demographic, clinical and analytical variables are analyzed, including TAC dose conversion factor, dose-adjusted intra-individual variability index (average of 6 months), weight-adjusted concentration/dose ratio (average of 6 months), renal function at one year, detection of donor-specific antibodies (DSA) at one year and adverse events.

Results: 25 patients are included, 40% were boys. The median age at KT was 12.2 years (range 1.7-17.95), being congenital anomalies of the urinary tract the main cause of chronic kidney disease (40%). 60% received LCP-TAC after IR-TAC and 40% after ER-TAC, and the immunosuppressive conversion was made at median of 1.7 years after KT (range 1-8.42). The main reasons were: better TAC adjustment (32%), facilitating the immunosuppressive regimen (32%) and a high intra-individual variability (28%). The conversion factor used was 0.7 (range 0.58-0.83), without observing significant changes in plasma levels. Greater bioavailability was observed with LCP-TAC compared to other formulations (p 0.003) and less intra-individual variability (p 0.007). No significant differences were observed in glomerular filtration rate at one year. In the analysis of subpopulations, when the reason for change was intra-individual variability, a significant reduction in variability was observed ($p < 0.001$). 1 patient developed DSA at one year after conversion but no rejection was observed in the biopsy, and 1 patient discontinued LCP-TAC due to the development of de novo diabetes. No other notable complications were observed.

Conclusions: LCP-TAC seems to be a safe formulation in paediatrics and could provide a better pharmacokinetic profile, especially in children with high intra-individual variability.

1256 - P2.201

LACK OF STANDART APPROACH FOR EPSTEIN-BARR VIRUS DNAEMIA IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS: A MULTICENTER QUESTIONNAIRE

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Aims/Purpose: In pediatric kidney transplant recipients (pKTR), Epstein-Barr virus (EBV) is often seronegative, while donors are mostly seropositive. Therefore, EBV DNAemia is more common in pediatric recipients compared to adults. This condition can lead to various significant issues including post-transplant lymphoproliferative disorder. There are significant variations in the definition of EBV DNAemia, testing methods, accepted threshold values, and patient management among centers. This study aims to elucidate this situation.

Methods: This survey involved 17 pediatric nephrology centers in Turkey. The survey questions were shared online with the centers, and responses were evaluated using the same system.

Results: A total of 39 pediatric nephrologist participated in the survey, including 12 consultants, 8 associate professors, and 19 professors. Kidney transplantation was performed in 83.3% of the centers. All centers reported routine screening for EBV post-transplantation. However, the timing of the first screening varied: one week (11.8%), one month (70.6%), and three months (5.9%), with two centers (11.8%) not performing routine screening. Polymerase chain reaction (PCR) and serological methods were used for testing, with percentages of 87.5% and 17.6%, respectively. The unit for EBV-DNA test results was predominantly reported as copies/mL (87.5%) and IU/mL (12.5%), with significant variation in the accepted threshold values, ranging from 50-1000 copies/mL to 10-4500 IU/mL. Follow-up frequency in the presence of EBV DNAemia was predominantly every two weeks (82.4%), followed by weekly (11.8%) and every three weeks (5.9%). Changes in immunosuppression were mainly made by reducing the dose of mycophenolic acid (94.1%), followed by reducing tacrolimus dose (52.9%) and steroid discontinuation (17.6%). Despite the reduction in immunosuppression, 88.2% of centers preferred intravenous immunoglobulin, and 29.4% chose rituximab in cases of persistent EBV DNAemia. Regarding the administration of rituximab, 53.9% of the centers reported no specific criteria, while 23.5% preferred rituximab at 3 months and 11.8% at 2 months of persistent EBV DNAemia.

Conclusions: While there were various recommendations for patient monitoring and management (especially regarding immunosuppressive changes, IVIG, and rituximab use) in the presence of EBV DNAemia in pKTR, there is a need for a best clinical practice recommendation.

1257 - P2.202

20-YEAR PATIENT AND FIRST KIDNEY TRANSPLANTATION SURVIVAL ANALYSIS BASED ON THE PAEDIATRIC KIDNEY REPLACEMENT THERAPY NATIONAL REGISTRY IN SPAIN (REPIR 1)

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Purpose: The Pediatric Kidney Replacement Therapy National Registry in Spain (REPIR 1), created in 1987 and sustained on behalf of the Spanish Society of Pediatric Nephrology (AENP), collects annually updated information from all pediatric nephrology centers in the country, regarding the initiation and maintenance of chronic dialysis and/or kidney transplantation in children. In this 20-year survival analysis, we aimed to evaluate patient and first kidney graft survival in our National cohort and determine the main prognostic factors involved.

Methods: Retrospective analysis of all first kidney transplant (KT) performed in pediatric programs in Spain, from 2002 to 2022, focused on graft and patient survival and main factors that potentially influence both items: type of donor (living, LD, or deceased, DD, donor), recipient age, donor age, HLA matching, presence of anti-HLA antibodies and underlying kidney disease. We compared those factors by the Kaplan-Meyer survival analysis.

Results: A total 1,149 KT were reported in the study period. 30 patients died during that time (2.6% mortality, half them, within the first year after KT) and 4 else were lost during the follow up. Although not significant, we observed higher patient mortality in recipients under 2 years-old. From the remaining 1,115 KT, 877 were DD (72.9%) and 238 were LD (27.1%). We found a 60.3% (IC95% 53-68.6) global graft survival at 15 years after transplantation, with better graft survival in LD (81.8%) than in DD (57.2%) ($p < 0.01$). These differences in graft survival based on donor type (LD vs DD) remained similar when comparing recipients younger and older than 6 years of age. Further, on the DD group, we observed higher graft survival rate in donors older than 6 years old (64.9%) than in younger than 6 years-old (49.3%) but no differences between donors younger than 3 years (n = 46) and in those between 3 to 6 year-old (n = 136). There was no differences in graft survival between recipient sex or primary kidney disease, either. Pre-emptive KT represented 32% of patients, but no differences in graft survival compared to patients on dialysis prior to KT were detected.

Finally, we observed similar graft survival when comparing HLA-matching (0-3MM vs 4-6MM) and comparing presence or absence of anti-HLA antibodies as well, although the number of patients with antibodies was very low (n = 32).

Conclusions: In this National Pediatric Transplant cohort of 1,149 KT in Spain, we confirm an overall better and extended graft survival in LD recipients, even in the youngest patients (under 6 years) in the long term (> 15 years). A KT from young deceased donors (under 6 years old, and similarly in under 3 or 3-6 years old) is the main risk factor that predicts a worst graft survival beyond the first year after transplantation. We found no differences between HLA-matching and graft survival. Patient mortality was low and we did not identified any single mortality risk factor.

1262 - P2.203

A RETROSPECTIVE ON DECEASED DONORS KIDNEY TRANSPLANTATION IN CHILDREN ACROSS CHANGES IN THE SWISS NATIONAL ORGAN ALLOCATION SYSTEM

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Aims/Purpose: Organ allocation systems aim to grant equal access to transplantation for patients on the waiting list, while ensuring optimal medical benefit. The Swiss National Organ Allocation System (SOAS) has undergone several changes since its introduction in 2007 (Figure 1). In 2012 it incorporated the presence of DSA in a priority score and waiting points shifted from being allocated from listing time to the time of starting dialysis. Between 2015 and 2017 the advantage of highly immunized patients in the priority score was lowered and points allocated out of dialysis reduced. These changes may have affected transplant access, patient's immunological matching and transplant outcome.

Methods: We retrospectively analyzed kidney allocation from deceased donors in Switzerland between 2007 and 2020 with focus on pediatric recipients (≤20 y.o.). Data were available through the Swiss Transplantation Cohort Study and SOAS. Access to transplantation was assessed in 3 periods (v0: 2007-2012; v1: 2012-2015, and v2: 2015-2020) by a two-way ANOVA and a left-censored time-to-event analysis (Long-Rank) considering patients' characteristics and the transplantation period. The outcome of performed transplantations was evaluated considering the time to first rejection.

Results: 91 children were successfully transplanted without deaths on the waiting list. Patients' characteristics were similar in the three periods, with the exception of gender. The mean age at transplantation was 13.0 ± 6y, with a mean donor age of 33.85 ± 13y. The mean time to transplantation was 222.1 ± 271 days, considerably shorter compared to the adults' waiting time (1067.2 ± 626 days). 25% were preemptively transplanted, 7% were considered highly immunized (cPRA ≥85), and 9% were transplanted across DSA. No difference was observed in time to transplantation for gender (p =0.96), diagnosis (p =0.63), ABO group (p =0.66), or immunization status (p =0.12) in the three time periods. Preemptive listed recipients were transplanted faster in v0 than recipients on dialysis (p =0.023), this advantage disappeared in v1 (p =0.524) and v2 (p =0.560) (Figure 2). The mean follow-up was 836 ± 922 days, similar in the three periods (p =0.20). The mean time to rejection was 585 ± 727 days, with no differences considering gender (p =0.78), ABO group (p =0.62), immunization status (p =0.76), diagnosis (0.82), and dialysis modality (p =0.45).

Conclusion: Changes in the Swiss Allocation System permitted a fair organ allocation in children, avoiding death on waiting list. In particular, highly immunized patients were transplanted as fast as other recipients and presented similar rejection-free time.

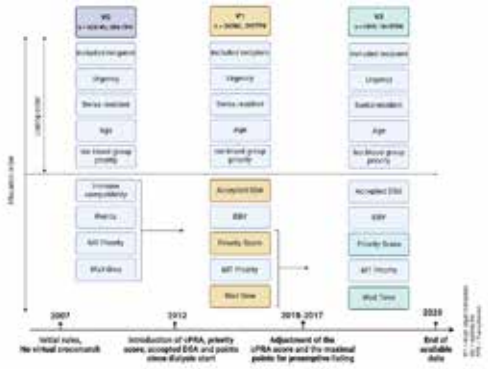

Figure 2. Changes in the Swiss Organ Allocation System between 2007 and 2020, defining 3 time periods.

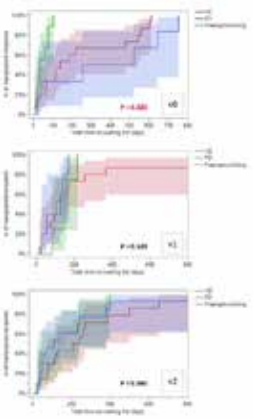

Figure 3. Time to transplantation analysis with modified Kaplan-Meier plots of patients with different dialysis modalities across the 3 periods.

1271 - P2.204

INFECTION-RELATED HOSPITALIZATIONS IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS

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Aims: Infections are the most common cause of hospitalizations and also one of the most common causes of mortality in renal transplant recipients. The aim of this study was to examine the clinical features of infection-related hospitalizations in pediatric renal transplant recipients.

Methods: The files of the patients who were followed up between January 2014 and November 2022 were reviewed retrospectively through the hospital electronic data system.

Results: A total of 226 patients, 124 (%54,9) boys, were included in the study. The mean age at kidney transplantation was 10.5 ± 5.4 years, and the median follow-up period was 5.5 years. During the follow-up period, 432 (68,9%) of 627 hospitalizations were due to infections. Of 139 patients hospitalized due to infections, 57 (%41,0) were hospitalized once, 33 (%23,7) twice, whereas 49 (%35,2) had three or more hospitalizations. We observed that the mean age of the patients hospitalized due to infections were younger than those without (9,7 ± 5,5 vs 12,0 ± 4,9 years, p =0,002). The most common causes of hospitalizations were urinary tract infections (UTI) (47,5%), followed by respiratory system infections (27,3%) and gastrointestinal system infections (11,1%). Risk factors for UTI-related hospitalizations were female gender (OR = 2,0), post-transplant first 6 months (OR:4,2), neurogenic bladder (OR:6,4), presence of post-transplant vesico-uretheral reflux (OR:15,3), and having a JJ stent (OR:5,0). The most common agents detected in patients with UTI were E.coli (43,7%) and Klebsiella (32,3%); bacterial resistance rate was 45,2%. The presence of a central venous catheter was found to be a significant risk factor for bacteremia (OR = 8,3). At follow-up, 7 patients died, 5 of whom were of severe infections. The risk factors for mortality were the presence of a central venous catheter (OR = 16,0), bacteremia (OR = 20,8), pneumonia (OR = 9,9), and the need for intensive care (OR: 350).

Conclusion: In our study, infections were both the most frequent cause of hospitalizations and mortality in pediatric renal transplant recipients.

1277 - P2.205

PARVOVIRUS B19 INFECTION RELATED ANEMIA IN THE EARLY PERIOD OF KIDNEY TRANSPLANTATION: A CASE REPORT

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Introduction: After kidney transplantation (KTx), anemia may occur in recipients for many reasons, including allograft dysfunction, dietary deficiencies, infections. However, Parvovirus B19 infection is less common than other causes. Here, we present a case of Parvovirus B19 infection that developed in the early period after KTx.

Case: An 11-year-old female patient diagnosed with end stage renal failure due to Stromme syndrome underwent peritoneal dialysis for 2 years and hemodialysis for the last 1 year. She underwent a living KTx from his mother. HLA mismatching showed no mismatches at A locus, 1 mismatches at B locus, and 1 mismatches at DR locus. The patient received induction with antithymocyte globulin (ATG) with a total dose of 5 mg/kg. The patient was discharged on postoperatif 15th day with maintenance immunosuppression consisting of tacrolimus, mycophenolate sodium, and prednisone. During the post-transplant second month, the patient developed resistant anemia, even though her graft functions were normal. During this time, the hemoglobin level decreased to 6.7 g/dl from baseline 11.5 g/dl. In other laboratory studies; hematocrit %21.2, platelets 313000 mm3; reticulocyte relative 0.19% (0.5-2.0), LDH 159 µ/l, ferritin 557 ng/ml, B12 231 pg/ml and folate 3.7 ng/ml. B12 and folic asid replacements were iniated. As a result of the worsening anemia, Parvovirus B19 serology and a qualitative RT-polymerase chain reaction (PCR) for parvovirus B19 was studied. Parvovirus IgM was 102.6 U/mL positive and Parvovirus B19 IgG was negative. Peripheral blood Parvovirus B19 PCR resulted as 835,717,434 copies/mL. The patient was started on intravenous immunoglobulin at a dose of 500 mg/kg for 4 doses. After treatment Hb was seen as 11,3 g/dL on the second week.

Conclusions: Parvovirus B19 should be considered in the differential diagnosis of anemia, even in the early period after kidney transplantation. This emphasizes the importance of early screening and treatment of this potentially life-threatening complication.

1294 - P2.206

SEVERE ANEMIA IN A KIDNEY TRANSPLANT PATIENT

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Case Presentation: A thirteen year-old male patient who underwent kidney transplantation from a living donor in another center, applied to our pediatric nephrology outpatient clinics with the complaint of fatigue at post transplant sixth month. His treatment protocol included prednisolone, tacrolimus, and mycophenolic acid. On physical examination, there was pallor in his skin and mucosa. The patient had normal blood pressure and slightly increased heart rate. Laboratory examination revealed a severe anemia with a hemoglobin level of 5.6 g/dL. Biochemical analysis showed a slightly increased serum creatinine level (0.83 mg/dL) with normal urea and normal electrolytes. Hemoglobin was 5,6 g/dL (12.5-16), hematocrit was 17% (36.5-47.5%) with low red blood cell count 2,17 (4.1-5.55) x1012/L and low RDW: %13.4 (%11.5-16) and normal MCV: 81 fL (78-93). Peripheral blood smear revealed normochromic normocytic anemia. Further analysis were made in order to elucidate the etiology of severe anemia. Anti-nuclear antibody and dsDNA antibody were negative. BK virus PCR was negative in both urine and blood. Parvovirus IgM and IgG were negative as well. Other viral markers were not informative. Despite several transfusions hemoglobin level fell to 4.3 g/dL. Bone marrow aspiration and biopsy showed 70% cellular marrow. In the interstitial area, there were huge pleomorphic cells with prominent nucleoli, and vesicles in nuclei which supports the suspicion of parvovirus or CMV infection. Blood Parvovirus and CMV PCRs were demanded and nearly two billion copies of parvovirus were detected in Parvovirus PCR analysis. The patient was diagnosed as Parvovirus B-19 related anemia. The patient was administered IVIG (400 mg/kg/day) for five days. Immunsupressive treatment was diminished. Our patients's control hemoglobin was 10.5 mg/dL on the 19th day of the treatment and it was 12.3 g/dL at the last visit after discharge. However, despite reduction of immunusuppression, anemia relapsed 3 months later, the patient was administered IVIG again, and tacrolimus treatment were changed to everolimus.

Conclusion: Acute and chronic persistent anemia may be seen in patients with Parvovirus B19 infection. Pure red cell aplasia is a life threatening complication of parvovirus infection which may be seen in immunsuppressive patients especially in bone marrow transplantation and solid organ transplants. In all cases of anemia with unknown etiology, in renal transplant receivers with a hemoglobin level < 10 g/dL, and in anemia irresponsive to erythropoietin treatment, one should kept in mind the possibility of infection with parvovirus B19. It is advised to order a Parvovirus PCR test when there is severe anemia in a young kidney transplant during the first months post-kidney transplantation. Close monitoring is essential to detect relapses.

