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CLINICAL CHARACTERISTICS AND CAUSES OF PEDIATRIC CHRONIC KIDNEY DISEASE IN NINEVEH PROVINCE

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ABSTRACT

Background: Chronic kidney disease is recognized as a major public health problem, determined by the presence of structural or functional abnormalities of the kidney, with or without decreased GFR for more than 3 months. **Aim of study**: To study the clinical characteristics and causes of CKD in children in Nineveh province. **Patients And Methods**: The study evaluated 81 patients aged 1-15 years with chronic kidney disease at Ibn-Sina teaching hospital in Nineveh province. Patients were followed up at the pediatric nephrology consultation clinic and dialysis units for 6 months. Patients with acute kidney injury or steroid sensitive nephrotic syndrome were excluded. GFR was estimated using the revised bedside Schwartz formula. Patients were divided into five stages of CKD. **Result**: The most frequent cause was obstructive uropathy 19.8%, The metabolic cause was the next, found in 16.0%, Glomerulonephropathy found in 13.6%. The most frequent age group was below 5 years representing 54.3% were the congenital anomaly of kidney and urinary tract the are most common cause. Children with CKD stage I and stage II comprised 9.9% and 7.4% respectively in the studied group, while those with stage IIIa, IV and V composed, 23.5%,25.9% and 33.3% respectively. Family history was 32.1% in this study. **Conclusion**: Children often develop kidney and urinary tract disorders (CKD) due to congenital anomalies, metabolic causes, and glomerulopathies. Early screening, early detection, and timely treatment of preventable causes could reduce CKD incidence.

KEYWORDS: Chronic Kidney Disease, Clinical characteristics, Pediatric age.

INTRODUCTION

End-stage kidney disease (ESKD) and early mortality are only two of the many problems that can arise from chronic kidney disease (CKD), a dangerous and rare condition.[1] It is diagnosed if the patient has either of the following criteria: kidney damage for ≥ three months, as determined by the presence of structural or functional abnormalities of the kidney, with or without decreased GFR, or a GFR < 60 mL/min/1.73 m2 for ≥ 3 months, with or without other signs of kidney damage.[2]

The fundamental etiology of chronic kidney disease is the main factor that determines rates and patterns of development. Congenital abnormalities of the kidney and urinary tract (CAKUT) are the most frequent cause of CKD and ESRD in children. Glomerular disease, neurogenic bladder, and other conditions are next in line. Diabetes and hypertension, two extremely uncommon causes of childhood CKD, account for more than 70% of adult patients' CKD.[3,4] Only 39.6% of children with ESRD have hypodysplasia, compared to 57.5% of those with CKD. Patients with focal segmental glomerulosclerosis or underlying chronic glomerulonephritis make up 10.7% of ESRD patients but 4.4% of CKD patients.[4]

Congenital, acquired, hereditary, or metabolic renal illness are the pathogenetic causes of juvenile chronic kidney disease (CKD); causes of kidney disease in children are often classified as either glomerular or no glomerular in origin. The main factor influencing the course of CKD is the development of tubulointerstitial fibrosis.[5]

The majority of CKD patients gradually advance to ESRD over many years, occasionally even decades. The development of renal damage in patients with established chronic kidney disease is mostly determined by disease-

independent processes. The gradual loss of kidney function is thought to be caused by a number of processes, such as proinflammatory cytokines, profibrotic growth factors, proteinuria, podocyte damage, hypertension, and disturbances in filtration or hemodynamics.[6] The cause determines the clinical signs of chronic kidney disease in children. While some children with glomerular disease may have more subtle symptoms including polydipsia, polyuria, nocturia, and enuresis due to the urine concentrating deficiency associated with CKD, others may have severe hematuria and/or edema.[5]

In conclusion, supportive care for chronic kidney disease (CKD) aims to enhance quality of life and maybe halt the course of renal failure. A pediatric facility that can offer interdisciplinary services, such as medical, nursing, social services, dietary, and psychological support, should treat children with chronic kidney disease (CKD). Managing CKD in juvenile patients requires careful attention to nutrition, fluid and electrolyte balance, and linear growth.[5,6]

AIM OF STUDY

To study the clinical characteristics (blood pressure, height, weight, and laboratory investigation) in children younger than 15 years old and to study the causes of CKD in children in Nineveh province.

