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Comparative Study between Obstructive and Non-Obstructive Renal Anomalies Among a Group of Iraqi Children

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Abstract

Background Congenital anomalies of the kidney and the urinary tract (CAKUTs) are relatively common birth defects and account for 40-50% of the etiology of chronic kidney disease (CKD) in children worldwide.

Objective To study the types of renal anomalies (RA) and to compare between obstructive and non-obstructive RA in relation to demographic data and complications.

Methods A descriptive study conducted in Al Imamein Kadhimein Medical City spanning the period from the 1st of February 2020, to the 30th of July 2020. Data collected were: type of renal anomaly, age of diagnosis, family history of RA, consanguinity, clinical presentation and associated complications.

Results In this study, 160 patients were included. Males were more affected than females 1.54:1. Most of the patients, 78 (48.8%), diagnosed were ≤5 age group. Most of the patients, 124 (77.5%), had negative family history, vesicoureteral reflux (VUR) was the commonest anomaly detected in 67 patients (41.9%), followed by renal agenesis in 24 patients (15.0%). Urinary symptoms were most common presentation in 93 patients (58.1%). A higher complication was urinary tract infection (UTI) (62.5%). Comparison between obstructive and non-obstructive RA, reveled age of diagnosis and hydronephrosis has significant difference. While family history, UTI, failure to thrive, and chronic kidney disease stages was not significant.

Conclusion The commonest renal anomaly was VUR, the most prominent complication was UTI. Gender, age of diagnosis and hydronephrosis has significant difference between obstructive and non-obstructive RA.

Keywords Renal, anomalies, children

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List of abbreviations: CAKUT = Congenital anomalies of the kidney and the urinary tract, CKD = Chronic kidney disease, ESRD = End-stage renal disease, FTT = failure to thrive, GFR = Glomerular filtration rate, HN = Hydronephrosis, MCDK = Multicystic dysplastic kidney, PUJ = Ureteropelvic junction obstruction, PUV = Posterior urethral valve, RA = Renal anomalies, UTI = Urinary tract infection, VUR = Vesicoureteral reflux

Introduction

Congenital anomalies of the kidney and the urinary tract (CAKUTs) are relatively common birth defects observed in 3-6 per 1,000 live births and account for 40-50% of the etiology of chronic kidney disease (CKD) in children worldwide [1-2].

Many different developmental abnormalities are classified as CAKUT, including underdevelopment or absence of a kidney (renal hypodysplasia or agenesis), a kidney formed of fluid-filled sacs called cysts {multicystic dysplastic kidney (MCDK)}, swelling

of the kidney resulting from the inability of urine to drain from the kidney into the bladder {hydronephrosis (HN)}, an extra ureter leading to the kidney (duplex kidney or duplicated collecting system), a blockage in a ureter where it joins the kidney {ureteropelvic junction obstruction (PUJ)}, an abnormally wide ureter (megaureter), backflow of urine from the bladder into the ureter {vesicoureteral reflux (VUR)), and an abnormal membrane in the urethra that blocks the flow of urine out of the bladder {posterior urethral valve (PUV)} [3].

The genes most commonly associated with isolated CAKUT are PAX2, which is also associated with renal coloboma syndrome. [4,5].

Inheritance of CAKUT is complex and not completely understood. About 10-20% of cases are thought to occur in families. When inherited, CAKUT most commonly follows an autosomal dominant pattern, less commonly follows an autosomal recessive pattern, while in many cases, the inheritance pattern is unknown or the condition is not inherited [6,7].

It is important to diagnose these anomalies early and initiate therapy to minimize renal damage, prevent or delay the onset of end stage renal disease (ESRD), and provide supportive care to avoid complications of ESRD [8].

This research aimed to study the types of renal anomalies (RA) in relation to clinical presentations, age of diagnosis, family history and complications and to study the difference between obstructive and non-obstructive types of RA according to demographic data and complications.

