RESEARCH PAPER

Clinical Spectrum of Congenital Anomalies of Kidney and Urinary Tract in Children

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Objective: To evaluate the clinical spectrum and patterns of clinical presentation in congenital anomalies of kidney and urinary tract. **Methods:** We enrolled 307 consecutively presenting children with congenital anomalies of kidney and urinary tract at the pediatric nephrology clinic. Patients were evaluated clinically, with serum biochemistry, appropriate imaging and radionuclide scans. **Results:** The most common anomaly was primary vesicoureteric reflux (VUR) (87, 27.3%), followed by pelviureteral junction obstruction (PUJO) (62,20.1%), multicystic dysplastic kidney (51 16.6%), non-obstructive hydronephrosis (32, 10.4%) and posterior urethral valves (PUV) (23, 7.4%). 247 (80.4%) anomalies had been identified during the antenatal period. Another 33 (10.7%) were diagnosed during evaluation of urinary tract infection, and 21 (6.8%) during evaluation for hypertension at presentation. Obstructive anomalies presented earlier than non-obstructive (7 (3, 22.5) *vs* 10 (4, 24) mo: (*P*=0.01)). The median (IQR) ages of presentation for children with PUV (*n*=23), VUR (*n*=87) and PUJO (*n*=62) were 4 (2, 14) mo, 10 (5, 27) mo, and 7 (3, 22.5) mo, respectively. Nine (2.9%) children had extrarenal manifestations. **Conclusions:** The median age at clinical presentation for various subgroups of anomalies indicates delayed referral. We emphasize the need for prompt referral in order to initiate appropriate therapeutic strategies in children with congenital anomalies of kidney and urinary tract.

Keywords: *CAKUT, Hydronephrosis, Multicystic renal dysplasia, Vesico-ureteral reflux.*

Congenital anomalies of the kidney and urinary tract (CAKUT) are an important cause of morbidity in children, and contribute significantly to end-stage renal disease (ESRD). About 30-60% of ESRD in children are due to CAKUT [1-4]. CAKUT includes a wide spectrum of anomalies such as pelviureteral junction obstruction (PUJO), multicystic dysplastic kidney (MCDK), renal hypodysplasia, horse-shoe kidney, ectopic kidney, primary vesicoureteric reflux (VUR), posterior urethral valve (PUV), and vesicoureteral junctional obstruction (VUJO). It is important to diagnose these anomalies and initiate therapy to prevent or delay the onset of ESRD. We therefore, studied the clinical presentation patterns in children with CAKUT. The primary objective of this study was to evaluate the clinical spectrum and patterns of clinical presentation in CAKUT. The secondary objectives were to study the clinical characteristics of obstructive and non-obstructive CAKUT, and to study the extrarenal manifestations in these patients.

Methods

This descriptive study was conducted at the Pediatric Nephrology outpatient clinic of a tertiary hospital from December 2015 through September 2017 after obtaining approval from the Institute Ethics Committee.

The study recruited consecutively presenting children aged <13 years with CAKUT. Children with polycystic kidneys and neurogenic bladder were excluded. Definitions of clinical entities – acute kidney injury (AKI) [5], urinary tract infection (UTI) [6], chronic kidney disease (CKD) [7] and hypertension [8] – were as per standard guidelines.The diagnosis and management of antenatal hydronephrosis was performed as per standard guidelines [9,10]. Weight for age *Z* scores were calculated from WHO growth charts [11]. The diagnostic criteria for various CAKUT were as follows:

(*a*) *PUJO:* PUJO was defined by an obstructive pattern on ethylenecysteamine (EC) diuretic renography *i.e.*, a curve that rises continuously over 20 minutes or plateaus, despite furosemide administration and post-micturition [10].

(*b*) *PUV:* The diagnosis was established by a micturating cystourethrography (MCU) showing dilated or

elongated prominent posterior urethra; and confirmed by cystoscopy.

(*c*) *Primary VUR:* MCU was performed for confirming the diagnosis of primary VUR, and then classified into grades I to V [12]. Secondary VUR was excluded by presence of bladder anomalies/ureterocele.

(*d*) *MCDK*: It was diagnosed by unilateral multiple cysts of varying sizes on ultrasound, with altered echoes without cortico-medullary differentiation; and a DMSA renal scan showing minimal/ no function.

