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ORIGINAL ARTICLE

Congenital anomalies of kidney and urinary tract (CAKUT) and associated extra-renal anomalies in fetal autopsies

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ABSTRACT

Objectives and Background: According to studies, 1% of all pregnancies have an abnormality, with 20–30% of those affecting the genitourinary system. Congenital abnormalities of the kidney and urinary tract (CAKUT) is one of the primary causes of perinatal and neonatal mortality in children. Many extra-renal congenital illnesses accompany these defects, affecting the patient's prognosis. This study aims to determine the subtypes, frequency, and extra-renal defects associated with congenital anomalies of the urinary system, which is the major cause of mortality in fetal and infant autopsies throughout the perinatal and neonatal eras. We believe that our study will contribute to the literature because few autopsy investigations can give this data. **Materials and Methods:** The study included 110 fetal autopsies between January 1997 and May 2019. 10% were newborns under the age of one year, and 90% were fetus autopsies. **Results:** Males accounted for 67.3% of the cases, while females accounted for 35 (31.8%) (the gender of one case could not be determined). Renal dysplasia was the most frequent CAKUT, with a rate of 22.73%, followed by renal agenesis, with a rate of 20.0%. Eighty-four cases (76.3%) showed disease in at least one other organ system. Musculoskeletal system (MSS) abnormalities were the most common associated system anomaly, with one or more MSS anomalies (34.55%) detected in 38 cases. **Conclusion:** Finally, we want to underline that CAKUT and its associated anomalies are not uncommon. Prenatal imaging, genetic investigation, and/or postmortem examination should all be used to screen for CAKUT. This information is helpful for the mother's future pregnancy management and parental genetic counseling.

KEY WORDS: Association, Autopsy, CAKUT, Development, pediatric nephrology, System anomalies

Access this article online

Website: www.ijpmonline.org

DOI: 10.4103/ijpm.ijpm_45_23

Quick Response Code:

INTRODUCTION

The ureteral bud (UB) and metanephric mesenchyme (MM) commence kidney formation in a multi-step process. The metanephric mesenchyme gives rise to nephrons, the minor functional portion of the urinary system, whereas the ureteral bud gives rise to collecting ducts, ureters, and the bladder. The kidneys take their final shape due to the mutual interplay of UD and MM structures.[1,2]

Growth factors involved in both nephrogenesis and UB formation, matrix proteins, particularly E-cadherin, mechanical requirements like MM and UB effect, essential signaling pathways like WNT, and many genes and gene products like WT-1, ODD-, angiotensin type 2 receptor gene, and BMP are all involved in this process.[3]

According to studies, 1% of all pregnancies have abnormalities, with 20–30% of those affecting the genitourinary system (GUS).[4]

Congenital abnormalities of the urinary tract (CAKUT), including the kidney, ureters, bladder, and urethra are embryonic urinary system disorders that cause problems during development.[5]

Submitted: 14-Jan-2023
Revised: 23-Apr-2023
Accepted: 07-May-2023
Published: 09-Nov-2023

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How to cite this article: Çobankent Aytekin E, Sanhal CY, Toru HS. Congenital anomalies of kidney and urinary tract (CAKUT) and associated extra-renal anomalies in fetal autopsies. Indian J Pathol Microbiol 0;0:0.

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Based on hospital registries, the prevalence of CAKUT is estimated to be 4–60 per 10,000 births, with variations in diagnosis methods and ethnic and country variances between studies.[6,7] While some forms of CAKUT are familial or associated with syndromes, they are frequently spontaneous and unrelated to syndromes.[4]

CAKUT can occur for various reasons; it enhances the likelihood of CAKUT being noticed in conjunction with other system pathologies by impacting multiple organ systems simultaneously and producing secondary pathophysiological alterations due to CAKUT. In research, the coexistence rate ranges from 0.16 per thousand to 48.4 per thousand.[8,9]

This study aims to evaluate the subtypes, frequency, and associated extra-renal anomalies of CAKUT, which is one of the leading causes of perinatal and neonatal mortality in fetal and infant autopsies. There are few perinatal autopsy investigations into CAKUT and related extra-renal abnormalities. This study briefly reports CAKUT and associated anomalies, which can be essential data for literature and further meta-analysis research.

