



Research Article

# Longitudinal Study of the Association between Antenatal Nephrourological Ultrasonographic Findings with Unfavorable Clinical Outcomes during Postnatal Period, Childhood and Adolescence, in Patients with Congenital Anomalies of the Kidney and Urinary Tract (CAKUT)

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## Abstract

**Background:** Advances in obstetric ultrasound have led to early diagnosis of Congenital Anomalies of the Kidney and Urinary Tract (CAKUT) during antenatal care. Patients with CAKUT may present with unfavorable clinical outcomes throughout life. **Objectives:** to associate antenatal nephrourological ultrasonographic findings with clinical outcomes during postnatal period, childhood and adolescence, in patients with CAKUT. **Patients and Methods:** Retrospective cohort study of 823 patients with CAKUT followed at the Fetal Medicine Center of the Federal University of Minas Gerais (UFMG) and referred to the Pediatric Nephrology Unit of Clinics Hospital from Federal University of Minas Gerais after delivery. Median follow-up time was 58.7 months. The nephrourological ultrasonographic findings detected at the last exam prior delivery were associated with the need for surgical treatment, occurrence of Urinary Tract Infection (UTI), urinary tract infection in patients on chemoprophylaxis, development of Chronic Kidney Disease (CKD), End-Stage Kidney Disease (ESKD) and death. Pearson's and Fisher's exact chi-squared tests were used in the statistical analysis. Odds ratio was used to determine the prognostic value of the antenatal ultrasonographic findings. **Results:** In patients with CAKUT, the nephrourological ultrasonographic findings that presented statistical significant association with the clinical outcomes, in comparison to patients with CAKUT without such findings were: unilateral hydronephrosis (reduction of 42.5% in the chance of UTI in patients on chemoprophylaxis, 82.9% in the chance of CKD, 89.8% in the chance of ESKD and 2.8% in the chance of death); unilateral isolated hydronephrosis (reduction of 57% in the chance of UTI in patients on chemoprophylaxis, 89.5%

in the chance of CKD, 87.7% in the chance of ESKD and 2.5% in the chance of death); bilateral isolated hydronephrosis (reduction of 30.7% in the chance of surgery and 90.7% in the chance of ESKD); unilateral renal cysts (66.1% reduction in the chance of surgery); bilateral hydronephrosis (1.7-fold increase in the chance of UTI in patients on chemoprophylaxis, 4.3-fold increase in the chance of CKD, 4.7-fold increase in the chance of ESKD and 4.8-fold increase in the chance of death); unilateral megaureter (2.9-fold increase in the chance of UTI); bilateral megaureter (5.9-fold increase in the chance of surgery, 7.7-fold increase in the chance of hypertension, 3.5-fold increase in the chance of UTI, 3.6-fold increase in the chance of UTI in patients on chemoprophylaxis, 11.8-fold increase in the chance of CKD, 17.9-fold increase in the chance of ESKD and 14.5-fold increase in the chance of death), megabladder (7.9-fold increase in the chance of surgery, 10.6-fold increase in the chance of hypertension, 3.9-fold increase in the chance of UTI, 4.4-fold increase in the chance of UTI in patients on chemoprophylaxis, 24.7-fold increase in the chance of CDK, 35.8-fold increase in the chance of ESKD and 15.4-fold increase in the chance of death); oligohydramnios (6-fold increase in the chance of surgery, 4.9-fold increase in the chance of UTI, 30-fold increase in the chance of CKD, 40-fold increase in the chance of ESKD and 14.5-fold in chance in the of death); unilateral hydronephrosis with megaureter (2.9-fold increase in the chance of CKD and 2.4-fold increase in the chance of UTI in patients on chemoprophylaxis); bilateral hydronephrosis with megaureter (6.8-fold increase in the chance of CKD, 10.8-fold increase in the chance of ESKD and 13.3-fold increase in the chance of death); bilateral hydronephrosis with megaureter and megabladder (10.8-fold increase in the chance of surgery, 12.7-fold increase in the chance of hypertension, 4-fold increase in the chance of UTI, 4.3-fold increase in the chance of UTI in patients on chemoprophylaxis, 10.1-fold increase in the chance of death, 12.2-fold increase in the chance of CKD and 15.5-fold increase in the chance of ESKD); bilateral hydronephrosis with megabladder and oligohydramnio (5.2-fold increase in the chance of surgical treatment, 23-fold increase in the chance of death, 150.8-fold increase in the chance of CKD and 93.8-fold increase in the chance of ESKD). Conclusion: Our study revealed the nephrourological ultrasonographic findings associated with the reduction and the increase of unfavorable clinical outcomes in a group of 822 patients with CAKUT.

**Keywords:** CAKUT; Ultrasonographic findings; Hypertension; Chronic kidney disease; End-stage kidney disease

## Introduction

With the advent of fetal screening scan, the detection of congenital anomalies of the kidney and urinary tract (CAKUT) in utero has allowed early management of these conditions [1]. CAKUT consists of a spectrum of malformations that occur at the level of the kidney (hypoplasia and dysplasia), collecting system (hydronephrosis and megaureter), bladder (e.g., ureterocele and vesicoureteral reflux), or urethra (posterior urethral valves) [2]. Antenatal hydronephrosis (ANH) affects 1-5% of all pregnancies and is one of the most common birth defects [3]. It is estimated that, through morphology scan, one structural anomaly is detected in every 100 pregnancies. Of these anomalies, approximately 50% are central nervous system alterations, 20 to 30% are related to the genitourinary tract, 15% to the gastrointestinal tract and 8% to the cardiovascular system [4].

CAKUT has aroused great interest in the scientific community, especially in recent years, due to advances in the prenatal detection of these malformations through morphology scan, as well as a better understanding of their etiology, pathophysiology and related genetic factors [5].

The Fetal Medicine Center of Clinics Hospital from Federal University of Minas Gerais (CEMEFE) has been following fetuses

with CAKUT for over twenty years. Patients with CAKUT are followed according to our clinical protocol and undergo sequential ultrasonographic evaluations. After birth, the neonates are followed at the Pediatric Nephrology Unit of Clinics Hospital from Federal University of Minas Gerais (UNP). The postnatal follow-up protocol consists of performing postnatal ultrasound after the first week of life, in addition to pediatric clinical and laboratory evaluations every six months. Routine laboratory tests include serum creatinine measurement to assess renal function and routine urinalysis and urine culture to rule out Urinary Tract Infection (UTI). Voiding cystourethrography and renal scintigraphy are requested according to the initial findings of each case.

## Patients and Methods

In this retrospective cohort study, the records of 832 patients with prenatally detected CAKUT, followed at the Fetal Medicine Center of Federal University of Minas Gerais, in Brazil, and admitted for postnatal follow-up at the at the Pediatric Nephrology Unit of Clinics Hospital from Federal University of Minas Gerais, between January 1986 and October, 2010, were reviewed.

At the Fetal Medicine Center, each fetus had undergone a detailed morphology scan to detect CAKUT and other anatomic anomalies. Specific ultrasound findings, such as renal, urethral or bladder involvement, and volume of amniotic fluid were recorded. Fetuses with multiple malformations or aneuploidy were excluded from the analysis, as well as 9 patients with duplicated records.

