CONGENITAL RENAL AND URINARY TRACT ANOMALIES IN SELECTED NEONATES

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ABSTRACT

BACKGROUND

Congenital anomaly of kidney and urinary tract (CAKUT) are among the most common anomalies diagnosed prenatally. Early diagnosis and timely intervention can preserve renal function and avoid morbidity.

AIMS AND OBJECTIVES

To screen, select at-risk newborns for congenital renal and urinary tract anomalies by postnatal ultrasound and to study the pattern of distribution, clinical presentation and its correlation with antenatal scan.

MATERIALS AND METHODS

It was a prospective study. Postnatal ultrasound of 40 subjects fulfilling the inclusion criteria was performed on 4th day of life. Postnatal ultrasound findings were compared with antenatal records and immediate postnatal clinical course was assessed.

RESULTS

Out of 40 high-risk selected screen patients, 14 subjects were identified to have CAKUT on postnatal USG on 4th day of life. Hydronephrosis was the most common congenital renal anomaly with statistically good correlation with antenatal and postnatal scan (P <0.0001). Mild hydronephrosis detected on antenatal scan (with anterior pelvic diameter 7-9 mm) showed resolution on postnatal ultrasound in 3 subjects. The congenital anomalies in 4 cases were missed on antenatal USG. The number of LBW babies in the screened population was 60% and 64% babies with CAKUT were LBW. Family predisposition was seen in 12.5% of CAKUT population.

CONCLUSION

Congenital renal and urinary tract anomalies can be easily identified on antenatal and post natal ultrasound. LBW babies with family history of CAKUT or high-risk factors warrant radiological screening and biochemical evaluation. Hydronephrosis is the most common finding consistent in both the scans and had a good resolution rate. Prenatal screening would help in early identification of CAKUT anomalies and possible early surgical or medical intervention to prevent or slow ESRD.

KEYWORDS

CAKUT (Congenital Anomaly of Kidney and Urinary Tract), Antenatal Hydronephrosis, ESRD (End Stage Renal Disease), LBW (Low Birth Weight), Antenatal Sonography, VUR (Vesicoureteric Reflux), PUJ (Pelvic Ureteric Junction).

HOW TO CITE THIS ARTICLE: Karambelkar GR, Malwade SD, Agarkhedkar S, et al. Congenital renal and urinary tract anomalies in selected neonates. J. Evid. Based Med. Healthc. 2016; 3(25), 1152-1157. DOI: 10.18410/jebmh/2016/264

INTRODUCTION: Congenital anomalies of kidney and urinary tract (CAKUT) occur frequently. They comprise a wide spectrum of structural and functional malformations that result from faulty renal system development. Some forms of CAKUT occur in combination of multiorgan malformation syndrome and most are nonsyndromic.[1] They constitute 15-20% of all prenatally diagnosed congenital anomalies.[2]

Submission 28-02-2016, Peer Review 14-03-2016,
Acceptance 22-03-2016, Published 28-03-2016.
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DOI: 10.18410/jebmh/2016/264

In the absence of any systemic disease, the prevalence of congenital anomalies of the kidney and the urinary tracts is found to be around 0.1% with antenatal ultrasonography[3] and over 1% with postnatal ultrasonography.[4]

They are responsible for 34-59% of chronic kidney disease and 31% of end-stage renal disease in children.[1] They not only affect growth but also affect maturation and cognition. They are cause of an enormous distress to the family and levy huge financial burden for treatment.

The epidemiological prevalence of CAKUT in the developing world is lacking. More so over there are no studies in high risk population to estimate their prevalence, clinical course and outcome in the developing world. Thus, this study was planned to help in early detection of congenital renal and urinary tract anomalies in high-risk

subjects. It also aimed at finding out accuracy of antenatal ultrasonography and to assess the immediate postnatal outcome of babies diagnosed with CAKUT.

MATERIAL AND METHODS: It was a prospective observational study conducted in 40 at-risk selected subjects in a tertiary care medical college over a period of two years from July 2012-July 2014. The written informed consent from the parents and approval from the institutional ethical committee was obtained.

Newborns who fulfilled inclusion criteria were termed as high-risk for this study. Newborns with family history of renal disease like polycystic kidney, history of congenital anomalies in previous siblings, positive history of consanguinity, history of antenatally detected oligohydramnios in the mother during the second and third trimester, antenatally diagnosed congenital renal or urinary tract anomaly, history of passage of first urine after more than 48 hours of birth, single umbilical artery, patent urachus, external ear anomalies and other associated congenital anomalies were enrolled in the study. Newborns, who did not fulfil the above criteria and whose parents refused to participate in the study were excluded from the study.

