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Chronic kidney disease in children: A report from a tertiary care center over 11 years.

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ABSTRACT

Background: Chronic kidney disease (CKD) is an overwhelming illness in children. Considering the importance of CKD in pediatric age group, in addition to the racial and ethnic differences in prevalence and etiology of CKD, epidemiologic studies are recommended. The majority of the results regarding the incidence of CKD have been achieved from studies on hospitalized children.

Objectives: This study evaluates the incidence and etiology of chronic renal failure (CRF) in children in a tertiary care center in Isfahan, the second large province of Iran.

Patients and Methods: A retrospective analysis of medical record data of children less than 19 years old, hospitalized for CKD at St Alzahra hospital, Isfahan, Iran, during the period of November 2001 until December 2011 was made. A total of 268 eligible cases were recruited. Patients were categorized into 5 groups according to glomerular filtration rate (GFR) and KDOQI guideline.

Results: Out of 268 patients, 144 patients were male (54%). The mean and median of age was 11.01± 0.39(SD) years and 12.5 years, respectively. Approximately 55% of patients had either systolic and/or diastolic hypertension. The most frequent etiology of CKD was glomerular diseases (34%) followed by reflux nephropathy (16.7%). Most patients (74.8%) had GFR less than 15 ml/min/m², when diagnosed. Anemia was the most prevalent laboratory abnormality (85%). Small-size kidneys were seen in 65.8% of patients. Kidney replacement therapy (either hemo- or peritoneal dialysis) was applied for 72.3% of the patients. The transplantation rate average was 7.2 per million children population. The annual incidences of CKD (mostly advanced stages) were 5.52 per million population (PMP) and 16.8 per million children population, respectively. The all cause of mortality rate was 18.4%. Younger age was the only independent predictor of mortality (p=0.005).

Conclusions: We concluded that glomerular diseases are the leading cause of CKD in our patients. In addition, the annual incidence of CKD is considerably high.

Original Article

Implication for health policy/practice/research/medical education:
Chronic kidney disease (CKD) is an overwhelming illness in children. This study evaluates the incidence and etiology of CKD in children in a tertiary care center in Isfahan, Iran. We found that, glomerular diseases are the leading cause of CKD in our patients. In addition, the annual incidence of CKD is considerably high.

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1. Background

Chronic kidney disease (CKD) is an overwhelming illness in children. The mortality rate of children receiving dialysis is 30-150 times greater than that of normal population (1, 2). While CKD affects 500 per million populations per year of adults, 1%-2% is in the pediatric age group (3). Irrespective of lower incidence of CKD in children, compared with adults, the cost of treating end- stage renal disease (ESRD) is still significant (4). Total economic cost of North American ESRD programs reached 25.2 billion dollars in 2002 and more increase in the following years was expected (4). Considering the importance of CKD in pediatric age group, in addition to the racial and ethnic differences in prevalence and etiology of CKD, more epidemiologic studies are recommended (5). However, differences in evaluating methods have flawed the data sources (5). Furthermore, the majority of the results regarding the incidence of CKD have been achieved from studies on hospitalized children. In this regard, we previously reported the incidence of acute kidney injury in our tertiary care center (6).

2. Objectives

In this study, we evaluated the incidence and etiology of pediatric CKD in our tertiary care center in Isfahan, Iran.

3. Patients and Methods:

A retrospective analysis of medical record data of children less than 19 years hospitalized for CKD at St Alzahra hospital, Isfahan, Iran, during the period of November 2001 until December 2011 was performed. CKD was defined as either kidney damage or glomerular filtration rate (GFR) < 60 ml/min/1.73m² for more than 3 months (table 1) (7). A total of 268 eligible cases were recruited. For every patient, demographic and anthropometric data, laboratory data (serum creatinine and electrolytes), electrocardiographic findings; ultrasound results, chest-x-Ray findings, and etiology of CKD were recorded. glomerular filtration rate (GFR) was calculated based on Schwartz formula (8). Patients were categorized into 5 groups according to GFR and KDOQI guideline (7).

Table 1: Stages of CKD according to KDOQI guideline

Stage	Description	GFR ml/min/1.73m²
1	Kidney damage with normal Or increased GFR	≥ 90
2	Kidney damage with mild decrease GFR	60-89
3	Moderate decrease GFR	30-59
4	Severe decrease GFR	15-29
5	Kidney failure	< 15