Pregnant women were characterized according to age and parity at the time of their evaluation. Minimum age was 15 years and the maximum age was 43 years (median 24; mean 26; standard deviation 6.67). The minimum parity was zero and the maximum was 7 (median 1 and standard deviation 1.25).

Patients with CAKUT were characterized according to gestational age at birth, sex and mode of delivery. The minimum gestational age at birth was 26 weeks and the maximum was 42 weeks (median 38; mean 37.6; standard deviation 2.59). There was a predominance of males neonates (67.7%), and 52.5% of the patients were born by vaginal delivery.

Pregnant women whose fetuses showed urinary tract malformations detected by morphology scan were enrolled at CEMEFE for specialized evaluation and sequential scans, if necessary. Morphology scans were carried out by CEMEFE team of obstetric sonographers, using an US apparatus with a 100 Hz acoustic filter and a 3.5 MHz sectoral probe. The interval between examinations was defined by clinical-obstetric indications. After each scan, the ultrasound findings of each fetus were recorded in a specific clinical record. For the analysis, we considered the last scan registered in the database before delivery.

The scan was divided into two phases. At first, fetal statics, biometry measurements and estimated fetal weight were determined. The amniotic fluid volume was measured using the Amniotic Fluid Index (AFI). The scanner will also described the placental site and the appearance of the umbilical cord. The structures of the central nervous system, face, spine, thorax, heart, lungs, abdomen, upper and lower limbs were carefully evaluated, in order to rule out associated malformations. In a second moment, the morphology of the kidneys and the fetal urinary tract were carefully evaluated, searching for the presence of hydronephrosis, megaureter, megabladder, renal hypoplasia, pelvic kidney, cysts, oligohydramnios and renal agenesis. The laterality of the lesion was also specified. For the study of the kidneys, their location, contour, echogenicity, volume, presence of cysts, their sizes and distribution were determined. Renal length was obtained by measuring the longitudinal diameter and the anteroposterior diameter in a cross-sectional view. Hydronephrosis was defined

as the presence of an anteroposterior diameter of the renal pelvis equal to or greater than 10 mm ( $DAP \geq 10$  mm). The presence of a megaureter was defined by the finding of an anechoic and irregular tubular dilation in the topography of the ureter. A megabladder was characterized by the presence of a rounded anechoic structure in the middle of the fetal abdomen (diameter greater than 5 mm and/or wall thickness greater than 4 mm). Oligohydramnios was defined by the presence of an Amniotic Fluid Index (AFI) lower than the 5<sup>th</sup> percentile for a given gestational age (severe oligohydramnios). AFI between the 5<sup>th</sup> and 95<sup>th</sup> percentiles was considered normal.

At the Pediatric Nephrology Unit of Clinics Hospital from Federal University of Minas Gerais, before 2000, infants were investigated according to a systematic protocol described elsewhere [6]. After 2000, they were followed through a more tailored clinical protocol [7-9], which included renal ultrasonography after the first week of postnatal life. Then, all infants with confirmed hydronephrosis underwent a Voiding Cystourethrogram (VCUG). After 2009, VCUG was performed only in a selected subgroup of patients. When the VCUG was normal but postnatal US had revealed Renal Pelvis Dilatation (RPD)  $\geq 10$  mm, renal scintigraphy was performed after the first month [10]. Antibiotic prophylaxis was started right after birth and maintained according to the definitive diagnosis. Clinical examination (including growth and blood pressure measurements), nephrourological scans and laboratory reviews (including routine urinalysis and urine culture, to rule out urinary tract infection; and serum creatinine to assess renal function) were scheduled at 6-month intervals.

Table 1 shows the frequency of the nephrourological ultrasound findings identified in the fetuses of the study. Unilateral hydronephrosis was the most frequently observed sonographic finding, occurring in 47.3% of patients. Isolated unilateral hydronephrosis was observed in 42.6% of the cases. Bilateral hydronephrosis was observed in 38.8%, while isolated bilateral hydronephrosis occurred in 32% of cases. The frequency of ultrasound findings compatible with unilateral cystic disease was 10.6% of cases. The ultrasound finding of bilateral renal cystic disease was approximately 8.8 times lower (1.2%). The combination of bilateral hydronephrosis findings with megaureter and megabladder was seen in 29 patients (3.5%).

Description of the ultrasonographic findings	n	%*
Unilateral hydronephrosis	389	47.3
Isolated unilateral hydronephrosis	351	42.6
Bilateral hydronephrosis	319	38.8
Isolated bilateral hydronephrosis	263	32.0
Unilateral megaureter	37	4.5
Bilateral megaureter	43	5.2
Megabladder	41	5.0
Unilateral renal cystic disease	87	10.6
Bilateral renal cystic disease	10	1.2
Oligohydramnios	13	1.6
Unilateral hydronephrosis with megaureter	35	4.2
Bilateral hydronephrosis with megaureter	14	1.7
Bilateral hydronephrosis with megaureter and megabladder	29	3.5
Bilateral hydronephrosis with megabladder and oligohydramnios	9	1.1
Unilateral renal hypoplasia	6	0.7
Bilateral renal hypoplasia	1	0.1
Unilateral renal agenesis	3	0.3
Unilateral pelvic kidney	1	0.1
Unilateral hydronephrosis with oligohydramnios	1	0.1
Bilateral hydronephrosis with oligohydramnios	3	0.3
Unilateral hydronephrosis with megabladder	2	0.2
Bilateral hydronephrosis with megabladder	1	0.1
Isolated unilateral megaureter	2	0.2
*Percentage in relation to the total number of records in relation to the total number of records		

**Table 1:** Frequencies of sonographic findings detected at the last antenatal ultrasound examination in patients with congenital anomalies of the kidney and urinary tract.

To determine which of the sonographic findings would be associated with the unfavorable clinical outcomes in patients with CAKUT, an observed frequency of at least 1% was considered as the cutoff point. Thus, as shown in Table 1, the correlated ultrasound findings were: unilateral hydronephrosis, isolated unilateral hydronephrosis, bilateral hydronephrosis, isolated bilateral hydronephrosis, uni and bilateral megaureter, megabladder, uni and bilateral cystic disease, oligohydramnios, unilateral hydronephrosis with megaureter, bilateral hydronephrosis with megaureter, bilateral hydronephrosis with megaureter and megabladder, bilateral hydronephrosis with megaureter and oligohydramnios. The postnatal unfavorable clinical outcomes of interest were Urinary Tract Infection (UTI), surgical interventions, hypertension, Chronic Kidney Disease (CKD), and death.

Patients with CAKUT were systematically investigated for the occurrence of UTI. Urine samples from all newborns were

obtained for urinalysis and urine culture after the first day of life. Urine tests were repeated at every visit or whenever there was clinical suspicion. The exams were collected and run at the Central Laboratory of HC-UFG, using standardized techniques. The presence of 5 or more leukocytes per field under the microscope at 400X magnification was defined as pyuria. Urine culture was considered positive when it identified a single microorganism, with a Colony Forming Unit (CFU) count greater than 100,000 per ml of urine.

