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Prenatal diagnosis and postnatal outcome of congenital anomalies of the kidney and urinary tract system: A single-center retrospective study

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Abstract

Aim: To evaluate the prenatal sonographic findings, prevalence, prognostic factors and postnatal outcome of congenital anomalies of the kidney and urinary tract (CAKUT).

Method: This single-center retrospective study was conducted from electronic health records of pregnant women between 18-40 weeks of gestation from January 2015 to January 2022. Babies who were diagnosed as having CAKUT in utero and followed prenatally and postnatally were enrolled in the study.

Results: Out of 15,460 fetuses, 417 fetuses had CAKUT with a frequency of 2.6%. The most common CAKUT was hydronephrosis/pelvis dilatation (n=476, 2.1%). Approximately 67% of CAKUT cases showed normalization or regression. A quarter of babies with CAKUT underwent surgery [75% of oligohydramnios cases, 20% of hydronephrosis/pelvis dilatation cases, 14% of megacystis cases, and 37% of multicystic dysplastic kidney disease (MCDK) cases]. The chromosomal anomaly incidence in babies with CAKUT was 1.2%. Eleven (2.7%) babies with CAKUT died in the perinatal period. All babies with bilateral renal agenesis and bilateral MCDK resulted in exitus.

Conclusion: CAKUT is a very common anomaly with a prevalence of 2.6%. Most of the CAKUT in our series showed spontaneous regression, and 25% of affected babies needed surgery. Oligohydramnios and bilateral anomalies were risk factors for adverse outcomes.

Keywords: Anomaly, congenital, kidney, prenatal, urinary system

Introduction

Congenital anomalies of the kidney and urinary tract (CAKUT) are the most common findings on fetal ultrasound (US) with a prevalence of 0.2-2% [1]. CAKUT is described as structural and functional anomalies of the kidneys and the urinary tract, accounting for up to 20% of all birth defects [2, 3]. These anomalies may occur in isolation as well as part of a syndrome. In recent years, detailed fetal US in the second trimester has become the standard of care. During this evaluation, fetal kidneys, the urinary tract and the bladder can be screened in detail, and a variety of CAKUT disorders can be identified with high accuracy. However, the predictive value of abnormal findings of the urinary system in the prenatal period is not easy to evaluate. Many factors in utero such as oligohydramnios, concomitant anomalies, and intrauterine growth restriction (IUGR) may adversely affect the prognosis for postnatal outcome [4]. Among the urinary system anomalies, solitary kidney associated with a posterior urethral valve, renal cysts, bilateral renal hypoplasia, and bladder outlet obstructions may have poor prognosis in the postnatal period [4,5].

CAKUT may be the main cause of 30-60% of chronic kidney diseases in childhood and may be a major cause of end-stage renal disease [6, 7]. Early diagnosis of urinary tract anomalies provides for the initiation of the best medical support/or surgical intervention as soon as possible before progression to chronic kidney disease [8]. This study aimed to evaluate the value of prenatal diagnosis and sonographic findings of CAKUT and to identify prognostic factors and postnatal outcomes.

Materials and Methods

This single-center retrospective study was conducted at a secondary referral center that specialized in maternal health care between January 2015 and January 2022. A total of 15, 460 pregnant women between 18-40 weeks of gestation were examined through obstetric

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US, and the babies who were diagnosed as having CAKUT were enrolled in the study.

The inclusion criteria were any kind of CAKUT diagnosed during obstetric US and followed-up prenatally and postnatally. Babies who were not able to be followed up postnatally were excluded from the study. Examinations were performed by an experienced radiologist using a highresolution US device with a convex 6-1.9-MHz probe (Toshiba Aplio 500, Japan). In all babies, the kidneys were identified carefully in different imaging planes. The length of both kidneys was measured in the sagittal plane and the full lengths and sizes of the kidneys were compared using nomograms in cases with abnormalities. In cases of pyelectasis, the anterioposterior diameter (APD) of renal pelvises was measured in axial planes. Fetal pyelectasis was considered when the anterior-to-posterior diameter of the renal pelvis was measured as >4 mm up to 28 weeks and as >7 mm at or after 28 weeks of gestation (9). The most common classification system, the hydronephrosis grading system of the Society for Fetal Urology (SFU), the Urinary Tract Dilatation (UTD) system, was used to classify hydronephrosis [9]. The fetuses in the high-risk group were monitored with an interval of 2-4 weeks until birth. The following criteria were also evaluated using US: the number, location, and echogenicity of the kidneys, the presence of solid/cystic mass in the kidneys, caliectasis, ureter dilatation, and the shape and size of the urinary bladder. Accompanying extrarenal malformations, the presence of oligo/polyhydramnios, and complications of pregnancy were also recorded. All images were recorded electronically and electronic health records with radiologic images were retrospectively analyzed. Written informed consent was obtained from all parents to participate in the study, and the investigation followed the guidelines for human studies and the World Medical Association Declaration of Helsinki. The study was approved by the local ethics committee (No: 23/175).

