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# Etiology of Chronic Kidney Disease in Children in Three pediatric Nephrology Centers in Baghdad

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**A B S T R A C T**

Chronic kidney disease is abnormalities of kidney structure or function, present for at least three months. Study the etiologies and stages of chronic kidney disease (CKD) in group of children and the correlation with some demographic criteria. Descriptive study included 100 patients with CKD, was conducted from the 1st of March to the end of August 2017. Demographic data were collected; examination of all patients and glomerular filtration rate (GFR) was calculated. Males were 49%, females were 51%. The most common cause of CKD was congenital anomalies in 34%, then secondary reflux nephropathy in 17%, glumerluopathies in 15%, hereditary causes in 10% of the patients. Congenital anomalies and Hereditary causes were diagnosed mainly before the age of 5 years in 52.9% and 88.9% respectively, while secondary reflux nephropathy and Glomerulopathy were diagnosed mainly after the age of 5 years in 64.7% and 73.3% respectively. The majority of patients were detected in stage V of CKD. Hypertension was found in 39% of patients, low weight for their age in 72%, short stature in 71%, and low PCV in 94%. The major causes of CKD are congenital anomalies, secondary reflux nephropathy, and glomerulopathies.

## Introduction

As described by the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI), Chronic kidney disease (CKD) is diagnosed if the patient had either of the following criteria are present[(1,2)]: 1. Kidney damage for ≥ three months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifested by one or more of the following features: Abnormalities in the composition of the blood or urine, abnormalities in imaging tests or abnormalities on kidney biopsy. 2. GFR < 60 mL/min/1.73 m2 for ≥ three months, with or without the other signs of kidney damage described above[(3)]. Risk factors affect CKD progression (non-modifiable): low nephron number as in low birth weight, growth periods

of rapid growth as in first year of life or after adolescent growth spurt, and acute kidney injury. Potentially modifiable risk factors: Hypertension. Proteinuria. Obesity. Acidosis. Anemia, Vascular disease, Tobacco, Uric acid, diet, Nutrition, and Metabolism and elevated serum alkaline phosphatase, low 25-OH vitamin D levels.[4, 5, 6, 7, 8]

Etiology of CKD, in children <5 years of age is associated mainly with Congenital malformations, Metabolic/genetic disorder and Congenital nephrotic syndrome. In those >5 years of age, etiology mostly of Glomerular disease [2].

Study the etiologies and stages of CKD in group of children from Nephrology centers in Baghdad city and the correlation with age groups. Study some demographic criteria of those children, and methods of diagnosis of CKD.

## Materials and Methods

A descriptive study was conducted in Pediatric Nephrology Clinic in AL Imamain Al-Khadmain Medical City from 1st of March to the end of August 2017.Study included 100 children with CKD, who were admitted to the wards or followed up in the consultation clinics or hemodialysis. Patients were collected from 3 Pediatric Nephrology Centers in Baghdad: AL Imamain Al-Khadmain medical City, Welfare Teaching Hospital, and Central Child Teaching Hospital. The duration of study was Etiology of chronic kidney disease was known from the files records of the patient with methods of diagnosis.

A well-constructed questionnaire was performed, in which direct interview was done between the patient and their relative and the doctors involved to collect data, which included the following: name, gender, age. Age at diagnosis of CKD. Etiology and clinical presentations of CKD, family history of renal disease and method of diagnosis of CKD.

Physical examination was performed to each patient at time of interview and the following measures were taken; height weight. Blood pressure (BP). Short stature is defined by height or length below 3rd centile or less than 2 standard deviations for that specific age and sex. Diagnosis of failure to thrive was considered if a child's weight is below the 5th percentile [3, 9]. Hypertension was defined as BP ≥95th percentile for age, height, and sex [4].

The following investigation done at time of recording: blood urea, Serum creatinine, Packed cell volume (because it is usually available in all centers)

Estimation of GFR by using Schwartz formula [2]

Patient were divided into five stages of CKD according to K/DOQI (The kidney disease outcomes quality initiative)[1,2]

Anemia is defined as a reduction of the hemoglobin concentration or red blood cell (RBC) volume below the range of values occurring in healthy persons. “Normal” hemoglobin and hematocrit (packed red cell volume) vary substantially with age and sex[10].

Statistical analysis: this is a descriptive study where most of the parameters were categorical so they are expressed as frequency and percentage except for some laboratory investigation parameters which were continuous so expressed as mean ± standard deviation.

## Results and Discussion

Total number of patients with CKD was 100 patients, 51% of them were females and 49% were males (F:M ratio 1.04:1).

