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Research Article

CHRONIC KIDNEY DISEASE: CAUSES AND OUTCOMES IN LIBYAN CHILDREN AT TRIPOLI CHILDREN HOSPITAL (2001-2021)

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Abstract

Background: Chronic Kidney disease (CKD) is a major public health problem worldwide. Causes of CKD are very different in children from those in adult. Congenital abnormalities of the kidney and urinary tract are the main cause of CKD in children. **The objectives** of this study are to determine the etiology and outcome of CKD in Libyan children at Tripoli Children Hospital. **Patients and methods:** Across sectional study included of 162 Libyan children with evidence of CKD, who followed up in nephrology unit at Tripoli Children Hospital from the year 2001 to 2021.CKD were defined and grading according to Kidney Disease Improving Global Outcomes (KDIGO) guidelines. **Results:** there, 56.8% of cases were less than 5 years, 59.3% of cases were males and male to female ratio was 1.45; with mean age of 11.4 years. The underlining causes of CKD in children were: Glomerulonephritis (14.8%), FSGS were the main cause of glomerulonephritis; hereditary nephropathy (17.3%) PH1were commonest cause of it; Congenital anomalies of kidney and urinary tract (CAKUT) (57.4%), PUV accounted for the most common underlining cause of congenital anomalies. The outcomes of these children, 30.4% was still follow up with CKD, 24.1% of cases reached end stage renal disease (ESRD), 8.6% of them were died and 16% of cases were missed follow up. **Conclusion:** The most common cause of CKD of these children were CAKUT with late presentation to pediatric nephrologist. Children who were at risk, need proper followed up and early conservative treatment to prevent the progression of CKD.

Keywords: Chronic Kidney disease, Obstructive nephropathy, Glomerulonephritis, Tripoli.

INTRODUCTION

Chronic Kidney disease (CKD)is a major public health problem worldwide. However, rising incidence and prevalence leading to poor outcomes associated with high cost[1]; 11–13% of the overall world's population suffers from CKD[2]. Kidney Disease Improving Global Outcomes (KDIGO) guidelines proposed a definition of CKD, as abnormalities of kidney structure or by a decline in glomerular filtration rate (GFR) below 60 mL/min/1.73 m^2 of body surface area, present for more than 3 months[3]. Most kidney diseases are asymptomatic or no findings until later in their course and are detected only when they are chronic[3]. Glomerular filtration rate (GFR) is widely accepted as the best index of kidney function[4]. However, it is generally reduced after widespread structural damage and most other kidney functions decline in parallel with GFR in CKD[3]. During the pediatric age, the presence of CKD at any stage is a strong predictor for deterioration of renal function later in lifetime [5]. Childhood CKD presents clinical features that are specific and totally peculiar to the pediatric age, such as the impact of the disease on growth [6]. The epidemiological studies that have been performed provide evidence that ESRD represents the "tip of the iceberg" of CKD and suggest that patients with earlier stages of disease are likely to exceed those reaching ESRD by as much as 50 times. [7, 8]Due to a lack of national registries, any semblance of incidence and prevalence data from developing countries primarily originates as reports from major tertiary care referral centers.[7]The mortality rate of children with CKD requiring renal replacement therapy is at least 30-times higher than the age-matched healthy children, and health outcomes are not improving[9].Several studies investigated the association between socio-demographic, economic and personal factors and CKD outcomes and revealed that this relation was complex and multifactorial [10]. It is essential to understand the epidemiology of CKD in children to make an accurate and early diagnosis, determine preventable or reversible causes of progression, predict prognosis, and help the counseling of the affected children and their families[11]. Causes of CKD are very different in children from those in adults.

In a recent NAPRTCS report congenital causes, including congenital anomalies of the kidney and urinary tract (CAKUT) (48%) and hereditary nephropathies (10%), Glomerulonephritis accounted for 14% of cases. The causes are usually related to age at presentation of renal impairment, CAKUT predominated seen in younger patients and glomerulonephritis was the leading cause in children older than 12 years of age[11]. With progressed CKD there are various complications occur and their frequency depends on the stage of CKD. The most important complication includes Anemia with the prevalence being 73% at stage 3 CKD and >93% at stage 5 CKD[12]. Growth impairment, occurring in 35% of children with CKD stages 2–4. 43% of patients with childhood onset end-stage renal disease (ESRD) do not achieve an adult height within the normal range [13].

In the absence of a national registry, the exact incidence and causes of CKD in Libyan children is not known. Therefore, the aims of this study are to determine the etiology and outcome of CKD in Libyan children at Tripoli Children Hospital.