PATIENTS AND METHODS

Subjects: This descriptive observational study was aimed at evaluating 81 patients aged 1day–15 years suffering from chronic kidney disease of all stages and followed-up at the pediatric nephrology consultation clinic and dialysis center in Ibn-Sina Teaching Hospital in Nineveh province, which provides tertiary medical care to children over a 6-months period from the first of October 2022 to the first of April 2023. Patients with acute kidney injury of any etiology or steroid-sensitive nephrotic syndrome were excluded from this study.

At the time of the interview, each patient had a thorough history and physical examination, and measurements of their height, weight, and blood pressure (BP) were made. Height or length below the third centile or less than two standard deviations for that age and sex is considered short stature. If a child's weight fell below the fifth percentile, failure to thrive was taken into consideration. The 95th percentile of blood pressure for age, height, and sex was considered hypertension.

At the time of recording, the following tests were performed: CBC, urinalysis, urine culture, UPCR, ultrasound of the abdomen, CT scan of the abdomen, voiding cystourethrography, urodynamic study, echocardiogram, serum creatinine, serum albumin, serum calcium, serum phosphorous, serum alkaline phosphatase, and C3, C4 (these tests were performed for some patient). Using the updated Schwartz formula at the bedside, the glomerular filtration rate (GFR) was calculated as [0.413*height(cm)/scr(mg/dl)]. According to the kidney disease outcomes quality initiative, or K/DOQI, patients were categorized into five phases of CKD.

Abnormalities in kidney structure or function that last for three months or more, with or without a decline in GFR, are referred to as chronic kidney disease. CKD stages as determined by the Kidney Disease Outcomes Quality Initiative (K/DOQI). Phase 1: GFR of 90 or above; Phase 2: 60 to 89; Phase 3a: 45 to 59; Phase 3b: 30 to 44; Phase 4: 15 to 29; Phase 5: <15.

Technique of blood pressure measurement: Instrument of measurement of blood pressure: Mercury sphygmomanometer according to the chart (B.P for height and gender) as shown in appendix, checking of BP while patient in sitting position the midline of cuff is placed in line with brachial artery 2-3 cm above the cubital fossa and the cuff should fit around the arm.

Statistical analysis: Microsoft Excel 2007 sheets contained a summary of the data gathered for the study. To conduct the statistical analysis, IBM SPSS 26 was used. The Shapiro-Wilk test was used to determine if these data were normal, and nonparametric tests were used. Whereas the nominal data was presented in frequencies and proportions, the numerical data was presented in medians and minimums with maximum values. The nominal data were subjected to the Chi square test. A p-value of less than 0.05 was deemed significant.

RESULTS

The distribution of the study sample according to socio-demographic characteristics was demonstrated in Table 1. The table elicited that the most frequent age group was 1–5 years, representing 45.7% with a statistically significant difference ($p = 0.000$). The male: female ratio was 1.25:1, and the males constituted 55.6% and the females represented 44.4% of the study sample; the difference was not significant. Most of the study sample (63.0%) was living in rural areas, while 37.0% of the study sample was living in urban areas, with a statistically significant difference ($p = 0.020$).

Table 1: Distribution of the study sample according to the socio-demographic characteristics.

Socio-demographic characteristics		Frequency	Percent	p-value*
Age	**<1y**	7	8.6	**0.000**
	1-5	37	45.7	
	6-10	17	21.0	
	11-15	20	24.7	
Gender	**Males**	45	55.6	0.317
	Females	36	44.4	
Residence	**Urban**	30	37.0	**0.020**
	Rural	51	63.0	

**Chi square test has been used*

A positive family history of CKD was found in 32.1% and was statistically significant (p = 0.001), as shown in table 2.

Table 2: Distribution of the study sample according to family history.

Family history	Frequency	Percent	p-value*
Positive	26	32.1	**0.001**
Negative	55	67.9	

**Chi square test has been used*

The distribution of the study sample according to stages of CKD was demonstrated in Table 3. It revealed that most of the study sample had stages 4 (25.9%) and 5 (33.3%), while stage 1 was found in 9.9%, stage 2 in 7.4%, stage 3a in 12.3%, and stage 3b in 11.1%. The difference was statistically significant (p = 0.000).

Table 3: Distribution of the study sample according to stages of CKD.

