

A Hospital Based Cross-Sectional Study to Evaluate the Spectrum of Congenital Anomalies of Kidney and Urinary Tract, and Clinico-Epidemiological Characteristics

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Received: September, 2019

Revised: October, 2019

Accepted: October, 2019

Abstract

Background and Aim: To determine the spectrum of congenital anomalies of kidney and urinary tract (CAKUT) in Indian children, and to evaluate its clinico-epidemiological characteristics.

Methods: A tertiary-care, hospital-based cross-sectional study conducted (November 2016-October 2018) at SCBMCH & SVPPGIP Hospital included children aged ≤ 14 years with a diagnosis of CAKUT. Incidence of individual congenital anomalies and clinico-epidemiological characteristics of each anomaly thus considered were evaluated.

Results: In 140 children, 9 types of congenital anomalies were reported; posterior urethral valve was most common (37.85%) followed by pelvi-ureteric junction obstruction (32.14%) and vesico-ureteric reflux (14.28%). Hypospadiasis (5%), renal agenesis (2.86%), multicystic kidney disease (2.86%), duplication of pelvi-calyceal system (2.14%), horseshoe kidney (1.42%) and ureterocele (1.42%) were other CAKUTs. A total of 68.57% were boys (girls=31.43%). The CAKUTs were observed more in children with: age 1-5 years (32.14%), unilateral disease (45%), and term delivery (67.86%), and in children of mother aged >30 years (58.57%). Diabetes was present in mothers of 4 children (gestational: 2, pre-gestational: 2), hypertension in 3, tobacco use in 5, oligohydramnios in 7 and polyhydramnios in 3 mothers. Majority of the children had asymptomatic (37.86%) manifestation followed by burning micturition (31.43%). Non-renal congenital anomalies were present in 15.71% children (gastrointestinal malformations: 5.71% were most common). Positive family history for CAKUT was seen in 7.8% cases.

Conclusion: The most frequent CAKUTs were posterior urethral valve and pelvi-ureteric junction obstruction in our study. The study also provided the clinico-epidemiological characteristics of CAKUT. These data can be helpful for prenatal counseling and management of CAKUTs.

Keywords: CAKUT; congenital anomalies; child; Indian.

Conflict of interest: The authors declare no conflict of interest.

Please cite this article as: Padhy SB, Pradhan SK. A Hospital Based Cross-Sectional Study to Evaluate the Spectrum of Congenital Anomalies of Kidney and Urinary Tract, and Clinico-Epidemiological Characteristics. *J Ped Nephrol* 2019;7(3):1-8.
<https://doi.org/10.22037/jpn.v7i4.27406>

Introduction

Congenital anomalies are defined as a wide array of functional, structural, biochemical or molecular abnormalities (1, 2). Congenital anomalies of the kidney and urinary tract (CAKUTs), a major group of pediatric diseases, constitute 20-30% of all congenital anomalies and occur in ~1 in every 500 live births (3, 4). CAKUT is responsible for several morbidities including urinary tract infection (UTI),

hypertension, and chronic kidney disease (CKD), and is responsible for 30-60% end-stage renal disease (ESRD) cases in children (3, 4). CAKUTs include renal abnormalities such as pelviureteric anomalies (upper urinary tract), vesicoureteric junction anomalies (lower urinary tract), and bladder and urethral abnormalities (5).

Several maternal, genetic and environmental factors including advanced maternal age, specific complications, abnormal family history, and maternal diseases (gestational diabetes, hypertension) are known to affect the incidence of CAKUTs (6, 7).

The current hospital based cross-sectional study was carried out to determine the spectrum of CAKUTs among the pediatric patients in India, and to evaluate the clinico-epidemiological characteristics of CAKUTs.

Methods

Study Design

This was a cross-sectional study performed over a period of 23 months (between November 2016 and October 2018) at a tertiary care hospital (Srirama Chandra Bhanja Medical College & Hospital [SCBMCH] and Sardar Vallabhbhai Patel Post Graduate Institute of Pediatrics [SVPPGIP], Cuttack, Orissa) in India.

The study was performed after approval from Institutional Ethics Committee and was performed in accordance with the Declaration of Helsinki. Informed consent was obtained from the parents of all participants included in the study.