4. Results

Out of 268 patients, 144 patients were male (54%) and 124 (46%) were female. Male to female ratio was 1.2/1. The mean and median age was 11.01± 0.39 (SD) years and 12.5 years, respectively. The mean of body weight was 25.4± 1.23 (SD) Kg. The means of age and body weight were not significantly different between male and female (p>0.05), (table 2). Approximately 55% of patients had either systolic and/or diastolic hypertension. The means of systolic and diastolic blood pressure were 124.72± 2.4 mmHg (SD) and 81.02± 1.65 mmHg (SD), respectively. Diastolic blood pressure was significantly higher in female than male patients (p=0.045) (table 2). The most frequent etiology of CKD was glomerular diseases (35.2%) followed by congenital anomaly of kidney and urinary tract (CAKUT) (34.5%). Nonetheless, in 21.7% of patients the etiology of CKD was unknown (table 3). Most patients (74.8%) had GFR less than 15 ml/min/m² when diagnosed (table 4). Anemia (hemoglobin <5th percentile) was reported in 85% of

patients followed by hyperphosphatemia (67.7%), hypocalcemia (55.1%) and acidosis (34.7%). The means of various biochemical parameters and electrolytes are shown in table 5. While increased renal echogenicity was the most frequent ultrasound abnormality (70.2%), small-size kidneys were seen in 65.8% of patients. Cardiomegaly (increased cardiothoracic ratio) was reported in 34.3% of patients. Only 13.6% of patients had pleural effusion. Kidney replacement therapy (either hemodialysis or peritoneal dialysis) was applied for 72.3% of patients. Up to December 2011, 97 patients (36.4%) were received kidney allograft, mostly from non-related living donors (75.3%). The transplantation rate averages were 7.2 per million children population. Out of 97 patients, 46.4% of them were female. Mean and median of age in kidney transplant recipients were 15.43± 0.38 (SD) and 16 years respectively. Mortality rate among kidney transplant recipients was 13.4% (13 patients). However, only two patients died from transplantation sequels shortly after surgery. The remaining (11 patients) died up to the date of completing survey because of severe systemic infections and or malignancy. Nephrectomy was performed for 2 patients owing to renal vein thrombosis. Mortality in kidney transplant recipients had reverse correlation with younger age (r=-0.307, p=0.002).

Table 2: Patients' demographic findings

Variable	Mean	±SD	P
Age (year)			
Female	11.5	±0.51	N.S
Male	10.6	±0.56	
Body weight (kg)			
Female	27.34	±1.77	N.S
Male	23.77	±1.70	
Systolic Blood pressure (mmHg)			
Female	128.100	±3.50	N.S
Male	122.480	±3.30	
Diastolic Blood Pressure (mmHg)			
Female	84.870	±2.55	P=0.045
Male	78.320	±2.13	

Table 3: Etiology of CKD

Etiology	frequency
Glomerular Disease	
Nephrotic syndrome (FSGS)	19.4%
Glomerulonephritis	15.8%
Congenital anomaly of kidney and Urinary tract (CAKUT)	
Reflux nephropathy	16.7%
Kidney cystic diseases	7.3%
Obstructive uropathy	6.3%
Kidney hypo-dysplasia	4.2%
Vasculitis	1.6%
Stone	2.8%
Cystinosis	4.2%
Unknown	21.7%

Table 4: Frequency of diseases based on CKD stages

GFR	Frequency	Valid Percent
<15	199	74.8
15- 29	34	12.7
30-59	9	3.4
60-89	14	5.4
≥90	10	3.7

Table 5: Mean of serum biochemical findings and electrolytes

Variables	Mean±SD
Creatinine (mg/dL)	5.37±0.27
Serum sodium (mEq/L)	137.11±0.36
Serum potassium (mEq/L)	4.61±0.06
Serum phosphate (mg/dL)	6.24±0.18
Serum calcium (mg/dL)	8.02±0.10
Alkaline phosphatase(U/L)	561.34±44.97
Parathyroid hormone (pg/mL)	291.21±53.77
Hemoglobin (g/dL)	8.3881±0.17
ESR (mm/hour)	63.28±3.88
Blood pH (pH units)	7.34±0.00
Serum bicarbonate (mEq/L)	14.20±0.42
$PaCO_2$ (mmHg)	23.16±0.65
Calcium× Phosphorus (mg^2/dL^2)	50.04±1.56

The all cause mortality rate was 18.4% (49 patients). Out of 49 patients, 13 patients (26%) were died after transplantation. The annual incidences of CKD (mostly advanced stages) were 5.52 per million population (PMP) and 16.8 per

million children population respectively. In addition, CKD prevalence in our province was 5.06 per million populations. There was no association between mortality and the following factors; serum PTH level, Ca x P product, CRP level, electrolyte levels and hemoglobin. In addition, no significant correlation was seen between mortality and systolic and/or diastolic hypertension, etiology of disease and body weight. Among all factors, only patient's age had reverse association with mortality (r=-0.291, p=0.001). Furthermore, after applying regression multiple analysis, younger age was the only independent predictor of mortality (p=0.005).

