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Original Article

Kidney Outcome Predictors in Congenital Anomalies of the Kidney and Urinary Tract

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ABSTRACT

Aim: Congenital anomalies of the kidney and urinary tract (CAKUT) are a leading cause of chronic kidney disease in children. This study aimed to evaluate the frequency of adverse renal outcomes and also to identify early risk factors for guiding long-term follow-up strategies.

Materials and Methods: We conducted a retrospective cohort study of children born between 2010 and 2023 with diagnoses of unilateral kidney agenesis, multicystic dysplastic kidney, or posterior urethral valves (PUV) followed up at a tertiary pediatric nephrology center. Clinical and demographic variables were extracted from the electronic health records. Adverse renal outcomes included proteinuria, hypertension and an estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73m^2 or age-equivalent thresholds. Univariate logistic regression analyses were performed in order to assess associations between potential predictors and adverse outcomes.

Results: Among the 104 patients [60% male; median age at last follow-up 7.2 years (interquartile range 6.9)], 13% developed adverse renal outcomes, most commonly proteinuria (7%). The median age at onset of these outcomes was 3.7 years. PUV, prematurity and a history of urinary tract infection (UTI) were significantly associated with adverse outcomes. Other factors, including low birth weight, additional CAKUT, reduced baseline eGFR, and kidney length to body length ratio at diagnosis, were not significantly associated with negative outcomes.

Conclusion: Adverse renal outcomes can occur early in children with CAKUT. Prematurity, UTI and PUV emerged as key determinants of adverse renal prognosis and may serve as valuable markers for identifying patients at higher risk who may require closer and more individualized follow-up.

Keywords: Congenital anomalies of kidney and urinary tract, pediatric, risk factors, chronic kidney disease

Introduction

Congenital anomalies of the kidney and urinary tract (CAKUT) represent a heterogeneous group of structural malformations resulting from disrupted urinary tract development during intrauterine life (1,2). They are among the most common congenital anomalies (3) and constitute the leading cause of chronic kidney disease (CKD) in children and young adults (4,5).

Clinically relevant forms of CAKUT include unilateral kidney agenesis (UKA), multicystic dysplastic kidney (MCDK), and posterior urethral valves (PUV). These conditions frequently result in a reduced nephron number, predisposing the remaining renal tissue to hyperfiltration injury, progressive fibrosis, and a subsequent loss of kidney function (6).

Long-term renal outcomes in children with CAKUT are highly variable. A considerable proportion of

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affected patients develop complications such as arterial hypertension, proteinuria, CKD, or kidney failure during childhood or adolescence. Although several studies have explored prognostic determinants, the available evidence remains incomplete, and early predictors of adverse renal outcomes have not been fully established (2,3).

The present study aimed to describe the frequency of adverse renal outcomes in a cohort of children with CAKUT followed at a tertiary pediatric nephrology center and to identify clinical and demographic factors associated with the increased risk of these outcomes.

Materials and Methods

We conducted a retrospective cohort study including pediatric patients diagnosed with UKA, MCDK, or PUV who were born between 2010 and 2023. Patients were excluded if the diagnosis could not be confirmed, if they were lost to follow-up, or if their demographic data were incomplete. This study was in accordance with the ethical standards of the institutional research committee and the principles of the Helsinki Declaration.

Data Collection

The data were extracted from the electronic medical records and included demographic variables (birth weight, gestational age, and antenatal diagnosis) and clinical parameters, including the presence of additional CAKUT (aCAKUT), a history of urinary tract infection (UTI), baseline estimated glomerular filtration rate (eGFR) and kidney length to body length (KL:BL) ratio. The clinical outcomes assessed included proteinuria, arterial hypertension, clinically significant CKD and kidney failure.

In those patients with multiple primary CAKUT diagnoses, PUV was prioritized over MCDK or UKA as the primary diagnosis. In those patients with PUV, hydroureter, hydronephrosis and vesicoureteral reflux were not classified as aCAKUT due to their pathophysiological relationship with bladder outlet obstruction.

Baseline eGFR was calculated using the Schwartz equation, using the first serum creatinine obtained after the seventh day of life to minimize maternal creatinine influence. In those patients with PUV, only eGFR values obtained after one year of age were considered. This approach was chosen because renal function measurements obtained earlier may reflect impairment related to obstructive uropathy before surgical decompression, potentially leading to inaccurate estimations of long-term renal function. Similarly, KL measurements used to calculate KL:BL were obtained from the first available ultrasound for UKA and MCDK and from the first measurement after one year of age for PUV.

Outcome Definitions

Proteinuria was defined as a urine protein-to-creatinine ratio >50 mg/mmoL in children aged 6 months to 2 years old or >20 mg/mmoL in children aged 2 years or above, confirmed in at least two samples collected three months apart.