According to the clinical protocol, many of the patients with CAKUT used chemoprophylaxis for UTI with first-generation cephalosporin. These patients were also systematically screened for the occurrence of UTI. For the analysis, the occurrence of UTI was divided into two outcomes. The first outcome was the occurrence of UTI. The second outcome was the occurrence of UTI even while undergoing chemoprophylaxis for UTI.

The National High Blood Pressure Education Program Working Group, in 2014, classified hypertension in children and adolescents according to the normal distribution in healthy children and adolescents, using percentiles adjusted for gender, age, and height. Blood pressure is considered normal when both systolic and diastolic pressure are below the 90th percentile. Prehypertension is defined as systolic and/or diastolic pressure greater than or equal to the 90th percentile, but lower than the 95<sup>th</sup> percentile, or when the pressure exceeds 120 x 80 mmHg. Hypertension is characterized by systolic and/or diastolic pressure greater than or equal to the 95th percentile measured on at least three different occasions.

Stage 2 hypertension in children is defined as systolic and/or diastolic blood pressure greater than or equal to the 99th percentile plus 5 mmHg. Lower values are classified as stage 1. For the analysis, patients were classified according to the occurrence or the absence of hypertension during clinical follow-up.

Patients who required surgical intervention were monitored in parallel by the Pediatric Surgery team. Data referring to the surgical treatment were duly recorded in the UNP clinical record. For the analysis, the need for surgical treatment during clinical follow-up was considered.

Newborns with suspected renal function impairment, as in cases of posterior urethral valve, had serum urea and creatinine levels checked right after birth. The other patients with CAKUT underwent blood collection for urea and creatinine levels after 72 hours of life. Subsequently, patients were periodically submitted to investigation of renal function, through serum creatinine and urea. Glomerular function was calculated from the formula by Schwartz et al, which estimates the glomerular filtration rate in neonates, children and adolescents based on plasma creatinine concentration [11]. Patients with chronic kidney disease were classified according to the National Kidney Foundation Kidney Disease Outcome Quality Initiative (NKF-K/DOQI). Stage 1 corresponds to the presence of renal damage with normal or even increased Glomerular Filtration Rate (GFR). Stage 2 is characterized by renal damage with a slight decrease in GFR. Stages 3 and 4 are characterized by moderate and severe decrease in GFR, respectively. Patients with end-stage kidney disease are classified as stage 5.

The NKF-K/DOQI classification does not apply to children younger than 2 years of age, as the GFR varies according to age group in these children [12,13]. Currently, CKD is also defined by the presence of kidney damage, characterized by structural or functional alterations of the kidney with or without alterations in the GFR, for a period longer than three months or by a GFR of less than 60 ml/min/1.73 m<sup>2</sup> that persists for more than three months, regardless of the presence of kidney damage.

For the analysis, the occurrence of chronic kidney disease was broken down into two outcomes: The first outcome was the occurrence of non-terminal chronic kidney disease, that is, kidney disease chronic in stages 1 to 4. The second outcome was the occurrence of end-stage kidney disease, that is, in stage 5. Cases that evolved to death due to CAKUT complications were duly registered in the database.

All categorical variables were evaluated according to their absolute and relative frequencies (in percentage). For categorical variables, the exact Pearson's chi-square test was used when 100% of the cells had an expected value above 5. When 20% of the cells in the contingency table had an expected value between 1 and 5, Fisher exact test was used.

As this is a retrospective study, the calculation of Odds Ratio (odds ratio) was used to determine the prognostic values of the sonographic findings in relation to the unfavorable outcomes of interest studied. The significance level used was 0.05 with a confidence level of 95%. For statistical analysis, the SPSS program (Statistical Package for Social Sciences) version 20.0 was used.

## Results

Table 2 shows the frequency of unfavorable clinical outcomes studied. We observed that the occurrence of UTI was the most frequent clinical outcome, occurring in 30% of cases. The occurrence of UTI in patients on chemoprophylaxis was also analyzed, occurring in 11.7% of cases. It is noteworthy that 231 patients (28.1%) required surgical intervention. Hypertension was detected in 2.7% of patients during clinical follow-up. Chronic kidney disease, stages 1 to 4, occurred in 6% of the patients, whereas 2.8% of patients developed end-stage kidney disease. During follow-up, 12 patients (1.5%) died.

Unfavorable Outcomes	N	(%)
Surgery	231	28.1
Hypertension	22	2.7
Urinary tract infection (UTI)	247	30.0
Urinary tract infection (UTI) on chemoprophylaxis	96	11.7
Death	12	1.5
Chronic Kidney Disease (CKD): stages 1 to 4	49	6.0
End-stage Kidney Disease: stage 5	23	2.8

**Table 2:** Isolated frequencies of unfavorable outcomes observed in patients with congenital anomalies of the kidney and urinary tract in the postnatal follow-up, childhood and adolescence.

The patients were followed at the UNP during the postnatal, childhood and adolescence periods. The mean follow-up time was 58.7 months, with the maximum follow-up time being 257 months (median 39; mean 58.7; standard deviation 57.8). In the group of

patients who required surgical treatment, the mean follow-up time until the first intervention was 12.7 months (median 7; mean 12.7; standard deviation 20.1), with the maximum time being 121 months. The mean follow-up until the occurrence of UTI was 15.1 months (median 7; mean 15.1; standard deviation 23.32). In the group of patients who developed hypertension, the mean follow-up time was 108.6 months (median 91; mean 108.6; standard deviation 80), with a maximum time of 243 months. The mean follow-up time for patients who developed chronic kidney disease was 69.9 months (median 23; mean 69.9; standard deviation 88.42), with the maximum follow-up time equal to 257 months. The mean follow-up time for patients who died was 4 months (median 0.50; mean 0.92; standard deviation 1.24).

Tables 3 to 16 show the prognostic value of each of the nephrourological ultrasonographic findings with the unfavorable clinical outcomes studied.

Table 3 shows an association between the ultrasonographic finding of unilateral hydronephrosis (isolated or associated) with the occurrence of UTI in patients on chemoprophylaxis, death, occurrence of chronic kidney disease (stages 1 to 4) and end-stage kidney disease.

Outcomes	n	Odds Ratio	Confidence interval (95%)	p-value	
Surgery	116	1.179	0.869 – 1.598	0.290	*
Hypertension	9	0.767	0.324 – 1.815	0.545	*
Urinary tract infection (UTI)	117	1.006	0.746 – 1.356	0.969	*
UTI on chemoprophylaxis	34	0.575	0.369 – 0.895	0.013	**
Death	0	0.972	0.957 – 0.988	0.001	*
Chronic Kidney Disease (stages 1 to 4)	7	0.171	0.076 – 0.385	<0.001	*
End-stage Kidney Disease: stage 5	2	0.102	0.024 – 0.436	<0.001	**

\*Person Chi-Square; \*\*Fisher's Exact Test

**Table 3:** Prognostic values of the ultrasonographic finding of unilateral hydronephrosis (isolated or associated) in fetuses with congenital anomalies of the kidney and urinary tract with unfavorable outcomes observed in the postnatal follow-up, childhood and adolescence.