Stages of CKD	Frequency	Percent	p-value*
1	8	9.9	**0.000**
2	6	7.4	
3a	10	12.3	
3b	9	11.1	
4	21	25.9	
5	27	33.3	
Not dialysis	10		
dialysis	17		
**Chi square test has been used*			

The distribution of the study sample according to initial presentation was demonstrated in Table 4 and revealed that recurrent UTI was the most frequent presenting feature, representing 16.9% of the study sample, followed by FTT 14.6%, polyuria/polydipsia/enuresis 10.1%, anemia 10.1%, proteinuria at 10.1%, hematuria 8.9%, edema non-specific 8.9%, decreased UOP 7.9%, 7.9%, and high blood pressure 4.5%; the difference was statistically significant (p=0.000).

Table 4: Distribution of the study sample according to Initial Presentation.

Initial Presentation	Frequency	Percent	p-value*
Recurrent UTI	15	16.9	**0.003**
F.T.T, short stature	13	14.6	
Polyuria, polydipsia, enuresis	9	10.1	
Anemia	9	10.1	
Proteinuria	9	10.1	
Hematuria	8	8.9	
Edema	8	8.9	
Non-specific (Vomiting, lethargy)	7	7.9	
Decreased UOP	7	7.9	
High blood pressure	4	4.5	
**Chi square test has been used*			

The distribution of the study sample according to causes of CKD was demonstrated in Table (5) and showed that the most frequent cause was obstructive uropathy (19.8%, 12 males and 4 females), with a median age of 4 years and an eGFR of 36.5 mL/min/1.73 m^2. The metabolic cause was the next, found in 14.8% (6 males

and 6 females) with an age of 5 years and an eGFR of 26.0 mL/min/1.73m^2. Glumerulo-nephropathy was found in 13.6% (9 males and 2 females).

Table 5: Distribution of the study sample according to causes of CKD.

Causes	Total	Male	Female	eGFR Median (Min, Max)	Age Median (Min, Max)
Obstructive uropathy	16(19.8)	12(26.7)	4(11.1)	36.5 (7.1,90.0)	4.0 (1.0,14.0)
Metabolic and Genetic	12(14.8)	6(13.3)	6(19.4)	26.0 (7.0,90.0)	5.0 (0.46,9.0)
Glomerulonephritis	11(13.6)	9(20.0)	2(5.6)	9.65 (0.5, 20.0)	5.0 (0.5, 15.0)
Hypoplasia	8(9.9)	2(4.4)	6(16.7)	40.5 (16.0,45.0)	11.5 (5.0,14.0)
Reflux nephropathy	8(9.9)	3(6.7)	5(13.9)	11.00 (5.0, 71.0)	10.5 (9.0, 13.0)
Neurogenic bladder	6(7.4)	4(8.9)	2(5.6)	30.9 (10.7,45.0)	5.0 (0.5,5.0)
Unknown	6(7.4)	2(4.4)	4(11.1)	40.0 (26.0,93.0)	8.0 (5.0,11.0)
Nephrotic syndrome	5(6.2)	3(6.7)	2(5.6)	26.0 (6.5,72.2)	13.0 (4.0,15.0)
Polycystic Kidney	5(6.2)	2(4.4)	3(8.3)	38.0 (28.0,42.0	5.0 (5.0,11.0)
Single kidney	3(3.7)	2(4.4)	1(2.8)	14.2 (8.5,52.7)	5.0 (5.0,11.0)
Total	81	45	36		

The distribution of the study sample according to age at presentation, whether below or above 5 years, was demonstrated in Table 4.6 and showed significant differences (p=0.000) concerning obstructive uropathy and (p=0.013) for metabolic causes in both cases. Glomerulo-nephropathy, hypoplasia, and reflux nephropathy among those below 5 years were significantly lower than those above 5 years with (p=0.035), (p=0.034), and (p=0.034) respectively, A single kidney was found in 3.7% (2 males and 1 female) with an age of 5 years and an eGFR of 14.2 mL/min/1.73 m^2.

Table 6: Distribution of the study sample according to age at presentation.

Etiology	Age at presentation			p-value*
	<5 years	>5 years	Total	
Obstructive uropathy	15	1	16	**0.000**
Metabolic and Genetic	10	2	12	**0.013**
Glomerulo-nephropathy	2	9	11	**0.035**
Hypoplasia	1	7	8	**0.034**
Reflux nephropathy	1	7	8	**0.034**
Neurogenic bladder	6	1	7	0.059
Unknown	2	4	6	0.414
Nephrotic syndrome	2	3	5	0.655
Polycystic Kidney	3	2	5	0.655
Single kidney	2	1	3	0.564
**Chi square test has been used*				

The distribution of the study sample according to study parameters was demonstrated in Table (7) and showed that hypertension was found in 25.9% of the study sample with a statistically significant difference (p=0.000) from the normal Bp. Low height and low weight were found in 60.4% and 41.9% of the study sample, respectively, with no significant statistical difference from normal height and weight. Anemia was found in 86.4% of the study sample with a statistically significant difference (p=0.000) comparing to normal Hb, ureamia, hypocalcaemia, and hyperphosphatemia found in 82.7%, 92.6%, and 61.7% respectively, with significant statistical differences at (p=0.000), (p=0.000), and (p=0.035) in that order.