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PATIENT AND METHODS

Across sectional study included the records of 162 Libyan children with evidence of CKD. These children were followed up in nephrology unit at Tripoli Children Hospital during the 21 years period from2001 to 2021. The following information were taken from patient's medical recordes: age, sex, origin city and date of diagnosis as CKD, Glomerular filtration rate (GFR) at presentation, cause of CKD, and clinical outcome of these patients. GFR was estimated by the Schwartz formula. The value of the variant K (according to age and gender).CKD were defined and grading according to KDIGO guidelines [3].

eGFR = [(length in cm) × k]/serum creatinine in mg/dL;

where k = 0.45 for infants 1–52 weeks old, k = 0.55 for children 1–13 year sold, k = 0.55 for adolescent females 13–18 years old and k = 0.7 for adolescent males 13– 18 years old. Individuals with eGFR values <60 mL/min/ 1.73 m^2 were defined as having CKD. The National Kidney Foundation criteria for CKD were used[14].

CKD and Stages According to the K/DOQI scheme, CKD is characterized by stage 1 (mild disease) through stage 5 (ESRD)[3].

Stages	GFR value ml/ min/1.73m2	Classification
I	>90	Normal or high
II	60-89	Slightly decreased
III A	45-59	Mild to moderately decreased
III B	30-44	Moderately to severely decreased
IV	15-29	severely decreased
V	<15	ESRD

The outcomes of these children were divided into follow up with CKD, children reached ESRD, died and missed follow up.

Statistical Analysis

Data was analyzed by using IBM SPSS Statistics for Windows, version 20 (IBM Corp., Armonk, N.Y., USA). Descriptive statistics such as frequency, percentage and mean ± standard deviation were used to present all results. Chi-squared ($\chi 2$)and Fisher's exact tests were used as the test of significance for categorical variables. A p value < 0.05 considered significant. Datawas anonymous, kept strictly confidential and was accessible only to the research team.

RESULTS

A total 162 cases with chronic kidney diseases were registered at nephrology clinic at Tripoli Children Hospital during study period. Results revealed that 55 (34%) of cases were less than 2 years, with mean age of 11.4 years; 96 (59.3%)were males; and male to female ratio was 1.45:1; Most of the cases their origin was from west Libya (71.6%). (Table 1). The underlining causes of CKD in children were: Glomerulonephritis (24, 14.8%), FSGS were the main cause of glomerulonephritis; hereditary nephropathy (20,17.3%), PH1were the commonest cause of it; Congenital anomalies of kidney and urinary tract (CAKUT)reported in 97(57.4%) of cases, PUV accounted for the most common underlining cause of congenital anomalies (Table 2). The outcomes of these children, 49(30.2%)was still follow up with CKD, 24.1% of cases reached ESRD, 8.6% of them were died and 16% of cases were missed follow up (Table 3).

Table 1. Demographic characteristics of the CKD cases at Tripoli Children Hospital

Character	Frequency (N=162)	%
Age :		
less than 2 years	55	34.0
2-4 years	37	22.8
5-10 years	50	30.9
More than 10 years	20	12.3
Sex:		
Male	96	59.3
Female	66	40.7
City origin		
West	116	71.6
Central	23	14.2
South	17	10.5
Unknown	6	3.7
GFR at presentation:		
Stage I Normal (120-80)	45	27.8
Stage II Mild (79-60)	12	7.4
Stage III Moderate (59-30)	47	29.0
Stage IV Sever (29-15)	36	22.2
Stage V ESRD (Less than 15)	22	13.6

Table 2. Chronic kidney disease causes among cases at Tripoli Children Hospital

Cause	No.	%
Glomerulonephritis	24	14.8
– FSGS	20	12.3
– HUS glomerulonephritis	2	1.2
– IgA nephropathy	1	0.6
– HSPN	1	0.6
Hereditary nephropathy	28	17.3
– PH1	16	9.9
– Bartter	2	1.2
– Familial nephronephitiasis	2	1.2
– RTA	1	.6
– Cystinosis	3	1.9
– Congenital nephrotic syndrome	4	2.5
Congenital anomalies of kidney and urinary tract	93	57.4
– PUV	21	13.0
– Neurogenic bladder	16	9.9
– Reflux nephropathy	15	9.3
– Hypoplasia/dysplasia	19	11.7
– Cystic disease	10	6.2
– Associated congenital anomalies	12	7.4
Unknown cause	17	10.5
Total	162	100.0

[FSGS: Focal Segmental Glomerulo Sclerosis, HUS: Hemolytic uremic syndrome, HSPN: Henoch Scholoin purpura nephritis, PH1: Primary Hyperoxaluria type 1, RTA : Renal tubular acidosis, PUV: Posterior urethral valve]

