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Prenatal diagnosis and postnatal outcomes of congenital kidney and urinary tract anomalies: results from a tertiary center

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Abstract

Background This study aimed to investigate the prenatal features, genetic findings, and perinatal outcomes of fetuses with congenital anomalies of the kidney and urinary tract (CAKUT), with a particular focus on associations with additional structural or chromosomal abnormalities.

Methods A retrospective cohort analysis was conducted on 277 fetuses diagnosed with CAKUT between December 2020 and December 2024 at a tertiary center. Data on anomaly subtypes, associated findings, genetic testing, pregnancy outcomes, and postnatal follow-up were evaluated. Logistic regression was used to identify predictors of termination.

Results Urinary tract dilatation was the most frequent anomaly (28.2%), followed by multicystic dysplastic kidney (11.6%) and bilateral renal agenesis (11.2%). Extrarenal anomalies were present in 33.9% of fetuses, primarily involving the CNS. Genetic testing was performed in 48.4%; chromosomal abnormalities were found in 17.3%, most commonly trisomy 21 (5.8%). Termination was significantly associated with early diagnosis (adjusted OR = 0.82; $p < 0.001$), oligohydramnios (OR = 4.94; $p < 0.001$), CNS (OR = 3.74; $p = 0.001$), and cardiac anomalies (OR = 4.21; $p = 0.002$). Neonatal death occurred in 29.2% of cases, and mortality was higher in non-isolated anomalies (60% vs. 32.9%, $p < 0.001$).

Conclusions Fetuses with CAKUT, particularly those with early diagnosis or coexisting anomalies, carry a higher risk of adverse outcomes. Prenatal detection, coupled with comprehensive genetic and structural evaluation, is essential for informed counseling and postnatal planning.

Keywords CAKUT, Prenatal diagnosis, Chromosomal anomalies, Pregnancy termination, Neonatal outcome

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Introduction

Congenital kidney and urinary tract anomalies account for approximately 20% of anomalies detected via antenatal ultrasonography [1]. These malformations represent a serious group that can progress to chronic kidney disease during childhood. This group includes both structural and functional malformations of the bladder, kidneys, ureters, and urethra [1, 2].

The development of the kidneys and urinary tract progresses through three stages: pronephros, mesonephros, and metanephros. Each stage plays an important role in

shaping the final urinary system and kidneys. Disruptions in these critical developmental steps—due to teratogenic exposures, monogenic defects, aberrant cellular migration, or altered transcription factor expression—can result in congenital anomalies of the kidney and urinary tract (CAKUT) [1, 3].

Some urinary system anomalies can lead to oligohydramnios, which may impair fetal lung maturation and cause deformities in the fetal face and extremities [4]. Due to their potential to affect other organ systems and predispose to chronic kidney disease in childhood, early recognition of these anomalies during the antenatal period is of great importance. In particular, obstructive urinary tract pathologies, if left untreated, may progress to end-stage renal disease [5]. Because these conditions often follow an asymptomatic clinical course, prenatal diagnosis and postnatal monitoring are essential. To prevent end-stage renal failure and to enable timely initiation of appropriate treatment, families must be thoroughly informed.

Several studies have demonstrated that CAKUT is frequently associated with chromosomal and syndromic anomalies. Approximately 12–20% of cases have an identifiable monogenic cause, with mutations described in more than 50 genes. Co-occurrence with anomalies of the central nervous system, cardiovascular structures, gastrointestinal tract and limbs is also common. Therefore, understanding the antenatal diagnosis, identification of associated anomalies, and postnatal outcomes of CAKUT are essential for comprehensive antenatal counseling and individualized postnatal care [6–8].

Our study aims to investigate the association between congenital urinary tract anomalies and chromosomal or other system abnormalities and to contribute to management and treatment planning through postnatal follow-up.

Materials and methods

Between December 1, 2020, and December 31, 2024, 396 fetuses diagnosed with congenital kidney and urinary tract anomalies were evaluated at the Perinatology Clinic of Başakşehir Çam and Sakura City Hospital. These cases were examined in a multidisciplinary council involving specialists from the departments of genetics, perinatology, and pediatric nephrology. Associated anomalies of the central nervous system, cardiovascular system, gastrointestinal system, and extremities were also recorded.

Twenty patients with more than two additional system anomalies were excluded from the study. Another 99 cases were excluded due to lack of antenatal/postnatal follow-up or an inability to reach the families. Ultimately, 277 fetuses with accessible hospital records were included in this retrospective analysis. A flow diagram illustrating the inclusion process is presented in Fig. 1.