5. Discussion

In the present study we assessed the prevalence of CKD over 11 years in a tertiary care center in Isfahan province. Since this center is the only tertiary pediatric nephrology center in our province, the results may give a good representation of CKD in our province. The results of our study revealed a noteworthy prevalence of new cases of advanced stages of CKD. Most available information regarding the prevalence of CKD comes from the observational but not epidemiological studies worldwide (5). Comparing with similar studies, we observed that the prevalence of CKD is higher in our province. The high percentage of young population in our country may be partly responsible of this difference. Mong Hiep et al. reported the average annual number cases of 4.8 per million child population native to Ho Chi Minh City (9). The cumulative annual incidence in Jamaica was 4.61 per million child population under age 12 years (10). However, the annual incidence of CKD in Wales was higher (8.60 in 1996) (11). Data from a prospective large sample-size study in Italy (ItalKid projects) revealed a mean incidence of 12.1 per million populations under 20 years (12). Data from Slovakia showed that the overall incidence of CKD in children (until 18 years of age) was 18.2 per million inhabitants and 71.7 per million children (13). Since various studies recruited different populations from different ethnicities, and the results showed diversity. Almost all children with advance stages of CKD have being referred to our tertiary pediatric nephrology center. Therefore, the results of this study demonstrated the incidence of advanced stages of CKD very close to total incidence of CKD in our province.We had a male preponderance in our patients. The similar results have been achieved by many studies (10, 14, 15). The median age of our patients was higher than the patients of southwest of Iran (12.5 years compared to 4.2 years) (14). The male patients referred to our center were at a younger age. Whether parents' attention to male child is the reason of this difference, and should be assessed precisely. The age of diagnosis of CKD varies widely. A part of this diversity rises from difference in responsible etiologies. In those countries that congenital anomalies of kidney and urinary tracts (CAKUT) are the most prevalent causes of CKD, the age of diagnosis was lower than those with a high frequency of glomerular diseases (10, 14, 16).Evaluating the clinical signs of our patients, revealed that hypertension (HTN) was the most prevalent sign (more than 50% of patients) followed by anemia. Surprisingly, in most cases, HTN was detected for the first time at hospital. Wilson et al. reported HTN in as frequent as 46% of their patients (17). A cohort study on 366 children showed that HTN was observed in more than 70% of patients, while anemia and growth retardation were reported in 37% and 12% respectively (18). Most of the patients of this study was placed in stage 1 and 2 CKD, while the majority of our patients were in

stage 5. Anemia has been known as a common abnormality in CKD (19). In 2011, a multicenter prospective children chronic kidney disease study showed that anemia was the most frequent finding in advance stages of CKD (20). In the same way, Mong Hiep et al. reported that HTN was the second most prevalent sign after anemia (9). We observed anemia in 85% of patients. It is not surprisingly to find anemia in most patients since anemia is detectable when GFR reaches 60 ml/min/1.73m^2 or less (21). Nonetheless, anemia is not infrequent in early stages of CKD (22).Considering the etiology of CKD, different results have been achieved from various studies. Neild et al. reported that CAKUT is the leading cause of CKD worldwide (23). While, CAKUT was the most frequent cause of CKD in Italy, Slovakia, Saudi Arabia, Jamaica, Serbia and southwest of Iran, we showed that glomerular diseases were the leading cause of CKD in our province (10,12-14, 16, 24). Similarly, data from Iraq and Australia, demonstrated that glomerular disease was the most single etiology of CRF (15, 25). Higher mortality was reported in CKD children with poor growth (26). We did not demonstrate such association. However, younger age was the only independent factor of mortality among our patient.Since most of our patients had GFR less than 15 ml/min/m^2 (approximately 75%), renal replacement therapy (either hemodialysis and or peritoneal dialysis) was applied for a majority of them. The rate of renal replacement therapy differs among different studies. Obviously, it is depend on patients' GFRs and also hemodynamic and electrolytes imbalance. In addition, feasibility of performing renal replacement therapy in every center may be responsible for dissimilarity among the results (5, 9, 10, 12-15). Most of our patients were received kidney transplantation from non-related living donors. Transplantation rate in our province was higher than Africa, southwest of Iran, Iraq and Saudi Arabia but lower than Spain and the USA (13-16, 27, 28).Given that CKD is becoming a health burden worldwide, strategic plans by health care providers and policy makers have been recommended to find patients at risk (29).The limitation of this study is gathering data from hospitalized patients and hence missing many patients with CKD stages 1 and 2. Nevertheless, the strength of this study is recruiting patients from only pediatric nephrology tertiary care center of our province.

6. Conclusions

We concluded that glomerular diseases are the leading cause of CKD in our patients. In addition, the annual incidence of CKD is high. Since, early stages of CKD may be detectable by screening tests, cohort studies and screening programs should be considered further. Furthermore, a pediatric CKD registry system should be launched.

Authors' contributions

AG defined the aim of research and the study design. SH, AM,SFT and YM participated in the design of the study and performed the statistical analysis and wrote some parts of the draft. AG prepared the manuscript. All authors read and approved the final manuscript.

Conflict of interest

The author declared no competing interests.

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