The number of patients who were under five years of age was 22 while those above five years is 78. Regarding age of diagnosis, the highest proportion of patients diagnosed when they older than five years 54% and 46% were below five years. Mean age of patient was 9.2 years, while mean age of diagnosis was 6.3 years. Family history was positive for renal disease in 28%, while it was negative in 72% as shown in table 1.

Table 2 shows distribution of patients according to the etiology of CKD, which showed that congenital anomalies represent the most common cause and found in 34% of patient in which hypoplastic kidney found in 17%, primary reflux nephropathy 12%, multicystic kidney disease 2%, posterior urethral valve 2%, and single kidney 1%. Secondary reflux nephropathy ranked the second cause of CKD found in 17% of patient.

Glomerulopathy, found in 15% in which focal segmented glomerulosclerosis (FSGS) found in 6%, MPGN,RPGN and congenital nephrotic syndrome each represented 2%, while IgA nephropathy, shunt nephritis, SLE nephritis each represented 1% of the patients.

In this study hereditary causes, hemolytic uremic syndrome and renal stones each found in 9% of patients.

Table 3 show methods of diagnosis of CKD in which ultrasound (US) was the most common method, used in 58% of patients followed by CT scan in 41% of patients, VCUG used in diagnosis of 31%, renal biopsy used in 17%, serological test (C3, C4) used in diagnosis of 10% of patients, CBC and blood film used in 9% and eye examination in 6% of patients.

Table 4 shows the etiology of CKD according to age of patients at the time of diagnosis and show that the congenital anomalies was diagnosed before the age of five years in 52.9%, while diagnosed after five years in 47.1 % out of 34 patients. In patients with secondary reflux nephropathy, the patients who diagnosed before the age of five years represented 35.3%, while in those who diagnosed after the age of five years represented 64.7%. In glomerulopathy, the majority of the patient was diagnosed after the age of five years and represented 73.3% out of 15 patients. Hereditary causes were mainly diagnosed before the age of five years (88.9% of patients). In hemolytic uremic syndrome, and in renal stone 55.6% of patients were diagnosed after five years while in 44.4% of patients were diagnosed before the age of five years.

According to the distribution of patients according to stages of CKD, the majority were included in stage V, (44 patients), stage IV (23 patients), stage III (24 patients), stage II (8 patients) and only 1 patient in stage I (Figure 1).

Table 5 shows the distribution of patients according to clinical examination parameters, 39% of the patients were hypertensive while 61% were normotensive. 72% of patients were below normal weight for their age, while 28% were normal. 71% of patient was short stature, while 29% were of normal height.

Regarding laboratory investigation, the mean ± standard deviation of blood urea was 136.77 ± 70.27, for serum creatinine 4.33 ± 3.08 and for PCV was 28.32 ± 3.47. However, 94% of our patient had low PCV for their age and sex, as shown in table 6.

In the current study, the proportion of female patients included in the study was approaching to that of male patients. Male predominance was found by a number of studies as those conducted in Iran (57%) [(11)], Saudi Arabia [(12)] Sudan 2006 (60.5%) [(13)], in Kuwait 2005 (73.1%) [(14)], and Iraq 2008 (58%)[(15).]

In this study, congenital anomalies represented the commonest etiology of CKD. Similar

result was found by previous Iraqi study 2008, when reported that the congenital abnormalities of the urinary tract was the most predominant cause of CRF and found in 36% of patients [15].

Also a study conducted in Italy 2003 in which they observed that leading causes of CKD were hypodysplasia associated with urinary tract malformations in 53.6% of study patients [16]. Another study conducted in Iran 2001 reported that the commonest etiology was congenital urological abnormalities in 47% of CKD patients and stated that children with vesicoureteral reflux (VUR) were the most common malformation [11].

Belgian registries in May 2010 was in agreement with current result in which they observed that congenital anomalies of kidney and urinary tract were the main causes of CKD, accounting for 59% of all cases [17]. Congenital anomalies usually presented earlier with sign and symptoms of CKD so the diagnosis made earlier. Different result was found by the Australia and New Zealand Dialysis and Transplant registry when reported that glomerulonephritis was the most common cause of end stage renal failure in children and adolescents (42%) [18].