When CAKUT was detected in antenatal US, at least one more screening was performed before birth depending on the severity of the findings. For ongoing renal pelvis dilatations in the 3rd trimester, US follow-up was performed on the third postnatal day at the earliest. In cases of bilateral severe hydronephrosis, US examinations were performed within the first 3 days. If the renal pelvis APD was measured as 5-9 mm, it was considered mild, if the APD was ≥ 10 -14 mm, it was considered moderate, and if the APD was ≥ 15 mm, it was regarded as severe. When anomalies of the urinary system persisted for 3 months or longer, further examinations such as scintigraphy, voiding cystourethrography (VCUG), and dimercaptosuccinic acid (DMSA) scintigraphy were recommended.

All CAKUT cases were classified as 'normalization,' 'regression,' 'persistence,' and 'progression' based on the radiologic findings at the first year of life. Normalization was defined as the normal size, location, configuration, and structure of the kidney and urinary tract system. Regression/progression was defined as a decrease/increase

in postnatal sonographic findings compared with the findings in the prenatal period. Persistence was defined as postnatal findings being the same as those in the prenatal period.

All statistical evaluations were performed using the Statistical Package for the Social Sciences package program (SPSS 22.0). The normality assumption of the variables was checked using the Shapiro-Wilk test. Mean, median, number, standard deviation (SD), and frequency were used as descriptive statistics.

Results

A total of 417 cases of CAKUT with a frequency of 2.6% were detected in antenatal US out of 15,460 fetuses. Of the 417 fetuses, 10 were excluded from the study due to a lack of postnatal evaluation. The characteristics of the patients included in the study are given in Table 1.

Five (1.2%) out of 407 babies with CAKUT had chromosomal anomalies (trisomy 21, trisomy 18) and 17 (4.1%) had concomitant extrarenal anomalies. All babies with trisomy 21 cases had mild renal pelvis dilatation, one baby with trisomy 18 had megacystis and the other had hydronephrosis. Oligohydramnios was diagnosed in 24 (5.8%) pregnancies (Table 1).

Prenatal diagnoses of CAKUT were classified diversely including urinary tract dilatations, developmental anomalies, and cystic kidney diseases. The numbers and incidences of different types of CAKUT (Figures 1-13) in the prenatal period and postnatal outcome are presented in Table 2.

Prenatal US showed renal pelvis dilatation in 329 fetuses, 182 unilateral and 147 bilateral dilatations. Out of 476 renal pelvis dilatations in utero, 96 (20.1%) showed normalization in the postnatal period (Table 2). Of the remaining 380 renal pelvis dilatations in the postnatal period, 320 (84.2%) were mild, 42 (11%) were moderate, and 18 (4.7%) were severe dilatations (Table 3). The types of urinary tract dilatations (Figures 4-9, 13) detected in prenatal US are presented in Table 4.

The median follow-up time was 32 (IQ: 23-66.2) months in the postnatal period. Overall, 102 babies (25%) underwent surgery (Table 2). Thirty-five of these babies underwent surgery within the first 3 months. Hydronephrosis/pelvis dilatation was the most common diagnosis in the surgery group (n=98, 96%) (Table 2). Of babies with hydronephrosis who underwent surgery, 39 had ureteropelvic junction obstruction (UPJO) (39.7%), 38 had vesicoureteral reflux (VUR) (38.7%), 15 had ureterovesical junction obstruction (UVJO) (15.3%), three had posterior urethral valves (PUV) (3%), two had urethral atresia (2%), and one (1%) had ureterocele. Eighteen (75%) of 24 patients with oligohydramnios underwent surgery.