A detailed obstetric history of any risk factor for development of congenital renal or urinary tract anomalies like history of oligohydramnios, poor weight gain or hypertension, diabetes, obesity, increase salt intake, alcohol consumption, exposure to teratogens, etc. during pregnancy was obtained from mother's hospital records.

The demographic variables which included age, weight, gravida, parity and consanguinity were recorded on a separate proforma. Standard definitions were used to define oligohydramnios, pregnancy induced hypertension, diabetes and obesity. Consanguinity was present if marriages were between cousins or niece and uncle. Details of postnatal events including gestational age, Apgar scores, birth weight were recorded and a thorough clinical examination was performed as per proforma. Presence of other associated congenital anomaly was also documented and was confirmed.

A postnatal ultrasonography was performed by a skilled observer using the ALOKA Prosound alpha 6 ultrasound machine having a frequency of 3 to 7 MHZ using curvilinear probe. It was performed on day 4-5 after birth as per the guidelines of the Paediatric Nephrology Society, as earlier evaluation would miss the diagnosis due to physiological dehydration.[5]

CAKUT in this study comprises of renal dysplasia, hydronephrosis, abnormalities of migration, abnormalities of the urethra and bladder and abnormalities of collecting systems as well as obstructive mega ureters.

The kidneys were assessed for their presence or absence, dimensional abnormality, presence or absence of normal renal echotexture, accompanying abnormalities such as cysts or tumours, the ureters were checked for any ureteral dilatation, duplication and ureterocoeles. The urinary bladder was checked for abnormalities in shape and wall. The anomalies of the urethra were also assessed and documented.

Hydronephrosis was defined and graded using renal APD (anteroposterior diameter) diameter in antenatal sonography and APD or SFU grade during postnatal evaluation. The subjects with hydronephrosis were classified into mild, moderate and severe hydronephrosis as per Society of Foetal Urology grading.

Antenatal hydronephrosis was present if the APD is >4 mm in second trimester and >7 mm in the third trimester. This is in accordance with the classification based on renal pelvic anteroposterior diameter, that is 4-6 mm in second trimester and 7-9 mm in third trimester was considered mild hydronephrosis; 7-10 mm in second trimester, 10-15 mm in third trimester as moderate. Severe hydronephrosis was considered if APD >10 mm in second trimester and >15 mm in third trimester.[6,7]

The ultrasonographic findings of postnatal scans were compared with antenatal scans that were performed as per the Society of Foetal Medicine 2013 guidelines for second trimester anomaly scan between 18-20 weeks of gestation, and were confirmed in the third trimester scans.[8] Blood was drawn aseptically in all subjects for assessment of renal biochemical abnormalities on postnatal day 4 or day 5. All subjects were followed up for three months to assess short-term outcome which included their growth monitoring, biochemical parameters and a repeat USG evaluation. All subjects diagnosed with CAKUT were put on the antibiotics prophylaxis as per the guidelines.

The collected data was analysed using the SPSS software (Statistical Package for the Social Sciences, version 2.1). The demographic variables were expressed in numbers and percentages. P values less than 0.05 were considered statistically significant.

RESULTS: In this prospective study, 40 eligible newborn infants were enrolled. Table 1 provides the demographic and clinical characteristics. The post natal scan demonstrated presence of congenital renal or urinary tract anomaly (CAKUT) in 14(35%) subjects. There was a male preponderance in the study as well as in CAKUT cohort, with 24(60%) males and 16(40%) females in study population and 10(71%) males and 4(29%) females in CAKUT cohort. Mean gestational age was 36.6 weeks. Of those 14 subjects with CAKUT, 9(64%) were low birth weight babies (weight <2.5 kg) and two (14%) subjects had history of some congenital renal disease in the family. Other associated congenital anomalies were present in 7(17.5%) subjects of study population including 3(21%) out of 14 in CAKUT cohort.

The postnatal scan demonstrated presence of congenital renal or urinary tract anomaly in 14(35%) subjects. The anomalies identified were as per Table 2. Hydronephrosis was found to be most common renal anomaly in these subjects (71%). The records of antenatal sonography demonstrated hydronephrosis in 11 subjects (27.5%), which was confirmed in 10 subjects (25%) on postnatal ultrasound. Three subjects (7.5%) having mild

hydronephrosis (APD diameter 7-9 mm) on antenatal scan demonstrated resolution of the anomaly on post natal scan while one hydronephrosis which was missed on antenatal scan was picked up postnatally. There was a statistically significant correlation between antenatal and postnatal scan (P <0.0001). Four cases with CAKUT (10%) were missed antenatally. The anomalies that were missed on antenatal scan were bilateral hydronephrosis with hydroureter with VUR (n=1), ectopic kidney (n=2) and PUJ obstruction (n=1). Disorders of parenchymal disease (dysplastic or hypoplastic kidney) and migration defects were uncommon.