Study Population

Neonates and children below 14 years of age who were identified with CAKUTs were included in this study. Patients having structural abnormality of the urinary tract which were secondary to any post-natal assaults (urolithiasis, tuberculosis and glomerulonephritis) were excluded.

Children, following the diagnosis of CAKUT, were examined and assessed systematically for the presence of any obvious congenital anomalies clinically related to every organ system.

Diagnosis of CAKUT was based on clinical evaluation by the pediatrician and other appropriate investigations such as pathological laterality and radio-imaging activity using ultrasonography (antenatal ultrasound Doppler studies), plain computed tomography (CT, with or without contrast micturating cystourethrogram), magnetic resonance imaging (MRI, MR urography, MR angiography), or radionuclide scan.

Study Assessments

The study endpoints included the spectrum of CAKUTs. We also evaluated the clinico-epidemiological characteristics of each anomaly

including child age, laterality of disease, maturity at delivery, maternal age at conception, maternal disease (diabetes, hypertension), substance abuse, amniotic volume, clinical manifestations in children, non-renal congenital anomalies and family history.

A detailed antenatal and maternal history including the age of the mother, parity or the history of consanguinity, different maternal medical conditions and habits were obtained by reviewing the maternal records and by interviewing the parents on the below mentioned guidelines:

1. Birth weights: Normal: >2.5 kg, low birth weight (LBW): <2.5 kg; very low birth weight (VLBW): <1.5 kg.
2. Maturity: Babies born at <37 completed weeks (i.e., < 259 days), calculated from the 1st day of the last menstrual period were considered as premature.
3. Standard definitions were used to define oligohydramnios, pregnancy induced hypertension, and diabetes.

The diagnostic criteria for various CAKUT were based on a previous report from India (3). Pelvi-ureteric junction obstruction was defined by an obstructive pattern on diethylenetriamine pentaacetic acid (DTPA) diuretic renography i.e., a curve that rises continuously over 20 minutes or plateaus, despite furosemide administration and post-micturition; posterior urethral valves: the diagnosis was established by a micturating cystourethrography (MCU) showing dilated or elongated prominent posterior urethra; and confirmed by cystoscopy; vesico-ureteric reflux: MCU was performed for confirming the diagnosis of primary VUR. Secondary VUR was excluded by presence of bladder anomalies/ureterocele; other anomalies such as renal hypoplasia/dysplasia, horseshoe kidney, crossed renal ectopia, duplex-collecting system were diagnosed on renal ultrasonogram (3).

Results

Spectrum of CAKUTs

A total of 140 patients with confirmed diagnosis of CAKUTs were included in this study. Altogether 9 types of congenital anomalies were identified. The most common CAKUT was posterior urethral valves (37.85%) followed by hydronephrosis due to a pelvi-ureteric junction obstruction (32.14%).

Vesico-ureteric reflux, not due to any other primary cause, was marked in 14.28% cases. The other congenital anomalies identified were hypospadias (5%), multicystic disease of the kidney (2.86%), renal agenesis (2.86%), duplication of pelvi-calyceal system (2.14%), ureterocele (1.42%) and horseshoe shaped kidneys (1.42%) (Figure 1).

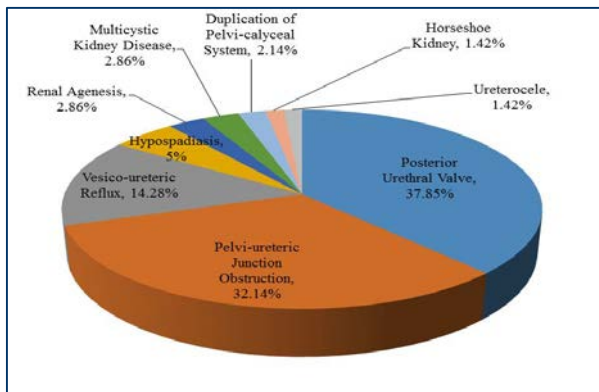


Figure 1. Spectrum of CAKUTs in study group.

Fetal characteristics and outcomes in CAKUTs

Among the study population with CAKUT, 68.57% were boys and 31.43% were girls. The most common age group ranged from 1 to 5 years age (32.14%), ~19% were found to be in their neonatal period and another 27% in infancy.

The youngest patient was 1-day old, having brought early due to diagnosis by antenatal ultrasound.

The oldest patient was 14 years of age.