Eleven (2.7%) babies with CAKUT died in the perinatal period (Table 2). One fetus with bilateral renal agenesis died in utero, and the others died soon after birth. Three babies with autosomal recessive polycystic kidney disease (ARPKD) died on the first day of life. One fetus with bilateral MKDB died soon after birth (Table 2).

Table 1: The characteristics of the patients included in the study

Maternal-Fetal demographic characteristics		Value (min- max)
Maternal age		27±3 (20-39)
Gestational age at diagnosis		18.5±2 (17-25) N (%)
F. ()	Male	247 (60.6%)
Fetus gender	Female	160 (39.3%)
	Cardiac anomalies	5 (1.2%)
	CNS anomalies	3 (0.7%)
Composition to entreposition	Extremity anomalies	6 (1.4%)
Concomitant extrarenal anomalies	Lung anomalies	1 (0.2%)
	Abdominal wall defect	1 (0.2%)
	Genital anomalies	1 (0.2%)
	Trisomy 21	3 (0.7%)
Aneuplody/ Genetic Syndromes	Trisomy 18*	2 (0.4%)
	Meckel-Gruber Syndrome**	1 (0.2%)
	Bilateral renal agenesis	4 (0.9%)
Olygohydromnias	Unilateral renal agenesis	1 (0.2%)
Olygohydramnios	ARPKD	7 (1.7%)
	ADPKD	2 (0.4%)
	MCKD	2 (0.4%)
	PUV	2 (0.4%)
	Urethral atresia	2 (0.4%)
	UPJO	4 (0.4%)

ARPKD Autosomal recessive polycystic kidney disease, ADPKD Autosomal dominant polycystic kidney disease, MCKD Multicystic dysplastic kidney disease, PUV Posterior urethral valve, UPJO Ureteropelvic junction obstruction

Table 2: Number and incidence of prenatally diagnosed CAKUT cases (more than one diagnosis per patient possible) and postnatal prognosis

CAKUT	(N, %)	Normalization	Persistant	Regression	Progression	Surgery	Death
Urinary tract dilatation	476 (2.1%)	96 (20.1%)	69 (14.4%)	276 (57.9%)	35 (7.3%)	98 (20.5%)	_
Bilateral renal agenesis	4 (0.02%)					_	4 (100%)
Unilateral renal agenesis	22 (0.14%)		22 (100%)			ı	_
Horseshoe kidneys	28 (0.18%)		28 (100%)			_	_
Ectopic kidneys	15 (0.09%)		15 (100%)			_	_
Megacystis	7 (0.04%)	1 (14.2%)	1 (14.2%)		5 (71.4)	1 (14.2%)	2 (28.5%)
Autosomal recessive polycystic kidney disease (ARPKD)	7 (0.04%)		1 (14.2%)		3 (42.8%)	_	4 (57.1%)
Autosomal dominant polycystic kidney disease (ADPKD)	3 (0.01%)		3 (100%)			ı	-
Multicystic dysplastic kidney disease (MCDK)	8 (0.05%)		5 (62.5%)		2 Bilateral (25%)	3 (%37.5)	1 Bilateral (12.5%)
Obstructive cystic renal dysplasia (OCRD)	6 (0.03%)		1 (16.6%)		5 (83.3%)	_	-

Table 3: Pelvis dilatation

Pelvic dilatation (AP diameter)	Prenatal (N, %)	Postnatal (N, %)
Mild	315 (66.1%)	320 (84.2%)
Moderate	129 (27.1%)	42 (11%)
Severe	32 (6.7%)	18 (4.7%)

Table 4: Types, incidence and accompanying features of urinary tract dilatations detected on prenatal ultrasound

Types	Number of Cases	Incidence (%)	Mean renal pelvis APD*	Calyx dilatation
Transient dilatation	262	55.0	4.5 mm	-
Ureteropelvic junction obstruction	96	20.1	6.5 mm	+++
Vesicoureteral reflux	70	14.7	5.6 mm	+
Ureterovesical junction obstruction	30	6.3	5.3 mm	++
Posterior urethral valve	5	1.0	5.4 mm	++
Urethral atresia	4	0.8	5.5 mm	+++
Ureter duplication	5	1.0	5.9 mm	+++
Ureterocele	3	0.6	5.1 mm	++
Primary megaureter	1	0.2	5.7 mm	++

^{*}APD: Anterioposterior diameter, +: Minimal, ++: moderate, +++: severe

^{*}The fetus with Trisomy 18 is presented in Figure 9.