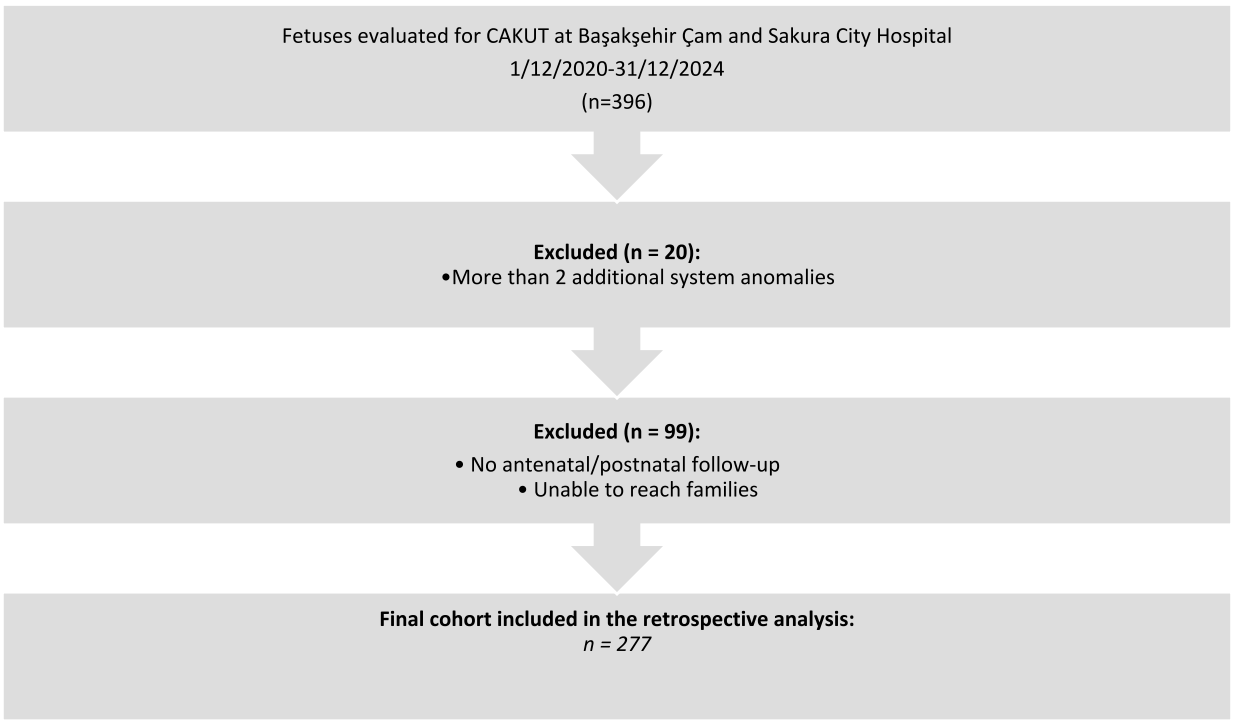

Fig. 1 Flowchart showing patient selection, exclusion criteria, and final classification of fetuses included in the study cohort

The diagnosis of CAKUT was based on prenatal ultrasound findings evaluated by experienced perinatologists using consistent criteria throughout the study period. In cases with available data, postnatal imaging and clinical follow-up were used to confirm the diagnosis. Fetuses showing spontaneous regression of urinary tract dilatation (UTD) during prenatal follow-up were excluded to reduce bias toward mild or transient conditions and to ensure that the cohort represented persistent structural anomalies. In contrast, cases that showed postnatal resolution were retained in the analysis and included in the final cohort.

Demographic data of the included patients—such as gravida, parity, gestational week at diagnosis, fetal sex, antenatal diagnoses determined by our multidisciplinary council, associated anomalies, termination status, postnatal clinical status, delivery timing, genetic and imaging results, and follow-up and treatment plans—were obtained from the hospital information system and through telephone interviews.

Urinary system anomalies were classified as urinary tract dilatation (UTD), lower urinary tract obstruction (LUTO), multicystic dysplastic kidney (MCDK), polycystic kidney disease, renal agenesis, duplication of the collecting system, ectopic kidney, bladder exstrophy, and megacystis. Antenatal urinary tract dilatation (UTD) is among the most frequently detected congenital anomalies during pregnancy. Renal pelvic diameter (RPD) was used to define and grade UTD. Measurements were taken in the transverse plane, and an anteroposterior diameter greater than 4 mm in the second trimester or 7 mm in the third trimester was considered indicative of UTD [9].

Following the council evaluation, appropriate invasive prenatal diagnostic tests were recommended to families based on gestational age. Diagnostic methods included chorionic villus sampling (CVS), amniocentesis (AS), cordocentesis (CS), or genetic analysis from fetal skin samples in cases where pregnancy was terminated. For families concerned about the risk of fetal loss, postnatal genetic evaluation was proposed.