Ultra-sound was the most common tool used and achieved diagnosis in 58% of CKD patients. I t is well known that US used in the diagnosis of hypo plastic kidney, hydronephrosis, dilated ureter, polycystic kidney disease, multicystic kidney disease nephrolithiasis, single kidney, Wilms tumor. CT scan yield diagnosis in 41% of patients. CT scan used in detection of hypoplastic kidney, nephrolithiasis, polycystic kidney disease, Wilms tumor. Micturating cysto-urethrogram yield diagnosis in 31% of patient and was used in reflux nephropathy.[1, 2, 3, 4, 19]

In this study, high blood pressure was recorded in 39% of patients. The height was low in 71%; also 72% of patients had low weight for age.and94% of patient had low PCV.

**Table.1** Distribution of patients according to demographic data

| **Parameter** | | **No.** | **Percentage** |
|---|---|---|---|
| **Sex** | Males | 49 | 49% |
| | Females | 51 | 51% |
| **Age of patients (Yr)** | ≤ 5 | 22 | 22% |
| | > 5 | 78 | 78% |
| **Mean ± SD (range)** | 9.2±4.27 (3.0 months-18.0 years) | | |
| **Age of patients at diagnosis (Yr)** | ≤ 5 | 46 | 46% |
| | > 5 | 54 | 54% |
| **Mean ± SD (range)** | 6.37±4.06 (1.0 month-14years) | | |
| **Family history of renal disease** | Negative | 72 | 72% |
| | Positive | 28 | 28% |

**Table.2** Distribution of patients according to etiology of CKD

| Etiology | | No. | Percentage |
|---|---|---|---|
| Congenital anomalies<br>Hypoplastic Kidney<br>Primary reflux nephropathy<br>Multicystic kidney disease<br>Posterior Urethral valve<br>Single kidney | <br>171<br>222<br>1 | 34 | 34% |
| Secondary reflux nephropathy | 17 | 17 | 17% |
| Glomerulopathy Focal segmental glomerulosclerosis Membrane proliferative glomerulonephritis Rapidly progressive glomerulonephritis Congenital nephrotic syndrome IgA nephropathy Shunt nephritis SLE nephritis | <br>622<br>211<br>1 | 15 | 15% |
| Hereditary Cystinosis Nephronophthiasis Polycystic kidney | 531 | 9 | 9% |
| Atypical hemolytic uremic syndrome | 9 | 9 | 9% |
| Renal stone | 9 | 9 | 9% |
| Diabetic nephropathy | 2 | 2 | 2% |
| Others Wilm's tumor Bardet Beidle syndrome | 11 | | 2% |
| Unknown | 3 | 3 | 3% |

**Table.3** Methods of diagnosis of cause of CKD

| Methods of diagnosis | No. | Percentage |
|---|---|---|
| Ultrasound | 58 | 58% |
| CT scan | 41 | 41% |
| VCUG | 31 | 31% |
| Renal biopsy | 17 | 17% |
| Serological test: C3 & C4 | 10 | 10% |
| CBC & blood film | 9 | 9% |
| Eye examination | 6 | 6% |

**Table.4** Etiology of chronic kidney disease according to age of diagnosis

| Etiology | Age≤ 5 years | Age> 5 years | Total |
|---|---|---|---|
| Congenital anomalies | 18 (52.9%) | 16 (47.1%) | 34 |
| Secondary reflux nephropathy | 6 (35.3%) | 11 (64.7%) | 17 |
| Glomerulopathy | 4 (26.7%) | 11 (73.3%) | 15 |
| Hereditary | 8 (88.9%) | 1 (11.1%) | 9 |
| Hemolytic uremic syndrome | 4 (44.4%) | 5 (55.6%) | 9 |
| Renal stones | 4 (44.4%) | 5(55.6%) | 9 |
| Diabetic nephropathy | 0 (0%) | 2 (100%) | 2 |
| Others | 1 (50.0%) | 1(50.0%) | 3 |
| Unknown | 1 (33.3%) | 2 (66.7%) | 3 |
| Total | 46 (46%) | 54 (54%) | 100 |