Methods

This descriptive study included 160 children with RA who were recruited at Pediatric Nephrology Clinics of Al Imamein Al-Kadhimein Medical City, Central Child Teaching Hospital, Child Wellfare Teaching Hospital and Karbala Pediatric Teaching Hospital spanning the period from the 1st of February 2020 to the 30th of July 2020.

A direct interview with the patients themselves or their parents, also review of patient's files; collecting the following data: type of renal anomaly, age of diagnosis, family history of renal anomalies, consanguinity, clinical presentation and associated complications.

Height and weight measurements for all patients was done. The following investigations: renal function test (blood urea, serum creatinine), urinalysis and urine culture, in addition to prenatal ultrasound.

The patients were categorized into two main groups:

Group 1: Obstructive anomalies including PUV, PUJ, VUJ, ureterocele, duplex system, megaureter.

Group 2: Non-obstructive anomalies including VUR, renal agenesis, MCDK, polycystic kidney diseases, renal hypoplasia, ectopic kidney, horse-shoe kidney, ectopic ureter.

Of the 160 studied patients with RA, 23 patients of them had combined renal anomalies; 14 patients out of these 23 had combined obstructive and non-obstructive, accordingly these 14 patients were excluded from comparison of obstructive and non-obstructive to avoid fallacies.

Urinary tract infection (UTI) was considered positive when patient had symptoms and findings on urinalysis, confirmed by a urine culture [9,10]. The diagnosis of failure to thrive (FTT) is considered if a child's weight is below the 5th percentile [11].

Reference values for normal blood urea and serum creatinine according to age was applied. [12]. Stages of CKD, was categorized according to estimated glomerular filtration rate (GFR) based on serum creatinine using Schwartz formula [13].

The study has been conducted in accordance to the terms of the code of ethics in research of Ministry of Health in Iraq and The Iraqi board of Medical Specialty Ethics Committee.

Statistical analysis

The data analyzed by the statistical package for social sciences (SPSS-version 23) and Microsoft

office Excel programs (2013) and Graph Pad Prism (6). Most of data were presented as frequency and percentage except for age of presentation and age of diagnosis which expressed as mean±standard deviation. Fisher exact test and Yates' chi square test was used to compare between frequencies, while unpaired t-test was used to compare between means. P value <0.05 was considered statistically significant and highly significant if <0.001.

Results

Age at time of presentation was ranged between 1 day to 16 years, and the mean was 47.07±49.89 months, while the age at time of diagnosis was ranged between prenatal diagnosis to 13 years old with a mean 31.36± 37.44 months. The most frequent age group at time of presentation was 1-5 years age group including 84 patients (52.5%). The most frequent age group at time of diagnosis also was 1-5 years including 78 patients (48.8%), followed by below one year of 48 patients (30.0%), including 13 patients diagnosed prenatally. There were 97 males (60.6%) and 63 females (39.4%) with male:female ratio 1.54:1. Most of the patients had negative family history 124 (77.5%), and most of their parents were not consanguineous (58.1%) (Table 1).

Table 1. Distribution of 160 Patients according to demographic data

Parameter		No.	%
Age at presentation (yr)	<1	41	25.6
	1-5	84	52.5
	5-10	27	16.9
	>10	8	5.0
Age at diagnosis (yr)	Prenatal Dx	13	8.1
	<1	48	30.0
	1-5	78	48.8
	5-10	19	11.9
	>10	2	1.2
Sex	Male	97	60.6
	Female	63	39.4
	M:F ratio = 1.54:1		
Family history	Positive	36	22.5
	Negative	124	77.5
Consanguinity	Positive	67	41.9
	Negative	93	58.1

Urinary symptoms were most common presented in 93 patients (58.1%), followed by fever detected in 77 patients (48.1%). UTI was the most frequent complication accounted for (62.5%), followed by renal impairment (34.4%) (Table 2).