Karyotype and chromosomal microarray analysis (CMA) was routinely performed in all fetuses with structural anomalies as part of our institutional genetic evaluation protocol. Whole exome sequencing (WES) was selectively offered in cases with syndromic suspicion or complex findings and required additional informed consent, as it was not covered by standard healthcare funding.

Before invasive procedures, all families received verbal and written information regarding the procedure and its potential complications, and informed consent was obtained. For fetuses diagnosed with aneuploidy or incompatible with life, termination of pregnancy was discussed and offered by the council, which included medical geneticists and perinatologists.

In the postnatal period, newborns followed for urinary anomalies were evaluated with abdominal ultrasonography performed by neonatologists to confirm prenatal diagnoses. Infants requiring further care were referred to the pediatric nephrology department for follow-up and treatment.

Statistical methods

Descriptive statistics were used to summarize demographic characteristics and the distribution of fetal urinary system anomalies. Categorical variables such as fetal sex, anomaly types, and karyotype results were presented as frequencies and percentages. Continuous variables such as maternal age and gestational age at diagnosis were expressed as medians with minimum and maximum values or interquartile ranges (IQR), depending on their distribution.

Comparisons between groups (e.g., trisomy vs. normal karyotype) were performed using appropriate statistical tests. For continuous variables that did not show normal distribution, the Mann–Whitney U test was applied. For categorical variables, either the Chi-square test or Fisher's exact test was used, depending on the expected cell counts.

A two-sided p-value of < 0.05 was considered statistically significant. All analyses were performed using IBM SPSS Statistics version 30 for Windows (IBM Corp., Armonk, NY, USA).

Results

The study group included 277 fetuses diagnosed with congenital kidney and urinary tract anomalies, diagnosed prenatally and confirmed either through postnatal evaluation or consistent antenatal follow-up. Cases demonstrating regression during prenatal follow-up were excluded from the analysis to ensure diagnostic consistency. Of these, 57.8% were male ($n = 160$), 37.9% were female ($n = 105$), and 1.8% ($n = 5$) had ambiguous genitalia. In 7 cases, fetal gender was not available. The mean maternal age was 28 years (range: 16–51), and the mean gestational age at diagnosis was 24 weeks (range: 11–40). The median gravida was 2 (range: 1–13), and the median parity was 1 (range: 0–9). Demographic data are presented in Table 1.

Among fetal urinary tract anomalies, the most frequently observed was urinary tract dilatation (UTD) (28.2%), with bilateral UTD being more common (19.9%). This was followed by unilateral multicystic dysplastic kidney (MCDK) (11.6%), bilateral renal agenesis (11.2%), and polycystic kidney disease (11.2%) (Table 2). Of the 277 fetuses, 94 (33.9%) had additional anomalies

Table 1 Frequency distributions of categorical variables

	N	%
Fetal Gender		
Female	105	37.9
Male	160	57.8
Ambiguous Genitalia	5	1.8
Unknown	7	2.5
Total	277	100.0
	Median	Min–Max
Maternal Age	28 years	16–51
Gestational age at diagnosis	24 weeks	11–40
Gravida	2	1–13
Parity	1	0–9

in other organ systems. The most common coexisting anomalies involved the central nervous system (CNS) (67.0%), followed by cardiac anomalies (39.4%), limb malformations (26.6%), and gastrointestinal system (GIS) anomalies (16.0%). The highest rates of co-occurring system anomalies were seen in fetuses with bilateral UTD (56.4%), ectopic kidney (52.9%), and megacystis (46.2%) (Table 7-Appendix).

Due to parental refusal of genetic testing, no genetic analysis could be performed in 51.6% of cases ($n = 143$). Among the invasive procedures, amniocentesis (AS) was the most frequently performed (26.4%), followed by fetal autopsy (13.4%), chorionic villus sampling (CVS) (5.0%), and cordocentesis (CS) (2.9%). Karyotype analysis revealed trisomy 21 in 16 cases (5.8%), trisomy 18 in 7 cases (2.5%), trisomy 13 in 2 cases (0.7%), and trisomy 16 in 1 case (0.3%). Other chromosomal anomalies were observed in 22 fetuses (8.0%), while no abnormalities were detected in 59 cases (21.3%). Karyotype data were not available for 170 fetuses (61.4%) (Table 3).

Fetuses diagnosed with renal anomalies were divided into three groups based on termination status and the presence of additional structural anomalies. Additionally, 42 fetuses with multisystem anomalies in which the pregnancy was continued were not included in this table, as they did not fit the classification criteria of the three primary groups. Tables 4 and 5 present a detailed overview of the genetic testing methods utilized across the study groups, along with the corresponding chromosomal findings. While invasive testing such as amniocentesis and autopsy was more frequently performed in terminated cases, chromosomal abnormalities, including trisomies and other structural anomalies, were more commonly identified in fetuses with multisystem involvement.