Table 7: Distribution of the study sample according to study parameters.

Parameter	State	Frequency	Percentage	p-value*
Blood pressure	High	21	25.9	**0.000**
	Normal	60	74.1	
Height	Normal	32	39.6	0.059
	Low	49	60.4	
Weight	Normal	44	54	0.437
	Low	37	46	
Hb	Normal	11	13.6	**0.000**
	Anemia	70	86.4	
Bl. Urea	Normal	14	17.3	**0.000**
	Uremia	67	82.7	
S. calcium	Normal	6	7.4	**0.000**
	Hypocalcaemia	75	92.6	
S. phosphate	Normal	31	38.3	**0.035**
	Hyperphosphatemia	50	61.7	
**Chi square test has been used*				

Distribution of H.T،short stature, low weight, anemia, uremia, hypocalcemia, hypocalcemia and hyperphosphatemia according to each stage of CKD as shown in Table 8.

Table 8: Distribution of the study parameters according to stages of CKD.

	Stages of CKD						p-value*
	Stage I (n=8)	Stage II (n=6)	Stage IIIa (n=10)	Stage IIIb (n=9)	Stage IV (n=21)	Stage V (n=27)	
Hypertension (n=21)	2 (25.0)	0 (0.0)	0 (0.0)	2 (22.2)	2 (9.5)	15 (55.6)	**0.05**
Short stature (n=49)	1 (12.5)	0 (0.0)	4 (40.0)	5 (55.5)	18 (85.7)	21 (77.8)	**0.000**
Under weight (n=37)	1 (12.5)	0 (0.0)	3 (30)	4 (44.4)	10 (47.6)	19 (70.4)	**0.000**
Anemia (n=70)	3 (12.5)	5 (33.3)	8 (80.0)	8 (88.9)	20 (95.2)	26 (96.3)	**0.000**
Uremia (n=67)	1 (12.5)	2 (33.3)	8 (80.0)	9 (100.0)	21 (100.0)	26 (96.3)	**0.000**
Hypocalcemia (n=75)	8 (100.0)	6 (100.0)	9 (90.0)	9 (100)	19 (90.0)	24 (88.9)	**0.002**
Hyperphosphatemia (n=50)	2 (25.0)	2 (33.3)	4 (44.4)	6 (50.0)	11 (58.0)	25 (92.6)	**0.000**
**Chi square test has been used*							

DISCUSSION

The most frequent age group was below 5 years, representing 54.3%, were the congenital anomalies of the kidney and urinary tract were the most common causes. This finding is similar to a study done in those in Egypt by Safouh et al, and in California by R. Tuttle et al (2019).[7]

Family history was found in 32.1% of cases, which might suggest that inherited disease is common in this study. This finding is similar to that of Ali et al 2019 (2019).[8]

The majority of patients were found in stage 5, accounting for (33.3%) followed by stage 4, accounting for 25.9%, while stage 1 was found in 9.9%. This is similar to a study done in Baghdad by Ali et al 2019[8] where stage 5 compromised 44% while stage 1 compromised 1% only, and in Egypt by Safouh et al 2015[9] where stages 1, 4, and 5 compromised 4.4%, 18.3%, and 57.6%, respectively.

In the current study, higher rates of ESRD are primarily attributable to very low public health awareness, delay in presentation or referral by primary and secondary care facilities, decrease awareness by doctors, poor access of patients from rural and remote areas to tertiary care facilities, and it's also possible that the majority of the patients came from consultation clinics and hemodialysis facilities. A research conducted in Serbia in November 2011 revealed conflicting findings, stating that the frequency of CKD stages II–IV is 2.4 times higher than that of CKD stage V.[10] but did not specify the explanation.