Of 140 cases, 67 (47.85%) had undergone antenatal ultrasound checkup and 32 (22.86%) were diagnosed or suspected by these prior ultrasonography tests. Of children having renal and ureteric pathologies (n=80), most of the patients were found to have unilateral disease (45%: left sided 26.42%, right sided 18.57%), and 17 (12.14%) children had bilateral anomalies including the ones with horseshoe kidneys (n=2, both female children). About 32% of the children were observed to have been born preterm (<37 weeks of gestational age) (Table 1).

Table 1. Pediatric patients’ characteristics and outcomes in study group

Parameters	N=140 n (%)
Gender	
Boy	96 (68.57)
Girl	44 (31.43)
Age group	
Neonates	26 (18.57)
Infants	38 (27.14)
1-5 years	45 (32.14)
>5 years	31 (22.14)
Antenatal ultrasound done	
Diagnosed	32 (22.85)
Undiagnosed	35 (25)
Maturity at delivery	
Term	95 (67.86)
Preterm	45 (32.14)

CAKUTs, Congenital anomalies of kidney and urinary tract system.

Maternal characteristics and CAKUTs

Congenital anomalies were observed in majority (58.57%) of the cases with maternal age > 30 years. There was no history of use of drugs with teratogenic potential during pregnancy in this study. Five of the mothers were found to be habituated to tobacco use. No abuse of alcohol was documented.

Mothers of 7 of the children were reported having either decreased amniotic fluid volume during the 3rd trimester of pregnancy while 3 of the mothers had increased amniotic fluid volume during that period (Table 2).

Table 2. Maternal characteristics in study group

Parameters	N=140 n (%)
Maternal age at the time of birth	
<20 years	8 (5.71)
20-29 years	50 (35.71)
30-39 years	76 (54.29)
>39 years	6 (4.29)
Substance abuse	
No	135 (96.43)
Yes	5 (3.57)
Amniotic fluid volume during pregnancy	
Normal volume	130 (92.86)
Oligohydramnios	7 (5)
Polyhydramnios	3 (2.14)
Maternal diabetes	
Non-diabetic	136 (97.14)
Gestational diabetes	2 (1.43)
Pregestational diabetes	2 (1.43)
Hypertension in pregnancy	
Non-hypertension	137 (97.85)
Hypertension	3 (2.15)

CAKUTs, Congenital anomalies of kidney and urinary tract system.

Table 3. Clinico-epidemiologic characteristics in study group

Parameters	N=140 n (%)
Asymptomatic	53 (37.86)
Symptomatic	87 (62.14)
Burning micturition	44 (31.43)
Decreased urination	32 (22.86)
Dribbling urination	23 (16.43)
Pain abdomen	14 (10)
Mass abdomen	8 (5.71)
Hematuria	6 (4.29)
Abdominal distention	3 (2.14)
Non-renal congenital anomalies n (%)	22 (15.71%)
Gastro-intestinal	8 (5.71)
Musculo-skeletal	5 (3.57)
Cardiovascular	4 (2.86)
Central nervous system	3 (2.14)
Ophthalmological	2 (1.42)
Family history	
Negative	129 (92.14)
Positive	11 (7.86)

CAKUTs, Congenital anomalies of kidney and urinary tract system.

Mothers of 4 children were identified as having deranged blood sugar levels; 2 of them had pregestational diabetes mellitus and 2 had developed gestational diabetes mellitus. Three

mothers had hypertension at the time of pregnancy; of which 1 had hypertension along with pregestational diabetes mellitus.

Clinico-epidemiologic characteristics in CAKUTs

The largest group of children with respect to specific clinical manifestations was the asymptomatic group of 53 (37.86%) children. These children were diagnosed with CAKUT incidentally on investigation, with or without antenatal suspicion. Amongst the symptomatic children, the most common presentation was burning micturition (31.43%, 44/140) that accounted for 50.57% (44/87) of all symptomatic children. A total of 22 (15.71%) children with diagnosed CAKUT were found to have other associated congenital anomalies; 8 (5.71%) had associated GI malformations (ano-rectal malformations being the most common, found in 5 patients), and 5 (3.57%) had musculoskeletal abnormalities. This study further revealed a positive family history for renal and urinary tract anomalies in 11 cases, about 7.8% of all cases. Table 3 provides the details about clinic-epidemiologic characteristics in this study and its effects on CAKUTs.