When comparing fetuses with trisomy ($n = 26$) and those with a normal karyotype ($n = 59$), there was no statistically significant difference in maternal age (median: 29.5 vs. 29 years; $p = 0.990$) or gestational age at diagnosis (median: 23 vs. 22 weeks; $p = 0.404$). However, the pregnancy termination rate was significantly higher in the trisomy group (61.5% vs. 29.3%; $p = 0.011$). In addition, bilateral UTD was substantially more frequent in the trisomy group (57.7% vs. 23.7%; $p = 0.005$). No significant difference was found between the groups regarding other types of urinary anomalies. Group comparisons based on karyotype are shown in Supplementary Table 1.

Table 6 presents the crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) for factors associated with pregnancy termination. Lower gestational age at diagnosis was independently associated

Table 2 The distribution of fetal urinary system anomalies and accompanying anomalies

	N	%	Accompanying anomalies (*n*)	Accompanying anomalies (%)
Antenatal Diagnosis				
Unilateral Urinary Tract Dilatation	23	8.3	9	39.1
Bilateral Urinary Tract Dilatation	55	19.9	31	56.4
Unilateral Multicystic Dysplastic Kidney	32	11.6	7	21.92
Bilateral Multicystic Dysplastic Kidney	11	4.0	2	18.2
Polycystic Kidney Disease	31	11.2	7	22.6
Unilateral Renal Agenesis	16	5.8	7	43.8
Bilateral Renal Agenesis	31	11.2	8	25.8
Ectopic Kidney	17	6.1	9	52.9
Megacystis	13	4.7	6	46.2
Bladder Exstrophy	7	2.5	-	-
Low urinary tract obstruction (LUTO)	28	10.1	3	10.7
Duplication of the collecting system	13	4.7	5	38.5
Total	277	100.0	94	33.9

Table 3 Karyotyping technique and results

Diagnostic Test	N	%
None	143	51.6
CVS	14	5.0
AS	73	26.4
Cordocentesis	8	2.9
Fetal Autopsy	37	13.4
Blood from Newborn After Birth	2	0.72
Total	277	100.0
Anomaly Diagnosis		
None	59	21.3
T21	16	5.8
T18	7	2.5
T16	1	0.3
T13	2	0.7
Other	22	8.0
Not Available	170	61.4
Total	277	100.0

with higher termination rates (adjusted OR = 0.82, 95% CI: 0.76–0.88, $p < 0.001$); indicating that each additional week of gestational age reduced the likelihood of termination by approximately 18%. Among fetal anomalies, oligohydramnios (adjusted OR = 4.94, 95% CI: 2.44–10.4, $p < 0.001$), CNS anomalies (adjusted OR = 3.74, 95% CI: 1.65–8.67, $p = 0.001$), and cardiac anomalies (adjusted OR = 4.21, 95% CI: 1.67–10.9, $p = 0.002$) were significantly associated with increased odds of termination. In contrast, GIS anomalies showed no association (adjusted OR = 1.00, $p = 0.997$). The initial association with limb anomalies (crude OR = 2.71, $p = 0.016$) lost significance after adjustment (adjusted OR = 1.43, $p = 0.528$), suggesting potential confounding by other anomalies.

Postnatal outcomes showed that 35 fetuses (17.3%) experienced spontaneous regression without the need for any intervention. Eighteen cases (8.9%) required surgical procedures, and 90 infants (45.6%) remained under follow-up. A total of 59 fetuses (29.2%) died in the antenatal or postnatal period. The most common conditions associated with mortality were bilateral renal agenesis ($n = 14$), polycystic kidney disease ($n = 11$), bilateral MCDK ($n = 9$), and bilateral UTD ($n = 9$). In contrast, only one death occurred in cases of unilateral UTD and unilateral MCDK. Figure 2 illustrates the number of fetal or neonatal deaths according to the type of urinary tract anomaly.

Among non-isolated urinary tract anomalies, the mortality rate was 60%, compared to 32.9% in isolated cases—a statistically significant difference ($p < 0.001$). The median gestational age at delivery was 34 weeks in non-isolated cases and 37 weeks in isolated cases ($p = 0.009$). These findings demonstrate that fetuses with

Table 4 Distribution of genetic testing according to termination status and multisystem involvement in fetuses with renal anomalies

Diagnostic Test	Multisystem anomalies with TOP (*n*=42)	Isolated renal anomalies with TOP (*n*=33)	Isolated renal anomalies with continuation of pregnancy (*n*=160)
None	9 (21.4%)	12 (36.4%)	116 (72.5%)
CVS	4 (9.5%)	4 (12.1%)	3 (1.9%)
Amniocentesis (AS)	15 (35.7%)	4 (12.1%)	36 (22.5%)
Cordocentesis (CS)	1 (2.4%)	2 (6.1%)	0 (0.0%)
Fetal Autopsy	13 (31.0%)	11 (33.3%)	4 (2.5%)
Blood from Newborn	0 (0.0%)	0 (0.0%)	1 (0.6%)