1307 - P2.207

KIDNEY TRANSPLANTATION IN PATIENT WITH URETERAL AND RENAL AGENESIS IN SIRENOMELIA: FIVE YEARS OF EXPERIENCE

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Aims/Purpose: Sirenomelia is a rare congenital malformation driven by fused lower extremities and associated with other anomalies of genital, urinary and gastrointestinal systems, single umbilical artery and sever oligohydramnios. It is a lethal condition in the perinatal period and only 1% of cases can survive the 1st week after birth. The survival and prognosis are closely connected to an appropriate kidney function.

Methods: We describe 5 years of experience after renal transplantation (RT) in a rare case of Sirenomelia.

Results: A 22-years-old gravida delivered at 40 weeks' gestation a 2450-g female infant. No malformations were documented prenatally. At the birth, the newborn presented sireniform malformation. Radiological imaging showed a single dysplastic and ectopic kidney located in pelvic region with bladder and urethral agenesis. Alteration of the excretory tracts was characterized by absence of ureteral with a cutaneous orifice that allowed the urinary outflow. A single median ovary was recognizable; but uterus, vagina and external genitals were absent. On second day of life a terminal ileostomy was performed for anorectal and descending colon atresia. Furthermore, a surgical team succeeded in total separation of the lower limbs. The girl had progressive chronic renal failure with initial serum creatinine of 1.7 mg/dL. Subsequently, during a pyelonephritis, she developed an acute kidney injury (serum creatinine 9.2 mg/dL). We started continuous renal replacement therapy. No improvement in clinical condition was observed; pelvic nephrectomy surgery had to be performed. The gradual resolution of illness allowed us to start intermittent hemodialysis. At 16 years old, the patient received cadaveric RT and contextual ureterocutaneostomy was performed. The induction regimen consisted in basiliximab; whereas the maintenance immunosuppressive treatment consisted of tacrolimus, mycophenolate mofetil and corticosteroid. No surgical or immunological complications were reported. Her post-transplant course was characterized by some infectious events, particularly pyelonephritis. Therefore, we decided to insert a ureteral stent to allow the urinary outflow. Five years after RT, patient presents good general condition with normal blood pressure. The ureteral stent is replaced every three weeks. The most recent laboratory test reveals normal blood count, creatinine 1.14 mg/dl (eGFR 69 mL/min/1.73mq), no electrolytic alteration, no inflammatory markers and negative screening for viruses.

Conclusion: We report a rare case of Sirenomelia with overall survival of approximately 21 years old and 5 years after RT. Our experience demonstrates a greater survival rate in patients with maintained renal function. The kidney transplantation may represent a management strategy in patient with similar urinary tracts anomalies.

1313 - P2.208

A RARE CAUSE OF PEDIATRIC KIDNEY TRANSPLANT RELATED TO RETROPERITONEAL FIBROSIS IN ERDHEIM-CHESTER DISEASE

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Aims/Purpose: Present a rare cause of chronic kidney disease with pathognomonic features

Methods: Case review of Erdheim-Chester Disease and solid organ transplantation in these patients

Results: Erdheim-Chester Disease (ECD) is a rare histiocytosis that has been recognized as a neoplastic disease, due to the discovery of recurrent mutations in the activating MAPK pathway (RAS-RAF-MEK-ERK). Typical findings in ECD include central diabetes insipidus, restrictive pericarditis, perinephric fibrosis, and sclerotic bone lesions. The histopathological diagnosis of ECD is challenging due to non-specific inflammatory and fibrotic findings on histopathological examination of tissue samples. Most ECD patients require treatment, except for a minority with minimally symptomatic mono-organ disease. In the literature, there were 800-1000 reported cases in adults, predominantly males, with onset typically between 40-70 years of age. Pediatric cases are very rare (approximately 20 cases). We describe a pediatric case that manifested ECD in the first few months of life, progressing to end-stage kidney disease requiring haemodialysis. The patient came to medical attention due to petechial skin lesions, fever, and lymphadenopathy. At three and a half years old, investigations for acute kidney injury (AKI) revealed peritoneal fibrosis associated with severe bilateral hydronephrosis, hepatosplenomegaly, numerous osteolytic lesions in the cranial area, one bone lesion in the tibial region, and one in the femoral region. Biopsy of an occipital lesion oriented towards the diagnosis of infiltration of foamy histiocytes, CD68+ in the absence of cellular elements attributable to Langerhans cells, supporting a diagnosis of ECD. She started hemodialysis at the age of 12, one year later she underwent a deceased donor kidney transplant. Remarkably, within approximately 24 hours post-transplant, she showed an early graft function.

Conclusion: To our knowledge, three cases of solid organ transplantation in adulthood have been described, including lung, kidney, and liver transplants, and this is the first case of organ transplantation in pediatric age due-to ECD. ECD should be considered by pediatric nephrologists, especially when evaluating the possibility of acute or chronic kidney disease and perirenal fibrosis. Despite its rarity, the complexity of the disease, the availability of specific therapies (BRAF/MEK inhibitors), and the hematologic risk (particularly chronic myelomonocytic leukemia) emphasize the importance of considering this condition.

1314 - P2.209

IS THERE A DIFFERENCE BETWEEN SUBCLINICAL REJECTION AND ACUTE ALLOGRAFT DYSFUNCTION ON PATHOLOGICAL EXAMINATION IN PAEDIATRIC KIDNEY TRANSPLANT RECIPIENTS?

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Aims/Purpose: Subclinical rejection refers to the presence of rejection findings on pathological examination due to donor-specific antibody (DSA) positivity, despite normal laboratory findings. The objective of this study was to compare the results of patients who underwent biopsy due to acute allograft dysfunction (AAD) and subclinical rejection.

Methods: A retrospective review was conducted on allograft biopsy data sent from the Pediatric Nephrology Clinic between 2014 and 2023. AAD was defined as an increase of 0.3 mg/dL in serum creatine level compared to the baseline level. The specimens were evaluated using Banff 2019 criteria by two senior nephropathologists at the Department of Pathology. The score for microvascular inflammation (MVI) was calculated by adding the scores for glomerulitis and peritubular capillaritis.

Results: A total of 206 biopsy specimens from 136 kidney transplant recipients were analysed. Indications for biopsy include AAD in 154 patients (74.7%), subclinical rejection in 21 patients (10.1%), primary disease recurrence in 11 patients (5.3%), polyoma virus nephropathy in 12 patients (5.8%), delayed graft function in 5 patients (2.4%), and unexplained proteinuria in 2 patients (0.9%). The serum creatinine values of patients with AAD at the time of biopsy were mean 2.04 ± 1.15 mg/dL, and the median time between renal transplantation and biopsy was 2.91 years (IQR 5.53 years). DSA was found to be positive in 37% of patients with AAD. Tubulitis (93.5%) and interstitial inflammation (85.7%) were the two most common findings in biopsies performed with the diagnosis of AAD. 14.3% of the sample had an MVI index of 2 or higher, while 51.9% had an MVI index of 1. C4d staining was positive in the peritubular capillaries of 16.2% of patients. Interstitial fibrosis and tubular atrophy were present in 88.3% and 87.0% of patients, respectively. When comparing biopsy findings of patients with subclinical rejection and AAD, the MVI, tubulitis, interstitial inflammation scores, and C4d positivity rates were found to be similar (p-values of 0.061, 0.459, 0.624, and 0.557, respectively). IF/TA scores indicating chronic involvement were more frequent in the AAD group (p 0.006 and 0.008, respectively). The subclinical rejection group had a longer follow-up time after biopsy (5.73 ± 2.64 vs 4.49 ± 2.59; p =0.044). The graft failure rate was 9.5% in patients with subclinical rejection and 38.1% in patients with AAD (p =0.012).

Conclusion: It is remarkable that subclinical rejection exhibits similar acute inflammation findings to AAD. Diagnosing rejection before clinical signs appear has allowed patients to experience a lower rate of graft failure.

1332 - P2.210

A CLINICAL TRIAL SIMULATION FOR PROSPECTIVE CLINICAL STUDIES ON THE LONGITUDINAL ASSESSMENT OF BIOMARKERS TO PREDICT ALLOGRAFT REJECTION IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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Aims/Purpose: The prospective study of non-invasive biomarkers in kidney transplantation (KTX) is becoming increasingly prevalent as the complexity of rejection is incompletely captured by routine laboratory testing. However, as the clinical course of these patients is subject to multiple irregular changes, single biomarker measurements, as frequently reported, may not suffice. This is especially relevant for rare events in small cohorts, i.e. rejection in pediatric KTX. The aim of this study was to simulate and compare clinical trial scenarios and statistical models for the assessment of longitudinal biomarkers to predict rejection in pediatric kidney transplant recipients.

Methods: By using real-world data of plasma Torque Teno virus (TTV) measurements in our pediatric KTX cohort (a biomarker reflecting patients' immunestatus) we conducted extensive simulations with 432 clinical trial scenarios to explore a broad range of different sample sizes, effect sizes, biomarker trajectories, and subcohorts. Therefore, we used permutational rejection sampling with mixed-effects model simulated biomarker trajectories to generate time-to-event data with 5000 replicates for each scenario. Estimation accuracy and statistical power were calculated and evaluated across different statistical models and clinical scenarios.

Results: Statistical power increased with sample size and biomarker observation time increase across most scenarios and statistical models. In scenarios with the smallest sample size (n = 100) and lowest event rate (4%) the highest statistical power was achieved by Cox regression with time-dependent covariates and generalized estimated equations (GEEs). Case-control comparisons using single measurements achieved similar results with parametric (t test) and non-parametric (Mann Whitney U) methods although with markedly decreased power in comparison to longitudinal models.

Conclusion: The utilization of longitudinal biomarker trajectories for the prediction of rare events in small cohorts, such as rejection in pediatric KTX, resulted in higher statistical power, especially upon increasing biomarker observation time. This was observed across different clinical scenarios and subcohorts. Clinical trial simulation and utilization of appropriate modeling approaches are crucial to identify non-invasive biomarkers with predictive potential for rejection, especially in small cohorts with rare events, and thereby to potentially reduce (repeated) invasive KTX biopsy.

1338 - P2.211

NEW ONSET IGA VASCULITIS IN A KIDNEY TRANSPLANT RECIPIENT-A CASE REPORT

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Aims/Purpose: IgA vasculitis (IgAV) is the most common pediatric small-vessel vasculitis. It usually involves the skin, gut, joints, and the kidney in 40% of cases. As far as we know, only a couple of cases of new-onset IgA vasculitis in kidney transplant recipients have been described and in these cases, kidney function was not affected.

Methods: A case report of the patient followed at our tertiary hospital.

Results: Our patient is a boy who was born with bilateral kidney hypoplasia and required peritoneal dialysis. At the age of two, the patient was transplanted with a kidney from his grandfather, after which, he was treated with triple immunosuppression: tacrolimus, mycophenolate mofetil (MMF), and prednisolone. Recurrent gastrointestinal and respiratory infections complicated the post-transplant period, and MMF was therefore changed to azathioprine. The patient also had moderate hypertension. Two years after the transplantation, the glomerular filtration rate was 40 ml/min/1,73 m2. At the age of four, after an episode of bacterial enteritis, our patient developed typical IgAV with purpura, abdominal pain, lower limb pain, and macroscopic hematuria. The kidney function deteriorated. Laboratory tests Creatinine rose from baseline 80 to 140 µmol/L, Urine albumin/creatinine ratio from 0 to 250 mg/mmol. Skin biopsy. Small cell vasculitis with neutrophil infiltrates and IgA depositions. Initial kidney biopsy Immunofluorescence confirmed the deposition of IgA in glomeruli. Activity scores included mesangial and endocapillary proliferation and tubulointerstitial inflammation, E1M1S1T1C1 according to the Oxford classification. Moreover, 50% of glomeruli had segmental sclerosis, and 7 of 49 (14%) glomeruli had crescents. The boy was treated with 3 methylprednisolone pulses 15 mg/kg followed by an increased dose of prednisolone from 5 mg every other day to 1 mg/kg daily. Azathioprine was increased from 1 mg/kg/day to 2 mg/kg/day. The concentration of tacrolimus was maintained at a higher level (5-6 ng/ml compared with a standard level of 3-5 ng/ml). The patient experienced two recurrences of rash and joint pain during upper respiratory tract infections during the first twelve months after the onset of IgAVN. After twelve months, the creatinine returned to its pre-vasculitis level and there was a complete regression of albuminuria. The doses of immunosuppression were decreased accordingly. Control kidney biopsy showed the entire resolution of previous inflammation. During the following four years, there was no relapse of vasculitis. Blood pressure and glomerular filtration rate remained stable.

Conclusions: As far as we know, this is the first case of new-onset IgA vasculitis in a kidney transplant recipient significantly affecting the graft function. Our patient was successfully treated with temporarily increased standard post-transplantation immunosuppression.

1390 - P2.212

HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR ACQUIRED SEVERE APLASTIC ANEMIA IN A KIDNEY TRANSPLANT RECIPIENT: CASE REPORT

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Aims/Purpose: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) can be offered to solid organ transplant recipients as a therapeutic treatment option for irreversible damage of hematopoiesis. Adult data suggests worse outcomes of allo-HSCT in kidney than liver transplant recipients but data in children remains scarce.

Methods: We present a challenging case of allo-HSCT to treat severe aplastic anemia (SAA) in a 14-year-old kidney transplant recipient.

Results: The patient developed SAA 6 years after kidney transplantation. Patient underwent deceased donor kidney transplantation at the age of 7 years due to stage 5 chronic kidney disease after Shiga toxin-associated hemolytic uremic syndrome (HUS) at 4 years of age. During the post-transplant course the patient developed absence epilepsy and leukopenia (leading to withdrawal of mycophenolate mofetil). At the age of 14 years, being on tacrolimus and two anticonvulsants the patient had SARS-CoV-19 infection and a month later developed fever and irreversible pancytopenia of unknown origin classified as acquired SAA. After 2 months of different therapeutic attempts peripheral hematopoietic stem cells were infused from a matched unrelated donor (9/10) under immunosuppression with cyclosporin and anti-thymocyte globulin. During the post-transplant period she became severely hypertensive whereas kidney function remained stable with several mild-to-moderate acute kidney injury (AKI) episodes. After timely neutrophil engraftment acute graft-versus-host disease (GvHD) grade II was diagnosed at day +38 and treated with steroids and mesenchymal stem cells. Later on, reactivation of cytomegalovirus (CMV) and BK virus was observed on day +45 managed with adoptive immunotherapy with CMV-specific T-lymphocytes and ganciclovir. On day +41 HSCT-thrombotic microangiopathy (TMA) was diagnosed and weekly eculizumab infusions were started (a total of 6). Although TMA markers improved, CMV-disease progressed and patient developed pericardial and pleural effusion requiring surgical drainage. The condition deteriorated gradually due to multiple organ failure with anuric AKI and despite all efforts the patient died on day +95 after allo-HSCT.

Conclusion: Our case illustrates the challenges of allo-HSCT in pediatric kidney transplant recipients, including unclear immunosuppressive regimens, need to adapt typical allo-HSCT practices and managing various complication while attempting to preserve kidney transplant function.

1430 - P2.213

EVALUATION OF CHATGPT 3.5 OUTPUTS FOR PEDIATRIC KIDNEY TRANSPLANT QUESTIONS REGARDING ACCURACY, RELEVANCE AND POTENTIAL HARM

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Aims/Purpose: To evaluate the ability of ChatGPT 3.5 to provide accurate and relevant outputs to patient questions regarding management, care, and challenges of pediatric kidney transplantation and assess its potential to be used as a web-based information source for adolescent transplant patients.

Methods: In this study, a set of 37 questions with three separate themes as 'General Knowledge', 'Management and Care', and 'Living with Transplantation' had been generated by the two authors who did not evaluate the outputs later. The questions were generated by drawing examples from openly available public and patient centered informative pages of known transplant centers and authors' personal experiences with transplant patients. Initial prompting of the ChatGPT involved a brief explanation about a hypothetical 16-year-old patient who was about to undergo kidney transplantation because of chronic kidney disease. ChatGPT was instructed to answer the questions in a manner that a doctor would do to a lay-person patient. After initial prompting of ChatGPT, the generated outputs were evaluated by two separate pediatric nephrologists with experience in kidney transplantation (R1 and R2). The evaluators rated the outputs of the ChatGPT according to their accuracy, relevancy, potential harm and extend of the potential harm using the Likert scale. In case of inconsistent scores, a third evaluator has been involved.