Among the study group, 183 renal anomalies were detected: 23 patients have combined renal anomalies. VUR was the most frequent seen in 67 patients (41.9%), 15 patients with VUR were associated with neurogenic bladder. Second rank was for renal agenesis in 24 patients (15.0%) (Table 3).

Table 4 shows that from total of 160 patients, 23 of them had combined RA, 14 patients out these 23 had combined obstructive and non-

obstructive RA, these 14 patients were excluded from comparison to avoid fallacies. The other 9 patients were involved, because they have either combined obstructive or combined non-obstructive RA, so regarded as same category. Accordingly, we have 146 patients for comparison. Regarding gender; most of those having obstructive RA were males 29/33 patients (87.9%), while only 60/113 patients (53.1%) of non-obstructive RA were males, this difference is highly significant P-value 0.0002. Regarding the age of diagnosis: most of the patients that had obstructive RA 23/33 (69.7%) diagnosed at or below 1 year, while most of the patients 66/113 (58.4%) of non-obstructive RA diagnosed at 1-5 age group, this difference had statistical highly significant P-value 0.0001. Seven patients of non-obstructive RA 7/113 (6.2%), and 5 patients out of 33 (15.2%) of obstructive RA diagnosed prenatally. Most of the patients with non-obstructive and obstructive RA had negative family history, (77.9%, 66.7%) respectively, P-value was not significant 0.6186.

Table 2. Distribution of 160 patients according to clinical presentation and associated complications

Clinical presentation	No.	%
Urinary symptoms	93	58.1
Fever	77	48.1
Abdominal symptoms	41	25.6
Acute kidney injury	15	11.9
Prenatal	13	9.4
Accidentally diagnosed	11	6.9
Improper weight or height gain	10	6.3
Complications	**No.**	**%**
Urinary tract infection	100	62.5
Renal impairment	55	34.4
Failure to thrive	38	23.8
Stones	15	9.4

*Patients may have more than one clinical presentation and more than one complication

Comparison between obstructive and non-obstructive RA in relation to complications as shown in table (5). UTI was seen in 74 patients (65.5%) non-obstructive RA and 20 patients (60.6%) with obstructive RA, p-value was statistically insignificant. Failure to thrive had insignificant difference between the 2 groups. Twenty-six (78.8%) of the obstructive patients' group had HN with only 35 patients (30.9%) of non-obstructive RA had HN, P-value was highly significant <0.0001.

CKD stage 1 was the commonest in 30 patients (20.6%), stage 1,2,3 mainly non-obstructive (22.1%), (4.4%) respectively, while stage 4 mainly obstructive (6.7%), the p-values was insignificant for CKD 0.6473.

Regarding ESRD: nearly equal figures of 8 patients (7.1%) non-obstructive RA, and 3 patients (9.1%) obstructive RA, P-value was not significant 0.7119.

Table 3. Patients' distribution according to types of renal anomalies

Anomaly	No.	%
Vesicoureteral reflux **	67	41.88
Renal agenesis (single kidney)	24	15.00
Ureteropelvic junction obstruction	20	12.50
Posterior urethral valve	12	7.50
Multicystic dysplastic kidney	11	6.88
Polycystic kidney	10	6.25
Renal Hypoplasia	8	5.00
Ectopic kidney	7	4.38
Uretocele	6	3.75
Vesicourethral junction obstruction	6	3.75
Duplex system	6	3.75
Others***	6	3.75

Number is 183, includes 23 patients combined anomalies. ** 15 patients with VUR were associated with Neurogenic bladder. *** Others includes ectopic ureter, Horse-shoe kidney, Megaureter

Table 4. Comparison between obstructive and non-obstructive Renal anomalies in relation to demographic data