MATERIALS AND METHODS

This research is a retrospective study; pediatric and perinatal autopsy cases were screened and evaluated between January 1997 and May 2019. Regarding the urinary system, 1526 autopsy reports and files were analyzed between these years. Perinatal autopsies are performed to termination, intrauterine exitus, and perinatal death cases; livebirth cases are called pediatric autopsies.

This retrospective observational study was conducted in a tertiary center pathology department, with an Institutional Ethics Committee Approval (Decision no: 452) following the Declaration of Helsinki.

Due to grade 3 maceration, 346 instances were only analyzed macroscopically, as some of the 346 cases did not have the requisite family consent for the autopsy procedure, and no information on urinary system pathology could be collected. One hundred and ten of the 1180 autopsy cases were urinary tract anomalies. This study included one hundred and ten patients with a congenital urinary system defect. Autopsy records, images of those with photographs, plain radiographs of those with plain radiographs, macroscopic findings, and microscopic findings were all investigated in these cases. Other than postmortem records, data from newborn and maternal files (molecular examination, infant age, gestational week, maternal age, and consanguineous marriage) were collected.

All fetal autopsies are performed on fresh material; before beginning the autopsy, the parent's consent to the autopsy and the type of consent granted was verified, as well as the newborn's identity and consulted with physicians to decide the questions that the autopsy must address.

A baby-gram radiograph of the entire body in mammography dosage is taken for all fetuses. Photographs of the fetus are taken for gross evaluation and recording. The crown-heel, crown rump, head circumference, foot length, and weight are all measured and compared to standard charts. The foot size is used to calculate gestational age, which is then compared to chronological age. Wigglesworth provides weights and measurements for stillborn and live-born infants using Women and Infants Hospital data.

Cranial, thoracic, and abdominal spaces are opened, and end-block dissection is performed. Each organ is sliced and examined, and at least one sample is collected for each organ, which is then fixed for around 24 h in 10% buffered formaldehyde. All organs are weighed and dimensioned before being fixed, and they are all evaluated for macroscopic anomalies. Each organ anomaly, as well as kidney anomaly, is recorded.

Histochemical and immunohistochemical tests are used to make conclusive diagnoses in cases that require further investigation. After detection and follow-up, slices of paraffin blocks stained with 0.4 mm of H and E were analyzed. The remaining organs are kept in the fixing solution to reevaluate if needed.

Cases are classified and defined by analyzing various classifications in the literature, particularly Potter-Osanthanondh's categorization.[10-12] [Appendix]

A preliminary diagnostic and/or diagnosis after examining the macroscopic and direct radiographs of the study group were established. Except for renal agenesis, all abnormalities were examined microscopically too.[13]

RESULTS

A congenital urinary system anomaly was detected in 110 of 1180 postmortem cases (9.3%). There were 11 (10%) children under the age of one year and 99 (90%) fetus autopsy. With a rate of 65.4%, it was shown that most fetus instances occurred in the second trimester. The smallest case was an 11-week-old fetus, while the largest involved a 200-day-old baby. Seventy-four (67.3%) of the 109 cases whose gender could be identified were male, while 35 (31.8%) were female. The age of the mother ranges from 14 to 41 years old. In 14.5% of the cases, there was growth and development retardation, and in 18.2%, there was maceration.

RD was the most prevalent renal anomaly, with a prevalence of 22.73%, and it was twice as common in men. In 18 of the cases, there was bilaterality.

RA was the second most prevalent anomaly, accounting for 20% of all cases. The cases were seen at a similar rate in the second trimester, and 72.7% were male. In ten of the cases, there was bilaterality. See Tables 1 and 2 for details on the frequency, gender, and bilaterality of different CAKUT kinds.