Results: The mean accuracy scores of all ChatGPT outputs were 4.40 (R1) and 4.52 (R2) out of 5. Mean accuracy scores of all outputs given by two different reviewers were coherent with each other. Only one output regarding the possible effects of being a transplant patient on pregnancy were evaluated as 'factually inaccurate' by one reviewer but mean accuracy of the respective output was 4.5 out of 5. When calculated separately, the mean accuracy scores of each group of questions were also over 4. In a similar manner, the overall mean relevancy/suitability scores of the outputs were 4.48 (R1) and 4.75 (R2). Overall rate of possible harm that could be triggered by the outputs was 30% (24% of them being minor inconvenience) according to R1 and 10% according to the R2 (8% of them being minor inconvenience).). Reviewer 1 attributed the decision to choose potential harm to the non-specificity of certain outputs that may underrate the importance of the personalized approach to a transplant patient especially in issues regarding lifestyle maintenance. Overall, the outputs were rated to be accurate, relevant and safe.

Conclusion: This study showed that the ability of the ChatGPT 3.5, a relatively inferior model, to produce accurate and relevant outputs with minor or no potential harm for a kidney transplant patient is significantly high. If known disadvantages of LLMs can be overcome by better prompting, and better versions, they can be valuable to streamline the workflow and for a source of information.

1463 - P2.214

CENTRAL BLOOD PRESSURE MONITORING IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS: A COMPREHENSIVE EVALUATION

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Introduction: Arterial hypertension in children after kidney transplantation is an important risk factor for graft loss and cardiovascular morbidity and mortality. Ambulatory blood pressure monitoring (ABPM) stands as the gold standard for diagnosing hypertension in children. Central systolic blood pressure (cSBP) more strongly reflects vascular changes than peripheral blood pressure (BP).

Objectives: Analyze the prevalence of arterial hypertension and left ventricular hypertrophy (LVH) in pediatric kidney transplant patients using ABPM and cSBP.

Methods: This was a retrospective observational, cross-sectional, study. Between October 2021 and June 2023 we performed ABPM and cSBP in 46 children and adolescents who had previously received kidney transplant. All of them had a functioning graft with GFR higher than 30 mL/min/1.73 m2, and had been stable for at least 6 months prior to study enrollment. We used SpaceLabs 90217 monitor (SpaceLabs Healthcare, Issaquah, WA) for all ABPM studies and Mobil-O-Graph (IEM: GmbH, Stollberg) for measurement of central blood pressure. Wall thickness and dimensions of the left ventricle were measured using M-mode. Left Ventricular Hypertrophy (LVH) was defined as left ventricular mass indexed (LVMI) to height 2.7 ≥95th percentile for gender and age. We examined the association between various BP parameters measured and presence or absence of LVH.

Results:

Patient characteristics are described in table 1. Based on values ≥95th percentile for cSBP and ABPM measurements and the use of antihypertensive medications, we grouped patients as normotensive, hypertensive, or with controlled hypertension (Figure 1). Regarding ABPM, the percentage of patients who had mean arterial pressure (MAP) ≥ 95th percentile in the different time periods was: 9% for 24-hour global MAP, 11% for diurnal and 13% for nocturnal. Patients identified with hypertension based on ABPM exhibited an increased likelihood of abnormal cSBP results in the multivariate analysis, with adjustments made for height z score and sex (OR: 1.06; 95%CI: 1.007- 1.14, p =0.03). cSBP showed an AUC = 0.72 (95% CI 0.57–0.87). The best cutoff was 110 mmHg with sensitivity of 0.75, and specificity of 0.65. Dimensions of the left ventricle were evaluated in 42 children, LVH was found in 13 (30%). All of them were hypertensive, 4 have abnormal ABPM and 6 abnormal cSBP, the remaining hypertensive children with LVH had controlled hypertension. Normotensive patients by ABPM and cSBP had lower LVMI than hypertensive patients (uncontrolled + controlled): 28 vs 36 g/m(2.7) (p =0,02).

Conclusions: Measurement of blood pressure by cSBP is an easy and simple method to be performed as part of the routine examination in the kidney transplantation clinic. Regular monitoring and trends over time might help identify changes in cardiovascular health and guide adjustments to medications.

Clinical and laboratory characteristics	Overal cohort (N =46)
Median age, yr (IQR)	14.5(11.6-16.9)
Male gender, n (%)	29(63)
Underlying Disease n (%)	
CAKUT	20 (43)
glomerular diseases	14(29)
STEC-HUS	4(9)
other	10(21)
Preemptive transplantation	10 (22)
time on dialysis(yr)	1.9± 2.8
Median eGFR as ml/min per 1.73 m2 by bedside Schwartz (IQR)	92.5 (60-80)
time since transplantation (yr)	5 (± 3.8)
BMI	22 (19-25)
Age- and sex-adjusted BMI z score	1.1 (0.3 1.7)
Height (cm)	149 (139-155)
Height z score	-1.7 (-2.5 -0.8)
LVMI n:42	35 (28-40.5)
Left ventricular hypertrophy n:42	13 (30)
Antihypertensive medication use	32 (67)
live related donor	23(50)

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ASSESSING PRE-TRANSPLANT HUMORAL AND CELLULAR RESPONSES, AND THE PREVENTIVE EFFICACY OF IV IMMUNOGLOBULINS FOR BK VIRUS REPLICATION AFTER PEDIATRIC KIDNEY TRANSPLANTATION

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Purpose: BK virus–associated nephropathy (BKVAN) is a major cause of kidney graft loss. No specific antiviral therapies are available. The current clinical approach relies on minimizing immunosuppression based on viral load monitoring. Nevertheless, this empirical strategy does not consistently yield success, underscoring the importance of identifying pretransplant predictors of BKV replication.

Methods: We assessed pre-transplant BKV neutralizing antibody (NAb) titers in pediatric kidney transplant recipients. Seronegative patients (BKV Genotype I NAb < 4 log10 IC50) were preemptively treated with intravenous immunoglobulin (IVIg: 0.4 g/kg/3 weeks for 6 months). Additionally, we conducted a retrospective evaluation of anti-BKV cellular responses, utilizing BKV-Elispot assay (VP1, LTA and pan-BKV peptides) on PBMC frozen on the day of transplantation, to assess its potential use as a predictive marker for BKV replication.

Results: We included 24 pediatric recipients with a median of 10.8 yo (mainly first transplant, with deceased donor, basiliximab induction and tacrolimus + MMF +/- steroids treatment). 8/24 patients (33.3%) were BKV Genotype I Nab positive before transplant. 18/24 patients received preventive IVIg treatment. Among the 24 patients, 6 (25%) experienced post-transplant BKV replication (including 2 with biopsy-proven BKVAN). Pre-transplant BKV Nab titer showed no significant difference between patients who experienced post-transplant BKV replication and those who did not (Figure 1). Out of the 24 patients, 14 BKV Elispot were performed on PBMCs frozen on the day of transplantation. While the limited sample size prevents us from reaching statistical significance, it's noteworthy that patients experiencing post-transplant BKV replication seem to exhibit lower pre-transplant cellular responses compared to those without post-transplant replication (Figure 2).

Conclusion: Anti-BKV cellular response may be a better predictor of post-kidney transplant BKV replication in pediatrics. The lack of association between pre-transplant NAb titers and BKV replication may be due to our systematic IvIg supplementation of seronegative patients and needs to be further investigated.

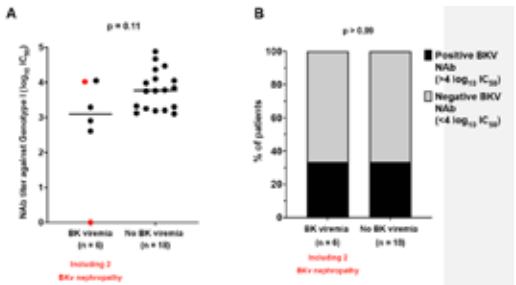

Figure 1. Pre-transplant anti-BK virus humoral responses

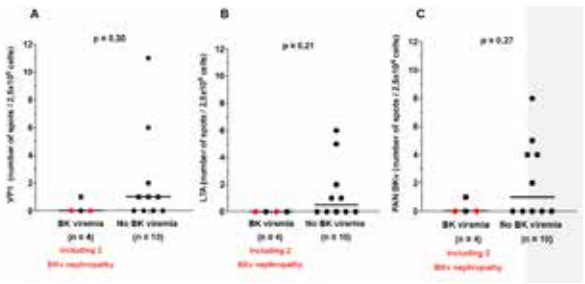

Figure 2. Pre-transplant anti-BK virus cellular responses

ABSTRACT ONLY

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BLOOD PRESSURE DIPPING IN CHILDREN WITH CAKUT. DATA FROM THE APRIC STUDY

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Hypertension (HTN) is a risk factor for progression of chronic kidney disease (CKD) in children. ABPM shows a nocturnal "dipping" (D) in blood pressure (BP) values during night-time; blunted D is a negative prognostic factor for CKD in adults. APRIC study is a multicentric study approved by the ESPN WG "CAKUT"; includes children with CAKUT in whom an ABPM was performed. Medical history, height, weight, office BP, laboratory data were registered. eGFR was calculated with the Schwartz formula. Non-dipping systolic (NDS) or diastolic (NDD) status was defined as nighttime systolic or diastolic BP average < 10% of the daytime BP average. The relation between dipping status and other variables was evaluated using both bivariate and multivariate statistical analysis. We have enrolled 131 children, 92 males (70.2%). Their age ranged from 5 to 18.8 years (mean 12.1, SD 4.2). Their diagnosis included: Vesico-ureteral reflux (11.5%), Reflux Nephropathy (22.1%), Renal Dysplasia (6.1%), Renal Agenesia (29.0%), Renal Hypoplasia (14.5%), Multicystic dysplasia (10 %), and other diagnoses (6,9%). Their eGFR ranged from 19.6 to 155.8 (mean 87.4, SD 20.8). Normal office BP was registered in 77 children (NORM BP, 58.8%); high office BP in 54 children (HIGH BP, 41.2%). 27 patients were on anti-hypertensive medication (BP MED, 20.6%). Non dipping systolic status (NDS) was registered in 97/130 (74.6%), and non-dipping diastolic (NDD) in 47/129 (36.4%). Reversal dipping was present in 14 (10.8%). In NORM BP, 47/77 (61.0%) were NDS vs 37/54 (68.5%) in HIGH BP (p =0.49). In NORM BP, 32/77 (41.6%) were NDD vs 32/54 (59.3%) in HIGH BP (p =0.07). In BPMED, NDS were 19/27 (70.4%) vs 65/104 (62,5%) in non BPMED (p =0.59). NDD were 12/27 (44.4%) in BPMED vs 52/104 (50,0%) in non BPMED (p =0.77). We compared age, sex, eGFR, CAKUT diagnosis, birth weight, BMI in NDS and NDD patients with the dipping status; sex was significantly different only in NDD (males 55.3% in ND vs 78.0% in dippers, p =0.01). In a simple regression model, neither systolic or diastolic dipping were predictors of eGFR (p =0.32 and 0.11). In a multiple regression model including age, sex, systolic and diastolic dipping and mean 24h systolic and diastolic BP, and type of diagnosis, only diastolic dipping was correlated with eGFR (p =0.03). In conclusion ND status is frequent in children with CAKUT including those with normal BP. NDD is related to lower eGFR and more frequent in females.

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DEMOGRAPHIC TRENDS AND DIAGNOSTIC INDICATORS IN PEDIATRIC PRIMARY VESICOURETERAL REFLUX NEPHROPATHY: INSIGHTS FROM A CLINICAL STUDY

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Aims/Purpose: This abstract aims to present the findings and analysis derived from a study conducted on patients diagnosed with congenital Vesicoureteral reflux (VUR) within the Nephrology Center of Tbilisi "I . Tsitsishvili Children's Clinic" in Georgia.

Methods: We conducted a retrospective analysis of patient records from the Nephrology Center of Tbilisi "I. Tsitsishvili Children's Clinic" in Georgia. Demographic data, reflux severity, and renal function confirmed by DMSA scintigraphy were evaluated. Additionally, mean platelet volume (MPV) and mean platelet count (MPC) were assessed as potential diagnostic markers. The study also explores the prospective integration of Neutrophil Gelatinase-Associated Lipocalin (NGAL) as a biomarker for kidney disease progression.

Results: Among the 23 pediatric patients with primary VUR induced nephropathy, males comprised approximately 60.9% of the cohort. The age at diagnosis ranged from 3 months to 10 years, with all patients exhibiting impaired renal function. Notably, 6 out of the 23 patients progressed to end-stage kidney disease, with 3 of them undergoing successful kidney transplantation. While the majority had reflux grades higher than 3, variability was observed in platelet parameters, with MPV below the normal range in 8.7% of cases. No significant abnormalities were noted in MPC.

Conclusion: Our findings shed light on demographic trends and diagnostic indicators in pediatric primary VUR induced nephropathy. The study underscores the importance of considering gender, age, reflux severity, and renal function in clinical assessment. Additionally, the potential integration of NGAL as a biomarker for monitoring kidney disease progression holds promise for enhancing clinical management strategies in the future.

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AN UNEXPECTED CAUSE OF METABOLIC ACIDOSIS IN A PATIENT WITH URINARY TRACT INFECTION

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Aims/Purpose: Urinary tract infection (UTI) is the most common bacterial infection in childhood. Children with obstructive urinary tract anomalies such as ureterovesical junction obstruction (UVJO) are at increased risk of developing UTIs. Severe cases may present with systemic symptoms and signs of urosepsis including metabolic acidosis.

Methods: Here, we present a patient with UVJO, diagnosed with UTI based on clinical and laboratory findings, but who did not improve despite UTI treatment.

Results: A term-born female infant presented due to dilation in the pelvicalyceal system detected on antenatal ultrasound (USG). A urinary USG performed at 40 days of age showed dilation in the renal pelvis with anterior-posterior diameter of 12 mm on the right and 10 mm on the left kidney; parenchymal thickness of 3 mm on the right and 6 mm on the left; and ureteral diameter of 13 mm on the right and 8 mm on the left. Bilateral UVJO was more prominent on the right side on Tc-99m mercaptoacetyltriglycine scintigraphy. Right ureterocutaneostomy was planned. The patient presented with vomiting at 2.5 months of age. There was significant pyuria (leukocytes 301/HPF) and metabolic acidosis (pH 7.22, HCO3 13.6 mEq/L). Hemoglobin was 8.1 g/dL and platelets were 76000/mL. Urine culture grew 100,000 colonies of Klebsiella pneumoniae. Despite UTI treatment, vomiting and metabolic acidosis with high anion gap persisted. Hypoglycemia and positive urinary ketones were detected. Despite low free carnitine [C0: 8.21 mmol/L (10-60)], there was a significant elevation in C3 [C3: 11 mmol/L (0.28-2.9)] on dry blood spot acylcarnitine analysis. High excretion of methylmalonic acid [1530 mmol/molcrea (< 11)] was found on urine. Genetic analysis revealed a homozygous missense variant (c.2179C > T, p.Arg727*) classified as pathogenic in the MUT gene, leading to a diagnosis of methylmalonic acidemia (MMA).

Conclusion: Organic acidemias result in metabolic acidosis due to the accumulation of metabolites, following an initial period of well-being. Metabolic decompensation in MMA can be triggered by stress conditions such as infection. Without considering metabolic disorders in the initial episode of metabolic acidosis, some patients may be misdiagnosed with sepsis. Therefore, even in patients with known underlying pathology, the possibility of another diagnosis that could contribute to the clinical picture should not be overlooked.

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ATYPICAL PICTURE OF MICTURATING CYSTOGRAPHY IN THE BOY WITH POSTERIOR URETHRA VALVE

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Aims/Purpose: Posterior urethral valve (PUV) is one of the most common and serious urinary tract malformations. This anomaly develops during fetal life and often leads to kidney dysplasia and chronic kidney disease. The golden standard examination to detect posterior urethral valves is micturition cystourethrography. We describe a case where the examination result is not typical, despite the presence of PUV.

Methods: A case report of the patient treated at our tertiary hospital during 2023.

Results: The male child was born full-term with induction due to oligohydramnios. After delivery, the baby needed short-term respiratory support. The child's general condition stabilized quickly, however, the patient developed hypertension, hyperkalemia, hyponatremia, metabolic acidosis, and creatinine levels rose rapidly. Considering these disturbances, the bladder was catheterized, despite a normal urine stream. Patient characteristics and outcomes are presented in the table:

Fetal ultrasound at 20th gestational week	Bilateral kidney pelvic dilation: AP diameter right 20 mm, left 14 mm
Postnatal ultrasound in the first week of life	Multicystic right kidney with severely reduced parenchyma; left kidney with increased echogenicity and small cysts; no residual urine in the bladder
Micturating cystourethrography	**No valve was detected.** After micturition, the bladder was empty.
Cystoscopy	Normal penile and bulbar urethra, proximal to the sphincter there was a classic arching and then a dilated posterior urethra. The bladder was partially trabeculated. **The valve was completely resected.**

Despite resection of the valve, the child developed kidney failure, which, however, did not require neonatal dialysis. Blood pressure, electrolyte as well as acid-base disturbances could be corrected conservatively.