Data		Non-Obstructive No.113 No. (%)	Obstructive No.33 No. (%)	Total 146 No. (%)	P value
Gender	Male	60 (53.1)	29 (87.9)	89 (61.0)	0.0002
	Female	53 (46.9)	4 (12.1)	57 (39.0)	
Age of diagnosis	<1	32 (28.3)	23 (69.7)	55 (37.7)	0.0001
	1-5	66 (58.4)	6 (18.2)	72 (49.3)	
	5-10	13 (11.5)	4 (12.1)	17 (11.6)	
	≥10	2 (1.8)	0 (0.0)	2 (1.4)	
Family history	Positive	29 (25.7)	5 (15.2)	34 (23.4)	0.6186
	Negative	88 (77.9)	22 (66.7)	110 (76.7)	

Discussion

In this descriptive study of CAKUT, male predominance (60.6%) was evident with an approximate male/female ratio 1.54:1. A population-based case-control study in Taiwan showed that males had a 1.83-fold greater risk of CAKUT than females as show in Tain *et al.* study [14], Katsoufis *et al*. study show 1.15:1 [15], which are nearly similar to our study. while in Turkish study by Bulum *et al.* in 2013 [16] showed a female predominance, M/F ratio 0:84, which is disagreed with current study, this was due to selection of patients of CAKUT in relative families only.

Authors noticed a considerable delay between the age of presentation (mean 47.07±49.89 months) and that of diagnosis (a mean 31.36±37.44 months), about 1.5 year, which occurred due to fact that the study was done in tertiary centers and patients had seen by different medical centers before referral. During comparison with Iraqi study by Hasoon in 2009 [17] we noticed there is nearly similar gap between age of presentation and age of diagnosis (about 1 year).

Table 5. Comparison between obstructive and non-obstructive Renal anomalies in relation to complications

		Non-Obstructive No.113 No. (%)	Obstructive No.33 No. (%)	Total 146 No. (%)	P value
UTI		74 (65.5)	20 (60.6)	94 (64.4)	0.6806
Failure to thrive		30 (26.5)	4 (12.1)	34 (23.3)	0.1033
Hydronephrosis		35 (30.9)	26 (78.8)	61 (41.8)	< 0.0001
Chronic kidney disease stages	I	25 (22.1)	5 (15.1)	30 (20.6)	0.6473
	II-III	5 (4.4)	1 (3.1)	6 (4.1)	
	IV	6 (5.3)	2 (6.7)	8 (5.5)	
End-stage renal disease		8 (7.1)	3 (9.1)	11 (7.6)	0.7119

Prenatal diagnosis was done for only (8.1%) of the patients, while in Gomez Huertas *et al*. study, fetal anomalies encountered approximately 30-50% of all malformations [18], this difference reflects our limited delay experience in prenatal diagnosis.

Positive family history found in 36 patients (22.5%), in Weber study, family history is identified in 10- 50% of affected children [7].

Positive consanguinity was seen in 67 patients (41.9%), which is nearly similar to Egyptian study 49.5% by Soliman et al. [19]. This reflects the high rate of consanguineous marriage in Arab population.

Regarding clinical presentation(s) of the study patients, urinary symptoms were the commonest (58.1%), followed by fever (48.1%), In Aksu et al. study, a significant number of children had low eGFR or hypertension at presentation [20].

UTI was the commonest complication (62.5%), this is similar to Capone study [3].

Different CAKUT have been identified, of which VUR was the commonest abnormality (41.9%), followed by renal agenesis (15.0%), then PUJ (12.5%). Soliman et al. [19] reported PUV (36.4%) as the commonest followed by primary VUR (19.6%) and PUJ followed by VUR in (18.7%). Aksu et al. [20] reported PUJO in (62.7%). This might be related to inclusion of patients from urology department in these studies.

During comparison of non-obstructive and obstructive RA in relation to demographic data, we notice that obstructive RA has male predominance, which is similar to Egyptian study by Soliman et al. 2015 (80.3%) [19]. Regarding age of diagnosis, most of the obstructive RA patients (69.7%) diagnosed at or below 1 year, while most of the patients of non-obstructive RA diagnosed at 1-5 age group (58.4%), this had statistical highly significant P-value 0.0001. Common obstructive RA like PUV presented early in life that led to earlier diagnosis [21,22]. Family history was of no significance statistically. A familial clustering of VUR has been described with a prevalence of 27-51% in siblings of patients with VUR and a 66% rate of VUR in children whose parents had reflux [23,24].