Oligohydramnios was observed in 11(27.5%) subjects in study population. There was no history of any other maternal risk factors observed in the mothers antenatally.

The subject's demonstrating CAKUT anomalies on postnatal ultrasound showed persistence of the anomaly on subsequent followup scan. Renal function tests were normal in all 40 subjects including 14 subjects of congenital renal or urinary tract anomalies at birth. Three subjects (21%) in CAKUT group, each with hypoplastic kidney, dysplastic kidney and bilateral hydronephrosis with hydroureter demonstrated deranged renal function test on biochemical evaluation at around 3 months of age (Table 3). The renal parameters were normal in unilateral disease and other milder form of diseases. All the subjects achieved appropriate anthropometry centiles on growth charts at 3 months of age. There was no mortality or morbidity during the study period.

Baseline and clinical characteristics	Total (n=40)	Neonates with CAKUT (n=14)	Neonates without CAKUT (n=26)
Gender			
Male	24(60%)	10(71%)	14(54%)
Female	16(40%)	4(29%)	12(46%)
Gestational age			
Preterm	16(40%)	6(43%)	10(38%)
Term	24(60%)	8(57%)	16(62%)
Birth weight			
<2500 g	26(65%)	9(64%)	17(65%)
> 2500 g	14(35%)	5(36%)	9(35%)
Consanguinity			
Yes	0	0	0
No	40(100%)	14(100%)	26(100%)
Family history			
Yes	5(12.5%)	5(12.5%)	0
No	35(87.5%)	9(87.5%)	26(100)
Oligohydramnios			
Yes	11(27.5%)	0	11(27.5%)
No	29(72.5%)	14(100%)	15(72.5%)
Other maternal risk factors (PIH, Diabetes, Smoking/alcohol, Obesity)			
Yes	0	0	0
No	40(100%)	14(100%)	26(100%)
Other congenital anomalies			
Yes	7(17.5%)	3(21%)	4(15%)
No	33(82.5%)	11(79%)	22(85%)

Table 1: Demographic distribution clinical characteristics of study group

Type of defect	Findings	Antenatal USG (n=13)	Postnatal USG (n=14)	P Value
Abnormalities of urinary collecting system (Hydronephrosis)				< 0.0001
1. Vesico ureteric junction obstruction	Right Hydronephrosis+Hydroureter	2	2	
2. Posterior urethral valve	B/L Hydronephrosis with Hydroureter with VUR	0	1	
3. PUJ obstruction	Right PUJ obstruction	1	1	
	Left PUJ obstruction	1	2	
	PUJ narrowing	1	1	
	Right Hydronephrosis with Cortical thinning	1	1	
	Right Hydronephrosis	3	1	
	Left Hydronephrosis	2	1	
Deformity of renal parenchyma	Right hypoplastic kidney	1	1	
	Right dysplastic kidney	1	1	
Migration defects	Left ectopic kidney	0	1	
	Right ectopic kidney	0	1	

Table 2: CAKUT anomalies identified on USG in study group

	At birth		At 3 months	
	Normal	**Deranged**	**Normal**	**Deranged**
Newborns without CAKUT (26)	26 (100%)	0	26 (100%)	0
Newborns with CAKUT (14)	14 (100%)	0	11 (79%)	3 (21%)
Total (40)	**40 (100%)**	**0**	**37(79%)**	**3(21%)**

Table 3: Renal biochemical abnormalities in study subjects

DISCUSSION: The study investigated the presence of congenital anomaly of kidney and urinary tract in at-risk selected babies. The incidence of CAKUT in selected population in our study is 35%. Earlier studies in literature have reported the incidence of CAKUT as 3-6 per 1000 live births in general population.[8-16] This increase in incidence in selected at-risk babies may not be a true reflection of the incidence as there are a large number of deliveries that take place at home.