Conclusions: Micturating cystourethrography remains the standard radiological examination for the diagnosis of anomalies of the male urethra. However, as our case indicates, the method does not reliably detect all the cases of PUV. Therefore, in case of typical clinical and laboratory presentation, we suggest keeping the urine catheter and proceeding to cystoscopy.

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UROLITIASIS AND ANOMALIES IN HORSESHOE KIDNEY

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Aim: Horseshoe kidney is the most common congenital fusion anomaly in children. The aim of this study was to evaluate the clinical characteristics of patients diagnosed with horseshoe kidney.

Purpose: The data of patients diagnosed with horseshoe kidney in the Pediatric Nephrology Outpatient Clinic were retrospectively analyzed.

Result: There were 115 patient (49 females). Follow-up period of 78 patients was 38.97 ± 39.28 months, median 29.5 months (1month-153 months). The follow-up period was one year or more in 51 patients. The most common urinary anomaly associated with horseshoe kidney was hypoplasic kidney. Extra renal anomalies included cardiac anomaly in two patients, Turner Syndrome in two patients and Kabuki Syndrome in one patient. Three patients (2.6%) had recurrent urinary tract infection. Urinary tract calculi were found in four patients (3.5%). None of the patients had deterioration in renal function during follow-up.

Conclusions: Horseshoe kidney may be associated with urinary and non-urinary anomalies. Our data suggest that urinary tract stone disease in children with horseshoe kidney is not more common than in the normal population

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UNVEILING RENAL LITHIASIS IN CONGENITAL STEINERT SYNDROME: A CASE REPORT

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Aims/Purpose: Congenital Steinert syndrome is a severe form of myotonic dystrophy that presents with abnormalities in sucking-swallowing, generalized hypotonia, facial diplegia, and respiratory alterations during the neonatal period. Inheritance is autosomal dominant with almost complete penetrance and variable expressivity. There are no published data on nephrourological involvement associated. The objective of this work is to present a paediatric clinical case diagnosed with congenital Steinert myotonic dystrophy and nephrourological involvement.

Methods: Retrospective review of the electronic medical record of a paediatric patient diagnosed with congenital Steinert myotonic dystrophy and nephrourological involvement.

Results: Two-year-old girl, born premature at 32 weeks, with normal ultrasound studies. Postnatal diagnosis of congenital Steinert's myotonic dystrophy with a tracheostomy.At 5 months of age, admitted for study of macroscopic haematuria. Ultrasound showed bilateral renal lithiasis of 3 mm and involvement of renal pyramids suggesting medullary microcystic kidney disease or microcrystal deposition. No other significant findings in the etiological study. Renal function was normal; therefore, conservative treatment was chosen. At 20 months of age, she had a febrile urinary tract infection with isolation of E.coli in urine culture. The ultrasound showed bilateral nephrolithiasis with right ureteral lithiasis (14 mm), causing right bilateral ureterohydronephrosis and multiple lithiasis in the left renal pelvis. Evaluated by paediatric urology, and treated with bilateral double J catheter insertion. At 21 months of age, she had a second febrile urinary tract infection caused by Pseudomonas aeruginosa. Comprehensive lithiasis study revealed hyperuricosuria (uric acid/Cr index 2.8 mg/ mg), hypercalciuria (Ca/Cr index 1.6 mg/ mg), and non-nephrotic range proteinuria (protein/creatinine index 1.1 mg/ mg), slightly elevated urinary oxalate (55.91 mg/ml), so, potassium citrate was indicated. Genetic study performed using complete exome sequencing for nephrolithiasis, polycystic liver disease, and nephrocalcinosis with negative results. Expulsion of lithiasis at 23 months, sent for study with the main component being calcium oxalate dihydrate. Currently stable, with GF rate > 90 ml/min/m2, awaiting lithotripsy.

Conclusion: It is the first case in the literature diagnosed with a congenital Steinert syndrome and nephro-urological involvement in a paediatric patient.

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POLYARTERITIS NODOSA (PAN) OF RENAL BLOOD VESSELS IN ADOLESCENT - CASE REPORT

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Aims/Purpose: Polyarteritis nodosa (PAN) is a necrotizing vasculitis of small- and medium-sized arteries that most often affects the kidneys, heart, and liver but can affect any organ system. The disease is rare in children, and its epidemiology probably imprecise due to poorly defined diagnostic criteria of the illness in the young, and the considerable degree of overlap in the clinical features of the vasculitis in childhood.

Methods: We presented a seventeen-year-old adolescent diagnosed with autism and epilepsy. He was admitted to our clinic after an epileptic seizure with severe impairment of consciousness. Urgent diagnostic workup confirmed a hypertensive emergency (HE) (arterial pressure 200/140 mmHg) and acute renal failure (urea 43.7 mmol/L, creatinine 1862 umol/L, anuria).

Results: Radiological diagnostics of the brain imaging revealed acute changes consistent with Posterior Reversible Encephalopathy Syndrome (PRES) in the context of HE. Renal ultrasound showed diffusely altered cortex of both kidneys with very poor perfusion, leading to kidney biopsy. Light microscopy findings suggested acute tubulointerstitial nephritis and acute post-infectious granulomatous glomerulonephritis. Ophthalmological fundus examination described bilateral optic nerve papilla with indistinct borders and abundant peripapillary retinal haemorrhages. Cardiac ultrasound diagnosed mild concentric left ventricular hypertrophy, diastolic dysfunction, and grade I aortic valve insufficiency. Treatment was initiated in the intensive care unit where he was monitored, sedated, mechanically ventilated, and underwent continuous veno-venous hemodiafiltration (CVVHDF) and antihypertensive therapy (urapidil). Three pulse doses of methylprednisolone were administered, followed by prednisone therapy. Doppler ultrasound of blood vessels revealed thickening and narrowing of radial artery walls. Subsequent electron microscopy findings described necrotizing vasculitis affecting muscular arteries without involvement of glomeruli, consistent with medium-sized vessel vasculitis - polyarteritis nodosa. PET-CT scan didn't show active vasculitis (it was done after one month of steroid therapy).Treatment with cyclophosphamide was initiated after definitive diagnosis. Following the first dose of cyclophosphamide, he developed a grand mal epileptic seizure, which was terminated with diazepam, a similar event occurred after the sixth cycle of cyclophosphamide. In 2023, he was referred to an adult rheumatologist, and treatment with mycophenolate mofetil was initiated. Estimated glomerular filtration rate (Bedside Schwartz formula) was 20 ml/min/1,7m2.

Conclusion: Here is described seventeen-year-old adolescent with autism and epilepsy whom is diagnosed very rare disease in children – polyarteritis nodosa.

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THE DIFFERENT FACES OF CHRONIC KIDNEY DISEASE

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The progression of chronic kidney disease(CKD) refer to an irreversible decline in glomerular filtration rate (GFR) as a result of parenchymal damage. Early diagnosis and treatment can slow the progression of renal disease. Aims: to present one of the masks of CKD - acute pancreatitis, as a reason for the diagnosis of End-stage Renal Failure (ESRF), resulting from bilateral renal hypo/dysplasia.Material and Methods: We report a case of a 17-year-old patient admitted as an emergency to Pediatrics for acute abdominal pain, repeated vomiting, including hematemesis and increasing faintness. Reports of right kidney hypoplasia in early childhood. No evidence of consultation with a pediatric nephrologist and follow-up. The physical examination revealed impaired general condition, afebrile, asthenic habitus, weight: 54kg,(-2 SDS) height 175cm. With pale- earthy skin colour; pale, dry visible mucous, no oedema. Diffusely reduced subcutaneous adipose tissue. Normal respiratory status, HR 90/min. BP 150/100 mm Hg. Abdomen- soft, with spontaneous and palpatory epigastric pain; diuresis 1.1ml/kg/h.Results: Laboratory and instrumental investigations revealed acute pancreatic injury (Lipase 951U/l, Amylase 960 U/l), ESRF - GFR 9.4 ml/min/1.73m2(creatinine 1196 umol/l, urea 52 mmol/l, uric acid 572 umol/l, anaemic syndrome, decompensated metabolic acidosis, hyperparathyroidism. Reference values of other biochemical indicators, including electrolytes(Na, K), coagulation profile, immunological tests(complement, immunoglobulins, negative test(anti-dsDNA, anti-GBM). Alpha-Galactosidase enzyme activity was normal and lyso-Gl-3was negative. There were proteinuria 2.7 g/(24.h), hyposthenuria, microhaematuria+, glucosuria+. Abdominal and chest radiography excluded acute intestinal obstruction, pneumoperitoneum and pulmonary hypervolemia. Abdominal ultrasound showed bilateral renal hypo/dysplasia, without abnormalities of other abdominal organs. ESRF protocol was followed and symptomatic treatment was started. A temporary central venous catheter was placed and 4 hemodialysis sessions were performed, with GFR 19.4 ml/min/1,73м2 and control of acute pancreatitis. Conclusions: We present a patient with 4 life-saving haemodialysis for ESRF, diagnosed due to acute pancreatitis as the first manifestation of CKD. After control of the acute condition, the patient undergoes chronic hemodialysis and is going to be prepared for renal transplantation.

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EVALUATION OF RED CELL DISTRIBUTION WIDTH IN CHILDREN WITH HYPERTENSION

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Aim: An index of the routine blood cell count, red cell distribution width (RDW) is a potent predictor of morbidity and mortality in a variety of settings, especially in many cardiovascular diseases. Aim of the study is to analyse the relationship between red cell distribution width(RDW) and systemic hypertension in children.

Method: In a cross-sectional study, data from patients who admitted to Pediatric Nephrology outpatient clinic and diagnosed as hypertension by ambulatory blood pressure monitor were analyzed. Patients were categorised as etiology and stage of hypertension. All patients underwent examinations for end organ damage for left ventricular hypertrophy (LVH) and hypertensive retinopathy. The patients' clinical and demographic characteristics including age, sex were obtained from patients files. RDW and hemoglobin levels before treatment were recorded and analysed. Children who had normal results of ABPM were included as control group.

Results: Totally 204 children were enrolled to our study and 91 were as control group. Mean age of patients were 14 ± 3 year (5-18 year). Mean RDW of patient and control group were similar (13.35 ± 1.17% and 13.39 ± 1.29% respectively, $p > 0.05$). Mean hemoglobin level was higher in patient group than control group (14 ± 1.89 g/dl and 13.6 ± 1.95 g/dl respectively, $p < 0.05$). Patient group was categorised as etiology, stage and end organ damage and results were at Table.

Characteristics of patient group	Red Cell Distribution Width (%)	p	Hemoglobin (g/dl)	p
Etiology -Primary hypertension (n = 138) -Secondary hypertension (n = 66)	 13.41 ± 1.04 13.24 ± 1.41	> 0.05	 14.07 ± 1.78 14.44 ± 2.10	> 0.05
Stage -Stage I (n = 85) -Stage II (n = 119)	 13.42 ± 0.99 13.31 ± 1.29	> 0.05	 14.41 ± 1.71 14.03 ± 2.01	> 0.05
Left ventricular hypertrophy (+ (n = 92) Left ventricular hypertrophy(-) (n = 112)	13.2 ± 1 13.4 ± 1.2	> 0.05	14.5 ± 2 13.9 ± 1.7	< 0.05*
Retinopathy (+) (n = 16) Retinopathy (-) (n = 188)	13.3 ± 1.1 13.3 ± 1.1	> 0.05	13.8 ± 2 14.2 ± 1.8	> 0.05

Conclusion: RDW was similar in children with hypertension and control group. RDW was similar in children with hypertension due to etiology, stage and end organ damage. Hemoglobin level was higher in children with hypertension, than control group. Hemoglobin level was higher in children with left ventricular hpertrophy than the children without left ventricular hypertrophy.

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RISK FACTORS FOR NEPHROLITHIASIS IN CHILDREN WITH CEREBRAL PALSY

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Cerebral palsy (CP) is a condition that includes a group of neurological disorders with motor disabilities as a result of lesions and/or abnormalities, which occurred in different stages of the brain's development. The poor bladder control, recurrent urinary tract infections (UTIs), limited physical activity, inadequate diet with reduced water intake are important risk factors for developing nephrolithiasis in children with CP, which may seriously affect kidney function. The aim of our study is to raise awareness of the risk factors and early diagnosis of nephrolithiasis in children with CP. Material and Methods: We present 3 clinical cases of children with CP and nephrolithiasis, in which the renal disorder was characterized by broad clinical heterogeneity. Results: First case is of 16-year-old girl with CP and mental retardation, which was referred for consultation with pediatric nephrologist because of severe anemic syndrome and azotemia. Ultrasonography of urinary tract showed staghorn calculi occupying the majority of pyelocaliceal system (PCS) of both kidneys with significant reduction of renal parenchyma. She was diagnosed with chronic kidney disease (CKD) and a supportive treatment was initiated. Afterwards, on the background of recurrent UTIs, a rapid progression of the CKD and a lethal end were observed. The second case presents a 6-year-old boy (born as third twin) with intrauterine diagnosed spina bifida and hydrocephalus. After birth he developed spastic quadriparesis, symptomatic generalized epilepsy and mental retardation. He was admitted for treatment due to microhematuria and transient azotemia. On ultrasonography and X-ray imaging, large concretions in the urinary bladder, impairing the urine drainage, were established. After recovering of renal function, surgical removal of calculi was recommended. The third case is of 2-year-old girl with spinal dysraphism, hydrocephalus and Chiari II brain malformation. Due to recurrent UTIs, nephrolithiasis with multiple calculi in PCS bilaterally was diagnosed. One week after diagnosis, the child was admitted in the clinic with severe dyspeptic syndrome that resulted in circulatory collapse. The laboratory tests showed acute kidney injury, severe hypernatremia and decompensated metabolic acidosis. Nephrolithiasis was verified by ultrasound and abdominal CT scan. Antibacterial treatment and rehydration therapy were performed. Conclusions: Nephrolithiasis is a serious problem with severe complications in pediatric patients with CP. Early diagnosis, adequate treatment and good control are granting protection of kidney function and better ongoing physical development of affected children.

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NEW ONSET OF TYPE 1 DIABETES MELLITUS WITH DIABETIC KETOACIDOSIS AND MACROSCOPIC HEMATURIA: A CASE REPORT

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Purpose: Diabetic ketoacidosis (DKA) often marks the initial presentation of type 1 diabetes (T1DM). Symptoms include polyuria, polydipsia, fatigue and dehydration. Pediatric nephrolithiasis is linked to structural abnormalities, urinary tract infections (UTI) and metabolic abnormalities which can occur in the context of genetic diseases. Hypercalciuria, is the most frequent abnormality and can result from increased intestinal absorption, renal losses, or bone resorption. Renal losses are amplified by factors such as dehydration, sodium load, acidosis, and hyperglycemia. Diabetic patients have an increased risk kidney function decline, exacerbated by factors like hypertension, obesity, and acute kidney injuries.

Methods: A 9-year-old girl presented to our emergency department with chest pain, altered consciousness, and macroscopic hematuria. Initial assessments showed severe DKA in the context of new-onset T1DM with hyperglycemia and acidosis with a slightly increased serum creatinine. Urinalysis confirmed macroscopic hematuria, proteinuria, ketonuria, and glycosuria. Bedside abdominal ultrasound revealed hyperechoic cortex and urine in the bladder. Treatment included normal saline infusion and insulin leading to a decrease in serum glucose and creatinine.

Results: Further assessments excluded hemolysis, UTI, or acute glomerulonephritis, as urine cultures were negative and both C3 and C4 complement fractions and autoimmune tests were globally normal. A repeat ultrasound showed nephrolithiasis with multiple hyperechoic spots in both renal pelvises. Diagnostic tests for nephrolithiasis showed hypercalciuria without hyperparathyroidism (Tab.1) One day post-admission urinary excretion of sand-like deposits occurred with subsequent regression of hematuria within 24 hours. Treatment at discharge included insulin and increased water intake. At one-month follow-up, no recurrence of nephrolithiasis or hypercalciuria.

Conclusion: This case highlights nephrolithiasis as a rare but significant complication of DKA, due to impaired renal calcium handling. It emphasizes the need for increased vigilance and preventive strategies for nephrolithiasis during acute metabolic disturbances. Awareness and ad-hoc measures are crucial for mitigating the risk of kidney injuries in this vulnerable population.