There was no statistically significant difference in the UTI, FTT and ESRD. This was similar to Egyptian study by Soliman et al. in 2015 [19]. But there was significant difference in HN between obstructive and non-obstructive RA, as (78.8%) of obstructive RA had HN, while only (30.9%) of non-obstructive RA had HN similar to study by Rasouly and Lu [25].

For the stages of CKD: compared to Egyptian study; obstructive group patients had advanced CKD stages (I: 45.5%, II–III: 22.7%, IV: 31.8%) in comparison to the non-obstructive group (I: 62.9%, II–III: 31.4%, IV: 5.7%) (P = 0.021). This difference might be due to high percent of PUVs in Egyptian study [19].

In conclusion, the commonest renal anomaly was VUR, followed by Renal agenesis, then PUJ. Most common presentation was urinary

symptoms. The most prominent complication was UTI. Gender, age of diagnosis and HN has significant difference between obstructive and non-obstructive RA.

Improving antenatal diagnosis, collaborative management between the obstetrician, the pediatric nephrologist and the urologist in order to provide optimal care for children with renal anomalies.

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Author contribution

Dr Ali: Concept of the article, collection of patients, data analysis, final supervision. Dr Kadhim: Data analysis, writing the parts of the article. Dr. Al-Obaidy: Concept of the article, collection of patients.

Conflict of interest

Authors declare no conflict of interest.