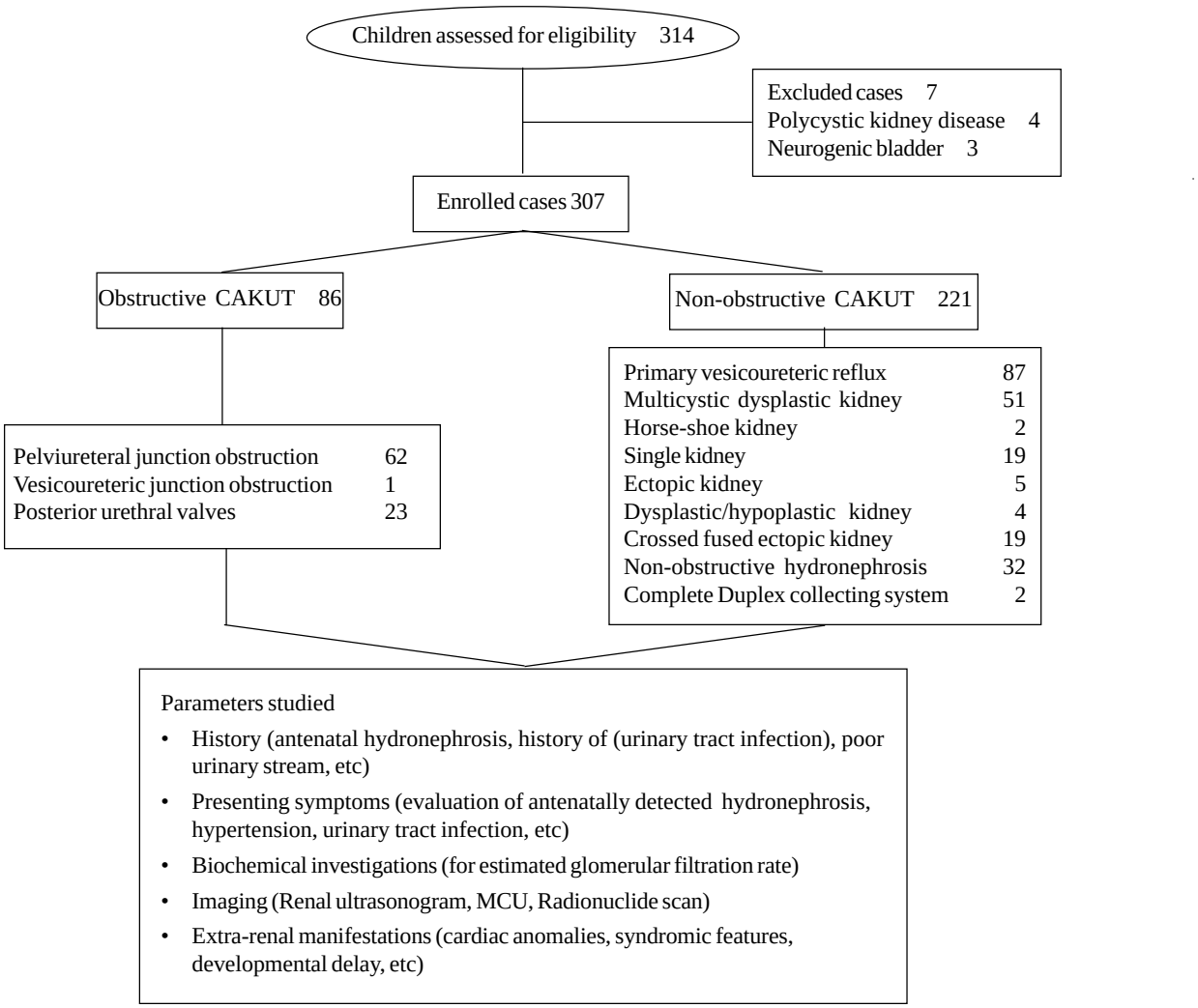
(e) *Other anomalies* such as renal hypoplasia/dysplasia, horseshoe kidney, crossed renal ectopia, duplex-collecting system were diagnosed on renal ultrasonogram.

Clinical and laboratory data were recorded in a cross sectional manner in a pre-designed structured proforma.

Statistical analyses: Normally distributed data was compared by Student's t-test, non-normally distributed data by Mann-Whitney U test, and proportions by chi-square test/ Fisher's exact test. SPSS 23.0 software (SPSS Inc. Chicago, Illinois) was used for analysis.

RESULTS

A total of 307 children with CAKUT were enrolled (***Fig*. 1**). Primary VUR was the commonest anomaly followed by PUJO and MCDK. The median ages of presentation of various anomalies are summarized in ***Table* I**.



MCU: micturating cysturethrogram; CAKUT: congenital anomalies of kidney and urinary tract.