Table 1. Laboratory tests at admission

	Value	Normal value		Value	Normal value
Serum creatinine (mg/dL)	0.52	0.5-0.7	**Parathormone (pg/mL)**	33.2	11.3-60
eGFR (CKiD U25) (mL/min/1.73m2)	91	>90	**Venous HCO 3- (mmol/L)**	5.9	24-26
Glycosuria (mg/dL)	>1000	0-10	**C3 (mg/dL)**	91	90-161
Urinary pH	5	5.5-6.5	**C4 (mg/dL)**	24	13-38
Calciuria/creatininuria (mg/mg)	1.6	<0.2	**ANA**	1:160	Negative
Calciuria (mg/kg/24h)	6.2	< 5	**ENA**	Negative	Negative
Serum calcium (mg/dL)	9.3	9.3-10.6	**ANCA**	Negative	Negative
Serum phosphorous (mg/dL)	5	4-5.6	**antidsDNA**	Negative	Negative
25OHVitamin D (ng/mL)	18	>30			

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TO REPAIR OR NOT TO REPAIR: NAVIGATING A COMMON COMPLICATION IN PEDIATRIC PERITONEAL DIALYSIS

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Background: Peritoneal dialysis (PD) is the preferred renal replacement therapy for children with end-stage kidney disease (ESKD). While infections are the most prevalent, mechanical complications can impact patients' health. Hernias are common due to increased intra-abdominal pressure and weakened abdominal wall connective tissue. This case report aims to highlight the risk factors and management of these complications.

Case: A 2-year and 4-month-old boy, weighing 13.4 kg, diagnosed with ESKD secondary to dysplasia and reflux nephropathy, initiated Continuous Ambulatory Peritoneal Dialysis (CAPD) at 1 year and 7 months of age. Dialysis was started at 250 ml/m^2 post-catheter placement for volume overload and refractory metabolic acidosis. Volume per cycle was gradually increased to maintain an effective concentration gradient. The home CAPD prescription included 5 daily exchanges of 500 ml at 1.5% glucose (833 ml/m^2). Intraperitoneal pressure measured 13 mmH2O. Residual diuresis was 150-200 ml/day. He experienced 2 episodes of bacterial peritonitis treated with intravenous antibiotics. Eight months after starting dialysis, he required surgery for umbilical hernia and a granuloma at the catheter site.The procedure involved excision the granuloma, omentectomy, and umbilical hernia repair. He transitioned to hemodialysis for 2 weeks without complications before returning to CAPD.

Discussion: The report discusses managing umbilical hernias in PD patinets, considering options like delaying surgery and alternative treatments. Unlike inguinal hernias that need surgical repair due to higher risk of incarceration necessitating surgical repair, umbilical hernias may not require immediate correction. Patients on CAPD can consider alternative treatments like automated peritoneal dialysis (APD) or kidney transplantation. Managing intraperitoneal pressure is crucial, as increased dialysate volume can exacerbate hernias. Maintaining intraperitoneal pressure below 14 cmH2O is advised to mitigate risks. Surgical considerations include laparoscopic hernia repair to reduce dialysate leakage risk. This can include combining hernia repair and catheter insertion in one procedure. Post-surgery, delaying PD initiation and adjusting dialysate volumes over days can help minimize complications. For children, adjustment of volumes is recommended based on age. Additionally, consider using hemodialysis for over 2 weeks following invasive abdominal procedures to aid healing and minimize complications.

Conclusion: Despite monitoring, the patient developed an umbilical hernia. Options like APD or renal transplatation could have avoided the need for surgery, but unvailable resources led to a different approach. This case underscores the importance of considering all options and tailoring management plans to each patient's circumstances and resources available.

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IMPROVING PREVENTION, DIAGNOSIS AND TREATMENT OF PERITONEAL DIALYSIS- ASSOCIATED PERITONITIS IN A TERTIARY PAEDIATRIC NEPHROLOGY UNIT

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Aims/Purpose: Peritoneal dialysis (PD)- associated peritonitis is a serious complication of PD and its prevention and treatment are important in reducing patient morbidity and mortality. We observed an increase in peritonitis rates in our centre, from 1.1 to 1.5 episodes/year in 2023-2024. The aim of this audit was to assess whether ISPD guidelines were being followed.

Methods: Data on peritonitis cases for 25 patients undergoing PD during the period of April 2023-March 2024, was retrospectively reviewed. Data included: PD fluid samples (white cell count, cell differential, culture), exit site inspection, exit site and gastrostomy swabs, antibiotic course and antifungal prophylaxis. Moreover, we examined catheter insertions for these patients and associated procedures at time of insertion, decolonisation regimes, antibiotics at induction, resting catheter times, and post-operative complications.

Results: 17 patients (68%) suffered PD peritonitis during this period. For these patients, 32 peritoneal fluid samples were sent. 14 were culture negative, however white cell differential was not processed. The most common cause was Staphylococcus (12 samples), 2 samples grew Pseudomonas, 1 sample grew Candida. In only 5 PD peritonitis episodes, was antifungal prophylaxis prescribed. Exit sites were swabbed in 78% of cases of suspected peritonitis (25 swabs). 9 out of 25 swabs had significant growth. Four swabs were untreated, one which grew Pseudomonas, and led to a catheter-related PD peritonitis. 21 catheters were inserted for 16 patients in that period, resulting in 8 catheter-insertion related infections. Of the patients who had catheter-insertion related peritonitis, 42% had a gastrostomy placed concurrently. Prior to all 21 catheter insertions, decolonisation was incomplete and, in 4 catheter insertions antibiotics were incorrectly administered. PD catheters with associated gastrostomy placement were rested on average 12.8 days. PD-peritonitis resulted in removal of catheters in 8 cases and transfer to haemodialysis in 5 patients.

Conclusion: Our audit identified incompliance with preventative measures and an increment of catheter-insertion related infections compared to previous years. We were unable to obtain cell count differentials in negative cultures, hindering diagnosis of eosinophilic peritonitis. Following audit results, we are implementing a quality improvement project. Using Plan-Do-Study-Act cycles we will capture results monthly. We have already disseminated results in education and governance meetings, designed a decolonisation pack for catheter insertion, as well as peritonitis diagnostic packs to ensure correct sampling, awaiting circulation. In view of the rise of catheter-insertion related infections with concurrent gastrostomy placement, our current recommendation is to insert gastrostomies prior to catheter insertion when possible.

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BIVALIRUDIN AS ANTICOAGULATION STRATEGY FOR ACUTE HEMODIALYSIS IN CHILDREN: TWO CASES WITH A SUMMARY OF RECENT LITERATURE

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Aims/Purpose: Unfractionated heparin (UFH) is the most used anticoagulative agent for extracorporeal settings in children, including acute hemodialysis modalities. In certain situations, such as heparin-induced thrombocytopenia, alternatives must be applied. The direct thrombin inhibitor bivalirudin has come forth as an attractive substitute. Bivalirudin is currently only approved for adult use in specific percutaneous coronary intervention settings. However, it has a growing off-label popularity in different contexts for both adult and pediatric patients. Experience with bivalirudin in children is mainly limited to extracorporeal membrane oxygenation, ventricular assist devices and during cardiopulmonary bypass surgery. Literature about its use as anticoagulation strategy for pediatric hemodialysis is very scarce. Here, we present two pediatric cases where bivalirudin was used during acute hemodialysis, followed by a short summary of recent literature.

Results: In our two cases, one session out of 7 was stopped prematurely because of circuit clotting, and no major bleeding events were seen. Both patients survived to cannulation and hospital discharge.

Conclusion: To date, experience regarding the use of bivalirudin in acute pediatric hemodialysis is lacking. We presented two pediatric cases in which bivalirudin was used successfully in acute hemodialysis on a PICU.

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GLOMERULOPATHY IN HORSESHOE KIDNEY

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Aims/Purpose: Horseshoe kidney (HR) is the most common fusion anomaly. It is usually asymptomatic, although some cases develop complications. Its association with polymalformation syndromes and chromosomopathies has been described. There are few reports on its association with glomerulopathies, these being especially proteinuric (membranous GN, nephrotic syndrome or FSGS). Renal biopsy is essential for diagnosis but can be challenging for the nephrologist.

Methods: We report an 15-year-old Ecuatorian boy who had presented an episode of gross glomerular hematuria with fever. Among the family history, terminal CKD of unknown cause in maternal uncle. Normal GFR and no HTA data. Ultrasound showed horseshoe kidney. Normal immune profile. AngioMRI shows 3 accessory polar arteries. During follow-up, he presented episodes of gross hematuria coinciding with infectious symptoms and persistent microscopic hematuria associated with significant proteinuria rising to the nephrotic range. Normal GFR and no HTA data. Ophthalmological study and normal audiometry.

Results: Treatment with antiproteinurics was started and a laparoscopic percutaneous renal biopsy was performed without obtaining an optimal sample. The study was extended with a genetic panel of glomerulopathies and familial hematuria (COL4A3, COL4A4 and COL4A5), which was negative. A new percutaneous renal biopsy with interventional radiology was performed, obtaining a viable sample where minimal glomerular alterations were evidenced without deposits in direct immunofluorescence. That suggested the possibility of disease with minimal changes. An electron microscopy study was requested and he started treatment with steroids at 60 mg/m2/day. The result of the study was compatible with thin basement membrane nephropathy, so the steroids were interrupted. He currently maintains microscopic hematuria and significant almost nephrotic proteinuria with normal GFR.

Conclusion: The coexistence of glomerulopathy, especially hematuric, and HR is rare. Renal biopsy is an essential tool for diagnosis, which can be a real challenge.

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RAPID PROGRESSIVE GLOMERULONEPHRITIS WITH SEVERE ENCEPHALOMYELITIS AND HYPERSECRETORY HYDROCEPHALUS POSSIBLY DUE TO SARS-COV-2 INFECTION. CASE REPORT

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Rapid progressive glomerulonephritis (RPGN) is often associated with acute/chronic kidney failure. RPGN with a systemic inflammation and severe encephalomyelitis is rare and has not been described in children. Normal developed 3-year-old Caucasian girl presented with headache and abdominal pain and 14 days (d) history of fever episode. She had not been vaccinated against SARS-CoV-2. Within 3d after admission kidney function deteriorated. Kidney biopsy showed diffuse endocapillary proliferative immunocomplex GN with glomerular thrombotic microangiopathy and signs of cryoglobulinemic deposits without sclerosis nor tubular atrophy. Her neurological state progressed to stupor. Cerebral magnetic resonance scan (cMRI) showed marked transependymal edema, signal alterations in corpus callosum and linear periventricular leucoencephalopathy due to hypersecretory hydrocephalus. Analysis of cerebrospinal fluid (CSF) showed mild increased cell count (40/µl) and marked increased amount of protein, immunoglobulins, ferritin and ß2-microglobulin. In CSF and blood microbiological, virological and autoimmune screens were negative. Thrombotic thrombocytopenic purpura/ hemolytic uremic syndrome and hematologic malignancy were excluded. Lymphocyte phenotyping showed IgM+IgG+ memory B cells, otherwise normal findings. Whole exome sequencing did not reveal an inborn error of immunity. A severe inflammation causing the RPGN with blood brain barrier disruption was suspected. Antimicrobial/-virological treatment was initiated. Plasmapheresis and immunosuppressive therapy with high-dose steroids, B-cell-depleting therapy (rituximab) and high dose iv IgG were indicated. AKI necessitated 16 days CVVH/-HD treatment. Due to increased intracranial pressure external ventricular drainage was applied. The course was complicated with ventricular bleeding. 2 month later she was discharged with normal neurological findings. 6 and 9 month later the patient presented with headache and vomiting. B-cells had regenerated. cMRI excluded pathology. CSF protein, ferritin and B2M were still elevated. Steroids improved symptoms and kidney function increased to GFR 23ml/min/1,73m^2. There was no proteinuria. Initially the serological and PCR assays did not show signs of SARS-CoV-2 infection (serum, CSF). SARS-CoV-2 spike 1-protein T cells were negative (while T cell-activity against other corona viruses was positive). Since the 6th week of admission the highly specific T cells have been repeatedly detected.

Fazit: We suppose that RPGN and encephalomyelitis were caused by SARS-CoV-2 infection. We suggest that the specific T-cell assay should be applied in unclear cases.

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A FAMILY VARIANT BARTTER SYNDROME TYPE III (CLINICAL CASE)

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Aims/Purpose: Bartter syndrome (SB) is a rare group of autosomal recessive salt-producing tubulopathies characterized by impaired transport mechanisms in the thick ascending section of the Henle loop, which leads to pronounced salt loss. The clinical phenotype of SB is represented by hypokalemia, metabolic alkalosis, secondary aldosteronism and arterial hypertension.

Methods: The case presented by us describes the family version of the type III SB. Type III SB occurs as a result of mutations of the CLCNKB gene affecting the CLC-Kb chloride channel in the distal tubules of the kidneys. Unlike the classic variant, type III SB has milder symptoms and mainly manifests from birth.

Results: This case presents a family version of the type III SB for three siblings. Two boys (10 and 8 years old) and one girl (1 year old) with an identical homozygous mutation of the CLCNKB gene. A genetic study of the proband mother and father revealed a nucleotide substitution of chr1:16378710G > A in the heterozygous state of the CLCNKB gene. The mutations were validated by direct Sanger sequencing. All sibs have similar clinical manifestations in the form of hypochloremic, hypokalemic, hyponatremic metabolic alkalosis, hypomagnesemia as a result of increased magnesium excretion, hyperreninemia, hyperaldosteronemia, hyperparathyroidism, decreased renal function. Each pregnancy was accompanied by polyhydramnios, polyuria, polydipsia and total hypoelectrolythemia were noted at birth. Therapy of patients with BS is aimed at maintaining normal electrolyte metabolism and controlling an increase in prostaglandin E2 levels. Currently, nonsteroidal anti-inflammatory drugs are the first-line drugs to control the increase in PGE2 levels, and oral forms of potassium are used to correct hypokalemia. For the purpose of renoprotection, reduction of angiotensin II and aldosterone, ACE inhibitors or ARBs are used.

Conclusion: Thus early diagnosis and timely therapy of SB in children makes it possible to form a prognosis of the disease and to regulate metabolic disorders.

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TWO SIBLINGS WITH CUBULIN MUTATION AND ISOLATED PROTEINURIA

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Aims: The primary cause of proteinuria is the dysfunction of the glomerular filtration barrier. Proteinuria could be caused also by defects in protein reabsorption in the proximal tubule (PT). Tubular proteinuria has a narrower range compared to glomerular proteinuria. One of the causes of these kind of proteinuria is linked to mutations of the cubilin (CUBN) and amnionless (AMN) genes. Cubilin, acts as a receptor for cobalamin in the ileum, but it also appears to be involved in the endocytic reabsorption of albumin in the renal PT. Mutation of the CUBN, causes Imerslund-Grasbeck syndrome a rare AR disease (1:200,000) with onset in childhood. It is characterized by non-nephrotic proteinuria, normal renal function, and vitamin B12 deficiency, which usually leads to megaloblastic anemia. These mutations can also be associated with isolated non-nephrotic proteinuria or isolated vit. B12 deficiency. Literature suggests that the proteinuria is due to tubular loss without glomerular involvement, and the prognosis is benign. In this case, we describe 2 siblings with biallelic pathogenic variants of the CUBN gene with a 5 year-follow-up, presenting with isolated proteinuria.

Methods: After incidentally detecting isolated non-nephrotic proteinuria in one out of 4 siblings in 2019, next-generation sequencing (NGS) for renal disease genes was performed in whole family.

Results: We report the case of two siblings aged 9 (male) and 5 (female), children of non-consanguineous parents, with isolated proteinuria. Along the paternal line the following has been reported: presence of renal lithiasis, an uncle died after years of dialysis. The siblings came to our attention in 2019 due to the incidental discovery of proteinuria in the older-one: urine test revealed proteins = 0.33 g/24h. Blood tests showed normal hematological parameters and creatinine (0,33 mg/dl). During clinical and laboratory follow-up, several urine tests showed non-nephrotic proteinuria (< 1 g/L) and renal ultrasound without abnormalities. Thereafter, the sister also revealed non-nephrotic proteinuria on urine tests with normal renal function, Vit. B12 and renal ultrasound. In Nov. 2019 NGS showed in both siblings 2 pathogenic variants on the CUBN gene inherited respectively from the father and mother (c.6359G > A:p.W2120X and c.8699C > A:p.A2900D).

Conclusion: Our cases corroborate the hypothesis that CUBN mutation can lead to a rare, and apparently benign and isolated non-nephrotic proteinuria condition. In particular, our case, considering the approximately 5 year follow up, emphasizes the benign nature of this condition. Therefore, in the presence of patients with isolated sub-nephrotic proteinuria, we consider it important to include CUBN mutation in the differential diagnosis, thus warranting genetic testing (NGS) with the possibility of avoiding invasive procedures and/or needless pharmacologic therapies.

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THE USE OF MACHINE LEARNING FOR RETROSPECTIVE ANALYSIS OF LITHOGENESIS FACTORS IN CHILDREN

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The range of factors conducive to the process of lithogenesis in the human body is constantly expanding, and the reasons for this phenomenon should be sought in e.g. incorrect eating habits, less physical activity, excessive supply of multivitamin preparations.

The aim of the study was to identify risk factors for the development of urolithiasis in the pediatric population depending on age and sex, based on a retrospective analysis of available medical documentation.