Hypertension was defined as systolic and/or diastolic blood pressure >95th percentile for age, sex and height on at least two separate occasions (7).

Clinically significant CKD was defined as eGFR<60 mL/min/1.73 m^2 in children aged 2 years or above, or 2 or more standard deviation (SD) below the mean if younger, confirmed on two measurements at least three months apart (8).

Statistical Analysis

Statistical analysis was performed using SPSS version 29. Continuous variables are expressed as mean and SD for normally distributed variables and as median and interquartile range (IQR) for non-normally distributed variables. Categorical variables are summarized as absolute and relative frequencies. Univariate logistic regression was conducted in order to evaluate the association between each predictor and adverse renal outcomes. Odds ratios (OR) with 95% confidence intervals (95% CIs) were calculated. Continuous variables were entered as linear predictors, and their ORs reflect the change in odds of the outcome per one-unit increase in the variable.

Given the limited number of outcome events, multivariable regression was not performed to avoid model overfitting and instability. Statistical significance was defined as $p<0.05$.

Results

A total of 104 patients were included. UKA was the most frequent CAKUT subtype (n=47, 45%). Male patients predominated (62, 60%). The median age at last follow-up was 7.2 years (IQR 6.9) and the median follow-up duration was 7.0 years (IQR 6.4).

Prematurity was present in 13 patients (13%), and low birth weight was identified in 12 patients (12%). Most patients had an antenatal diagnosis (n=88, 85%). Non-renal congenital anomalies were identified in 15 patients (14%), and 21 patients (20%) presented aCAKUT (Table I).

Adverse renal outcomes were identified in 13 patients (13%), with proteinuria being the most frequent

Table I. Characteristics of the cohort

	Combined cohort (n=104)	UKA (n=47)	MCDK (n=45)	PUV (n=12)
Male sex (%)	62 (59.6)	27 (57.4)	23 (51.1)	12 (100)
Age at last follow-up (years)	7.7±3.9	6.5±3.8	8.7±3.7	8.6±3.5
Antenatal diagnosis (%)	88 (84.6)	37 (78.7)	41 (91.1)	10 (83.3)
Gestational age (weeks)	39 (IQR 2)	39 (IQR 2)	39 (IQR 2)	38 (IQR 2)
Preterm birth (%)	13 (12.5)	8 (17.0)	3 (6.7)	2 (16.7)
Birthweight (g)	3,216 (IQR 706)	3,195 (IQR 745)	3,180 (IQR 702)	3,295 (IQR 747)
Low birth weight (%)	12 (11.5)	7 (14.9)	4 (8.9)	1 (8.3)
Post-natal diagnosis (Months)	5 (IQR 83)	8.5 (IQR 80)	0; 4*	144*
UTI (%)	28 (26.9)	11 (23.4)	8 (17.8)	9 (75.0)
Additional CAKUT (%)	21 (20.2)	9 (19.1)	8 (17.8)	4 (33.3)
First eGFR<90/-1 SD (%)	48 (51.1)	22 (51.2)	21 (53.8)	5 (41.7)
KL:BL ratio	9.6 (IQR 2.3)	10.4 (IQR 1.7)	8.9 (IQR 3.0)	9.0 (IQR 1.5)

Values are presented as mean ± standard deviation for normally distributed variables and median (interquartile range) for non-normally distributed variables. *For variables with less than three data, individual values are shown
CAKUT: Congenital anomalies of the kidney and urinary tract, eGFR: Estimated glomerular filtration rate, KL:BL: Kidney length to body length, MCDK: Multicystic dysplastic kidney, PUV: Posterior urethral valves, UKA: Unilateral kidney agenesis, UTI: Urinary tract infection.

manifestation (7% of the total cohort, present in 54% of patients with adverse outcomes). The median age at onset of adverse renal outcome was 3.7 years old (IQR 2.6). Kidney failure occurred in one patient with PUV, who started dialysis at 13 months of age.

In univariate logistic regression analyses, prematurity (OR=6.48; 95% CI: 1.71-24.57, p=0.004) and a history of UTI (OR=13.52; 95% CI: 3.37-54.25; p<0.001) were the strongest predictors of adverse renal outcomes.

Regarding the CAKUT subtype, MCDK was associated with a lower likelihood of adverse outcomes (OR=0.20; 95% CI: 0.04-0.97; p=0.045), whereas PUV was associated with a significantly increased risk (OR=7.5; 95% CI: 1.93-29.15; p=0.004).

Other variables, including antenatal diagnosis, low birth weight, a CAKUT, reduced baseline eGFR, and the KL:BL ratio, were not significantly associated with adverse renal outcomes (p>0.05). Detailed results are presented in Table II.