FIG. 1 *Flow chart depicting methodology of the study.*

Out of the 307 children, 247 (80.4%) were detected antenatally. Of this subgroup, 214 children had antenatal hydronephrosis. The others included MCDK (*n*=26), single kidney (*n*=3), crossed fused ectopic kidney (*n*=3) and ectopic kidney (*n*=1). In 33 (10.7%) children, CAKUT was identified during work up for UTI, while in 21 (6.8%), hypertension at presentation led to identification of CAKUT. Eighteen children were incidentally detected to have CAKUT, five were found to have CAKUT during evaluation for low eGFR, one child during evaluation for poor urinary stream at 10 years of age, and one child during evaluation for AKI. In two children, CAKUT was detected during evaluation of nephrotic syndrome (one had primary VUR and another had PUJO).

TABLE I PROFILE OF CHILDREN WITH CONGENITAL ANOMALIES OF KIDNEY AND URINARY TRACT (N=307)

Diagnosis	*No. (%)*	*Gender (male: female)*	*Age at diagnosis (mo) median* (IQR)
Primary VUR	87 (28.3)	54:33	10 (5, 27)
Grade 1	4		
Grade 2	35		
Grade 3	31		
Grade 4	14		
Grade 5	3		
PUJO	62 (20.1)	42:20	7 (3, 22.5)
Unilateral	58		
Bilateral	4		
MCDK	51 (16.6)	29:22	9 (2, 20)
Right sided	34		
Left sided	17		
Non obstructive hydronephrosis*	32 (10.4)	22:10	8 (4, 12)
PUV	23 (7.4)	23:0	4 (2,14)
Single kidney	19 (6.1)	13:6	13 (6, 36)
Crossed fused ectopic kidney	19 (6.1)	11:8	10 (4, 36)
Left to right	12		
Right to left	7		
Ectopic kidney	5 (1.6)	2:3	12 (6,24)
Dysplastic/Hypoplastic kidney	4 (1.3)	4:0	30 (3.75, 70)
Duplex collecting system	2 (0.6)	0:2	8 and 12[#]
Horse-shoe kidney	2 (0.6)	0:2	48 and 158[#]
VUJO	1 (0.3)	1:0	25[#]

*PUV: Posterior urethral valve, PUJO: Pelviureteral junction obstruction, MCDK: Multicystic dysplastic kidney, VUR: Vesicoureteric reflux, VUJO: vesicoureteric junction obstruction; *MCU and EC diuretic Renogram normal;* [#]actual ages.

Among primary VUR (*n*=87), grade 3 was the commonest. Primary VUR was bilateral in 29 (33.7%) children. Three children (3.4%) were diagnosed during CKD work-up; 28 (32.1%) were detected during workup for UTI. The mode of presentation of PUJO (*n*=62) included antenatal detection in 90.4%; incidental detection in 6.5%, following work up of UTI (1.6%) and during evaluation for nephrotic syndrome (1.6%). Bilateral involvement was seen in 6%.Two children had primary VUR in the contralateral kidney. Among MCDK cases (*n*=51), 8 children were incorrectly reported antenatally as hydronephrosis. Three of these cases had primary VUR (2 in contralateral, 1 ipsilateral). Among PUV cases (*n*=23), 86.9% had antenatal hydronephrosis; 78.2% presented with low eGFR.

The median (IQR) ages of presentation for children with PUV (*n*=23), VUR (*n*=87) and PUJO (*n*=62) were 4 (2,14) months, 10 (5,27) months and 7 (3, 22.5) months respectively. Among these three CAKUT categories, 20 (86.9%), 54 (62.1%) and 56 (90.3%) had evidence of hydronephrosis in the antenatal ultrasounds.

Among the 307 enrolled children with CAKUT, weight for age Z-score <-3 was noted in 29 (9.4%) children, while weight for age Z-score between -2 to -3 was noted in 28 (9.1%) children.

Obstructive CAKUT presented earlier than non-obstructive CAKUT (*P*=0.01) (***Table* II**). A greater proportion of obstructive CAKUTs were identified

TABLE II COMPARISON BETWEEN OBSTRUCTIVE AND NON-OBSTRUCTIVE ANOMALIES

	Obstructive (n=86)*	*Non-Obstructive **(n=221)*	*P value*
Antenatal diagnosis	77(89.5)	170 (76.9)	0.01
Male sex	56 (65.2)	140 (63.3)	0.02
UTI	5 (5.8)	28 (12.6)	<0.01
[#$]eGFR	60 (48.3,64.3)	62.8 (60,73.3)	<0.01
Hypertension at *presentation*	7 (8.1)	14 (6.3)	0.12
[#]Age at diagnosis (mo)	7 (3,22.5)	10 (4,24)	0.01

Comprised of Posterior urethral valve, Pelviureteral junction obstruction, and Vesico-ureteric junction obstruction;comprised of primary vesicoureteric reflux, Multicystic dysplastic kidney, Renal agenesis, Renal hypo-dysplasia, pelvic kidney, horse shoe kidney, crossed fused ectopia, Complete duplex collecting system; [$]in mL/min/173m^2; All values in n(%) except [#]median (IQR).*

WHAT THIS STUDY ADDS?