Material and methods. Retrospectively, data were analyzed from 528 patients (287, 241) hospitalized in the Pediatric Nephrology . The eligibility criterion for the study was the diagnosis from the group: N20.0 - N20.9 according to ICD10. This population was divided into 2 groups depending on the presence of the deposit confirmed by imaging (USG, CT, RTG). 161 patients with urolithiasis were included in the urolithiasis group (KUM); 120 children were included in the urolithiasis emergency group (SZK). Both groups were divided depending on the age of the children into 4 subgroups: 1st subgroup: 0 - 1 year of age (infants), 2nd subgroup: 1 – 4 years, 3rd subgroup 4 – 12 years, 4: 12 – 18 years. Retrospective analysis included medical data contained in patient's information sheets for selected laboratory markers marked in blood, urine portion and daily collection .

In addition, using the XGBoost algorithm, the most significant risk factors for the development of urolithiasis were identified for a selected population of children.

Results. In the KUM group were found (aged 1 – 18 years):

a. Positive correlations between daily phosphorus excretion and:

- daily excretion of oxalic acid, - P / creatinine index and diurnal magnesium excretion.

b. Negative correlations between the patient's age and:

- P / creatinine ratio, - blood phosphorus concentration, - daily urinary excretion Ua.

In the SZK group were found (aged 1 - 18 years):

a. Positive correlations between daily excretion of phosphorus in the urine and:

- daily excretion of oxalic acid, - daily excretion of magnesium, - P / creatinine ratio.

b. Negative correlations:

- daily excretion of Ua,- blood phosphorus concentration,- P / creatinine ratio.

Analysis of the medical database, using the XGBoost algorithm, showed that 3 areas have the greatest prognostic significance in the development of urolithiasis: calcium and phosphate metabolism (including blood levels of vitamin 25(OH)D3) and daily excretion of oxalic acid.

Conclusion: The diagnosis of KUM according to this algorithm is associated with higher calcemia values, calcium ion concentration in DZM, plasma levels of 25(OH)D3 and the Ca / creatinine ratio. In the field of phosphate management, the XGBoost algorithm linked lower average phosphatemia values and daily phosphorus excretion with the diagnosis of KUM, and higher with the diagnosis of SZK. Of the clinical symptoms, the occurrence of renal colic is prognostic in the XGBoost algorithm.

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FOUR SYRIAN SIBLINGS DIAGNOSED WITH PRIMARY HYPEROXALURIA TYPE 1 WITH BENING COURSE

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Aims/Purpose: Primary hyperoxaluria is a rare disease that is characterized by an increased oxalate excretion from urine.Here, we present four Syrian siblings diagnosed with Primary Hyperoxaluria type 1 whose disease course is slowly.

Methods: A 7-year-old male patient was presented with inability to urinate and flank pain. His physical examination was normal.Family history revealed that his 4-year-old sister had kidney stones and chronic kidney failure and died while being followed up with hemodialysis, and his 10-month-old brother had kidney stones and kidney failure and died from pneumonia. We learned that both of them had been using potassium citrate solution since infancy. He had acute renal failure and pyelonephritis. Urinary system ultrasonography revealed bilateral hydroureteronephrosis and multipl stones in the bladder.4 stones removed by cyctoscopy.Due to the high oxalate excretion and homozygous mutation in the AGXT gene potassium citrate and vitamin B6 was started as primary hyperoxaluria Type 1.His 4-year-old sister and 6 month-olg-brother had stones in kidneys.Kidney function tests were of the girl was normal but urea of the boy was high.Their oxalate excretion was increased.Even though genetic counseling a fourth brother was born and had oxalate excretion.Currently, the 12-year-old patient's urea:40-50 mg/dl, creatinin:0.8-0.9 mg/dl, while the other 3 children's were normal.Homozygous mutation was detected in the AGXT genes of the first 3 patients, the fourth's one hasn't been concluded. Since diagnosis, the oxalate excretions were always high, and after treatmen oxalate excretions tend to decrease.Glycolic acid excretion of all cases was within normal limits, but oxalic acid excretion was slightly high.

Conclusion: Primary hyperoxaluria Type 1 patients are known to have high urine oxalate, glycolic acid and oxalic acid levels. This disease can result with systemic oxalosis and end-stage renal failure.Our patient's renal functions were decreased to normal levels or stayed in normal range.We estimate this bening course might be due to shift in the reaction towards the oxalic acid rather than glycolic acid. However, as rapid deterioration may occur, close follow-up and continuous treatment are essential.

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GENETIC SEQUENCING UNLOCKS ALPORT SPECTRUM-COL4A3: TAILORED INSIGHTS AND EVOLVING FRONTIERS IN CLINICAL DECISION-MAKING

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Aims/Purpose: The study aimed to elucidate the diagnostic odyssey of a patient presenting with isolated microhematuria at age 11, leading to the identification of a heterozygous pathogenic variant (c.1855G > A p.(Gly619Arg)) in the COL4A3 gene, affirming an autosomal-semidominant manifestation of Alport syndrome type 3 (ADAS). This investigation sought to comprehensively analyze the clinical and genetic intricacies associated with this variant within the broader Alport Spectrum-COL4A3 framework.

Methods: A comprehensive diagnostic approach was employed, incorporating various modalities such as urinary and audiometric evaluations. Genetic sequencing was performed to identify the underlying pathogenic variant. Clinical assessments were conducted to characterize the phenotypic manifestations, particularly focusing on renal and extrarenal involvement, in alignment with the milder phenotype typical of ADAS. Literature review and consultation with ClinGen working groups aided in contextualizing the variant within the spectrum of Alport syndrome.

Results: The diagnostic journey culminated in the detection of the heterozygous pathogenic variant in the COL4A3 gene, associated with ADAS. This variant, previously observed in both autosomal recessive and dominant Alport syndrome cases, accentuated the clinical complexities inherent in the Alport Spectrum-COL4A3. The nuanced presentation observed in the patient, including the rarity of ocular involvement in autosomal-dominant cases, underscored the diverse phenotypic expressions linked to COL4A3 gene variants.

Conclusion: Our findings highlight the critical role of genetic sequencing in achieving precise diagnosis and prognosis in Alport syndrome cases, particularly emphasizing its importance in predicting the likelihood of end-stage renal disease in late adulthood. This case contributes to the evolving landscape of genetic-based diagnostics, emphasizing the necessity of precision in managing Alport Spectrum-COL4A3 cases and shaping the future of personalized medicine. The insights gained from this diagnostic journey underscore the growing significance of genetic sequencing in unraveling the complexities of Alport syndrome and guiding tailored patient care strategies.

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CYSTINURIA

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A 15 years old girl was suffering with intermittent abdominal pain lasting 2-3 months. The pain occured several times a week, macroscopic hematuria in urine was observed. Dysuria negated, the girl was afebrile. The examination of the morning urine revealed a microscopic haematuria, macroscopic haematuria was diagnosed in afternoon urine. Moreover, cystine crystals were found in the morning urine, for which she was hospitalised at the University Hospital in Ostrava for further investigation. On admission to the hospital another urine analysis was performed, cystine crystals were found, additionally, a quantitative level of cystein in the urine was higher. Ultrasonographic examination of the urinary tract revealed a concrement filling the right renal pelvis and both renal parenchyma. An abdominal X-ray was approved calcifications findings in both kidneys. CT scan showed pyelolithiasis findings on the right and lithiasis of the middle calyx on the left. Cystoscopy results shown orifice on the eyelash, a number of whitish small concrements around the left orifice. Stent was inserted on the right, laser fragmentation and extraction of the concrements were performed. After repeated urological interventions, kidney was free of concrements. Nephrologist started kalium citrate treatment to alkalize urine and maintain urine pH at 7.5. A magnesium, vitamin B and vitamin D were added to the patient treatment. Drinking 3-4 litres of fluids per day were recommended, additionally salt restriction and limiting foods with methionine (meat, milk, cheese, dairy products) was established. Genetic examination found a SLC7A9 gene disorder - autosomal recessive cystinuria, carried by both parents. These genes encode a protein that mediates the transport of cystine and dibasic amino acids in the proximal tubules of the kidney and in the small intestine. Recently, the girl is without any problems. Cystine urolithiasis is caused by cystinuria. Cystinuria significate to increased excretion of the cystine amino acid, ornithine, arginine, and lysine into the urine. The dibasic amino acids ornithine, lysine, and arginine are completely soluble in urine, unlike cystine, which is relatively insoluble in urine of 5-7 pH range. Only at urine pH values above 7 the solubility of cystine increase 2 to 3 times. Cause: malfunction of the tubular transport system for cystine and dibasic amino acids (lysine, arginine, ornithine).

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CHALLENGING IN MANAGING INFANTILE CYSTINOSIS: INSIGHT FROM A CENTER IN ALGERIA

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Aims/Purpose: Infantile cystinosis (IC) is an autosomal recessive generalized lysosomal storage disease. Three clinical phenotypes, of which the nephropathic or infantile form is by far the most frequent. The reported incidence of the disease is about 0.5–1:100,000 live births. The aim of this retrospective study is to examine the clinical presentation, diagnostic approaches, and treatment strategies of Infantile Nephropathic Cystinosis (INC) in an Algerian center.

Methods: A retrospective cohort study including 08 patients at one center of care was conducted. Data on time of diagnosis, Chronic Kidney Disease (CKD) stage, leukocyte cystine levels (LCL), extrarenal manifestations, and treatment was collected from medical files and analyzed.

Results: Patients were diagnosed at a median age of 29 months. Oral cystine-depleting therapy (i.e., cysteamine) was prescribed at a median dose of 1.3 g/m2 per day. LCL measurements was done at diagnosis but not in measured after due to local condition. The overall median height of the patients was at the 3th percentile. 40.5% of the values were ≤ the 3rd percentile. Patient sex and year of birth were not associated with age at initiation of KRT, but patients diagnosed before the age of 18 months required KRT significantly later than those patients diagnosed at the age of ≥ 18 months median renal survival was 12 years.

Conclusion: Infantile cystinosis is a rare disease. Managing it in an emerging country like Algeria makes things even more challenging. Even with the availability of treatment, the biological monitoring of it is not feasible, making the follow-up of these patients difficult. However, thanks to Cysteamine, progression to end-stage renal disease has been delayed.

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GITELMAN SYNDROME, A CASE REPORT

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Aim/Purpose: The Gitelman Syndrome, is caused by inactivating mutations in the SLC12A3 gene, which codifies the Na-Cl cotransporter thiazide, sensitive to the distal convoluted tubule, thus producing a urinary loss of sodium chloride It usually begins in late childhood or adolescence, with eagerness for salt, excessive tiredness, weakness and muscle cramps. A small proportion of children may have failure to thrive. They do not have hypertension nor decreased glomerular function. In some patients clinical manifestations are mild and diagnosis may be delayed .

Methods: Description of a case with Gitelman syndrome.

Results: A 10-year-old boy presented with a one-year history of polyuria, salt craving and muscle cramps that increased with exercise. His weight was in percentile 25 and his height in percentile 10. He remained with normal blood pressure . No personal or family history of diseases. His laboratory tests revealed hypokalemia (potassium 1.7 mEq/L) normal sodium (Na 134.2 mEq/l) and low chloride (cl91.6mEq/l). He had normal renal function (creatinine 0.41 mg/dl glomerular filtration rate 104.50 ml/min/1.73m2 urea 25 mg/dl) normal calcium 9.2 mg/dl and phosphorus 3.23 mg/dl together with hypomagnesemia 1.2 mg/dl and metabolic alkalosis (ph 7.45 bicarbonate 30 meq/l base excess +5). His urinalysis revealed : density 1005, pH 8, normal sediment. Urine ions: K 17.5 mEq/l, Cl 10 mEq/l, Na 7 mEq/l; Na urine/K urine 0.4. Elevated potassium Fractional excretion (36%), and normal fractional excretion of Na (1.6%) and Cl (0.11%) . Elevated potassium transtubular gradient 6. Ca/Cr ratio 0.56 mg/ mg. Renal ultrasound was normal The electrocardiogram confirmed hypokalemia due to PR prolongation. Treatment with intravenous potassium and magnesium supplements was started, and electrolytes were gradually corrected. At discharge potassium was 3.5 mEq/l and Magnesium 1.9 mg/dl. Given the fact that the patient presented with hypokalemia and high urinary loss of potassium, hypomagnesemia, metabolic alkalosis, elevated renin and aldosterone without nephrocalninosis, a tubulopathy was suspected . Genetic testing was performed The patient eas found to be heterozygous in two variants of the SLC12A3 gene, located on chromosome 16. Gitelman syndrome was confirmed The patient is under a diet rich in potassium and magnesium together with oral supplements of potassium and magnesium and spironolactone in order to maintain serum potassium levels of 3.1-3.5 meq/l . He has been able to resume sports without presenting cramps His height has increased from percentile 10 to 25 (4 cm in one year)

Conclusion: Tubulopathies are rare diseases and patients may spend years without diagnosis It is important to have a high grade of suspicion in order to consider them in the differential diagnostic process. An early diagnosis with prompt treatment can modify the patients quality of life and prognosis.

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WHOLE EXOME SEQUENCING REVEALS A NOVEL VARIANT IN ANKRD11 GENE AS A POSSIBLE MONOGENIC CAUSE OF UROLITHIASIS

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Aims/Purpose: Urolithiasis in early childhood is commonly associated with CAKUT, metabolic perturbations, and/or various other syndromes. Therefore, in conjunction with standard diagnostic modalities such as imaging and laboratory assessments, infants presenting with urolithiasis frequently require genetic testing to delineate potential monogenic etiologies, especialy when accompanied by concurrent indicative clinical features.

Methods: We present a case of an infant with nephrolithiasis along with delayed psychomotor development, facial dysmorphism and skeletal anomalies.

Results: The presented patient was born from pregnancy of non-consanguineous parents complicated by oligohydramnios and preterm delivery after 29 weeks of gestation. Immediately after birth the right-side diaphragmatic hernia was observed and in the following week surgical repair and repositioning of intestines, liver and upper kidney pole was performed. The follow up abdominal ultrasound revealed right kidney malrotation, grade IV hydronephrosis and was suggestive of nephrolithiasis. During the first year of life contrast enhanced voiding urosonography (ceVUS) revealed right sided vesicoureteral reflux grade IV, MAG3 renal scintigraphy indicated partial mechanical obstruction in the pyelocaliceal system of the right kidney, while CT urography confirmed nephrolithiasis. Since the extensive metabolic workup revealed no distinctive abnormalities, genetic evaluation was warranted. Considering delayed psychomotor development along with dysmorphic features of face and extremities on top of nephrolithiasis, whole exome sequencing had been performed revealing a heterozygous frameshift variant c.1598_1605dup, p.(Pro536Serfs*41) in the ANKRD11 gene. This variant is predicted to lead to a loss of normal protein function and was previously undescribed in the medical literature or reported in variation databases.

Conclusions: Monogenic influences on the pathogenesis of urolithiasis have traditionally been regarded as uncommon. Nevertheless, advancements in sequencing technologies have facilitated the identification of novel genetic determinants, indicating that a significant proportion of urolithiasis cases may have a monogenic basis. Although previously unrecognized as a contributor to urolithiasis, pathogenic variants in the ANKRD11 gene have been linked to KBG syndrome, a rare genetic disorder characterized by variable expressivity and non-specific features. Given the involvement of the disrupted protein encoded by the ANKRD11 gene in bone development, speculation arises regarding its potential role in calcium homeostasis and its conceivable contribution to stone formation. While other etiologies of urolithiasis cannot be conclusively ruled out in our patient, the presented case potentially represents the inaugural association of urolithiasis with KBG syndrome.

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A RARE CAUSE OF NEPHROTIC SYNDROME: GALLOWAY MOWAT SYNDROME

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Aims/Purpose: Proteinuria may occur in structural lesions of GBM, in electrical charge disturbance of GBM or in filtration hemodynamic The OSGEP gene is found in the cytoplasm and nuclei of human podocyte cells. This A mutation in the gene can lead to proteinuria and nephrotic syndrome. Galloway-Mowat Syndrome early onset neophrotic syndrome is associated with microcephaly, gyral anomalies of the brain and psychomotor retardation. Most patients have dysmorphic facial appearance, ear anomalies, hypertelorism and micrognathia. WDR73, OSGEP, LAGE3, TP53RK, and TPRKB genes may be associated with this syndrome.

Methods and Results: A 17-month-old girl was referred to the nephrology department duo to proteinuria. It was learned that she was born term and had no consanguineous marriage and prenatal history of abnormality. Physical examination findings are dysmorphic facial appearance, microcephaly, micrognathia, depressed nasal root, hypertelorism, spasticity in the lower extremities and clonus in the left foot. Urine protein was 75 mg/dl in a complete urinalysis. Urine microprotein/creatitine ratio was 3.68. Total Protein was 5.56 g/dL, Albumin was 3.56 g/dL, BUN was 12.3 mg/dL, Creatinine was 0.25 mg/dL. Whole Exom Sequencing genetic analysis was detected a heterozygous mutation in the OSGEP gene.

Conclusion: OSGEP gene mutation can associate with from isolated proteinuria to end-stage renal failure and neurodegenerative findings. Consequently, careful evaluation of patients with proteinuria in terms of concomitant other systemic abnormalities may be useful in protecting the patient from complications related to possible immunosuppressive use.