Table 4 describes the prognostic values of the ultrasonographic finding isolated unilateral hydronephrosis with the evaluated outcomes. We observed an association between this ultrasonographic finding with the occurrence of UTI in patients on chemoprophylaxis, death, development of chronic kidney disease (stages 1 to 4) and end-stage kidney disease in patients with CAKUT.

Outcomes	N	Odds Ratio	Confidence Interval (95%)	p-value	
Surgery	101	1.063	0.782 – 1.445	0.697	*
Hypertension	6	0.496	0.192 – 1.280	0.139	*
Urinary tract infection (UTI)	97	0.820	0.605 – 1.111	0.199	*
UTI on chemoprophylaxis	25	0.433	0.268 – 0.699	<0.001	*
Death	0	0.975	0.960 – 0.989	0.002	**
Chronic Kidney Disease (stages 1 to 4)	5	0.141	0.055 – 0.358	<0.001	*
End-stage Kidney Disease: stage 5	2	0.123	0.029 – 0.528	<0.001	**

\*Person Chi-Square; \*\*Fisher's Exact Test

**Table 4:** Prognostic values of the ultrasonographic finding of isolated unilateral hydronephrosis in fetuses with congenital anomalies of the kidney and urinary tract with unfavorable outcomes observed in the postnatal follow-up, childhood and adolescence.

The prognostic values of the sonographic finding of isolated or associated bilateral hydronephrosis with the unfavorable clinical outcomes of the study are shown in Table 5. Se observed an association between these finding with UTI in patients on chemoprophylaxis, death, development of CKD (stages 1 to 4) and End-Stage Kidney Disease (ESKD) in patients with CAKUT.

Outcomes	N	OddsRatio	Confidence Interval(95%)	p-value	
Surgery	99	1.268	0.931 – 1.728	0.132	*
Hypertension	10	1.327	0.566 – 3.108	0.514	*
Urinary tract infection (UTI)	100	1.109	0.818 – 1.504	0.506	*
UTI on chemoprophylaxis	48	1.683	1.097 – 2.580	0.016	*
Death	9	4.848	1.303 – 18.046	0.014	**
Chronic Kidney Disease (stages 1 to 4)	35	4.313	2.282 – 8.154	<0.001	*
End-stage Kidney Disease: stage 5	17	4.672	1.822 – 11.980	<0.001	*

\*Person Chi-Square; \*\*Fisher’s Exact Test

**Table 5:** Prognostic values of the ultrasonographic finding of bilateral hydronephrosis (isolated or associated) in fetuses with congenital anomalies of the kidney and urinary tract with the unfavorable outcomes observed in the postnatal follow-up, childhood and adolescence.

Table 6 shows the prognostic value of the ultrasonographic finding of isolated bilateral hydronephrosis with the unfavorable outcomes studied. We observed an association between this ultrasonographic finding with the need for surgical intervention and development of end-stage kidney disease in patients with CAKUT.

Outcomes	N	OddsRatio	Confidence Interval (95%)	p-value	
Surgery	61	0.693	0.494 – 0.972	0.033	*
Hypertension	4	0.465	0.156 – 1.388	0.245	**
Urinary tract infection (UTI)	67	0.722	0.519 – 1.003	0.052	*
UTI on chemoprophylaxis	30	0.964	0.609 – 1.525	0.875	*
Death	2	0.421	0.092 – 1.937	0.356	**
Chronic Kidney Disease (stages 1 to 4)	12	0.676	0.346 – 1.318	0.248	*
End-stage Kidney Disease: stage 5	1	0.093	0.013 – 0.696	0.002	*

\*Person Chi-Square; \*\*Fisher’s Exact Test

**Table 6:** Prognostic values of the ultrasonographic finding of isolated bilateral hydronephrosis in fetuses with congenital anomalies of the kidney and urinary tract with the unfavorable outcomes observed in the postnatal follow-up, childhood and adolescence.

Table 7 shows an association between the ultrasonographic finding of unilateral megaureter with UTI in patients with CAKUT.

Outcomes	N	OddsRatio	Confidence Interval(95%)	p-value	
Surgery	15	1.799	0.916 – 3.533	0.084	*
Hypertension	2	2.189	0.492 – 9.735	0.260	**
Urinary tract infection (UTI)	20	2.897	1.490 – 5.632	0.001	*
UTI on chemoprophylaxis	8	2.188	0.970 – 4.936	0.054	*

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Death	0	0.985	0.976 – 0.993	1.000	**
Chronic Kidney Disease (stages 1 to 4)	1	0.427	0.057 – 3.182	0.719	**
End-stage Kidney Disease: stage 5	0	0.971	0.959 – 0.983	0.619	**

\*Person Chi-Square; \*\*Fisher’s Exact Test

**Table 7:** Prognostic values of the ultrasound finding of unilateral mega ureter in fetuses with congenital anomalies of the kidney and urinary tract with the unfavorable outcomes observed in the postnatal follow-up, childhood and adolescence.

Table 8 shows the prognostic values of ultrasound finding the bilateral megaureter. It is noteworthy that we observed an association between this sonographic finding with all outcomes studied in patients with CAKUT.

Outcomes	N	OddsRatio	Confidence Interval (95%)	p-value	
Surgery	29	5.927	3.071 – 11.441	<0.001	*
Hypertension	6	7.743	2.864 – 20.935	<0.001	*
Urinary tract infection (UTI)	25	3.491	1.868 – 6.525	<0.001	*
UTI on chemoprophylaxis	13	3.639	1.826 – 7.251	<0.001	*
Death	5	14.530	4.407 – 47.903	<0.001	*
Chronic Kidney Disease (stages 1 to 4)	15	11.754	5.749 – 24.031	<0.001	*
End-stage Kidney Disease: stage 5	10	17.879	7.305 – 43.756	<0.001	*

\*Person Chi-Square; \*\*Fisher’s Exact Test

**Table 8:** Prognostic values of the ultrasonographic finding of bilateral mega ureter in fetuses with congenital anomalies of the kidney and urinary tract with the unfavorable outcomes observed in the postnatal follow-up, childhood and adolescence.

Table 9 shows the prognostic values of the ultrasound finding of megabladder. We observed an association between this sonographic finding and all clinical outcomes studied in patients with CAKUT.

Outcomes	N	Odds Ratio	Confidence Interval (95%)	p-value	
Surgery	30	7.883	3.879 – 16.022	<0.001	*
Hypertension	7	10.527	4.028 – 27.513	<0.001	*
Urinary tract infection (UTI)	25	3.941	2.065 – 7.523	<0.001	*
UTI on chemoprophylaxis	14	4.426	2.232 – 8.779	<0.001	*
Death	5	15.377	4.653 – 50.814	<0.001	*
Chronic Kidney Disease (stages 1 to 4)	20	24.729	12.086 – 50.598	<0.001	*
End-stage Kidney Disease: stage 5	13	35.843	14.478 – 88.738	<0.001	*

\*Person Chi-Square; \*\*Fisher’s Exact Test

**Table 9:** Prognostic values of the ultrasonographic finding of megabladder in fetuses with congenital anomalies of the kidney and urinary tract with the unfavorable outcomes observed in the postnatal follow-up, childhood and adolescence.