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Table 1: Distribution of urinary system anomalies I

Renal Anomaly	*N*	*E*	*K*	*Overall Percentage (n:1180)*	*Case percentage (n:110)*
Renal ectopia	3	2	1	0,25%	2,73%
Fusion	12	6	6	1,01%	10,91%
Renal agenesis (B/U)	22	16	6	1,86%	20,00%
Renal hypoplasia (B/U)	7	5	2	0,59%	6,36%
Renal tubular dysgenesis (B/U)	1	1	0	0,084%	0,91%
Renomegaly	1	1	0	0,084%	0,91%
Renal dysplasia* (B/U)	25	17	8	2.11%	22,73%
Polycystic kidney disease (B/U)	15	10	4	1,27%	13,64%
Cortical cysts and others	7	4	3	0,59%	6,36%

*Renal dysplasia including multi-cystic dysplastic kidney, cystic dysplastic kidney

Table 2: Distribution of urinary system anomalies II

Bladder, Ureter, and Urethra Congenital Malformations	*N*	*E*	*K*	*Overall Percentage (n:1180)*	*Case Percentage (n:110)*
Bladder dilatation	4	4	0	0,33	3,64
Bladder hypoplasia	4	2	2	0,33	3,64
Bladder agenesis	5	5	0	0,42	4,55
Urachal remnants	2	2	0	0,16	1,82
Prune belly syndrome	1	1	0	0,08	0,91
Urethra atresia	1	1	0	0,08	0,91
Ureter duplication	3	3	0	0,25	2,73
Ureter atresia*	22	16	6	1,86	20,00
Urethral obstruction	1	1	0	0,08	0,91
Urethra posterior valve	1	1	0	0,08	0,91
Hydroureteronephrosis UPD, (B/U)	18 (6/12)	11	7	1.52%	16.3%

*Only seen in cases of renal agenesis

Kidneys with cystic formations, where the typical kidney structure had vanished, were seen in some RD cases. One instance had fibrosis in the liver tissue, while another had dysplasia in the pancreas. Primitive forms, immature mesenchymal tissue, lobe abnormality, and the presence of cartilage tissue were all found during the microscopic inspection of these patients [Figure 1].

The macroscopy of (ARPKD) instances revealed cystic formations. Radially orientated cysts bordered with short cuboidal epithelium were detected under the microscope. The cysts had normal tubules and glomeruli. There were no primitive channels or immature tissue found. The liver was enlarged in five cases, with microscopical evidence of congenital hepatic fibrosis in the form of expanded portal tracts with Porto-portal bridging.

RD was found in two of the five instances with hydroureteronephrosis (HUN), both macroscopically and microscopically. GTKD in two cases, tubular cystic dilation (TCD) in two patients, and bilateral proximal tubule in one case did not distinguish when examined microscopically (renal tubular dysgenesis). Macroscopic and microscopic findings congruent with the diagnosis described in the material method section were discovered in all other cases.

In 65 cases, at least one or more dysmorphism findings were found (59.09%). Potter's facial appearance, which included

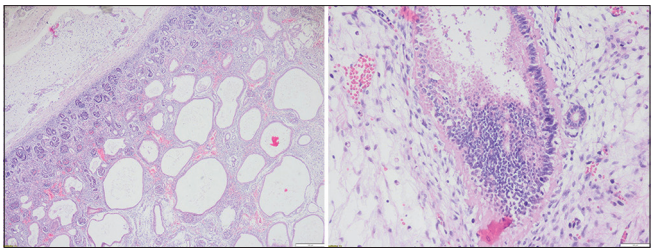


Figure 1: Renal dysplasia microscopic inspection; cystic formations, primitive structures, immature mesenchymal tissue, lobulation abnormality

a low ear, micrognathia, and a flat nasal root, was the most prevalent dysmorphism among them, accounting for 46.1% of cases. It was predominantly seen in renal dysplasia cases (76%). There have been seven cases of cleft-palate cleft lip, two cases of hypertelorism, two cases of lack of eyelid and eye-opening, three cases of head deformity, two cases of ear developmental anomaly, one case of ectropion, and three cases of short-thick neck. [Figure 1-3]

In our analysis, 84 (76.3%) subjects exhibited disease in at least one other organ system. While this link was found in every case of RA, it was followed by ARPKD, renal dysplasia, renal fusion, renal hypoplasia, renal ectopia, and others.

MSS anomalies were the most prevalent concomitant system anomaly, with one or more MSS anomalies found in 38 (34.55%) cases. Table 3 lists the associated anomalies and their frequency.

In RD cases, MSS abnormalities were the most common (12/25) congenital anomaly. MSS anomalies with CAKUT were most commonly associated with finger abnormalities (17 cases). [Figure 2] Polydactyly (ten cases), syndactyly (two cases), clinodactyly (two cases), conspiratorial (two cases), scoliosis (three cases), sternum developmental defect (one case), limb absence (three cases), vertebral defect (one case), limb hypoplasia (three cases), developmental defects of ribs (three), pes equinovarus (six cases), and abnormal limb joint positions (15 cases) were all observed.