The study found that the leading cause of CKD was CAKUT, which accounted for 56.9%. This is consistent with similar studies conducted in various parts of the world. For instance, in Egypt, CAKUT accounted for 46% (9), in Belgium, 59%[11] were CAKUT, and in Iran, CAKUT was responsible for 38.4% of cases, according to Shahdani's 2019 study.[12]

In this study, the most frequent cause was obstructive uropathy, accounting for 19.8%; the metabolic cause was next, found in 14.8%; glomerulo-nephropathy was found in 13.6%; and an unknown cause was found in 7.4%. These findings are consistent with the study done by Safouh et al (2015)[9], in which CAKUT accounted for 46%, primary glomerulonephritis was the second among CKD etiologies, familial or metabolic disorders were third, and an unknown cause was found in 20.6% and also consistent with the study done by Ali et al 2019[8] where CAKUT presented in 34%, secondary reflux nephropathy in 17%, and glomerulopathy in 15%, while in 20% the cause is unknown.

However, in Sudan, a different study discovered that primary glomerulonephritis was the leading cause of CKD, accounting for 25.4% of cases. The cause was unidentifiable in 40% of cases, while congenital urological malformations accounted for 17.5%.[13] The reason for this variation in findings was unclear.

In this study, congenital anomalies were typically found at an earlier age, usually before the age of five, and manifested with signs and symptoms of CKD. Therefore, the diagnosis was established earlier than cases caused by glomerular issues, which tended to present after the age of five. These findings are consistent with a 2019 study conducted in the United States by R. Tuttle et al et al.[7]

In contrast to developed country, where antenatal screening enables early detection and corrective surgery soon after birth, congenital urological problems in our country are often diagnosed late. As a result, there is a delay in intervention.

In this study, high blood pressure was found in 25.9% of patients, with 71.5% of these cases occurring at stage 5. These findings are consistent with previous research by Ali et al, which reported uncontrolled blood pressure in 39% of cases, with prevalence increasing as CKD progressed to later stages. Additionally, Staples et al (2010)[9] found that 46.9% of patients with CKD were hypertensive.

The study conducted by Chiou et al in Taiwan in 2016[14] showed a different result, with only 10.5% of patients having hypertension. This difference could be attributed to variations in the severity of CKD, as most of the children in our study were in Stages 4 and 5, while the majority of children in the other study were in Stages 1 and 2.

In this study, it was observed that 60.4% of patients had short stature and 41.9% had low body weight. These findings are similar to a study conducted by Ali et al[8] in Baghdad, where 72% of patients were below the normal weight for their age, with only 28% falling within the normal range. Furthermore, 71% of the patients had short stature, while 29% had normal height.

There are many factors that contribute to the low height and weight for age in patients with CKD. CKD is a chronic disease that is associated with several comorbidities, including undernutrition, anemia, CKD-MBD, and growth hormone resistance.

These findings are similar to a prior report and are also similar to a study carried out in Darussalam in 2016[8], which reported that poor growth in children with CKD is linked to higher morbidity and mortality rates, and a considerable percentage of the study participants had weight (25.3%) and height (31.1%) below the 5th percentile.

Furthermore, following CKD stage 3, the prevalence of short stature and failure to thrive significantly increased. For children with CKD stage 3 or above, we advise exercising caution when developing treatment programs for optimum nutrition supplements and routine growth monitoring.

The prevalence of lower hemoglobin levels in this current study among CKD patients may be attributed to the fact that the patients were collected from tertiary centers and had a long duration of CKD, with most of them in end-stage renal disease (ESRD). This finding is consistent with a study conducted by Ali et al.[8]

In this study, uremia, hypocalcemia, and hyperphosphatemia were found in 92.6% and 61.7%, respectively, of patients, most of them in stages 4 and 5. This is similar to the study done by Chiou et al, when hypocalcemia and hyperphosphatemia were common and most of them in stages 4 and 5.[14]

LIMITATION

The main drawback of this study was that most of the research was done in hospital settings, which might have an impact on how broadly the findings can be applied. This conclusion may be further validated in a bigger sample size, extended duration, and multicenter investigation. Prognosis cannot be predicted due to the short study period and absence of community-based CKD-related research. The gold standard for determining GFR is insulin clearance, however it is no longer easily accessible.

CONCLUSION

The main frequent causes of CKD include congenital abnormalities, metabolic reasons, and glomerulopathies. The majority of congenital malformations and genetic reasons are diagnosed before the age of five, whereas

glomerulopathies are generally diagnosed after the age of five. The majority of CKD patients were in Stages 4 and 5, and the majority of CKD patients had poor growth and short stature.

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