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FAMILIAL HYPONATREMIA CONDITIONED BY THE R137C MUTATION WITH CONSTITUTIVE ACTIVATION OF THE VASOPRESSIN RECEPTOR

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Aim: The authors described a familial nephrogenic syndrome of inappropriate antidiuresis (NSIAD) in two boys with hyponatremia and activating mutation of the vasopressin receptor.

Methods: Hyponatremia can occur in endocrinological diseases, neoplasms, kidney diseases, and acquired or genetically conditioned disorders of vasopressin levels. Genetic testing for an AVPR2 receptor activating mutation is crucial in patients with hyponatremia, normovolemia, hypoosmolality, and low copeptin level.

Results: Case 1. A 2.5-year-old boy was admitted to the hospital due to respiratory tract infection with a fever of up to 40˚C. He refused to drink water; his diuresis was 300 ml/day with no signs of dehydration or edema. Laboratory tests showed CRP 44.5 mg/dL, WBC 19.7x103/uL, Na 125 mmol/L, normal K, creatinine, and urea levels. Chest X-ray revealed peribronchial changes. Abdominal ultrasound and brain MRI were normal. In history, the boy has always consumed small amounts of fluids (about 600 mL/day). After treatment with intravenous 0.9% NaCl, cefuroxime, and paracetamol, Na was 132-127 mmol/L, with stable low urine uric acid level (1 mg/dL). Following infection resolution, hyponatremia, serum osmolality 260 mOsm/kg H2O with hypouricemia, and increased fractional sodium excretion (21%) were observed. Hormone levels (thyroid, ACTH, cortisol, renin, aldosterone) were normal. Due to low copeptin level, genetic testing for AVPR2 receptor activating mutation was performed, revealing a hemizygous pathogenic variant c.409C > T in one AVPR2 gene allele, resulting in Cysteine substitution for Arginine at position 137. NSIAD was diagnosed. Case 2. His 7-month-old brother had reduced activity and muscle tone, Na 117 mmol/L, and serum osmolality 249 mOsm/kg H2O due to the family history of genetic testing for NSIAD. This same variant of AVPR2 activating mutation was confirmed. The boys were recommended to restrict oral fluid intake to 1000 ml/m2 and sodium supplementation, achieving sodium levels of 128-132 mmol/l.

Conclusions: NSIAD requires genetic analysis to diagnose. Patients with NSIAD require continuous monitoring of electrolyte levels and limiting oral fluid intake and sodium supplementation.

Keywords: Nephrogenic Syndrome of Inappropriate Antidiuresis, hyponatremia, activating mutation of the vasopressin receptor

1204

SWITCHING FROM CONVENTIONAL TREATMENT WITH PHOSPHATES AND ALFACALCIDOL TO ANTI- FIBROBLAST GROWTH FACTOR 23 MONOCLONAL ANTIBODY: 12-MONTH FOLLOW-UP IN A 7-YEAR-OLD FEMALE WITH X-LINKED HYPOPHOSPHATEMIA

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Aims / Purpose: X-linked hypophosphatemia (XLH) is a hereditary form of rickets. Loss-of-function mutations in the phosphate regulating with homologies to Endopeptidases on X-chromosome (PHEX) gene result in renal phosphate wasting mediated by increased levels of Fibroblast Growth Factor 23 (FGF23). Conventional treatment of XLH rickets consists of daily oral administration of phosphates and active vitamin D analogs. Since 2018, targeted treatment with anti- Fibroblast Growth Factor 23 monoclonal antibody (Burosumab) has been successfully used in patients with XLH. We describe our 12-month experience of treatment with Burosumab in a 7 years old girl. with X-linked hypophosphatemia, scaphocephaly, Chiari syndrome type I and syringomyelia.

Methods: A 7-year-old girl presented in infancy with increased head circumference, and scaphocephaly due to sagittal synostosis. At the age of 15 months hypophosphatemia was revealed during investigation for genu varum (Figure 1). The presence of hypophosphatemia and bone deformities supported the diagnosis of hypophosphatemic rickets and at the age of 2 years, oral daily treatment with phosphates and alfacalcidol was initiated. Brain- spinal cord MRI at the age of 4 years revealed a 5-mm descent of the cerebellar tonsils below the level of the foramen magnum (Chiari syndrome type I), syringomyelia (Figure 2). The diagnosis of XLH was confirmed by genetic testing at the age of 5 years showing a de novo acceptor splice-site mutation in the PHEX gene (Intron 9, c.1080-3C > G). Due to non-improvement of hypophosphatemia, monotherapy with Burosumab was initiated administered in subcutaneous injection twice a month.

Results: The patient was treated with phosphates and alfacalcidol for 4 years (from 2 to 6 years old). During the last 12 months the patient is under monotherapy with Burosumab showing significant improvement of hypophosphatemia, achieving normal serum phosphorus levels (> 3.5 mg/dl) and normal phosphorus reabsorption values (> 85 %) and TmP/GFR.

Conclusion: In our patient, conventional treatment did not improve hypophosphatemia, whereas switching to the new therapy with Burosumab during the last 12 months resulted in significant improvement of serum phosphate and phosphorus reabsorption values. Burosumab is likely to emerge as the main treatment for XLH in the future.

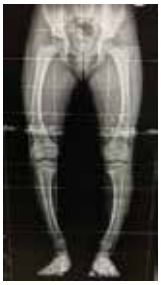

Figure 1. Anteroposterior radiograph of the femur and tibia, shows increased axial height of the physis. The metaphyseal area is widened and there is bowing of the axis of the femur and tibia.

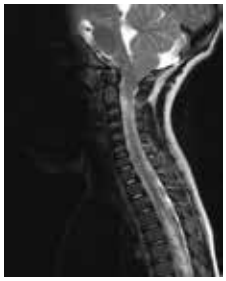

Figure 2. MRI of the craniovertebral junction, cervical and thoracic spine at the age of 4 years. There is crowding at the level of the foramen magnum (Chiari syndrome type I) and syringomyelia from the T3/T4 level and caudally.

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A RARE PRESENTATION OF KELLEY SEEGMILLER SYNDROME WITH ACUTE RENAL FAILURE

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Aims/Purpose: To present a case of a 13 year old boy with Kelley Seegmiller syndrome and acute renal failure.

Background: Kelley Seegmiller syndrome is caused by mutations in HPRT1 gene causing partial hypoxanthine guanine phosphoribosyl transferase deficiency. The affected males usually present with hyperuricemia, hyperuricosuria, gout and urolithiasis.

Case presentation: A 13 year old boy presented with 5 day history of fever with no other symptoms. He had routine blood tests one year ago that showed a uric acid of 11.7 mg/dl that was not further investigated. On admission to our hospital, his laboratory investigations showed: urea 220 mg/dl, creatinine 5 mg/dl, CRP 320 mg/L and uric acid 36 mg/dl. His urine culture grew E.Coli > 100.000 and his renal USS showed increased echogenicity in the renal pyramids bilaterally and a stone measuring 7 mm in the calyces of the right kidney. During his admission, we treated his urine infection with antibiotics and his AKI with supportive measures. Due to the very high uric acid on presentation, he received a dose of rasburicase and his uric acid improved to 7.2 mg/dl and increased again to 9.9 mg/dl and then remained to this level. His I acute renal injury resolved and he completed a 2 week course of oral antibiotics. His urine uric acid excretion was elevated (2386 mg/24h and 36 mg/kg/day) and his Fe uric acid was 14.5%. His genetic testing showed a missense mutation in the HPRT1 gene, most likely pathogenic (c.112C > G [p.Pro38Ala]) hence, a diagnosis of X-linked Kelley Seegmiller was made. His mother was harboring the same mutation and was asymptomatic. The patient is now stable on treatment with allopourinol and has normal renal function.

Conclusion: Kelley Seegmiller syndrome, if undiagnosed, can result in severe complications like acute renal failure on the basis of nephrolithiasis. High uric acid levels on routine blood tests should not be ignored but investigated with urine uric acid excretion and if abnormal, genetic testing can facilitate diagnosis, prognosis and treatment plan.

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AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE - A FIVE YEAR EXPERIENCE IN MARIBOR

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Aims/Purpose: Autosomal dominant polycystic kidney disease (ADPKD) is the most common genetic cause of renal failure worldwide, historically termed "adult" polycystic kidney disease. Its clinical presentation in young age is increasingly being recognized as significant cause of morbidity. Early management is important to slow down the progression of the disease and to delay renal failure in adulthood. The aim of our study was to review the patients with ADPKD treated in our paediatric centre in the last five years and to evaluate their clinical features and outcome.

Methods: We retrospectively extracted data from our computer system for all patients diagnosed with ADPKD and further analysed the information.

Results: Over the past five years, our centre treated 25 patients diagnosed with ADPKD, comprising 6 males and 19 females, with a median age of 14 years (interquartile range (IQR) 9 years). The median age at diagnosis was 10 years (IQR 10.5 years). While the majority had a positive family history, two cases confirmed de novo mutations. Eight patients received a confirmed genetic diagnosis, with six affected by mutations in PKD1 and two in PKD2. Genetic results are pending for five patients. Apart from one patient with reduced kidney function, all others exhibited normal kidney function, with median serum creatinine levels of 52 µmol/l (IQR 31 µmol/l) and cystatin C levels of 0.89 mg/l (IQR 0.19 mg/l), along with mild deviations in urinary albumin/creatinine ratio (median 1.6 g/mol, IQR 2.2 g/mol) and daily proteinuria (median 0.14 g/day, IQR 0.12 g/day). Elevated blood pressure was observed in four patients, while kidney stones were identified in two of them. One patient experienced a urinary tract infection within the last year. Five patients (20%) were recommended therapy with angiotensin-converting enzyme inhibitors, but two failed to adhere, one due to pregnancy and the other due to non-compliance. All patients received recommendations for healthy lifestyle. Vaptan therapy was not introduced in any of them.

Conclusion: In our patient cohort, ADPKD manifested mildly and accordingly to other reports; nevertheless, the necessity for treatment in a fifth of cases and one instance of reduced kidney function underscore the importance of regular screening for ADPKD in at-risk children along with performance of increasingly more accessible genetic testing.

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DENT'S DISEASE IN CHILDREN: IS EARLY DIAGNOSIS POSSIBLE?

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Aims: To present genetic, clinical and laboratory features of Dent's disease (DD) can be used for timely diagnosis

Methods: All patients with DD seen in 2nd City Children's Clinical Hospital since 2005 were included in the study. All 6 patients (from 5 families) were boys, age 10 (8–11) years, half of them had type 1 DD and 50.0% had type 2.

Results: The onset of the DD occurred at the age of 1.5 (1.0–2.0) years for all patients with proteinuria 0.477 (0.043–0.562) g/l. Biochemical blood test were normal: creatinine 36.1 (30.1–50.3) μmol/l, urea 3.2 (2.7–3.9) mmol/l, uric acid 2008.6 (1032.0–2062.0) μmol/l, potassium 4.4 (4.3–4.6) mmol/l, calcium 2.42 (2.40–2.49) mmol/l, phosphorus 1.69 (1.55–1.83) mmol/l. Acid-base state as normal: pH 7.39 (7.36–7.43), BE -1.6 (-2.5–-0.9) mmol/l, HCO3 23.5 (22.0–24.1) mmol/l. Urinary protein, calcium, phosphorus were 0.12 (0.08–0.26) g/24 h, 1.84 (0.94–3.90) μmol/24 h, 9.2 (6.0–13.1) mmol/24 h respectively. The first urinary US examination established the presence of microcalcinates in 2/6 patients. Excretion of oxalates was 2.1 (1.1–2.7) mg/24 h, so the first diagnosis was oxalate crystalluria. 4/6 boys had a positive family history of kidney disease (proteinuria, urolithiasis, CKD in maternal male relatives) and increasing proteinuria during further observation and treatment. 2-microglobulin levels exceeded 4 mg/l (normal 0–0.015 mg/l) in all patients. 2/6 patients had congenital cataract and impaired psycho-speech development (two siblings). This allowed us to assume hereditary nature of the disease and recommend genetic study. In 3/6 a mutation in CLCN5 gene was found, in 2/6 a mutation in OCRL gene (two siblings), in 1/6 genetic study wasn't performed. Thus, the age of diagnosis of DD was 6 (5–8) years. After 7 (5–9) years 4/6 patients were diagnosed with CKD stage 2–4.

Conclusion: Dent's disease is a difficult to diagnose but carefully collected hereditary anamnesis, the possibility of genetic testing allows timely diagnosis and prescription of therapy, thus slowing down the progression of CKD.

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IMMUNOLOGICAL CHARACTERISTICS OF TUNISIAN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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Aim: Kidney transplantation (KT) has revolutionized the prognosis of children with renal insufficiency; however, the course of the disease can be marked by complications. The aim of this study was to investigate the immunological characteristics of Tunisian children undergoing KT.

Methods: This was a retrospective and descriptive study that included pediatric renal transplant recipients followed at the pediatric nephrology department of Charles Nicolle Hospital in Tunis over a period of 34 years (from January 1, 1989, to December 31, 2022). We included patients who underwent KT at an age younger than 20 years. The detection of HLA antibodies relies on cellular methods (microlymphocytotoxicity assay + flow cytometry) and acellular methods (ELISA method + Luminex method). The lymphocytic cross-match was performed using donor cells obtained from peripheral blood in the case of living donors and from lymph nodes or, if unavailable, from the spleen in the case of deceased donors. For recipients, the sera used included the serum obtained on the day of transplantation and any previously positive sera stored in the Immunology Laboratory's serum bank.

Results: In our study, 97 patients were included. The median number of incompatibilities in the HLA system was 3 [2 - 3]. Complete compatibility was observed in seven cases (7.2%). A number of HLA mismatches 1-2 were observed in 20 cases (20.6%), and a number of 3-5 mismatches were observed in 70 cases (72.2%). The distribution of kidney transplants based on the number of incompatibilities per locus for the A, B, and DR loci was as follows: HLA-A: 0 incompatibilities (16.5%), 1 incompatibility (64.9%), 2 incompatibilities (18.6%). HLA-B: 0 incompatibilities (11.3%), 1 incompatibility (69.1%), 2 incompatibilities (19.6%). HLA-DR: 0 incompatibilities (25.8%), 1 incompatibility (72.2%), 2 incompatibilities (2%). The prevalence of patients with pre-transplant HLA antibodies was 7.2% (n = 7). Among them, 28.6% subsequently experienced rejection. Post-transplant, HLA antibodies were detected in 31 (32%) of the transplant recipients, of whom 12 (38.7%) later experienced rejection. The median time for the appearance of these antibodies post-transplant was 56 months [1.4 - 106.4].

Conclusions: Immunological monitoring is crucial for the success of kidney transplantation.

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INFECTIOUS COMPLICATIONS FOLLOWING PEDIATRIC KIDNEY TRANSPLANTATION: TUNISIAN SERIES

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Aim: To investigate the main infectious complications following pediatric KT in Tunisian children.

Methods: This is a retrospective and descriptive study that included pediatric kidney transplant recipients followed at the Pediatrics Department of Charles Nicolle Hospital in Tunis over a period of 34 years (from January 1, 1989, to December 31, 2022). Included were children and young adults aged less than 20 years at the time of transplantation.

Results: In total, 97 patients were included. 78 patients (80.4%) experienced at least one infectious complication post-transplantation (TR), of which 20 (25.6%) subsequently experienced rejection. Among our transplant recipients, 24 (24.7%) developed early post-KT infections, of whom 5 (20.8%) later experienced rejection. Early infections were primarily dominated by urinary tract infection (UTI) in 45.8% (n = 11) of cases and cytomegalovirus (CMV) infection in 20.8% of cases (n = 5). Forty-three patients (44.3%) experienced at least one UTI post-KT, of whom 9 (20.9%) later experienced rejection. The median number of UTIs per patient post-KT was 2 [1 - 4]. Indeed, 26.8% (n = 26) of our transplant recipients experienced more than one episode of UTI post-KT. The most common pathogen was Escherichia coli, in 23 cases, followed by Klebsiella pneumoniae in 15 cases. Seventeen patients (17.5%) experienced at least one pulmonary infection post-TR, of whom 4 (23.5%) later experienced rejection. A total of 21 documented pulmonary infections were recorded. These consisted of bacterial pneumonia in 14 cases, documented viral pneumonia in four cases, and fungal pneumonia in two cases. Two patients died from acute respiratory distress syndrome (ARDS). Twenty-one patients (21.6%) experienced at least one digestive infection post-TR, of whom 9 (42.9%) later experienced rejection. Gastritis due to Helicobacter pylori (HP) was found in two patients. Infectious esophageal involvement was found in three cases. This included mycotic esophagitis in two cases and CMV esophagitis in one case. Gastrointestinal infections were predominantly viral gastroenteritis. Infection with Giardia intestinalis was documented in one case. Viral diarrhea was the most common digestive infection in our series, accounting for 61.9% (n = 13) of digestive infections post-KT. The outcome of digestive infections in our transplant recipients was favorable in all cases. Fourteen patients (14.4%) experienced septicemia post-KT, of whom 5 (35.7%) later experienced rejection. The most commonly implicated pathogen in our series was Staphylococcus aureus in 35.7% of cases. The outcome was favorable in 13 cases. One death due to septicemia caused by Acinetobacter with multi-organ failure was noted.