Discussion

The current study of pediatric nephrology provides the spectrum of different congenital anomalies in a specific group of pediatric population from one hospital. The pattern and incidence of these anomalies generally varies over time or with geographical location, reflecting a complex interaction of known and unknown genetic and environmental factors including socio-cultural, racial and ethnic variables. In the developing world, with advancements in medical science, we have been successful in curtailing morbidity and mortality due to the associated infectious and nutrition deficient conditions to a great extent. This renders a greater significance to congenital anomalies, in ensuring a safe and sound childhood and a bright future thereafter.

The spectrum of CAKUT in this study showed that the most common anomaly is posterior urethral valve (~38%). This was followed by pelvi-ureteric junction obstruction (~32%) and vesico-ureteric reflux disease (~14%). Hypospadias, renal agenesis, multicystic kidney disease, duplication of ureters, horseshoe kidneys and ureterocele were also reported. The CAKUT spectrum observed in this study slightly differs from a recent Indian study by Radhakrishna and colleagues, (5) where pelvi-ureteric junction obstruction (40%) was the most

common anomaly followed by posterior urethral valve (32%) and vesico-ureteric reflux (19%) (5).

This study finds that CAKUT was present in 69% boys as compared to 31% girls, which is in accordance with previous studies by Karambelkar and colleagues, (60% boys and 40% girls) (8). However, a male preponderance was observed in the study by Radhakrishna and colleagues (boys: 86% vs. girls: 14%) (5). The only exception found in this study, in this respect, was the abnormality horseshoe kidney, wherein both the patients detected with this condition were females, which is found in abundance in males in general (9). The most common age group of presentation in this study was between 1 to 5 years accounting for about 32% of all patients, consistent with the study by Radhakrishna and colleagues (41% in the 1-5 year age group; 28% infants, ~19% aged >5 years and ~10% neonates) (5).

Only 47% of mothers of the patients had undergone an antenatal ultrasound in our study, which could be attributed to the lack of appropriate awareness and ambivalent attitude, particularly among the rural population, this coupled with lack of basic health infrastructure that persists in several nearby regions till date. Only about 23% of total cases and 48% of all cases that had undergone antenatal ultrasound were diagnosed or suspected as having any CAKUT similar to the study by Soliman et al.,(10) that reported diagnosis of ~37% cases antenatally. Radhakrishna et al.,(5) showed that ~93% of the mothers had undergone antenatal ultrasound and about 65% of all the cases and 70% of cases undergoing antenatal ultrasound were either confirmed or suspected of having a CAKUT, contrary to our results.

In our study, about 57% cases were of renal or ureteric origin and 45% of these cases and 26% of all cases had congenital anomaly on the left side and ~19% were right sided. Of the total cases, 12% had bilateral anomalies. Radhakrishna and colleagues, (5) reported 30% left sided lesions of all cases and bilateral cases plus urethral anomalies combinedly constituted 54% of total cases. Melo et al., reported 22% of left sided lesions in their study and 65% urethral diseases and bilateral diseases combined (11).

In our study, 32% of the affected children were found to have been born preterm and almost 68% were term delivery. Karambelkar and colleagues (8) reported 43% of the CAKUT cohort with preterm

delivery. Tain and colleagues, (12) reported ~40% cases of CAKUT in their study to have been preterm (<37 weeks of gestational age).

This study reveals that most (~54%) of the mothers delivered their children diagnosed with CAKUT in the age range of 30-39 years. Around 34% delivered their babies between 20-29 years. Only around 10% of the women were either less than 20 years or 40 years and above. Tain and colleagues, (12) reported similar data with 49% mothers belonging to 30-39 years age group and 47% mothers belonging to 20-29 years age group. Only 4% women were found to have delivered before 20 years or 40 years or thereafter.