Anomalies of the CNS came in second with a prevalence of 25.4%. Among 110 cases, 17 cases of neural tube defects (15.45%), including five encephaloceles, four spina bifida, three meningoceles, and two anencephalies, were detected. It shows a higher frequency of neural tube defect (NTD) in cases with ARPRD cases (4/15).

Aside from NTD cases, eight patients had hydrocephalus, three had lateral ventricular dilatation, one had Arnold Chiari Malformation, and one had Dandy-Walker Malformation. Except for NTD, CNS abnormalities were more common in UPD (5/11) cases.

GUT anomalies were observed in the third place with a rate of 22.73%. The most common one was ureteral agenesis (22 cases),

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Table 3: Associated malformations of other organ systems

Renal Anamoly	*Dysmorphism*	*MSS*	*GIS*	*GUS*	*RS*	*CVS*	*NTD*	*CNS*	*Syndrome*	*DİĞER*
N	65	38	20	25	21	18	17	11	22	12
%	59.09%	34,55%	18,18%	22,73%	19,09%	16,36%	15,45%	10%	20%	10,91%
Renal ectopia	1	1	0	0	1	1	0	0	1	1 a
Fusion	5	3	4	0	3	3	2	0	3	0
Renal agenesis	15	10	8	11	7	4	4	1	5	7 b
Renal hypoplasia	4	1	0	3	1	0	0	0	0	0
Renomegaly	0	0	0	1	0	0	0	1	0	0
Hydroureteronephrosis	3	1[c]	0	0	0	0	0	1	0	0
Renal dysplasia	19	12	6	7	5	6	4	3	6	2[d]
ARPKD	9	6	7	2	2	2	4		5	1[e]
Cortical cyst	2	0	1	0	1	1	1	1	1	0
Bladder dilatation	2	1	0	0	0	0	0	1	0	0
UPD-BUVPD	4	4	1		1	1	2	3	1	0
Ureter duplication	1	0	0	1	0	0	0	0	0	0

a: Thymic hypoplasia, b: adrenal and spleen malformation, c: osteochondroplasia, d: choroid plexus papilloma, cystic adrenal gland, e: cavernous hemangioma



Figure 2: Finger abnormalities; syndactyly, polydactyly. dysmorphism findings; ear developmental anomaly

accompanying all RA cases. A total of 28 GUT anomalies were observed. HUN/UPD (seven cases), bladder agenesis (four cases), double ureter (one case), urethra (one case), hypoplastic bladder (three cases), bladder dilatation (one case), undescended testis (three cases), external genital organ agenesis (two cases), uterine anomaly (three cases), urachus remnant (two cases), and bifid scrotum (one case) are among them. Figure 4 is an example of HUN/UPD.

With a rate of 19.09%, the RS came in fourth. Lung hypoplasia was the most prevalent abnormality, which we found in nine patients. Five of the RD cases had SS anomalies, all of which were lung hypoplasia. Seven different respiratory system defects were detected, including pulmonary hypo-lobulation (four cases), CPAM (two cases), diaphragmatic hernia (three cases), and lung aplasia (two cases). The most common RS abnormalities were found in cases of renal agenesis (7/22). In Figure 5, left lung agenesis and pulmonary hypoplasia are given.



Figure 3: Meckel-Gruber; neural tube defect (NTD) case was associated with ARPRD, polydactyly, Potter sequence, hydrocephalus

With a rate of 18.18%, the GIS is in the fifth line among the associated anomalies. Anorectal anomalies were the most prevalent abnormality found in nine patients. Other associated GIS anomalies were congenital hepatic fibrosis (six cases), including five cases linked to ARPKD, tracheal-esophageal fistula (two cases), ectopic pancreas (two cases), hypoplastic/dysplastic pancreas (two cases), and colon agenesis (one case). There were a total of 21 GIS abnormalities discovered. In addition, five of the individuals had an anterior abdominal defect [Figure 6]. The most common link between GIS abnormalities and cases of renal agenesis was found (8/22). According to our findings, GIS anomalies were nearly never accompanied by RE, RH, or UPD instances.