^{**}The fetus with Meckel-Gruber Syndrome is presented in Figure 10.

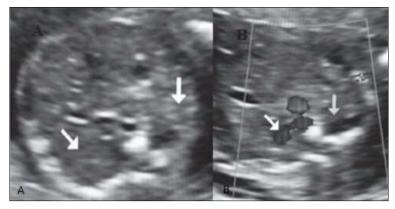


Fig 1: Unilateral renal agenesis. (A) An empty renal fossa is observed on one side in an 18-week pregnant woman (B) In color Doppler ultrasound (CDUS), one of the renal arteries (right renal artery) is not observed.

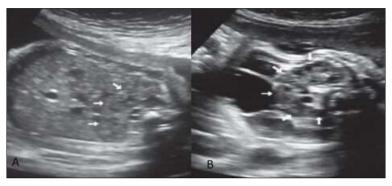


Fig 2: Horseshoe kidney. (A) Both renal lower poles are seen fused across the midline in a 23-week-old fetus. (B) Another horseshoe kidney is seen in a 36-week-old fetus whose mother also had a horseshoe kidney anomaly.



Fig 3: Ectopic kidney. (A) An empty right renal fossa is observed in the transverse section of the abdomen in a 26-week pregnant woman. (B) In the coronal plane, the right kidney is located lower than the left kidney and is adjacent to the bladder. (C) Ectopic kidney located in the pelvic region adjacent to the bladder is observed in another 24-week pregnant woman.



Fig 4: Measurement of the renal pelvises. The APD of the right renal pelvis was 5.5 mm showing mild dilatation in the 24-week-old fetus. The APD of the left renal pelvis is 3.8 mm and is in the normal range.

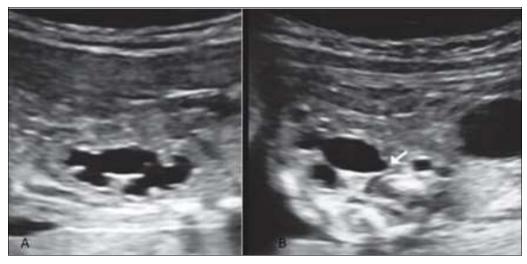


Fig 5: Ureteropelvic junction obstruction (UPJO). (A) Dilatation of the calyces in the fetal kidney (B) Narrowing of the renal pelvis as a pen tip. Arrow indicates UPJO.

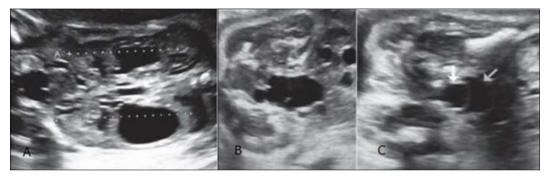


Fig 6: Bilateral duplicated collector system. (A) At 28 weeks of pregnancy, both kidneys increased in size and upper calyxes are dilated. (B) Ureterocele is seen in the urinary bladder. (C) When the bladder is slightly emptied, the ureterocele indicated by the white arrow is clearly visible.



Fig 7: Vesicoureteral reflux (VUR). (A) Hydronephrosis in the right kidney of a 28-week-old fetus. (B) Right ureter appears to be tortuous and dilated. (C) In the transverse section of the abdomen a dilated right renal pelvis is observed.