Maternal diabetes mellitus has been considered a very significant contributor in the pathogenesis of CAKUT in many of the studies. We report that ~3% of the mothers had deranged random blood sugar either due to gestational diabetes mellitus or pre-existing diabetes. Tain and colleagues, (12) reported only 2% of the mothers in their study as having diabetes. Most of them had gestational diabetes mellitus that was diagnosed in their current pregnancies. Only about 0.5% had pre-established diabetes. Karambelkar and colleagues, (8) did not find any of their patients to be having diabetic mothers. Postoev and colleagues, (13) found that about 5.7% of the CAKUT cases were associated with diabetes in the mother. Shnorhavorian and colleagues, (14) reported 5.88% of their patients with congenital urinary anomalies to be having diabetic mothers. Similarly, 2% of the mothers were hypertensive in our study, which is in line with study by Tain and colleagues, (12) (2.4%), whereas Karambelkar and colleagues, (8) reported that none of the mothers in their study were hypertensive. The use of therapeutic drugs with teratogenic potential has always been considered an important risk factor. However, in this study, no such drug use was documented. The substance abuse and use of alcohol, tobacco and recreational prohibited drugs such as cannabinoids have a key role in the pathogenesis of CAKUT.(15, 16) Our study revealed that about 3.5% of the mothers were addicted to tobacco chewing. No intake of alcohol or recreational drugs was revealed. Karambelkar and colleagues (8) did not document any use of these substances. Tain and colleagues (12) revealed that only about 0.5% of their patient's mothers had substance abuse.

Decreased amniotic fluid volume or oligohydramnios, prior to their delivery, was reported in 5% women. This reflects decreased renal function of urine formation that contributes to amniotic fluid or severe urinary tract obstruction. In contrast about 2% of the women were reported to be having polyhydramnios during their pregnancies. Rest 93% had normal amount of amniotic fluids. Tain and colleagues (12) reported oligohydramnios or polyhydramnios in ~7% of their patient's mothers. Radhakrishna et al.,(5) reported only 2.5% of the mothers in their study to be having oligohydramnios, which is half when compared with our study findings. Karambelkar et al.,(8) reported none of the mothers as having oligohydramnios. Majority (38%) of the patients in our study were asymptomatic. They were either detected prenatally on ultrasound examination or after birth upon being investigated for other disease etiologies or non-specific complaints. Among the symptomatic patients, the most common presentation was that of burning micturation (31%) indicative of UTI and decreased urination (23%) indicative of compromise of renal function. Radhakrishna and colleagues, (5) reported about 32% of their study population to be having asymptomatic disease with incidental finding on radiological investigation, 22% had UTI and 32% had features suggestive of renal compromise. Non-renal anomalies were present in 16% of the patients with gastro-intestinal anomalies being the most common (5.7%). Musculoskeletal (3.5%) and cardiovascular (2.9%) and central nervous system (2%) anomalies were other important anomalies. In the study by Radhakrishna and colleagues, (5) 14% of their patients with CAKUT had extra renal anomalies (5% ano-rectal malformations, 3% undescended testes and musculoskeletal anomalies). Karambelkar and colleagues, (8) reported that 21% of their CAKUT patients had extra-renal malformations.

In our study, a positive family history for renal and urinary tract anomalies was reported in ~8% children who had at least one family member with a CAKUT. These findings are similar to the study by Karambelkar and colleagues, (8) who reported a family association with CAKUT in 12.5% of the patients. Bondagji and colleagues, (17) reported that 7% of the cases had familial affection of CAKUT.

Conclusion

Overall, the most frequent CAKUTs observed in our study were posterior urethral valve and pelvi-ureteric junction obstruction. The study also provided the clinico-epidemiological characteristics of CAKUTs such as male preponderance, age 1-5 years, unilateral disease, term delivery, clinical manifestations, maternal age, preexisting or gestational diabetes, hypertension, tobacco use volume of amniotic fluid in mothers, non-renal congenital anomalies and family history.

Acknowledgements

The authors thank Ms. Bhumi Modi (Lambda Therapeutic Research Ltd.) for drafting the manuscript, Mr. Shreekant Sharma (CMPP™, ISMPP, Lambda Therapeutic Research Ltd.) for medical writing and follow-up with the journal/publisher, Dr. Venugopal Madhusudhana (CMPP™, ISMPP, Lambda Therapeutic Research Ltd.) for additional editorial assistance, and Drs. Jaykumar Sejpal and Mujtaba A Khan (Intas Pharmaceuticals Ltd) for medical review inputs.

Conflict of Interest

The authors declare no conflicts of interest.

Financial Support

The manuscript development was supported by Intas Pharmaceuticals Limited, Ahmedabad, India.

Patient Consent

Informed consent was obtained from the parents of all participants included in the study.

Authors Contributions

SKP takes responsibility for the content of the manuscript, including the data and analysis. SKP and SBP contributed to the acquisition of data, reversion of the manuscript and final approval.

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