Hydronephrosis was the most common anomaly identified on postnatal scan (71%) that correlated well with the antenatal records (78%). PU junction obstruction was the most common cause of hydronephrosis. A similar observation was also made in a study by Nabeel S. Bondagji,[17] where hydronephrosis was reported in 51.1% and antenatal diagnosis was confirmed postnatally in 90.1% of all CAKUT cases. Blyth et al, Sairam et al, Chandran and Levi et al also reported that the incidence of hydronephrosis varied between 0.6-4.5% in non-selected population.[18,19,20,21]

The severity of hydronephrosis was graded as per APD diameter. Mild variants with APD diameter <10 mm on antenatal scans of this anomaly were transient and resolved spontaneously on subsequent followup scans. In a systemic analysis on 25 studies by Sidhu et al,[22] it was demonstrated that isolated ANH resolved in 98% patients with APD <12 mm as compared to 51% with larger APD. In 2 other studies by Elder JS and Koff SA,[2,23] it was reported that antenatally detected dilatation was transient and resolved spontaneously in more than 50% of cases.[27-28] Severe forms of hydronephrosis (APD>12 mm) persisted on postnatal scans. A recent meta-analysis by Lee et al[24] reported that every dilatation of the urinary tract irrespective of the degree was associated with an overall increased risk of underlying uropathy, up to (36%). Thus, prenatal diagnosis of any form of hydronephrosis warrants for a critical followup postnatally for prevention of urinary infections and further renal damage. Dysplastic kidney disease and ectopic kidney were the other anomalies identified in our study as also in various other studies.

Duplicate urinary collecting system, followed by hydroureter and pelvic kidney were the most likely abnormalities to be missed antenatally. Four cases (10%) were missed in this study that include disorders of migration-ectopic kidney (n=2), bilateral hydronephrosis with hydroureter with VUR (n=1) and PUJ obstruction (n=1). 9.9 % cases were missed in Bondagji study.[17] This reiterates the importance of postnatal scans in high-risk groups.

There was a male predominance amongst the subjects screened for CAKUT in the study that was also reported in other studies by Nabeel S. Bondagji,[17] Hsain-Lan Chein,[25] Chandran[20] and Hindryckx.[26]

The maternal risk factors like diabetes, obesity, alcohol consumption and exposure to teratogens were not observed in the study though a positive family history of renal diseases was obtained in five subjects suggestive of a genetic predisposition. There is a familial occurrence of nonsyndromic CAKUT reported in various studies. All the 5 familial cases were of nonsyndromic CAKUTs and there are reports in the literature of occurrence of high incidence of CAKUT and diverse forms of CAKUT in the same family suggesting specific genetic mutations but the final phenotype is influenced by genetic or environmental factors.[27-31]

In the multi-centre European study by Wiesel et al.[16] it was observed that there was an association of CAKUT and non-renal congenital anomalies in about 30% of cases. The present data showed the presence of non-renal congenital anomalies in 17.5% of the study population and 21% of CAKUT cohort. Ear anomalies were the most common anomaly, consistent with reports from other studies.[16]

Oligohydramnios was observed in 27.5% of study population. There is high association of oligohydramnios and renal anomalies in reported studies but in our study none of the mothers with oligohydramnios had babies with renal abnormalities. The possible explanation for this could be that none of the study group babies had renal agenesis and severe renal outflow tract obstruction.

Although biochemical parameters were normal at birth for most of the babies, cases with renal parenchymal disease- hypoplastic and dysplastic kidney, or bilateral disease progressed to have deteriorating renal function on followup as early as 3 months (n=1). One baby had fulguration for severe PU Valve during the study period while rest of the babies were managed conservatively.

There was high incidence of low birth weight babies in this study (65%). A longitudinal study from Finland showed the risk of ESKD is increased to 70% in LBW babies whereas the risk in normal weight babies is 30-40%. The outcome of CAKUT in LBW babies is associated with higher morbidity.[32]

Prenatal diagnosis by ultrasound at the hands of skilled observer remains a good diagnostic modality to identify CAKUT though unfortunately this facility is accessible to only 50% of pregnant mothers as per NFHS III data.[33] The true burden of these anomalies becomes obvious only when symptoms of chronic kidney disease have manifested. Early screening and diagnosis may allow the opportunity to suggest the best medical and/or surgical treatment to be implemented as rapidly as possible, preventing or at least slowing down an evolution toward chronic kidney disease.

There are limitations to this study. The sample size is small and we have taken only high-risk population. Long term followup of these patients was unavailable due limited study period.

CONCLUSION: Antenatal ultrasound is an effective modality for screening of CAKUT. LBW babies with family history of CAKUT or high-risk factors warrants postnatal radiological and biochemical evaluation of urinary tract. There are potential clinical implications for the study findings. Among the notable finding was the highest incidence of hydronephrosis antenatally as well as postnatally. There is a good resolution rate with mild hydronephrosis. We encourage further research in this select population to find out the epidemiological burden of CAKUT in developing world for early intervention and better outcome.

ACKNOWLEDGEMENT: The authors thank the families for their participation in the study. We thank the Department of Radiology, the Department of Urology and Nephrology and the Department of Obstetrics and Gynaecology for their help. We also thank the hospital staff for their cooperation to collect the data.

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