- The most common congenital anamalies of the kidney and urinary tract (CAKUT) in our series were vesicoureteric reflux, pelviureteric junction obstruction, multicystic dysplastic kidney, non-obstructive hydronephrosis and posterior urethral valves.
- About one-fifth of anomalies had not been detected antenatally.
- Obstructive CAKUT presented earlier than non-obstructive CAKUT.

antenatally as compared to non-obstructive CAKUTs (P=0.01). There was a male preponderance in both groups. The proportions of children with UTI in the obstructive versus non-obstructive CAKUT groups were 5.8% versus 12.6% respectively (P<0.01). The median eGFR for obstructive and non-obstructive CAKUTs were 60 (48.3, 64.3) and 62.8 (60, 73.3) mL/min/1.73 m^2 (P<0.01).

Overall, 9 children (2.9%) had extrarenal manifestations. One primary VUR case had Down syndrome, another had VACTERL association. Three children with MCDK had cardiac anomalies [ventricular septal defect (VSD): 2, atrial septal defect: 1], while 2 primary VUR cases had cardiac anomalies (VSD: 1, TOF:1). One child with PUJO had VSD; and 1 child had developmental delay.

DISCUSSION

This cross-sectional study assessed the clinical profile in a cohort of 307 CAKUT cases. Obstructive CAKUTs presented earlier causing significant impairment of e-GFR as compared to the non-obstructive CAKUTs. This finding is comparable to earlier studies [13,14]. Primary VUR was the commonest CAKUT followed by PUJO, MCDK, non-obstructive hydronephrosis and PUV. In contrast, Soliman, *et al*. [13], reported PUV (36.4%) as the commonest followed by primary VUR (19.6%) and PUJO (18.7%). Aksu, *et al*. [15], reported PUJO in 62.7% followed by VUR in 16.6%. It is notable that we encountered quite delayed presentations of various CAKUTs, particularly PUV and PUJO. This can be inferred from the fact that though a majority of these CAKUTs had evidence of antenatal hydronephrosis, their median age at presentation to us was at a much later point of time. A significant number of children had low eGFR or hypertension at presentation, which is comparable to a previously published report [15]. Though a significant number of children were detected antenatally, approximately 19.5% of the CAKUTs had not been antenatally identified, and a majority of this sub-group were identified after UTI.

We encountered significant number of MCDK cases (16.6%) in contrast to previously reported studies [13], possibly due to a referral bias. We also found only 2.9% prevalence of extrarenal features in children with CAKUT. These extrarenal anomalies were detected in primary VUR, PUJO and MCDK cases, but not in children with PUV. This finding is different from a previous Egyptian report, wherein 57% of 107 CAKUT children had extrarenal features. The reasons for this could be related to different ethnicity. The parental consanguinity in our study cohort was 21% whereas it was 50.5% in this report [13].

There is paucity of published studies on the profile of CAKUT from India; and this study provides valuable information regarding this subject. Our study has few limitations. The study was conducted at referral hospital and the profile of enrolled subjects may not be representative of the disease profile at the community level. Also, we could not perform genetic testing of patients enrolled in this study.

It is known that a percentage of milder forms of CAKUT can be diagnosed later in life. Nevertheless, the median ages of presentation (despite a majority of them having had evidence of antenatal hydronephrosis) suggests a delayed referral. This study emphasizes the need for prompt referral by trained professionals in order to initiate appropriate therapeutic strategies in children with CAKUT and improvise the care bundle provided to these children.

Contributors: BHK: collected the data and drafted the first version of the manuscript; SK: conceptualized the study, was responsible for medical management of the cases, interpreted the data and critically revised the manuscript. RA: confirmed the radiological findings and critically reviewed the manuscript. VC: responsible for surgical management of cases and critically reviewed the manuscript. All authors approved the final version of the manuscript, and are accountable for all aspects of the study. SK: shall act as guarantor of the paper.
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