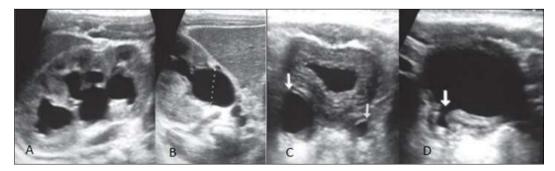


Fig 8: On the postnatal 7th day of the same fetus in figure 7 (A), hydronephrosis persisted in the right kidney. (B) Right renal pelvis APD is 10 mm and dilated. (C) White arrows indicate the distal sections of the ureters, the right ureter is prominent relative to the distal end of the left ureter. (D) The right ureterovesical junction is shown with a white arrow and is wider than normal. Findings confirm the diagnosis of VUR. The diagnosis was also confirmed through micturition cystourethrography.

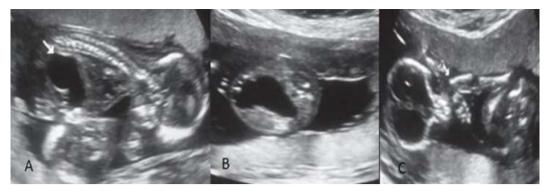


Fig 9: Megacystis. At 17 weeks of a dichorionic diamniotic twin pregnancy, (A) in sagittal and (B) transverse planes, a white arrow indicates the dilated bladder. (C) Radial ray malformation is detected in the same fetus. The karyotype result of the fetus was trisomy 18.



Fig 10: Autosomal recessive polycystic kidney disease (ARPKD) in a 26-week-old fetus (A) Bilateral hyperechoic large kidneys are seen in the coronal plane. (B) Hyperechoic kidneys and a millimetric cyst (white arrow) in the left kidney. Concomitant polydactyly (C) and vermian agenesis (D) are observed in the same fetus. The fetus was diagnosed as having Meckel-Gruber syndrome.

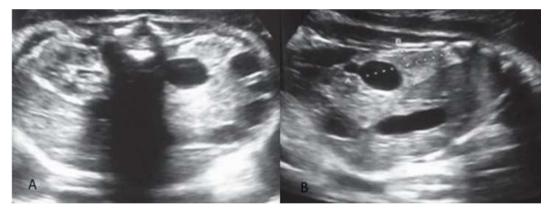


Fig 11: Multicystic dysplastic kidney disease (MCDK). Cysts of varying sizes and random distribution with increased left kidney size in a 28-week-old fetus. (B) MCDK in 32-week fetus.

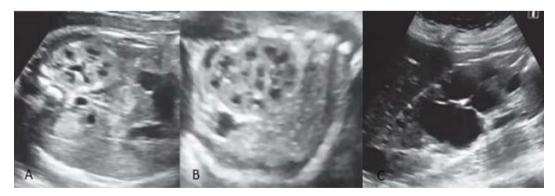


Fig 12: Autosomal dominant polycystic kidney disease (ADPKD). In a 29-week-old fetus, kidneys slightly increased in size and echoes are observed in the transverse (A) and sagittal (B) planes. No cyst is observed in the kidneys in this week, and amniotic fluid is sufficient. (C) ADPKD is also observed in the mother's kidneys.

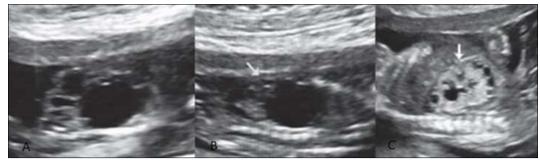


Fig 13: Obstructive cystic renal dysplasia (OCRD). (A) Hydronephrosis secondary to obstructive uropathy at the 17th gestational week. (B) Persistent hydronephrosis is seen at 21 weeks of gestation. (C) Dysplasia develops secondary to obstruction at 26 weeks (increased renal echogenicity and subcortical cysts are observed)

Discussion

In this study, a wide range of urinary system anomalies from mild renal pelvis dilatation to severe anomalies were evaluated. The prevalence of CAKUT was found as 2.6% and the most common type was hydronephrosis/dilatation with a prevalence of 2.1%. Most of the babies who were diagnosed as having CAKUT in the intrauterine period showed good prognosis in the postnatal period and it was determined which babies would need surgery in the postnatal period. This is one of the largest studies of CAKUT including prenatal and postnatal follow-up performed to date.