Table 3. Outcomes of the CKD cases at Tripoli Children Hospital

Outcome	No.	%
Follow up with CKD	49	30.2
ESRD (HD, PD)	39	24.1
Transplanted	23	14.2
Transfer to adult clinic	11	6.8
Died	14	8.6
Missed follow	26	16.0
Total	162	100

Glomerulonephritis and congenital anomalies of kidney and urinary tract were reported more among males, while hereditary nephropathy reported more among females; but there was no statistical significant difference between causes and sex, (P=0.34). (Table 4). Glomerulonephritis was more common among age group 5 years or more (70.8%), while congenital anomalies of kidney and urinary tract was more reported among children aged 4 years or less (68.8%).

Table 4. Distribution of cause of CKD according to sex

Cause	Sex		Total	P value
	Male	**Female**		
Glomerulonephritis	15 (17.6%)	9 (15.0%)	24 (16.6%)	0.34
Hereditary nephropathy	13 (15.3%)	15 (25.0%)	28 (19.3%)	
Congenital anomalies of kidney and urinary tract	57 (67.1%)	36 (60.0%)	93 (64.1%)	
Total	85 (100%)	60(100%)	145(100%)	

Table 5. Distribution of cause of CKD according to age

Cause	Age				**Total**	**P value**
	< 2 years	**2-4 years**	**5-10 years**	**> 10 years**		
Glomerulonephritis	2 (3.8%)	5 (13.9%)	14 (35.0%)	3 (17.6%)	24 (16.6%)	0.003
Hereditary nephropathy	10 (19.2%)	7 (19.4%)	5 (12.5%)	6 (35.3%)	28 (19.3%)	
Congenital anomalies of kidney and urinary tract	40 (76.9%)	24 (66.7%)	21 (52.5%)	8 (47.1%)	93 (64.1%)	
Total	52 (100%)	36 (100%)	40 (100%)	17 (100%)	145 (100%)	

Table 6. Distribution of outcomes of CKD according to sex

Outcomes	**Sex**		**Total**	**P value**
	Male	**Female**		
Follow up with CKD	31	18	49	0.26
	39.2%	31.6%	36%	
ESRD (HD, PD)	22	17	39	
	27.8%	29.8%	28.7%	
Transplanted	16	7	23	
	20.3%	12.3%	16.9%	
Transfer to adult	4	7	11	
	5.1%	12.3%	8.1%	
Died	6	8	14	
	7.6%	14%	10.3%	
Total	79	57	136	
	100%	100%	100%	

Table 7. Distribution of outcomes of CKD according to causes

Outcome	Causes			Total	P value
	Glomerulonephritis	**Hereditary nephropathy**	**Congenital anomalies of kidney and urinary tract**		
Follow up with CKD	5	4	37	46	<0.0001
	23.8%	15.4%	49.3%	37.7%	
Follow up with ESRD (HD, PD)	10	8	14	32	
	47.6%	30.8%	18.7%	26.2%	
Transplanted	3	3	15	21	
	14.3%	11.5%	20%	17.2%	
Transfer to adult	0	2	7	9	
	0.0%	7.7%	9.3%	7.4%	
Died	3	9	2	14	
	14.3%	34.6%	2.7%	11.5%	
Total	21	26	75	122	
	100%	100%	100%	100%	

There was a statistical significant difference between age and causes of CKD in children (P=0.003) (Table 5). Most of boys and girls were following up with CKD (39.2%, 31.6% respectively). Transplantation was more among boys, while death was more among girls. There was no statistical significant difference between outcomes and sex, (P=0.26) (Table 6). The study showed that 10(47.6%) of glomerulonephritis cases develop ESRD and on hemodialysis or peritoneal dialysis, while 8(30.8%) of hereditary nephropathy cases ended by ESRD and9 (34.6%) of them were died. There was a statistical significant difference between cause of kidney disease and outcomes in children at Tripoli Children Hospital, (P<0.0001) (Table7).

DISCUSSION

CKD is recognized as a global public health problem[15, 16]. This study reported the important causes and outcomes of CKD in pediatric patients referred to Tripoli Children Hospital. We found males were more predominate (59.3%) which was nearly similar to many other studies in the world.