Table 10 shows was an association between the ultrasonographic findings compatible with unilateral cystic kidney disease and the need for surgical intervention in patients with CAKUT.

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Outcomes	N	Odds Ratio	Confidence Interval (95%)	p-value	
Surgery	11	0.339	0.177 – 0.651	0.001	*
Hypertension	2	0.842	0.194 – 3.667	1.000	**
Urinary tract infection (UTI)	20	0.669	0.397 – 1.130	0.131	*
UTI on chemoprophylaxis	8	0.746	0.349 – 1.595	0.448	*
Death	1	0.766	0.098 – 6.009	1.000	**
Chronic Kidney Disease (stages 1 to 4)	3	0.536	0.163 – 1.760	0.469	**
End-stage Kidney Disease: stage 5	1	0.377	0.050 – 2.835	0.499	**

\*Person Chi-Square; \*\*Fisher’s Exact Test

**Table 10:** Prognostic values of the ultrasonographic findings of unilateral cystic renal disease in fetuses with congenital anomalies of the kidney and urinary tract with unfavorable outcomes observed in postnatal, childhood and adolescence follow-up.

Table 11 shows that the sonographic findings compatible with bilateral cystic renal disease were not associated with any of the outcomes in patients with CAKUT in our study.

Outcomes	N	Odds Ratio	Confidence Interval (95%)	p-value	
Surgery	2	0.638	0.134 – 3.025	0.734	**
Hypertension	1	4.190	0.508 – 34.597	0.239	**
Urinary tract infection (UTI)	4	1.564	0.437 – 5.591	0.498	**
UTI on chemoprophylaxis	3	3.318	0.843 – 13.053	0.100	**
Death	1	8.101	0.944 – 69.543	0.137	**
Chronic Kidney Disease (stages 1 to 4)	2	4.074	0.842 – 19.727	0.115	**
End-stage Kidney Disease: stage 5	1	3.995	0.485 – 32.917	0.248	**

\*Person Chi-Square; \*\*Fisher’s Exact Test

**Table 11:** Prognostic values of the ultrasonographic findings of bilateral cystic renal disease in fetuses with congenital anomalies of the kidney and urinary tract with unfavorable outcomes observed in postnatal, childhood and adolescence follow-up.

Table 12 shows the prognostic value of the ultrasonographic finding of oligohydramnios with the outcomes in our study. We observed an association between this sonographic finding and the need for surgical treatment, UTI in patients on chemoprophylaxis, death, occurrence of CKD (stages 1 to 4) and end-stage kidney disease in patients with CAKUT.

Outcomes	N	Odds Ratio	Confidence Interval (95%)	p-value	
Surgery	9	5.959	1.817 – 19.548	0.002	*
Hypertension	0	0.973	0.962 – 0.984	1.000	**
Urinary tract infection (UTI)	7	2.771	0.922 – 8.331	0.059	*
UTI on chemoprophylaxis	5	4.938	1.582 – 15.416	0.002	*
Death	2	14.545	2.848 – 74.284	0.014	**

**Citation:** Krettli WSC, Leite HV, Cabral ACV, Reis ZSN, Quirino ILG, et al. (2023) Longitudinal Study of the Association between Antenatal Nephrourological Ultrasonographic Findings with Unfavorable Clinical Outcomes during Postnatal Period, Childhood and Adolescence, in Patients with Congenital Anomalies of the Kidney and Urinary Tract (CAKUT). *J Community Med Public Health* 7: 334. DOI: <https://doi.org/10.29011/2577-2228.100334>

Chronic Kidney Disease (stages 1 to 4)	8	30.010	9.401 –95.794	<0.001	*
End-stage Kidney Disease: stage 5	6	39.983	12.145 – 131.634	<0.001	*

\*Person Chi-Square; \*\*Fisher’s Exact Test

**Table 12:** Prognostic values of the ultrasonographic finding of oligohydramnios in fetuses with congenital anomalies of the kidney and urinary tract with the unfavorable outcomes observed in the postnatal follow-up, childhood and adolescence.

Table 13 shows an association between the ultrasonographic finding of unilateral hydronephrosis with megaureter in patients with CAKUT with the outcomes UTI and UTI in patients on chemoprophylaxis.

Outcomes	N	OddsRatio	Confidence Interval (95%)	p-value	
Surgery	14	1,754	0.876 –3.512		*
Hypertension	2	2,327	0.522 – 10.375	0.239	**
Urinary tract infection (UTI)	19	2,917	1.474 –5.772	0.001	*
UTI on chemoprophylaxis	8	2,357	1.039 –5.349	0.035	*
Death	0	0,985	0.976 –0.993	1.000	**
Chronic Kidney Disease (stages 1 to 4)	1	0,453	0.061 –3.384	0.716	**
End-stage Kidney Disease: stage 5	0	0,971	0.959 –0.983	0.619	**

\*Person Chi-Square; \*\*Fisher’s Exact Test

**Table 13:** Prognostic values of the ultrasonographic finding of unilateral hydronephrosis with megaureter in fetuses with congenital anomalies of the kidney and urinary tract with the unfavorable outcomes observed in the postnatal follow-up, childhood and adolescence.

Table 14 shows an association between the ultrasonographic finding of bilateral hydronephrosis with megaureter in patients with CAKUT with the occurrence of death and development of CKD (stages 1 to 4) and end-stage kidney disease in patients with CAKUT.

Outcomes	n	OddsRatio	Confidence Interval (95%)	p-value	
Surgery	6	1.947	0.668 –5.673	0.214	*
Hypertension	0	0.973	0.962 –0.984	1.000	**
Urinary tract infection (UTI)	7	2.371	0.823 –6.833	0.100	*
UTI on chemoprophylaxis	3	2.100	0.575 –7.664	0.218	**
Death	2	13.317	2.631 – 67.403	0.016	**
Chronic Kidney Disease (stages 1 to 4)	4	6.791	2.050 – 22.499	0.007	**
End-stage Kidney Disease: stage 5	3	10.759	2.785 – 41.566	0.006	**

\*Person Chi-Square; \*\*Fisher’s Exact Test

**Table 14:** Prognostic values of the ultrasonographic findings of bilateral hydronephrosis with megaureter in fetuses with congenital anomalies of the kidney and urinary tract with the unfavorable outcomes observed in the postnatal follow-up, childhood and adolescence.

Table 15 shows an association between the ultrasonographic finding of bilateral hydronephrosis with megaureter and megabladder in patients with CAKUT with all unfavorable clinical outcomes of our study.