Table 5 Distribution of genetic results according to termination status and multisystem involvement in fetuses with renal anomalies

Anomaly Diagnosis	Multisystem anomalies with TOP (*n*=42)	Isolated renal anomalies with TOP (*n*=33)	Isolated renal anomalies with continuation of pregnancy (*n*=160)
None	8 (19.0%)	9 (27.3%)	17 (10.6%)
Trisomy 21	7 (16.7%)	2 (6.1%)	4 (2.5%)
Trisomy 18	7 (16.7%)	0 (0.0%)	0 (0.0%)
Trisomy 16	1 (2.4%)	0 (0.0%)	0 (0.0%)
Trisomy 13	2 (4.8%)	0 (0.0%)	0 (0.0%)
Other	5 (11.9%)	7 (21.2%)	7 (4.4%)
Not Available	12 (28.5%)	15 (45.5%)	132 (82.5%)

Table 6 Crude and adjusted odds ratios (OR) with 95% confidence intervals (CI) for predictors of pregnancy termination. Adjusted ORs were estimated using multivariate logistic regression including amniotic fluid index (AFI), central nervous system (CNS) anomalies, gastrointestinal system (GIS) anomalies, cardiac anomalies, and limb anomalies

Variable	Crude OR	95% CI (Crude)	*p*-value (Crude)	Adjusted OR	95% CI (Adj)	*p*-value (Adj)
Gestational age	0.82	0.77–0.87	< 0.001	0.82	0.76–0.88	< 0.001
Oligohydramnios (vs Normal AFI)	4.52	2.58–7.92	< 0.001	4.94	2.44–10.4	< 0.001
SSS anomaly (vs No)	3.03	1.68–5.48	< 0.001	3.74	1.65–8.67	0.001
GIS anomaly (vs No)	0.96	0.3–3.11	0.945	1.00	0.23–3.98	0.997
Cardiac anomaly (vs No)	3.39	1.67–6.89	< 0.001	4.21	1.67–10.9	0.002
Limb anomaly (vs No)	2.71	1.18–6.25	0.016	1.43	0.47–4.30	0.528

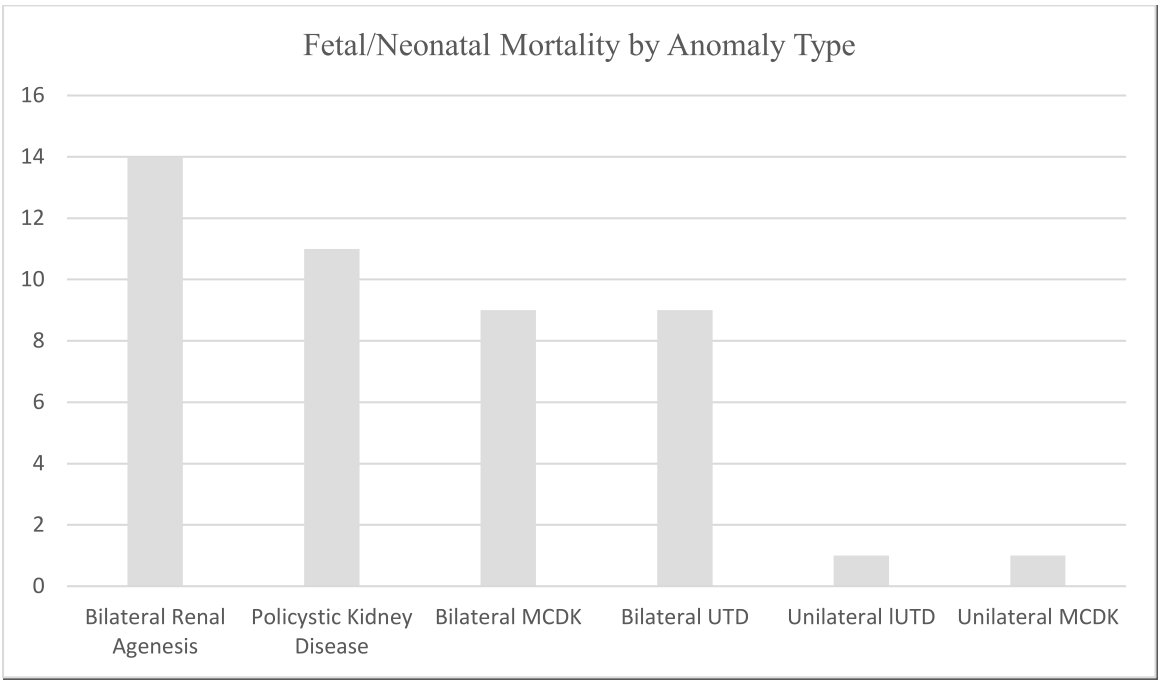

Fig. 2 Number of fetal or neonatal deaths according to the type of urinary tract anomaly

isolated renal anomalies have better postnatal prognosis compared to those with additional structural anomalies.

Discussion

Genetic findings

CAKUT may present in isolation or as part of a monogenic or syndromic condition. Therefore, it is recommended that these patients undergo not only karyotype analysis but also advanced genetic evaluations such as chromosomal microarray (CMA) and whole-exome sequencing (WES). These anomalies can also be accompanied by malformations in other organ systems. In particular, co-occurrence with central nervous system (CNS) and cardiac anomalies increases the risk of an underlying chromosomal disorder. The most common CNS anomalies included ventriculomegaly, agenesis of the corpus callosum, neural tube defects and Dandy–Walker malformation. In our cohort, 33.9% of cases had associated anomalies, most frequently involving the CNS, consistent with other national studies [10, 11].

Informed decision-making regarding genetic testing or pregnancy termination may be influenced by sociocultural norms and perceived procedural risks, particularly when fetal loss is explicitly mentioned in consent documentation. As a result, genetic testing was performed in 48.4% of cases. Moreover, 27 families declined to receive the results despite consenting to testing. The most common result was normal karyotype

(21.3%). Trisomy 21 was identified in 5.8% of cases, followed by trisomy 18 (2.5%), trisomy 13 (0.7%), trisomy 16 (0.3%), 69 XXX (2 cases) and Turner syndrome (1 case).

CMA and WES enabled detection of other clinically significant variants, including PKHD1 mutations ($n=$ 3), DiGeorge syndrome ($n=$ 2), variants suggestive of Meckel–Gruber syndrome (1 case), deletions at 1q21.1 and Xp21.1, and a combined 4p16.3 deletion with 8p23.1 duplication consistent with Wolf–Hirschhorn syndrome [12].

Variants of uncertain significance (VUS) were identified in nine cases. In one fetus, a VUS/likely pathogenic deletion on the X chromosome, combined with ultrasonographic findings, Beckwith–Wiedemann syndrome was suspected; however, WES could not be performed. The remaining VUS findings—including those in the CRB2 and PKD1 genes and a 15q11.2 deletion—remained uninformative during pregnancy, highlighting the challenges of interpreting uncertain results in the prenatal setting. Families were informed about the ambiguous nature of these results, and decisions regarding clinical care were guided by the infant's postnatal presentation rather than genetic data alone. Ongoing genetic consultation was recommended, given the possibility that future research may shed light on these uncertain findings. In two fetuses, a second invasive procedure was necessitated by concerns of maternal DNA contamination in the initial sample. Both families declined further testing.

Although using WES in our cohort was limited due to financial constraints, it revealed clinically relevant findings in selected cases. In a study of neonates with kidney anomalies, WES contributed to a diagnosis in 36.1% of cases [13]. Similarly, Saha et al. reported a 46% diagnostic yield with WES, with nearly 20% receiving a revised diagnosis that impacted clinical management [14]. Importantly, pathogenic variants were identified even without a family history, supporting the inclusion of WES regardless of familial background. While genetic abnormalities were less common in isolated renal anomalies (3.1%), our results confirm that syndromic or monogenic causes cannot be excluded based solely on the absence of extrarenal findings. Nevertheless, each patient should be counseled regarding the potential risks and benefits of diagnostic testing, as chromosomal abnormalities may still occur in a small proportion of cases.

UTD is a common ultrasonographic marker in Down syndrome cases in the antenatal period. In the presence of coexisting anomalies, invasive diagnostic testing is recommended [15]. In our study, bilateral UTD was found to be significantly more frequent in the trisomy group, consistent with the literature (57.7% vs. 23.7%; $p=0.005$). On the other hand, no statistically significant association was observed between other types of urinary tract anomalies and trisomies [16, 17].

In a study of 439 fetuses with Down syndrome, Demir GÜ et al. [18] reported a mean maternal age of 32.1 ± 7.0 years and found congenital heart disease in 69.5% of the cases. Although advanced maternal age is a well-known risk factor for trisomies [16], no significant age difference was observed between the trisomy and non-trisomy groups in our cohort. However, fetuses with trisomy had a significantly higher rate of associated anomalies compared to those with normal karyotypes (76.9% vs. 37.3%), $\chi^2(1, N= 85) = 11.00$, $p= 0.001$. These findings underscore the importance of careful anomaly scanning and genetic assessment regardless of maternal age. These findings reinforce the importance of detailed sonographic evaluation and genetic testing in fetuses with multisystem anomalies.

Predictors of termination

The decision to terminate pregnancy was most frequently made in fetuses with bilateral renal agenesis (22.1%), polycystic kidney disease (18.2%), and bilateral urinary tract dilatation (14.3%). Fetal contribution to the amniotic fluid begins at the 8 th week of gestation and constitutes the majority of the fluid by the 16 th week. In cases where the renal parenchyma is non-functional (such as renal agenesis, polycystic kidney disease), the resulting absence of fetal urine leads to anhydramnios, which causes Potter sequence, characterized by pulmonary hypoplasia, limb contractures, retrognathia, and a flattened nasal bridge. Anhydramnios is a critical ultrasonographic marker considered during the decision-making process for pregnancy termination [4, 19].

In our termination group, 57% of fetuses had oligohydramnios or anhydramnios, compared to 22.0% in the group where pregnancy was continued. Additionally, congenital heart defects and CNS anomalies were significantly more common in terminated fetuses (25% vs. 9%, $p= 0.002$; 39% vs. 17%, $p< 0.001$). CNS anomalies were the most prevalent associated anomalies in the overall cohort, and their frequency was notably higher in the termination group. The high prevalence of oligo/anhydramnios and the increased rate of cardiac anomalies observed in the termination group are consistent with previous literature findings [10, 11, 18]. While limb abnormalities initially appeared to influence outcomes, this association diminished after accounting for coexisting anomalies, implying that the observed effect may be attributable to those accompanying conditions rather than the limb defects themselves.

In a study by Syngelaki et al., it was demonstrated that renal anomalies such as multicystic kidneys, UTD, LUTO, and renal agenesis can be detected as early as the

first trimester. In our study, since the most frequent terminations occurred in this group, the earlier gestational age at diagnosis in terminated cases is consistent with the literature [20].

Notably, pathologies such as bilateral UTD (56.4%), ectopic kidney (52.9%), and megacystis (46.2%) were frequently accompanied by anomalies in other systems. A 2024 study by İnan et al. found such associations in 24% of ectopic kidney cases, supporting the view that it often coexists with structural or genetic abnormalities. Similarly, Fontanella et al.emphasized the need to consider syndromic anomalies in megacystis cases [21, 22].

Postnatal outcomes and results of fetal intervention

When examining postnatal outcomes, 35 cases (17.3%) showed spontaneous regression without the need for any intervention. Follow-up ultrasonography was performed beyond the neonatal period to confirm the persistence of the resolution. These cases were thus not considered transient or false negative findings as described in Gaeta et al., and were retained in the study cohort [23]. Surgical procedures were required in 18 cases (8.9%), and 90 infants (44.6%) remained under follow-up. A total of 59 patients (29.2%) died during follow-up. Among the deceased cases, the most common renal anomalies were bilateral renal agenesis ($n = 14$), polycystic kidney disease ($n = 11$), and bilateral UTD ($n = 9$). The least associated anomalies with mortality were unilateral UTD and unilateral MCDK, each observed in only one deceased patient.

The median gestational age at birth for these fetuses was 34 weeks. The mortality rate was significantly higher among non-isolated cases (60%) compared to isolated cases (32.9%), and this difference was statistically significant ($p < 0.001$). Similarly, when comparing gestational ages, non-isolated cases had a median gestational age of 34 weeks at birth, while isolated cases had a median of 37 weeks ($p = 0.009$). In line with these findings, a large-scale population-based study by Al-Dewik et al. also reported that fetuses with congenital anomalies tended to be born earlier. That study further emphasized that fetal mortality was significantly higher in cases with multisystem anomalies, and that delivery occurred at earlier gestational ages [24]. Our results show the prognostic importance of distinguishing isolated from complex CAKUT and support the need for individualized prenatal counseling and multidisciplinary postnatal care.

In addition to postnatal outcomes, six fetuses in our study underwent prenatal intervention with vesicoamniotic shunt (VAS) placement due to severe lower urinary tract obstruction (LUTO) or megacystis. LUTO predominantly affects male fetuses and has an estimated incidence of 2.2 per 10,000 live births [25]. The most common cause of LUTO is posterior urethral valves (PUV), accounting for approximately 63% of cases [26]. In our study, 66.4% of fetuses with LUTO were also suspected to have PUV, which is consistent with previous studies.

Among the six fetuses who underwent VAS (three with LUTO and three with megacystis), one was female and five were male. Genetic analysis was available in only two of these patients, and both were interpreted as having normal karyotypes. An experienced perinatologist performed all vesico-amniotic shunt procedures to minimize the risk of technical errors. Unfortunately, all six fetuses experienced intrauterine demise between the 16 th and 17 th gestational weeks.

Strizek et al. reported a 75% survival rate in a small cohort of 10 patients who underwent VAS [27]. However, a comprehensive meta-analysis by Nassr et al., which included 423 studies, concluded that although short-term outcomes may appear favorable, VAS is not effective in improving survival over a two-year follow-up period [25]. In our study, VAS was considered only in cases with LUTO or megacystis without sonographically apparent additional anomalies. However, due to reduced reliability of ultrasound due to anhydramnios, the early gestational age at intervention and parental refusal of genetic testing; we cannot definitively exclude the possibility of complex CAKUT in these fetuses. All six families were counseled regarding the poor prognosis and were offered pregnancy termination; however, none accepted this option. These factors could partly explain why our results deviated from previously published data. Our experience with six VAS procedures in fetuses with severe LUTO or megacystis showed uniformly poor outcomes, despite tecnically successful interventions. Limited ultrasound visibility and absence of genetic data likely influenced both prognosis and decision-making. These cases emphasize the need for careful evaluation when considering fetal therapy, where individualized management is essential.

Strengths and limitations

With a sizable cohort of 277 fetuses, this study offers a substantial dataset that enhances the generalizability and clinical relevance of its findings in the context of CAKUT. All cases were evaluated by a multidisciplinary team including specialists in perinatology, medical genetics, and pediatric nephrology, which strengthens the clinical and diagnostic accuracy. Furthermore, antenatal diagnoses were confirmed postnatally through imaging and clinical follow-up, enhancing the reliability of findings. The study also presents a wide genetic spectrum, including cases analyzed via karyotype, CMA, and in selected cases, WES offering a comprehensive evaluation of genetic etiologies. Additionally, this research reflects real-world clinical practices in a

tertiary center and addresses socio-cultural factors such as the parental refusal of genetic testing, which is especially relevant in countries with similar healthcare contexts.

Nevertheless, our study has certain limitations. Being a retrospective analysis, data were obtained from hospital records, and some clinical details were missing or unavailable during follow-up. Genetic testing could not be performed in a substantial proportion of cases due to lack of informed consent. Furthermore, financial constraints prevented many families from undergoing advanced genetic analyses such as WES, potentially limiting the identification of the full spectrum of genetic causes. Lastly, the presence of variants of uncertain significance (VUS) posed interpretation challenges due to their unclear clinical relevance. In addition, there is a potential risk of selection bias related to missing data or unclear documentation of fetal demise. Lastly, as part of the postnatal follow-up data was obtained through telephone interviews rather than from medical records, the possibility of recall bias should be acknowledged.

Conclusion

With increasing access to advanced imaging technologies, second-trimester ultrasonography has become more widespread. This has facilitated the antenatal diagnosis of congenital kidney and urinary tract anomalies. These anomalies can progress during pregnancy, and due to their frequent association with structural and chromosomal abnormalities, prenatal diagnosis plays a crucial role in guiding postnatal follow-up. Since earlier diagnosis is often linked to more severe forms of CAKUT, timely detection may facilitate less traumatic decision-making processes for families, including early termination when indicated.

Accurate classification and a multidisciplinary approach are essential for planning appropriate postnatal care and interventions. Given the wide clinical spectrum of CAKUT, proper antenatal diagnosis is vital for improving neonatal outcomes and ensuring early and appropriate management.

Furthermore, due to the high incidence of coexisting other system anomalies in fetuses with CAKUT, meticulous antenatal evaluation of the fetal anatomy should be considered a critical component of prenatal care.

Appendix

Accompanying anomalies (number of patients with anomalies=94)

CNS	63	67.0
GIS	15	16.0
Cardiac	37	39.4
Limb	25	26.6

Abbreviations

CAKUT	Congenital Anomalies of the Kidney and Urinary Tract
UTD	Urinary Tract Dilatation
LUTO	Lower Urinary Tract Obstruction
MCDK	Multicystic Dysplastic Kidney
WES	Whole Exome Sequencing
CMA	Chromosomal Microarray
PUV	Posterior Urethral Valve
VUS	Variant of Uncertain Significance
AS	Amniocentesis
CVS	Chorionic Villus Sampling
CS	Cordocentesis

Supplementary Information

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Supplementary Material 1.

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Authors' contributions
İ.P. and H.Ö.Ç designed the study, E.O, T.N.Ç.Ç, H.Ö.Ç and D.A collected the data, N.Ç.Ç and H.Ö.Ç conducted the analysis,H.Ö.Ç, M.Ç, and S.Y. drafted the manuscript. The author read and approved the final manuscript.

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Data availability
The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee of Başakşehir Çam and Sakura City Hospital (approval number: E-96317027–514.10–253798061) on September 17, 2024. All procedures were conducted in accordance with the institutional ethical standards and the 1964 Declaration of Helsinki and its subsequent revisions. Informed consent was obtained from all participants or their legal guardians.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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