This is largely related to the high incidence of congenital urological malformations among males with CKD. In Egyptian study males accounted as 56.7%[8]. In Sudanese study males accounted as 60.5%[17]. Harambat et al. reported that the exact prevalence of CKD is not known and it depends on the country and it ranges from 55–60 to 70–75 per million of the age-related population (pmarp) in Spain and Italy, as the disease at its early stages does not show any specific symptoms and is difficult to diagnose [11].However, in the Middle East (Kuwait) and Southeast Asia (Brunei Darussalam) countries, it is considerably greater and accounts for 329 and 736 pmarp, respectively[11, 18]. Due to lack of national registry of CKD in the pediatric population word wide, explained the insufficient data on epidemiology of CKD. The most common known cause of CKD in present study is due to congenital anomalies of kidney and urinary tract (CAKUT) accounted as 57.4%. Obstructive uropathy in form of posterior urethral vale represented 13% of the cases, this may be related to late presentation of theses case to pediatric nephrologist. In a study done by Safouh et al reported that the most common single cause of CKD was obstructive uropathy (21.7%), followed by

primary glomerulonephritis (15.3%), reflux/urinary tract infection (14.6%), aplasia/hypoplasia (9.8%) and familial/metabolic diseases (6.8%); unknown causes accounted for 20.6% of the cases[8].On the other hand, in Sudanese children, the most common cause of CKD was primary glomerulonephritis (25.4%) and the CAKUT causes come the second common causes accounted for (17.5%)[17].A meta-analysis was done on 13 studies conducted on 3,596 Iranian children. They found that the main causes of CKD were CAKUT, urological disorders, and glomerulonephritis, these cause accounted as 38.40%, 22.28%, and 18.21%, respectively[19].The second causes of ESRD were glomerulopathy and nephrotic syndrome. Congenital and hereditary disorders followed this. Chronic pyelonephritis was the third frequent cause of ESRD. However, in a substantial number of patients (40), no cause was recorded. These results are similar to the data reported by Wood et al. in the North American Pediatric Renal Transplant Cooperative Study[20].While in Banaga et al. indicated that the hypertension is a leading cause of ESRD in Sudan followed by chronic glomerulonephritis among adult patients[21]. In many developed countries, the leading cause of CKD is CAKUT [11,22]. Our findings regarding CAKUT as a cause of CKD was 57.4% which show agreement with the data from United States, Italian, Belgian, and Serbian CKD registries, for 48%, 58%, 59%, and 58% of all CKD causes, respectively[23]. Hereditary nephropathy with the corresponding prevalence rates of 17.3% vs. 10% in the United States and 9% vs. 19% in Belgium[23]. Meta-analysis was done on 13 studies conducted on 3,596 Iranian children. They found that the main causes of CKD were CAKUT, urological disorders, and glomerulonephritis, these cause accounted as 38.40%, 22.28%, and 18.21%, respectively[19].

A study done in Tripoli, Libya in 2004, by Fituri et al, revealed that the posterior urethral valves(PUV) was the most common cause of severe obstructive uropathy in infants and children accounted (53%) of cases in Tripoli Children Hospital. Furthermore, the second cause was hereditary nephropathies (25%) and Glormulopathies accounted for (4%) [24]. From another study in Benghazi by El Tabbal et al there was a higher occurrence of obstructive uropathy among men caused by the presence of congenital posterior urethral valve [25]. In current study about 17(10.5%) of cases had unknown etiology this may be related to late presentation of patient to pediatric nephrologist.

In a study of adults, Zaied et al. in two major hospitals showed that the most cases are caused by hypertension, followed by obstructive uropathy, glomerulonephritis in decreasing frequencies[26]. A similar study done in Misurta, Libya demonstrated that the most common causes of ESRD were diabetes and hypertension affecting young-age population followed in order by undetermined causes, glomerulonephritisin, chronic pyelonephritis due to drug nephrotoxicity [27]. Other less common causes such as obstructive uropathy, polycystic kidney disease, gout, and IgA nephropathy also was reported in Misurta study [27]. The clinical outcomes of this study reveal that 30.2%of our patients continued follow up with CKD nearly similar to Sudanese children (25%) however, 24.1% underwent ESRD and required hemodialysis and peritoneal dialysis which is similar to a study on Sudanese children. 26% of our patients missed follow up and 22% in Sudanese children with CKD[17].

Conclusion

The clinical profiles, causes, and outcome of CKD and ESRD at Tripoli Children Hospital were documented. Most of cases of CKD were males; the most common cause of CKD of these children was Congenital anomalies of kidney and urinary tract (CAKUT) which is more common in males; With late presentation and delayed referral to pediatric nephrologist associated with poor outcomes. Additional actions were needed in form of early detection and referral associated with early treatment. Antenatal screening for renal anomalies (PUV) may decrease the prevalence of CKD and ESRD especially if an early surgical intervention of obstructive uropathy were done. Children, who were at risk, need proper followed up and early conservative treatment to prevent the progression of CKD.

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