Conclusion: Infectious complications are common post-KT and can be serious.

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CALCINEURIN INHIBITORS IN PEDIATRIC KIDNEY TRANSPLANTATION: VARIABILITY AND COMPLICATIONS

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Aim: Calcineurin inhibitors (CNIs) are a cornerstone in the immunosuppressive treatment after pediatric kidney transplantation (KT). However, this treatment is associated with complications. The aim of our study was to investigate the intra-individual variability of calcineurin inhibitors on one hand and their toxicity on the other hand.

Methods: This is a retrospective and descriptive study that included pediatric renal transplant recipients followed at the Pediatric Department of Charles Nicolle Hospital in Tunis over a period of 34 years (from January 1, 1989, to December 31, 2022). We included children under the age of 20 at the time of KT. (CNIs) were prescribed as maintenance therapy after KT. The doses were adjustable according to pharmacological monitoring of residual levels. The evaluation of intra-individual variability of calcineurin inhibitors was based on calculating the coefficient of variation (CV) of the drug levels. This coefficient was calculated using the formula: CV(%) = /M, where: M = The mean of trough levels (C0) for Tacrolimus and Cyclosporine. = The standard deviation of all available through levels (C0) of the studied immunosuppressive treatment for each patient.

Results: The median value of the CV for Tacrolimus was 20.4% [17.5 - 29.2]. Nineteen out of the patients (33.3%) receiving Tacrolimus had a CV greater than or equal to 27%, of which 10 (52.6%) subsequently experienced rejection. The median value of the CV for Cyclosporine was 52% [25 - 63.5] (Rejection (+): 52% [34 - 66] vs. Rejection (-): 51% [31 - 63]). Renal toxicity from CNIs was found in 20.6% of our transplant recipients (n = 20). This consisted of acute toxicity in 5 cases and chronic toxicity confirmed by urinary protein/creatinine ratio (PBG) in 15 cases. Acute toxicity from CNIs was secondary to the use of Cyclosporine in 4 cases and Tacrolimus in 1 case. Chronic toxicity from CNIs confirmed by kidney graft biopsy was found in 9 patients receiving Cyclosporine and 6 patients receiving Tacrolimus. Stomatological involvement was noted in five of our transplant recipients, all of whom were receiving Cyclosporine. In our series, the switch from Cyclosporine to Tacrolimus was justified by the severity of adverse effects related to Cyclosporine in 5 out of 6 cases. This included marked gingival hypertrophy in two cases and renal toxicity from CNIs in three cases.

Conclusions: Monitoring of trough levels of CNIs as well as surveillance of their side effects is essential.

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SUCCESSFUL RENAL TRANSPLANTATION IN A PAEDIATRIC RECIPIENT WITHIN TWO WEEKS OF ACUTE COVID-19 INFECTION

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Purpose: To report the successful outcome of a renal transplant carried out two weeks after acute COVID-19 infection.

Background: A 13-year old boy with end-stage kidney disease on in centre haemodialysis secondary to Townes-Brock syndrome after failed renal transplant has dialysis access issues. He has recurrent bacteraemias and line infections, and without time to form two stage transposition for complex arteriovenous fistula to mature knowing that he had three failed attempts to insert peritoneal dialysis catheter previously.

Results: There are no living donor options so he was placed on clinically urgent scheme (both donation after brain and circulatory death donors) with mismatch 2, 2, 2 as running out of dialysis access for re-transplantation. He previously had four COVID-19 vaccinations and admission for COVID-19 infection. He was called in for DCD four days later but had very mild symptomatic COVID-19 infection with blocked nose but otherwise clinically well with SARS-CoV-2 PCR RNA CT of 27.7 on NPA. The offer was declined and he was suspended from the "waiting list" for transplantation. He started anti-viral treatment with remdesivir and his SARS-CoV-2 PCR RNA increased from 26.95 to 36.511 over three days and was negative the following week. He did not receive sotruvimab or paxlovid. He went back on call for re-transplantation two weeks later and was successfully retransplanted with DBD within two days. There were no intra or post-operative anaesthetic or respiratory concerns, he has remained negative for COVID-19 infection since transplantation, with stable renal allograft function (estimated glomerular filtration rate of 72mls/min/1.73m2).

Conclusions: This is the first description of clinically urgent renal transplantation two weeks after acute symptomatic COVID-19 infection. Viral load was undetectable after remdesivir use and transplantation took place without intra- or post-operative complications. We did not wait the advised seven weeks post COVID-19 infection due to urgent requirement for transplantation. While there are generally positive outcomes in renal transplant recipients with COVID-19 infection, there are no published reports of renal transplantation during acute COVID-19 infection. For some patients, renal transplantation may be considered where the anaesthetic and respiratory risks are balanced against the clinically urgent requirement for transplantation, and the important role of remdesivir to decrease viral load.

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A CASE REPORT UNCOVERING ULTRA-RARE ANGIOTENSIN CONVERTING ENZYME GENE MUTATIONS AFTER KIDNEY TRANSPLANTATION

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Aims/Purpose: Renal tubular dysgenesis (RTD) is a rare condition, which is caused by various mutations in genes encoding components of renin – angiotensin system. We report a patient with novel bi-allelic mutations in angiotensin-converting enzyme (ACE) coding gene.

Case report: A boy from non-consanguineous parents was born at 40 weeks of gestation (threat of terminations at the 6/7th gestation week). He did not have respiratory distress, but anuria was noticed after birth, spontaneous urine output on the third day. Persistent hyperkalemia from birth, blood pressure below 75. percentile by age, height and gender, high serum renin and normal aldosterone (measured at the age of two months), enlarged hyperechogenic kidneys on ultrasound and native kidney biopsy (at the age of three months) revealed vacuolated, degenerative tubules predominantly in distal tubules. Peritoneal dialysis was initiated at the age of 11 months because of end-stage chronic kidney disease and anuria and switched to hemodialysis six years later. He received a kidney transplant from his father at the age of 10 years. Immunosuppression consisted of basiliximab as induction therapy and tacrolimus, mycophenolate and metilprednisolone as maintenance immunosuppression. Two weeks after transplantation, the patient developed severe hypotension and hypoperfusion leading to allograft dysfunction. Blood serum tests revealed high serum renin concentration (above reference interval - 500 mcU/ml) and low ACE and aldosterone were detected (below reference intervals). He required noradrenaline infusion to maintain sufficient blood pressure. His primary diagnosis was unclear and a genetic testing (Blueprint Genetics, Helsinki, Finland) was performed revealing a novel likely pathogenic inframe deletion c.969_974del, p.(Phe323_Val325delinsLeu) and additionally two homozygous missense variants c.605C > T, p.(Pro202Leu), c.1454C > G, p.(Pro485Arg) in ACE gene suggesting renal tubular dysgenesis. Fludrocortisone (0.1 mg twice daily), desmopressin and midodrine initiated and because of severe negative fluid balance unilateral native kidney nephrectomy was performed. His graft function stabilized, and renin concentration normalized.

Conclusion: Renal tubular dysgenesis may present with variable clinical manifestations depending on underlaying mutation. Early diagnosis and treatment are crucial especially in transplant recipients.

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REJECTION AND SURVIVAL OF TUNISIAN CHILDREN WITH KIDNEY TRANSPLANTS: A TUNISIAN STUDY

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Aim: To study the impact of kidney transplant rejection on the survival of transplanted children in Tunisia

Methods: This was a retrospective and descriptive study that included renal transplanted children followed at the Pediatrics department of Charles Nicolle Hospital in Tunis over a period of 34 years (from January 1, 1989, to December 31, 2022). We included patients who underwent a kidney transplant at an age < 20 years. For patients who underwent more than one transplantation, each kidney transplant was considered as an independent transplantation.

Results: In our study, 97 patients were included, comprising 56 boys and 41 girls, resulting in a male-to-female sex ratio of 1.4 [Rejection (+): M/F = 0.8 versus (VS) Rejection (-): M/F = 1.6]. The average age of the recipients at the time of kidney transplantation was 15.4 ± 3.2 years [Rejection (+): 15.4 ± 2.4 VS Rejection (-): 15.4 ± 3.5 years]. The median time between the start of dialysis and kidney transplantation was 23 months [15 – 43.6] [Rejection (+): 19.5 months [12.5 – 41.7] VS Rejection (-): 23.8 months [15.4 – 44]]. The cumulative survival of transplant recipients was 90% at 5 years, 87% at 10 years, and 59% at 20 years post-transplantation. We did not find a statistically significant association between rejection and transplant survival in our study. The survival of patients who experienced rejection was 100% at 5 years, 95% at 10 years, and 80% at 20 years.

Conclusion: The absence of an impact of rejection on the survival of pediatric kidney transplant recipients reflects the significant progress made in the treatment of rejection in pediatric nephrology.

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EARLY VASCULAR REJECTION NOT ASSOCIATED WITH ANTI-HLA ANTIBODIES WITH GOOD MEDIUM AND LONG TERM PROGNOSIS. CASES REPORT

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Aims: To describe clinical and pathological findings in 3 patients with early vascular rejection with negative HLA antibodies.

Method: Retrospective review of clinical reports and biopsy samples.

Results: Patient 1: 9 y.o boy. Primary disease: SRNS. Negative pre-tx antiHLA antibodies. Kidney tx (cadaveric donor). Induction: basiliximab, steroids, MMF and IV cyclosporine. Good initial course, on day +3 presented oligoanuria, severe hypertension and pathological US. Kidney biopsy (day +5) showed severe endarteritis, mild glomerulitis, interstitial edema with macrophage infiltrate and negative C4d staining. Anti-rejection treatment: switch to tacrolimus, high-dose steroids, plasma exchange, immunoglobulins, rituximab and bortezomib. Follow-up biopsies (+15 and +97) showed progressive resolution of vascular injury and chronic glomerular and vascular TMA. C4d staining and anti-HLA antibodies remained negative. Follow up: gradual recovery of GFR. Proteinuria partially controlled with ARB. 10 years after tx, eGFR 40 mL/min/1.73m2. Patient 2: 14 y.o girl. Primary disease: ANCA-associated vasculitis. Negative pre-tx antiHLA antibodies. Kidney tx (cadaveric donor). Standard induction: basiliximab, steroids, MMF and tacrolimus. Surgery without complications, 24h after surgery she became anuric, severely hypertensive and with pathological US. Urgent biopsy (+2): preserved glomeruli, moderate macrophagic inflammatory interstitial infiltrate and severe endarteritis lesions. No C4d deposits. Anti-rejection treatment: high-dose steroids, plasma exchanges and thymoglobuline. At day +7 restarted diuresis with progressive recovery in GFR. 8 months later, eGFR 74 mL/min/1,73m2; no proteinuria. Negative antiHLA antibodies. Patient 3: 14 y.o boy. Primary disease: chronic interstitial nephritis. Negative pre-tx antiHLA antibodies. Living-related kidney tx (mother). Standard induction. Immediate diuresis in the OR, at 24h oligoanuria with severe hypertension and pathological US. Renal biopsy (+5): endarteritis, glomerulitis and capillaritis with macrophagic infiltrate. Negative C4d staining. Anti-rejection treatment: high-dose steroids, plasma exchanges, thymoglobuline and rituximab. Clinical course complicated with perirenal hematoma on day +15. Second biopsy (+28): resolution of rejection lesions, evolved acute tubular necrosis with interstitial edema.Follow up: gradual improvement of GFR. 3 months later, eGFR 71 mL/min/1.73m2; no proteinuria. Negative antiHLA and non- HLA antibodies.

Conclusion: Our patients share common clinical (very early presentation, severe hypertension) and pathological (endarteritis, macrophagic infiltrate) findings. We could not demonstrate an antibody-mediated mechanism. Despite severe presentation, prompt and aggresive treatment led to significant improvement in renal outcome.

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PREDICTION OF CKD PROGRESSION WITH KIDNEY FAILURE RISK EQUATION - EVALUATION OF A PORTUGUESE COHORT

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Aims/Purpose: The kidney failure risk equation (KFRE) was initially developed to guide clinical decision-making in adults with chronic kidney disease (CKD). Its applicability in pediatric patients has been explored, showing promising results as a predictor of risk of progression to end-stage kidney disease (ESKD). With this study, we aimed to assess the effectiveness of the 4-variable and 8-variable KFRE in predicting the risk of progression to ESKD in children with CKD.

Methods: We performed a retrospective analysis of CKD patients, followed in a Portuguese Paediatric Nephrology tertiary center, from January 2010 to December 2022. Patients aged ≤16 years-old with an estimated glomerular filtration rate (eGFR) < 60mL/min/1.73m2 were eligible for inclusion. The eGFR was estimated with the bedside Schwartz formula. The 4-variable (age, sex, eGFR, and albumin to creatinine ratio) and 8-variable (4 variables plus serum calcium, phosphate, bicarbonate, and albumin) KFRE calibrated to a non-North American population was computed. The primary outcome was time to ESKD, defined as the initiation of dialysis or kidney transplant, whichever occurred first. The association between the KFRE score and time to ESKD was examined using Cox proportional hazards model. Discrimination of ESKD risk by the KFRE was assessed using C statistics, with a value of greater than 0.80 indicating strong discrimination.

Results: Forty-six patients were included in the study (29 (63.0%) males), with a median age at inclusion of 9 (IQR 5-13) years. The median eGFR was 37 (IQR 25-52) mL/min/1.73m2 and 37 (80.4%) patients had a nonglomerular cause of CKD. The median follow-up time was 4.4 (IQR 2.2-7.3) years; 8 (17.4%) and 17 (37.0%) patients progressed to ESKD within 2 and 5 years after enrollment, respectively. The 4-variable KFRE scores discriminated risk of ESKD, with C statistics of 0.82 (95% CI, 0.69-0.95) and 0.77 (95% CI, 0.65-0.88) for the 2- and 5-year risk scores, respectively. Results were similar using the 8-variable equation. The performance of the KFRE showed no significant differences by gender, age, and cause of CKD.

Conclusion: The KFRE is a simple yet effective tool that provides excellent discrimination of the risk of ESKD in children with CKD. Our results suggest that both the 4-variable and 8-variable KFRE equation could be integrated into the clinical management of pediatric CKD patients to aid anticipatory guidance. However, larger studies are warranted to validate and reinforce our findings.

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ASSESSING THE VALIDITY OF THE KIDNEY FAILURE RISK EQUATION FOR PREDICTING GRAFT FAILURE IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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Aims/Purpose: Kidney transplantation (KT) is the gold standard treatment for end-stage kidney disease (ESKD). Graft failure remains a very significant post-transplantation concern, demanding reliable predictive tools to identify individuals at higher risk. The Kidney Failure Risk Equation (KFRE) has emerged as a promising prognostic tool to estimate the risk of progression to ESKD. Nevertheless, its applicability in pediatric cohorts, particularly in predicting kidney graft failure still remains poorly explored. With this study we aim to evaluate the validity of the KFRE in predicting graft failure among pediatric KT recipients, followed in a Portuguese pediatric nephrology division.

Methods: We performed a retrospective observational study including 59 pediatric KT recipients (KT between January 2007 and December 2017). The glomerular filtration rate (eGFR) was estimated with the creatinine based-CKiD U25 equation. The KFRE scores for each patient was computed with data obtained at 1-year post-transplant. ROC analysis was used to assess the adequate discriminative ability of the 4-variable KFRE in predicting the 2- and 5-year risk of graft failure in patients with functioning graft 1-year post-transplant.

Results: Among the 59 patients, 41 (69.5%) were male. Median age at the time of the KT was 12.4 (IQR 9.1-15.7) years, 11 (18.6%) being living donor recipients. Median eGFR at 1-year post-transplantation was 62.4 (IQR 53.1-72.5) mL/min/1.73m2; 1 (1.7%) and 4 (6.8%) patients developed graft failure within 2 and 5 years from the point of the 1-year post-transplantation evaluation, respectively. This model predicts that individuals with a 2-year risk above 5.82% or a 5-year risk above 2.4%, will have graft failure before 2 and 5 years, respectively. The discrimination was excellent for the 2-year risk (AUC 0.966, 95% CI 0.914-1.000) and very good for the 5-year risk (AUC 0.899, 95% CI 0.756-1.000). Calibration plots showed an imprecise calibration. However, the small sample size and the low number of patients with graft failure require caution in the interpretation of these plots.

Conclusion: The KFRE equation seems to have potential utility in predicting the progression of graft failure among pediatric KT recipients based on data collected 1-year post-transplant. Still, to validate these initial observations and to ensure the reliability of these conclusions, it is necessary to undertake more extensive studies on a larger scale.


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