**Citation:** Krettli WSC, Leite HV, Cabral ACV, Reis ZSN, Quirino ILG, et al. (2023) Longitudinal Study of the Association between Antenatal Nephrourological Ultrasonographic Findings with Unfavorable Clinical Outcomes during Postnatal Period, Childhood and Adolescence, in Patients with Congenital Anomalies of the Kidney and Urinary Tract (CAKUT). J Community Med Public Health 7: 334. DOI: <https://doi.org/10.29011/2577-2228.100334>

Outcomes	n	Odds Ratio	Confidence Interval (95%)	p-value	
Surgery	23	10.800	4.337 – 26.892	<0.001	*
Hypertension	6	12.685	4.548 – 35.382	<0.001	*
Urinary tract infection (UTI)	18	4.037	1.877 – 8.682	<0.001	*
UTI on chemoprophylaxis	10	4.333	1.951 – 9.622	<0.001	*
Death	3	10.064	2.573 – 39.361	0.007	**
Chronic Kidney Disease (stages 1 to 4)	11	12.158	5.366 – 27.544	<0.001	*
End-stage Kidney Disease: stage 5	7	15.472	5.783 – 41.392	<0.001	*

\*Person Chi-Square; \*\*Fisher's Exact Test

**Table 15:** Prognostic values of the ultrasonographic finding of bilateral hydronephrosis with megaureter and megabladder in fetuses with congenital anomalies of the kidney and urinary tract with the unfavorable outcomes observed in the postnatal follow-up, childhood and adolescence.

Table 16 shows the prognostic values of the sonographic findings of bilateral hydronephrosis with megabladder and oligohydramnios in patients with CAKUT with the unfavorable clinical outcomes studied. We observed an association between these ultrasonographic findings with the need for surgical intervention, death, development of CKD (stages 1 to 4) and end-stage kidney disease in patients with CAKUT.

Outcomes	n	OddsRatio	Confidence Interval(95%)	p-value	
Surgery	6	5.236	1.298 – 21.112	0.018	**
Hypertension	0	0.973	0.962 – 0.984	1.000	**
Urinary tract infection (UTI)	5	2.955	0.787 – 11.097	0.137	**
UTI on chemoprophylaxis	3	3.876	0.953 – 15.761	0.077	**
Death	2	22.971	4.236 – 124.579	0.007	**
Chronic Kidney Disease (stages 1 to 4)	8	150.829	18.425 – 1234.721	<0.001	**
End-stage Kidney Disease: stage 5	6	93.765	21.628 – 406.504	<0.001	**

\*Person Chi-Square; \*\*Fisher's Exact Test

**Table 16:** Prognostic values of the ultrasonographic findings of bilateral hydronephrosis with megabladder and oligohydramnios in fetuses with congenital anomalies of the kidney and urinary tract with the unfavorable outcomes observed in the postnatal follow-up, childhood and adolescence.

Table 17 presents a summary of the prognostic values of the sonographic findings that showed statistically significant relationship with the clinical outcomes of our study (presented in tables 03 to 16).

**Citation:** Krettli WSC, Leite HV, Cabral ACV, Reis ZSN, Quirino ILG, et al. (2023) Longitudinal Study of the Association between Antenatal Nephrourological Ultrasonographic Findings with Unfavorable Clinical Outcomes during Postnatal Period, Childhood and Adolescence, in Patients with Congenital Anomalies of the Kidney and Urinary Tract (CAKUT). J Community Med Public Health 7: 334. DOI: <https://doi.org/10.29011/2577-2228.100334>

Risk factor	Outcomes	n	OR	↑Chance	Reduction	p-value
	UTI on chemoprophylaxis	34	0.575	-	42.5 %	0.013
Unilateral hydronephrosis	Death	0	0.972	-	2.8 %	0.001
	Chronic Kidney Disease	7	0.171	-	82.9 %	<0.001
	End-stage Kidney Disease	2	0.102	-	89.8 %	<0.001
	UTI on chemoprophylaxis	25	0.433	-	57.0 %	<0.001
Isolated unilateral hydronephrosis	Death	0	0.975	-	2.5 %	0.002
	Chronic Kidney Disease	5	0.141	-	85.9 %	<0.001
	End-stage Kidney Disease	2	0.123	-	87.7 %	<0.001
	UTI on chemoprophylaxis	48	1.683	1.7 x	-	0,016
Bilateral hydronephrosis	Death	9	4.848	4.8 x	-	0,014
	Chronic Kidney Disease	35	4.313	4.3 x	-	<0,001
	End-stage Kidney Disease	17	4.672	4.7 x	-	<0,001
Isolated Bilateral Hydronephrosis	Surgery	61	0.693	-	30.7 %	0.033
	End-stage Kidney Disease	1	0.093	-	90.7 %	0.002
Unilateral Megaureter	UTI	20	2.897	2.9 x	-	0.001
	Surgery	29	5.927	5.9 x	-	<0.001
	Hypertension	6	7.743	7.7 x	-	<0.001
	UTI	25	3.491	3.5 x	-	<0.001
Bilateral Megaureter	UTI on chemoprophylaxis	13	3.639	3.6 x	-	<0.001
	Death	5	14.530	14.5x	-	<0.001
	Chronic Kidney Disease	15	11.754	11.8 x	-	<0.001
	End-stage Kidney Disease	10	17.879	17.9 x	-	<0.001
	Surgery	30	7.883	7.9 x	-	<0.001
	Hypertension	7	10.527	10.6 x	-	<0.001
	UTI	25	3.941	3.9 x	-	<0.001
Megabladder	UTI on chemoprophylaxis	14	4.426	4.4 x	-	<0.001
	Death	5	15.377	15.4 x	-	<0.001

	Chronic Kidney Disease	20	24.729	24.7 x	-	<0.001
	End-stage Kidney Disease	13	35.843	35.8 x	-	<0.001
Unilateral Renal Cystic Disease	Surgery	11	0.339	-	66.1 %	0.001
	Surgery	9	5.959	6.0 x	-	0.002
	UTI on chemoprophylaxis	5	4.938	4.9 x	-	0.002
Oligohydramnios	Death	2	14.545	14.5 x	-	0.014
	Chronic Kidney Disease	8	30.010	30.0 x	-	<0.001
	End-stage Kidney Disease	6	39.983	40.0 x	-	<0.001
Unilateral hydronephrosis with megaureter	UTI	19	2.917	2.9 x	-	0.001
	UTI on chemoprophylaxis	8	2.357	2.4 x	-	0.035
Bilateral hydronephrosis with megaureter	Death	2	13.317	13.3 x	-	0.016
	Chronic Kidney Disease	4	6.791	6.8 x	-	0.007
	End-stage Kidney Disease	3	10.759	10.8 x	-	0.006
	Surgery	23	10.800	10.8 x	-	<0.001
	Hypertension	6	12.685	12.7 x	-	<0.001
Bilateral hydronephrosis with megaureter and megabladder	UTI	18	4.037	4.0 x	-	<0.001
	UTI on chemoprophylaxis	10	4.333	4.3 x	-	<0.001
	Death	3	10.064	10.1 x	-	0.007
	Chronic Kidney Disease	11	12.158	12.2 x	-	<0.001
	End-stage Kidney Disease	7	15.472	15.5 x	-	<0.001
Bilateral hydronephrosis with megabladder and oligohydramnios	Surgery	6	5.236	5.2 x	-	0.018
	Death	2	22.971	23.0 x	-	0.007
	Chronic Kidney Disease	8	150.829	150.8 x	-	<0.001
	End-stage Kidney Disease	6	93.765	93.8 x	-	<0.001

**Table 17:** Summary table of significant prognostic values among the ultrasonographic findings of fetuses with congenital anomalies of the kidney and urinary tract with the unfavorable outcomes observed in the postnatal follow-up, childhood and adolescence.