Approximately 67% of babies with CAKUT showed normalization or regression. Most babies who showed normalization/regression were those with renal pelvis dilatation. Some 66% of renal pelvis dilatations in the prenatal period were mild, and the rate of those with mild dilatation in the postnatal period was 84%. Severe renal pelvis dilatation accounted for 6.7% of all dilatations in utero, whereas they accounted for 4.7% in the postnatal period. In the study conducted by Nef et al., unilateral/bilateral renal pelvis dilatation was found to be the most common among babies showing normalization [10]. pelvic intrauterine dilatations regression/normalization in the postnatal period in this study.

Renal pelvis dilatation accounted for 80% of all cases of CAKUT in our study

The most common cause of intrauterine renal pelvis dilatation was transient renal pelvis dilatation with a rate of about 55%. In transient renal pelvis dilatation, the average APD was found as 4.5 mm in the second trimester and was significantly smaller compared with the APD value in UPJ and VUR (p<0.005). However, calyx dilatation was observed in cases of UPJ, VUR, and PUV, but it was not observed in transient renal pelvis dilatations. Transient renal pelvis dilatation should be considered in fetuses with a renal pelvis APD of p<5 mm in the second trimester and not accompanied by calyx dilatation.

UPJO is the second most common etiology of hydronephrosis, and its incidence was found as 20% in the present study. Oligohydramnios accompanied in four of the UPJ cases, and three were bilateral UPJO. In bilateral UPJO cases accompanied by oligohydramnios, progression was observed in the postnatal period. In these babies, anuria developed along with renal failure and surgery was performed in the neonatal period. Noe *et al.* reported that a fetus with bilateral UPJO and oligohydramnios was referred to preterm delivery and surgery, similar to our cases [11]. It

can be assumed that bilateral hydronephrosis and oligohydramnios would have an unfavourable outcome in the absence of an early prenatal diagnosis.

Approximately one-quarter of babies with CAKUT underwent surgery in this study. Of those, about one-third had surgery in the first 3 months of life. In the study of Quirino *et al.*, 28% of babies required surgery and the most common leading cause was UPJO, similar to our study [12]. Nef *et al.* reported that one-third of babies with CAKUT required surgery, also that PUV and UPJO were the most common conditions requiring surgery in the first months of life [10]. The reason for the lower number of babies requiring surgery in the present study may be the shorter median follow-up period. In our study, 75% of the babies with oligohydramnios underwent surgery. The need for surgery increases in high-risk group patients, especially in oligohydramnios.

About 34% of babies with CAKUT showed persistence in the postnatal period without requiring surgery. These anomalies were generally unilateral or mild bilateral hydronephrosis, horseshoe kidneys, ectopic kidneys, and unilateral MCDK and ADPKD. Bilateral MCDK and most babies with ARPKD cases had unfavourable prognoses leading to death. Most babies with oobstructive cystic renal dysplasia (OCRD) and megacystis showed progression. Bilateral anomalies and the development of dysplasia were significant risk factors for unfavourable outcomes in the postnatal period.

The incidence of chromosomal anomalies in babies with CAKUT was 1.2%. All babies with trisomy 21 had transient mild renal pelvis dilatations, whereas those with trisomy 18 had persistent anomalies. Both trisomy 21 and trisomy 18 were accompanied by extrarenal malformations, and no aneuploidy was detected in any of the isolated urinary system anomalies. About 14% (n=1/7) of babies with megacystis had aneuploidy (Trisomy 18), which is consistent with the study of Taghavi *et al.*, reporting a rate of 15% [13].

The difficulty in evaluating a heterogeneous study population including a wide range of urinary system anomalies was one of the limitations of our study. The relatively short median follow-up time and absence of laboratory data were other limitations, due to the lack of a multidisciplinary approach in our hospital. However, the main aim of this study was to focus on imaging findings, diagnosis, and follow-up of different types of urinary system anomalies.

In conclusion, CAKUT is the most common intrauterine anomaly with a prevalence of 2.6%. It can be diagnosed with a careful sonographic evaluation in utero. Most babies

with CAKUT show spontaneous regression and only onequarter need surgery in the postnatal period. Particular risk factors, such as oligohydramnios and bilateral anomalies were predictive factors for adverse outcomes. Intrauterine diagnosis allows for prenatal counseling for parents and appropriate management for the babies.

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Conflict of Interest

Not available

Financial Support

Not available

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