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References

1. Rodriguez MM. Congenital anomalies of the kidney and the urinary tract (CAKUT). Fetal Pediatr Pathol. 2014; 33(5-6): 293-320. doi: 10.3109/15513815.2014.959678.
2. Harambat J, van Stralen KJ, Kim JJ, et al. Epidemiology of chronic kidney disease in children. Pediatr Nephrol. 2012; 27(3): 363-73. doi: 10.1007/s00467-011-1939-1.
3. Capone VP, Morello W, Taroni F, et al. Genetics of congenital anomalies of the kidney and urinary tract: The current state of play. Int J Mol Sci. 2017; 18(4): 796. doi: 10.3390/ijms18040796.
4. Hwang DY, Dworschak GC, Kohl S, et al. Mutations in 12 known dominant disease-causing genes clarify many congenital anomalies of the kidney and urinary tract. Kidney Int. 2014; 85(6): 1429-33. doi: 10.1038/ki.2013.508.
5. Bower M, Salomon R, Allanson J, et alL. Update of PAX2 mutations in renal coloboma syndrome and establishment of a locus-specific database. Hum Mutat. 2012; 33(3): 457-66. doi: 10.1002/humu.22020.
6. Nicolaou N, Renkema KY, Bongers EM, et al. Genetic, environmental, and epigenetic factors involved in CAKUT. Nat Rev Nephrol. 2015; 11(12): 720-31. doi: 10.1038/nrneph.2015.140.
7. Weber S. Novel genetic aspects of congenital anomalies of kidney and urinary tract. Curr Opin Pediatr. 2012; 24(2): 212-8. doi: 10.1097/MOP.0b013e32834fdbd4.
8. Song R, Yosypiv IV. Genetics of congenital anomalies of the kidney and urinary tract. Pediatr Nephrol. 2011; 26(3): 353-64. doi: 10.1007/s00467-010-1629-4.
9. Elder JS. Congenital anomalies and dysgenesis of the kidneys. In: Kliegman RM, Stanton BF, St Geme JW, et al. (eds). Nelson textbook of pediatrics. 20th ed. Philadelphia: Elsevier; 2015. p. 2554-6.
10. Hodson EM, Craig JC. Urinary tract infections in children. In: Avner ED, Harmon WE, Niaudet P, et al (eds). Pediatric nephrology. 7th ed. Berlin Heidelberg: Springer. Verlag; 2016. P. 1695-714.
11. Buchanan AO, Marquez ML. Pediatric undernutrition. In: Marcdante KJ, Kliegman RM (eds). Nelson essentials of pediatrics. 7th ed. Philadelphia: Saunders Elsevier; 2015. p. 93-6.
12. Sharma J, Vasudevan A. Normal reference values of blood and urine chemistries. In: Phadke K, Goodyer P, Bitzan M (eds). Manual of pediatric nephrology. New York: Springer; 2014. p.n533-610.
13. Wong CS, Mak RH. Chronic kidney disease. In: Kher KK, Schnaper HW, Makker SP. Clinical pediatric nephrology. 2nd ed. UK: Informa Ltd. 2007. p. 339-52.
14. Tain YL, Luh H, Lin CY, et al. Incidence and risks of congenital anomalies of kidney and urinary tract in newborns: A population-based case-control study in Taiwan. Medicine (Baltimore). 2016; 95(5): e2659. doi: 10.1097/MD.0000000000002659.
15. Katsoufis CP, DeFreitas MJ, Infante JC, et al. Risk Assessment of severe congenital anomalies of the kidney and urinary tract (CAKUT): A birth cohort. Front Pediatr. 2019; 7: 182. doi: 10.3389/fped.2019.00182.
16. Bulum B, Ozçakar ZB, Ustüner E, et al. High frequency of kidney and urinary tract anomalies in asymptomatic first-degree relatives of patients with CAKUT. Pediatr Nephrol. 2013; 28(11): 2143-7. doi: 10.1007/s00467-013-2530-8.
17. Hasoon FC. Obstructive uropathy and vesicoureteric reflex: An important causes of chronic kidney diseases in Iraqi Children. A thesis submitted for Iraqi Board of Medical Specialization, 2009.
18. Gómez Huertas M, Culiañez Casas M, Molina García FS, et al. Complementary role of magnetic resonance imaging in the study of the fetal urinary system. Radiologia. 2016; 58(2): 101-10. English, Spanish. doi: 10.1016/j.rx.2015.12.003.
19. Soliman NA, Ali RI, Ghobrial EE, et al. Pattern of clinical presentation of congenital anomalies of the kidney and urinary tract among infants and children. Nephrology (Carlton). 2015; 20(6): 413-8. doi: 10.1111/nep.12414.
20. Aksu N, Yavaşcan O, Kangin M, et al. Postnatal management of infants with antenatally detected hydronephrosis. Pediatr Nephrol. 2005; 20(9): 1253-9. doi: 10.1007/s00467-005-1989-3.

21. Malin G, Tonks AM, Morris RK, et al. Congenital lower urinary tract obstruction: A population-based epidemiological study. BJOG. 2012; 119(12): 1455-64. doi: 10.1111/j.1471-0528.2012.03476.x.
22. Haeri S. Fetal lower urinary tract obstruction (LUTO): A practical review for providers. Matern Health Neonatol Perinatol. 2015; 1: 26. doi: 10.1186/s40748-015-0026-1.
23. Giannotti G, Menezes M, Hunziker M, et al. Sibling vesicoureteral reflux in twins. Pediatr Surg Int. 2011; 27(5): 513-5. doi: 10.1007/s00383-010-2821-0.
24. Pirker ME, Colhoun E, Puri P. Renal scarring in familial vesicoureteral reflux: is prevention possible? J Urol. 2006; 176(4 Pt 2): 1842-6; discussion 1846. doi: 10.1016/j.juro.2006.04.089.
25. Rasouly HM, Lu W. Lower urinary tract development and disease. Wiley Interdiscip Rev Syst Biol Med. 2013; 5(3): 307-42. doi: 10.1002/wsbm.1212.

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