## Discussion

Congenital anomalies of the kidneys and urinary tract (CAKUT) comprise a wide spectrum of structural and functional malformations that can occur in the kidneys, collecting system, bladder or urethra (Song and Yosypiv, 2011).

Our main objective was to study the association between antenatal nephrourological ultrasonographic findings with the prognostic of patients with CAKUT in the postnatal follow-up, childhood and adolescence. Indeed, much attention has been given to studying the postnatal clinical course of individuals with CAKUT [14]. However, in literature there is still a lack of studies

that associate the antenatal ultrasound findings of CAKUT with the chance of the occurrence of certain clinical complications in these individuals.

Thus, our initial objective was to determine the frequency of the different ultrasonographic findings of CAKUT in the studied patients. As the alterations can be unilateral or bilateral, it is important to determine the laterality of the findings. Several patients had a single isolated ultrasound finding, but different alterations could coexist in the same individual. Therefore, the determination of the frequency of a given ultrasound finding varied according to the presence of that same finding in other combinations. Among

CAKUT, the sonographic finding of hydronephrosis corresponds to 50% of cases in most series (Reddy and Mandell, 1998). In our study, the echographic finding of isolated unilateral hydronephrosis occurred in 42.6% of the cases, while the echographic finding of unilateral hydronephrosis affected 47.3% of the patients. The finding of isolated bilateral hydronephrosis occurred in 32% of the cases, while the presence of bilateral hydronephrosis was found in 38.8% of the cases. In our study, the ultrasound findings compatible with cystic kidney disease occurred in 11.8% of the fetuses, being unilateral in most cases. The ultrasonographic finding of isolated unilateral megaureter occurred in only 0.2% of patients. However, the ultrasonographic finding of unilateral megaureter occurred in 4.5% of the cases, which can be explained by the presence of the unilateral megaureter finding in a significant number of patients who presented this finding in combination with other alterations. No patients had isolated bilateral megaureter, whereas the presence of bilateral megaureter occurred in 5.2% of the cases, which can be explained by the presence of the bilateral megaureter finding in a significant number of patients, who presented this finding in combination with other alterations.

The great variety of combinations of ultrasound findings detected in our patients was noteworthy: the combination of ultrasonographic findings of unilateral hydronephrosis with megaureter occurred in 4.2% of the cases; the presence of bilateral hydronephrosis with megaureter affected 1.7% of patients; the classic combination of bilateral hydronephrosis with megaureter and megabladder affected 3.5 of the patients; the presence of bilateral hydronephrosis with megaureter and oligohydramnios affected only 1.1% of the cases.

The frequency of oligohydramnios was small in our study, affecting 1.6% of the cases, which can be explained by the fact our database did not include patients with oligohydramnios and pulmonary hypoplasia that died in the neonatal period. Another explanation lies in the definition of oligohydramnios used in our study, which included only severe oligohydramnios.

In order to determine which nephrourological ultrasonographic findings would be correlated with unfavorable clinical outcomes in patients with CAKUT, an observed frequency of at least 1% was considered as the cutoff point. However, less frequent ultrasound findings included unilateral and bilateral renal hypoplasia; unilateral renal agenesis; unilateral pelvic kidney; unilateral hydronephrosis with oligohydramnios; bilateral hydronephrosis with oligohydramnios; unilateral hydronephrosis with megabladder, bilateral hydronephrosis with megabladder and isolated unilateral megaureter. No cases of bilateral renal agenesis were detected in our study, which was explained by the death of these patients in the neonatal period.

The occurrence of urinary infections in patients with

CAKUT may be accompanied by major complications, such as pyelonephritis or sepsis, especially in certain age groups [15]. Renal fibrosis may result from infectious processes [16]. Our study confirms the findings of the literature, which shows that special attention should be given to the occurrence of UTI episodes in patients with CAKUT. It is observed that the occurrence of UTI was the most common clinical outcome observed in our study, occurring in 30% of cases. UTI occurred in 11.7% of the patients on chemoprophylaxis. The frequency of UTI in our patients, throughout the clinical follow-up, demonstrates the importance of chemoprophylaxis, if necessary. Patients should also be instructed to inform about the signs and symptoms of UTI and seek urgent care if they have symptoms.

Our study did not intend to analyze the course of surgical treatment in cases in which this type of treatment was indicated. Our interest was only to determine the frequency of the need for surgical intervention in our patients, throughout the clinical follow-up. It is noteworthy that 231 of the 823 patients (28.1%) required surgical intervention.

Kidney diseases are the main cause of hypertension in children, occurring in approximately 68% of cases. Endocrinological and renovascular diseases account for 11% and 10% of cases, respectively [17].

Several diseases of the renal parenchyma can predispose to the development of hypertension. In glomerulonephritis, the mechanisms involved in the development of hypertension are volume expansion and activation of the renin-angiotensin system [18]. Fibrosis of the renal parenchyma may occur as a sequela of pyelonephritis or be associated with vesicoureteral reflux. Children with CAKUT may develop renal fibrosis and subsequent hypertension [19]. In our study, arterial hypertension was detected in 2.7% of patients with CAKUT during follow-up.

CAKUT are responsible for 30 to 50% of cases of chronic kidney disease in children and adolescents, and early treatment can minimize kidney damage. They may also correspond to 30 to 50% of cases of end-stage chronic kidney disease. Thus, it is essential that the diagnosis be made as soon as possible, so that adequate follow-up and treatment are promptly instituted [20].

In the present study, chronic kidney disease, stages 1 to 4, occurred in 49 out of 823 patients (6%), while 2.8% of individuals (23 out of 823 cases) evolved with end-stage kidney disease. During follow-up, 12 patients (1.5% of cases) died.

One of the limitations of the study is the absence of a control group. Therefore, the prognostic values must be interpreted taking into account the universe of fetuses with CAKUT. Thus, in the present study, patients with an antenatal ultrasonographic finding of unilateral hydronephrosis showed a 42.5% reduction

in the chance of UTI occurring during chemoprophylaxis, a 2.8% reduction in the chance of death, an 82.9% reduction in chance of developing chronic kidney disease (stages 1 to 4) and also an 89.8% reduction in the chance of developing end-stage chronic kidney disease, when compared to other CAKUT patients with other ultrasound findings.

The presence of isolated unilateral hydronephrosis on antenatal US indicates a 57% reduction in the chance of UTI occurring during chemoprophylaxis, a 2.5% reduction in the chance of death, an 85.9% reduction in the chance of chronic kidney disease (stage 1 to 4), as well as an 87.7% reduction in the chance of developing end-stage chronic kidney disease.

The prognostic values of the antenatal echographic finding of unilateral hydronephrosis, isolated or not, show that compared to the other possible echographic findings in patients with CAKUT, this sonographic finding indicates a lower chance of occurrence of the aforementioned complications.

The analysis of the prognostic values of the antenatal ultrasound finding of isolated bilateral hydronephrosis shows a 30.7% reduction in need for surgical intervention and a 90.7% reduction in the chance of the occurrence of end-stage chronic kidney disease.

However, the prognostic values of the antenatal ultrasound finding of bilateral hydronephrosis indicate a 1.7-fold increase in the chance of UTI among patients with CAKUT who were on chemoprophylaxis. We also observed a 4.8-fold increase in the chance of death, a 4.3-fold increase in the chance of chronic kidney disease (stages 1 to 4) and a 4.7-fold increase in the chance of developing end-stage chronic kidney disease.

The importance of determining the prognosis of the antenatal ultrasound finding hydronephrosis, unilateral or bilateral, isolated or not, in relation to unfavorable clinical outcomes, should be emphasized, since hydronephrosis corresponds to the most common sonographic finding detected in prenatal ultrasound in patients with CAKUT.

Discussing the importance of the ultrasonographic finding of megaureter is a difficult task for the sonographer or the obstetrician. The megaureter corresponds to the second main cause of hydronephrosis in neonates, preceded by obstruction of the ureteropelvic junction. Megaureter classification depends, however, on postnatal investigation, which allows checking for reflux and/or obstruction. In this context, any information about the prognostic value of this antenatal ultrasound finding can be of great value to the obstetrician and to the neonatologist's initial approach.

In our study, patients with an antenatal ultrasound finding of unilateral megaureter had a 2.9-fold increase in the chance of a

single outcome: UTI.

On the other hand, the prognostic value of the bilateral antenatal ultrasound finding megaureter indicates an increase in the chance of occurrence of all clinical outcomes. We observe an increase of: 5.9 times in the need for surgery; 7.7 times in the chance of developing hypertension; 3.5 times in the chance of UTI; 3.6 times the chance of UTI on chemoprophylaxis; 14.5 times in the chance of death; 11.8 times in the chance of developing chronic kidney disease (stages 1 to 4) and 17.9 times in the chance of developing end-stage chronic kidney disease.

The megabladder antenatal ultrasound finding indicates: a 7.9-fold increase in the chance of surgery; a 10.6-fold increase in the occurrence of hypertension; a 3.9-fold increase in the chance of having UTI; a 4.4-fold increase in the chance of UTI on chemoprophylaxis; a 15.4-fold increase in the chance of death; a 24.7-fold increase in the chance of developing chronic kidney disease (stages 1 to 4); and a 35.8-fold increase in the chance of end-stage chronic kidney disease.

In our database used, ultrasound findings of one or more cysts, as well as the presence of a multicystic aspect, were generically grouped as compatible with cystic renal disease, uni or bilateral. Among the 87 patients with sonographic findings compatible with unilateral cystic kidney disease, 73 had a sonographic appearance compatible with the appearance of a unilateral multicystic kidney.

Considering the analysis of the prognostic values of antenatal ultrasound findings compatible with unilateral cystic kidney disease, a 66.1% reduction in the chance in the need for surgical intervention was detected in individuals with CAKUT.

Antenatal ultrasound findings compatible with bilateral cystic kidney disease were not associated with any unfavorable clinical outcomes, but only 1 of the 10 patients in this group had an antenatal ultrasound appearance of a bilateral multicystic kidney. The other 9 patients had ultrasound findings compatible with simple cysts, of minor clinical importance, without involvement of the parenchyma. Moreover, several with ultrasound findings of bilateral multicystic kidney or bilateral polycystic kidney disease were not included in the database of our study, as they died in the immediate neonatal period. Our database consists of patients who survived the neonatal period.

The analysis of the prognostic values of the antenatal ultrasonographic finding of oligohydramnios indicates a 6-fold increase in the chance in the need for surgical treatment, a 4.9-fold increase in the chance of UTI on chemoprophylaxis. It also indicates a 14.5-fold increase in the chance of death, a 30-fold increase in the chance of chronic kidney disease (stages 1 to 4) and a 40-fold increase in the chance of end-stage chronic kidney disease.

The antenatal ultrasonographic finding of unilateral hydronephrosis with megaureter indicates a 2.9-fold increase in the chance of UTI and a 2.4-fold increase in the chance of UTI on chemoprophylaxis. The antenatal ultrasound finding of bilateral hydronephrosis with megaureter indicates a 13.3-fold increase in the chance of death, a 6.8-fold increase in the chance of chronic kidney disease (stages 1 to 4), and a 10.8-fold increase in the chance of end-stage kidney disease in patients with CAKUT.

The analysis of the prognostic values of the antenatal ultrasound finding of bilateral hydronephrosis with megaureter and megabladder indicates a 10.8-fold increase in the need for surgical intervention, a 12.7-fold increase in the chance of developing hypertension, a 4-fold increase in the chance of UTI, a 4.3-fold increase in the chance of UTI on chemoprophylaxis, a 10.1-fold increase in the chance of death, a 12.2-fold increase in the chance of developing chronic kidney disease (stages 1 to 4), and a 15.5-fold increase times the chance of developing end-stage kidney disease in patients with CAKUT.

The prognostic values of the antenatal ultrasound finding of bilateral hydronephrosis with megabladder and oligohydramnios indicate a 5.2-fold increase in the need for surgery, a 23-fold increase in the chance of death, a 150.8-fold increase in the chance of chronic disease (stages 1 to 4), and a 93.8-fold increase in the chance of developing end-stage kidney disease.

The findings of this study must be considered taking into consideration the potential limitations of its design. Because it is a retrospective study, the investigator must analyze data that were recorded in the database by other people. These studies are also more subject to selection and analysis biases. However, it must be emphasized that, before starting any statistical analysis, we were careful to validate the quality of the information contained in our database. Another concern was to perform adequate statistical treatment, reducing possible analysis bias. Moreover, certain characteristics of this historical cohort increase the strength of our findings. Among these, we can mention the follow-up time of more than 20 years, the sample size, the fact that the prenatal US exams were performed by the same team of ultrasonographers from CEMEFE, as well as the fact that the follow-up was performed by the same group of physicians at the UNP, according to well-established protocols.

Our study revealed the nephrourological ultrasonographic findings associated with the reduction and the increase of unfavorable clinical outcomes in a group of 822 patients with CAKUT.

After decades of systematic approach to antenatal detection of nephrouropathies at The Fetal Medicine Center of Clinics Hospital from Federal University of Minas Gerais (CEMEFE), our

understanding of antenatal care and the natural history of CAKUT has clearly improved. Our retrospective study revealed the antenatal nephrourological ultrasonographic findings associated with the reduction and the increase of unfavorable clinical outcomes in a group of 822 patients with CAKUT.

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