With a rate of 16.06%, CVS anomalies came in sixth. There were 24 CVS anomalies found, including cardiomyopathy (CMP) (one

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Figure 4: HUN/UPD case with ureteropelvic dilation of both kidneys

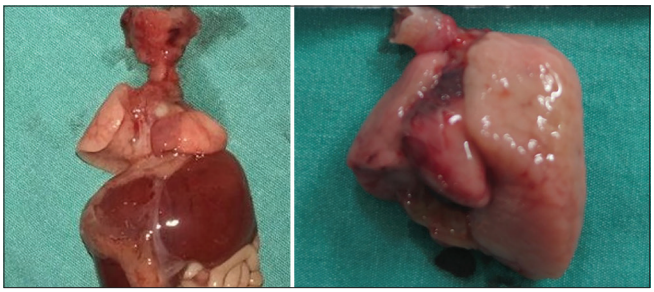


Figure 5: Left lung agenesis (left) and pulmonary hypoplasia (right)



Figure 6: Omphalocele (anterior abdominal defect)

case), transposition of the great arteries (TGA) (one case), pulmonary artery atresia (one case), and hypoplastic heart (two cases). The most prevalent abnormalities were atrial septal defect (ASD) (four cases) and ventricular septal defect (VSD) (four cases). A single umbilical artery was also observed in four cases, two linked to renal abnormalities. RD (6/25) and RF (3/12) are the most common CVS abnormalities.

In addition, one case has spleen agenesis, two instances have ectopic spleens, six cases have adrenal anomalies, three of which have adrenal agenesis, one case has a congenital choroid plexus tumor, one case has a cavernous hemangioma, one case has osteochondroplasia, and one case has thymic hypoplasia.

Phenotypic findings and genetic test results diagnosed trisomy and Turner syndrome cases. The syndrome was diagnosed in 22 CAKUT cases. These are trisomy 13 (three cases), Meckel-Gruber syndrome (MGS) (seven cases) [Figure 3], Down syndrome (one case), prune belly syndrome (one case), hydrolethalus syndrome (one case), hereditary renal agenesis-renal dysplasia syndrome (one case), hereditary renal dysplasia (one case), Turner syndrome (one case), XYY syndrome (one case), fetal notochord syndrome (one case), polysplenia syndrome (one case), Townes-Brocks (one case), pentalogy of Cantrell syndrome (one case), Di George (one case), and VACTERL association was detected in two cases [Table 4]. Prenatal radiological images and autopsy findings diagnosed other syndromes and associations.

DISCUSSION

While the incidence of CAKUT is reported to be 3–4% in studies involving babies in the neonatal period after delivery, it jumps to 10% in studies involving postmortems.[11,14]

Our investigation found CAKUT in 110 (9.3%) of the 1180 autopsy cases examined. This percentage has been found to range from 6.1% and 27% in the literature.[15,16] Although a few articles claim lower rates, CAKUT was significantly more common in studies that included postmortem investigation.[11,13,17,18]

RA, RD, and ARPKD have relatively poor prognoses. As a result, these are the most frequently observed CAKUT cases in autopsy research. The most common CAKUT cases encountered in autopsy studies were renal dysplasia cases. Male predominance and bilaterality have been reported in these.[13,19,20] These cases appear more frequently in autopsy investigations due to their incompatibility with life, especially when bilateral and/or part of a syndrome.

Our study found the syndrome more frequent in those with RD and RA, which is consistent with the literature.[13]

RA was the second most common CAKUT in our investigation and the other partner of the most prevalent CAKUT ranking in the literature. The incidence of RA was 1.84% in all autopsies in our sample, which is consistent with the literature.[13,16,17] This percentage is higher than research involving the general population, especially regarding bilaterality, which is incompatible with life. Bilaterality was 1.01% in our study, which is consistent with the literature.[12] Male gender predominated in both the literature and our investigation.[6,11,19]

ARPKD was reported in 1.27% of all autopsy cases and 13.64% of CAKUT cases in our autopsy study group, which is greater than other autopsy investigations.[13,16] ARPKD had similar macroscopic and microscopic properties to those described by Husayin A. and