Table II. Univariate analysis: odds ratios for the outcome by each factor

	Odds ratio	95% CI	p value
Malformation type			
UKA	1.05	0.33-3.35	0.941
MCDK	0.20	0.04-0.97	0.045
PUV	7.50	1.93-29.15	0.004
Antenatal diagnosis	0.42	0.05-3.50	0.424
Prematurity	6.48	1.71-24.57	0.006
Low birth weight	0.37	0.09-1.60	0.183
Urinary tract infections	13.52	3.37-54.25	<0.001
Additional CAKUT	0.52	0.12-1.88	0.316
Diminished baseline eGFR	0.71	0.21-2.44	0.591
KL:BL	0.94	0.70-1.26	0.295

Continuous variables were analyzed using univariate logistic regression; odds ratios represent the change in odds per one-unit increase in the variable
CAKUT: Congenital anomalies of the kidney and urinary tract, CI: Confidence intervals, eGFR: Estimated glomerular filtration rate, KL:BL Ratio of kidney length to body length, MCDK: Multicystic dysplastic kidney, PUV: Posterior urethral valves, UKA: Unilateral kidney agenesis.

Discussion

In this cohort of pediatric patients with CAKUT, 13% developed adverse renal outcomes, with proteinuria being the most frequent manifestation. Notably, these complications occurred at a median age of 3.7 years, suggesting that clinically significant renal impairment may develop early in life.

Children with CAKUT are known to be at increased risk of progressive kidney injury. Therefore, close clinical surveillance during early childhood is warranted, regardless of the initial presentation. The early identification of high-risk patients may allow for the timely implementation of nephroprotective strategies aimed at delaying or preventing CKD progression (3).

Among the variables analyzed, PUV, prematurity and a history of UTI were significantly associated with adverse renal outcomes. These findings are consistent with the current knowledge regarding nephron endowment and secondary renal injury mechanisms (2,5). PUV causes persistent bladder outlet obstruction, leading to increased intravesical and intrarenal pressures which often begin during fetal life. This process may result in renal dysplasia and progressive kidney injury. Furthermore, abnormal bladder function may persist even after surgical valve ablation, contributing to ongoing renal damage (9).

Prematurity is associated with reduced nephron number due to incomplete nephrogenesis. This reduced nephron endowment predisposes affected individuals to hyperfiltration injury and long-term renal dysfunction (10). Similarly, UTI may act as additional injurious events in structurally abnormal kidneys and so accelerate CKD progression.

Interestingly, and in contrast to some previous studies, the presence of aCAKUT, reduced baseline eGFR and reduced KL:BL ratios were not significantly associated with adverse outcomes in our cohort. This finding may be explained by the limited statistical power due to the relatively small number of outcome events (3,5).

Our results also suggest a protective association between MCDK and adverse renal outcomes. However, this finding should be interpreted with caution, as it may reflect the limited number of adverse events and the univariate nature of the analysis rather than a true protective biological effect. Larger studies are needed in order to further clarify this association.

Overall, our findings support the clinical relevance of easily identifiable early-life risk factors, such as prematurity and a history of UTI, in guiding risk-adapted follow-up strategies for those patients with CAKUT. Risk stratification based on these characteristics may facilitate targeted surveillance and timely interventions, potentially mitigating long-term kidney damage.

Study Limitations

The strengths of this study include the use of real-world data from a tertiary pediatric nephrology center and the inclusion of more than a decade of clinical experience.

However, several limitations must be acknowledged. First, the absence of a standardized follow-up protocol regarding the timing of laboratory and imaging evaluations may have introduced variability in data availability. Secondly, the relatively small number of outcome events limited statistical power and contributed to wide CIs for some predictors.

Despite these limitations, the identification of significant associations between adverse renal outcomes and prematurity, UTI, and PUV suggests that these factors represent clinically relevant predictors. Future multicenter studies with standardized follow-up protocols and larger cohorts are needed in order to validate these findings and refine risk stratification tools.

Conclusion

In this cohort of 104 children with CAKUT, 13% developed adverse renal outcomes, frequently occurring at an early age (median 3.7 years). PUV, prematurity, and a history of UTI were significantly associated with an increased risk of poor renal prognosis. These findings highlight the importance of incorporating early clinical risk factors into individualized follow-up strategies for those children with CAKUT.

Ethics

Ethics Committee Approval: According to the principles of the local ethics committee, observational retrospective studies with guaranteed anonymity are exempt from formal review.

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: M.M.C., M.M., C.N., C.C., Carm. C., C.G., Design: M.M.C., M.G.L., Data Collection or Processing: M.M.C., M.G.L., M.M., C.N., Analysis or Interpretation: M.M.C., M.G.L., C.C., Carm. C., C.G., Literature Search: M.M.C., M.G.L., C.N., C.C., Carm. C., Writing: M.M.C., M.G.L.

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