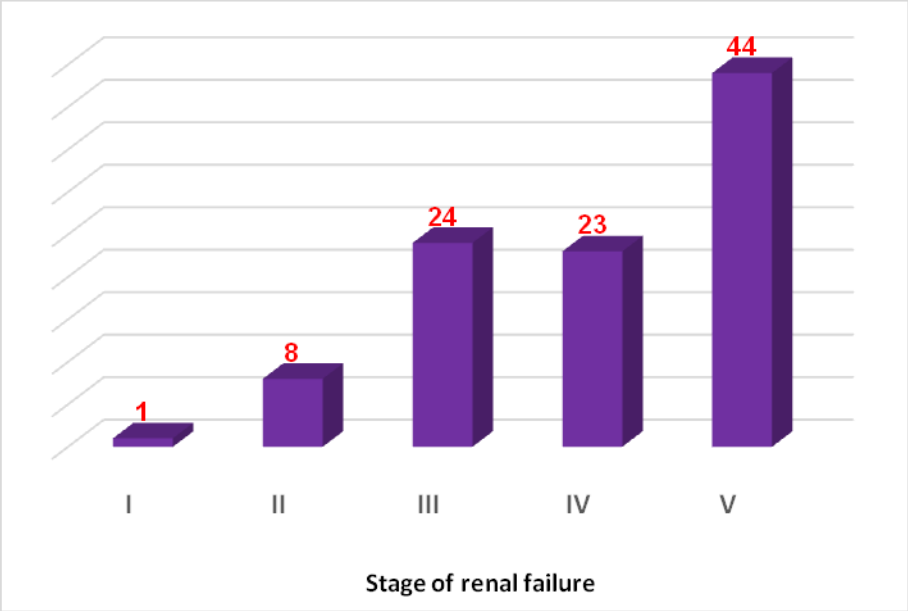
**Table.5** Distribution of the patients according to clinical parameters

| Parameter | State | No. | Percentage |
|---|---|---|---|
| Blood pressure | Normal | 61 | 61% |
| | High | 39 | 39% |
| Height | Normal | 29 | 29% |
| | Low | 71 | 71% |
| Weight | Normal | 28 | 28% |
| | Low | 72 | 72% |

**Table.6** Distribution of patients according to laboratory investigations

| **Lab. Investigation** | | **Mean ± SD** |
|---|---|---|
| **Bl. Urea(mg/dl)** | | 136.77±70.27 |
| **S. Creatinine(mg/dl)** | | 4.53±3.08 |
| **PCV%** | Mean ± SD | 28.32±3.47 |
| | No. of Normal | 6 (6%) |
| | No. of Low | 94 (94%) |

**Fig.1** Frequency of patients according to stage of CRF




A study conducted in Darussalam in 2016 observed that Poor growth in children with CKD is associated with increased morbidity and mortality and a significant proportion of study patients were below the 5th percentile for weight (25.3%) and height (31.1%). This is not unusual for children with CKD due to congenital predisposition, electrolyte imbalances, malnutrition, bone disease and medications. Blood pressure measurement in the same study yield high reading in (34%) of patients, and anemia found in 23.2% of them. [(20)]. Higher BR readings, and lower PCV values in the current study may be due to

collection of patients from tertiary centers, where the patients had long duration of CKD and most of them in ESRD (44%). In this study, end stage renal failure (ESRD) (stage V) had the highest proportion in 44 patients (44%), while stage I diagnosed in one patient (1%) only. This result was in accordance with 2 studies conducted in Turkey and Vietnam in which they observed that majority of the patients were in stage V (32.5%) and (85%) respectively [21, 22]. Different result was recorded in a study conducted in Iraq 2008 as it showed that 20% of patients were in the end stage of renal disease while the majority was in the moderate stage (32%) [15]. Different result was shown in a study conducted in Serbia in Nov 2011 when reported that prevalence of CKD stages II–IV is 2.4 times greater than the prevalence of CKD stage V [23]. Higher rates of ESRD in the current study mostly due to the collection of patients from hemodialysis centers.

The current study showed that congenital anomalies were diagnosed in 52.9% in ≤ 5 years old while Glomerulopathy constituted the major cause of CKD in patients > 5 year old. A study conducted in India in Nov 2003 in which they observed that obstructive uropathy diagnosed in 31% of the study patients with highest proportion at age 0-5 years (15.4%) followed by chronic glomerulonephritis that diagnosed in (27.5%) of study patients with highest proportion at age 11-18 years (13.4%) [24]. In another study conducted in Thailand in Jul 2008, results obtained showed that etiologies of CKD were significantly different in each age group, with genito-urinary anomalies and glomerulonephritis being the major causes of CKD in children aged ≤ 6 years (55.6%) and > 6 years (61.5%), respectively.[25]

In conclusion, the major causes of CKD are congenital anomalies, secondary reflux nephropathy, and glomerulopathies. Most of the congenital anomalies and hereditary causes diagnosed before 5 years of age while secondary reflux nephropathy, and glomerulopathies mostly diagnosed after 5 years of age. The majority of patient with CKD were included in Stage V and most of patient with CKD had poor growth and short stature.

## Recommendation

Early detection of CKD by screening test and laboratory investigations and referral to pediatrics nephrologists to receive their proper management in pediatric nephrology center.

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