Table 4: Detailed findings of recognized syndromes

Syndromes	*CAKUT*	*Dysmorphism*	*Other Findings*
Hydrolethalus	Renal dysplasia, UPD	Potter, maxillary hypoplasia, midline defect	Polydactyly, colon agenesis, pituitary agenesis, lateral ventricular dilatation, pulmonary hypoplasia
Prune belly syndrome	Renal dysplasia		Not seen
Fetal notochord syndrome	Fusion (horseshoe kidney)		Omphalocele CCAM type 3 anencephaly
Meckel-Gruber syndrome (MGS)	ARPKD	Microcephaly	Polydactyly, pulmonary hypoplasia, encephalocele
Meckel-Gruber syndrome (MGS)	Renal dysplasia		Polydactyly anencephaly
Meckel-Gruber syndrome (MGS)	Fusion (horseshoe kidney) renal agenesis	Potter, hypertelorism	Arnold Chiari Type 2, cerebellar herniation meningomyelocele clinodactyly (R-L), pes equinovarus (R-L), simian line
Meckel-Gruber syndrome (MGS)	Fusion (horseshoe kidney)	Foot inversion low ear	Diaphragm hernia situs inversus thoracal-lumbal NTD
Meckel-Gruber syndrome (MGS)	Renal dysplasia	Potter	Pes equinovarus, encephalocele
Meckel-Gruber syndrome (MGS)	ARPKD		Hypomelia, polydactyly, external genital agenesis, CMP, meningomyelocele

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Pysher T.[12] Hepatic fibrosis is frequently related to ARPKD.[13] Hepatic fibrosis was also present in five of our instances. The recurrence rate of ARPKD in subsequent pregnancies is around 25%, and postmortem detection is a critical factor in subsequent pregnancies.[21]

Previous investigations could not reach a clear consensus on the frequency of renal hypoplasia because it was included along with dysplasia in certain publications. When RH is unilateral, it is usually sporadic, and no abnormalities in the lower urinary tract are present. When it is bilateral, it is lethal.[12] Our investigation found seven RH, one of which was bilateral, which contradicts the literature. Three of the six unilateral RH patients had lower urinary tract anomalies, and one had laryngeal atresia.

Fusion abnormalities were found at a rate of 1.01% in all autopsy cases and 10.9% in CAKUT cases in our investigation, which is consistent with other studies.[11,16,17] The most prevalent kidney in the literature is the horseshoe kidney, which has been observed to be more common in men.[12,19] Despite most of our cases having horseshoe kidneys, like in the literature, they are female-to-male in gender and do not fit the literature.

On average, 85.46% of CAKUT fetuses had renal parenchyma-related anomalies (agenesis, polycystic kidney disease, and horseshoe kidney), while 14.54% of CAKUT fetuses had pelvic-ureteral system malformations. This rate is lower than reported in the literature.[11,17,22] The number of pelvic abnormalities and renal aberration instances is 38 (36%), consistent with the literature.[17,22]

In our study, 84 (76.3%) subjects had a disease in at least one other organ system. This link was found in every incidence of renal agenesis. Associations with other anomalies have been observed in a broad spectrum of autopsy studies, ranging from 10% to 100%.[13,16,19,22]

While oligohydramnios is the most common antenatal finding of CAKUT, postnatal findings include abdominal bulk, single umbilical artery, abdominal wall muscle abnormalities, and undescended testis.[22,23] In our investigation, abdominal wall muscle defects were found in five patients (4.5%), which was greater than the literature rate, which was reported to be lower in the literature (2.3% to 3.79%).[9,13]

A single umbilical artery has been linked to various defects, most notably urinary system pathologies.[24] A single umbilical artery was discovered at a rate of 3.6% in our study. Even though the rates reported in the literature differ, this link was highlighted.[13,16]

In this study, NTDs were the most common CNS anomaly, consistent with the literature.[9,13,19] The most prevalent organ system anomaly associated with NTD was observed in studies that included abnormalities associated with NTD.[25] We believe that common etiological factors such as maternal folate insufficiency caused by food or the use of anti-folate medicines, as well as a common genetic condition like ARPKD, are to blame for this link.[5] Our research found that NTD was most frequently associated with ARPKD cases (26.6%).

According to the literature, the Potter sequence was the most common dysmorphic finding, accounting for 27.3% of all cases.[9,11,13,15,19]

Only a tiny percentage of our patients have resulted from genetic testing (six cases). Aside from these cases, we also reported 16 syndromic cases for which genetic testing was impossible. In syndromic instances, we found the most RD. The number of samples for which chromosomal analysis was carried out or for which findings were received was limited. As a result, the number of cases with genetically determined chromosomal problems may have been lower than in earlier studies. This rate, however, was comparable with the literature when all syndromic instances (22 cases) were examined.

Although there are variances between studies[19,20,26,27] due to increases in ultrasound resolution and the experience of the physicians performing the imaging, this agreement has risen in recent years. The main limitation of this study is poor genetic data and prenatal USG data. However, plenty of morphological data are available.

Finally, we want to underline that CAKUT and its associated anomalies are not uncommon. As a result, prenatal imaging, genetic investigation, and/or postmortem examination should all be used to screen for CAKUT. This information is helpful for the mother's future pregnancy management as well as parental genetic counseling.

In patients with CAKUT, routine screening for other congenital anomalies, particularly those of the musculoskeletal, central nervous, and digestive systems, should be examined. Genetic counseling is justified in most of these problematic cases.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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APPENDIX

Classification And Definitions Of CAKUT

Renal position

A. Ectopia (cross-fused ectopic kidney, pelvic ectopia) : Abnormal location of the kidneys

B. Fusion (horseshoe kidney): A fused kidney extends across the midline and is fused to the lower pole of the normally positioned contralateral kidney.

Horseshoe kidney: Kidneys are fused posteriorly forming a horseshoe shape

Renal quantity

A. Agenesis (B/U)): Unilateral or bilateral kidney is not developed at all.

B. Hypoplasia (B/U): Kidney weight less than -2 standard deviations according to the gestational week and the kidney contains fewer lobes microscopically

C. Renal tubular dysgenesis: Insufficient or no differentiation of the proximal tubule in the prenatal period.

D. Renomegaly: Increased bilateral kidney size secondary to increased number or size of normally developed nephrons

E. Duplication :The presence of two separate pelves in the same kidney accompanied by complete or partial duplication of the ureter

F. Supernumerary: Being born with an extra kidney

Hydronephrosis: Dilation of the renal pelvis and calyces (>15 mm) secondary to increased urine retention.

Renal dysplasia/cystic diseases (gross and/or microscopic): Presence of primitive structures, immature mesenchymal tissue, lobe anomaly, cartilage tissue

A. Renal dysplasia:
1. Sporadic (bilateral, unilateral)
2. Hereditary
3. With malformation syndromes

B. Polycystic kidney disease: in which there are multiple renal cysts.
1. Autosomal recessive (infantile type)
2. Autosomal dominant (adult type)

C. Medullary cysts:
1. Medullary sponge kidney
2. Medullary cystic diseases

D. Cortical cysts:
1. Glomerulocystic disease (s): histologically by cystic dilation of Bowman spaces and atrophy of the glomerular tufts.
2. Simple cysts: Single cyst
3. Microcysts tubular dilatation: Microcystic dilatation of tubules

E. Renal cysts with hereditary syndromes: Meckel-Gruber syndrome, Joubert syndrome, Fryns syndrome, Zellweger syndrome, glutaric acidemia tip 2, trizomiler, tuberous sclerosis vs von Hippel Lindau syndrome

Congenital malformations of the ureters, bladder, and urethra

1. Anomalies of the bladder:
A. Dilatation: Over-enlarged bladder with flattened urothelium
B. Agenesis: Bladder is not developed
C. Duplication: Two ureteric buds
D. Urachal remnants: Urachal relics
E. Prune belly syndrome: Genetic disorder including cryptorchidism, abdominal wall defects, and findings of genitourinary defects

2. Anomalies of the urethra
A. Posterior valves: The obstructing membrane in the posterior male urethra
B. Atresia: Absence of the urethra

3. Anomalies of the ureter
A. Duplication: Unilateral or bilateral duplication of the ureter and renal pelvis may be accompanied by duplicated kidneys; outlet system may backflow or be clogged
B. Dilatation/ureterocele: A congenital cystic dilation of the intravesical portion of the distal ureter.
C. Atresia: Absence of ureter
D. Ureteral obstruction: Occlusion of the ureter at one point

Renal disease uncertain classification: