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Original Article (Pages: 2105-2112)

Etiology and Outcome of Chronic Kidney Disease in Iranian Children

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Abstract

Background

Considering the significant geographical and ethnical differences in pattern of incidence, etiology and outcome of chronic kidney disease (CKD), the present study aimed to assess the etiology and outcome of CKD in Iranian children.

Materials and Methods

In a cross-sectional study etiology and outcome of 372 children aged 3 months to 18 years with CKD was studied during the period 1991 –2014. Children (186 boys, 186 girls) with Stage 3 to 5 CKDs, defined as a glomerular filtration rate below 60 ml/min per 1.73 m2body surface area, were identified.

Results

Etiology was congenital anomalies of the kidney and urinary tract in 125 (33.60%), cystic/ hereditary/ congenital diseases in 91 (24.46%), glomerulopathy in 73(19.62%), and cause unknown in 71 (19.09%) patients. Forty-eight (13.22%) were on conservative treatment, 174(47.93%) had end-stage renal disease (ESRD) with chronic hemodialysis, 24 (6.61%) were on continuous ambulatory peritoneal dialysis. Sixty-eight (18.74%) underwent on renal transplant which was successful in 52 (14.33%) patients but was associated with abnormal renal function in 16(4.41%) children. Finally, 49 (13.50%) patients died.

Conclusion

A large number of children developed CKD secondary to congenital anomalies of the kidney and urinary tract. Planning for screening, early detection and instituting timely treatment of preventable causes could lead to a lower incidence of CKD in this group of children.

Key Words: Acute kidney injury; Etiology; Children; CAKUT; End-stage renal disease.

*Please cite this article as: Ataei N, Hosseini M, Baikpour M, Ataei F, Bloori Jirandeh H, Bazargani B, et al. Etiology and Outcome of Chronic Kidney Disease in Iranian Children. Int J Pediatr 2016; 4(7): 2105-12.

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Received date Mar 05, 2016 ; Accepted date: Mar 22, 2016

1- INTRODUCTION

Chronic kidney disease (CKD) is considered as one of the most common health problems worldwide (1). Although the prevalence of CKD is much lower in children compared to adults (2), but the more complications observed in children and the much higher costs of treatment in these age groups impose a great burden on the patients and their families and have a significant effect on their quality of life (3, 4). For instance, children with CKD suffer from growth retardation and abnormal development along with constant problems in various organs including cardiovascular, endocrine and gastrointestinal systems (5, 6). Even some studies have reported a significant association between CKD and cognitive disorders in children (7).

Early detection and treatment of CKD plays a key role in management of CKD in pediatric patients. Therefore, identification of different etiologies and outcomes can be helpful in preventing development of CKD in children (8). Considering the significant geographical and ethnical differences in pattern of incidence, etiology and outcome of CKD in children (4), further studies should be carried out in various geographic regions and among different ethnicities. Iran is a developing country of 70 million people, of whom 50% are below 18 years of age. Due to the lack of a central reporting agency, little is known about the incidence, etiology, and treatment of CKD of Iranian children. Accordingly, the present survey aimed to evaluate the etiologies and outcomes of CKD in Iranian children.

2- MATERIALS AND METHODS

2-1. Study design and setting

This cross-sectional study was conducted on children younger than 18 years old with stage 3 to 5 CKDs, having had referred to Children's Hospital Medical Center in Tehran, Iran, during 1991-2014. Informed written consent was obtained from the patients' parents. The protocol of the survey was approved by the ethics committee of Tehran University of Medical Sciences. All the authors adhered to the declaration of Helsinki principle throughout the project.

2-2. Participants

All the children with stage 3 to 5 CKDs were included in the study, consecutively. Exclusion criteria included being younger than 3 months old and previous inclusion in the study population. Stage 3 to 5 CKDs were defined as an estimated Glomerular Filtration Rate (eGFR) of less than 60 ml/min/1.73m2 (9). Schwartz' formula was used to calculate the subjects' GFR.
Considering the severity of CKD, subjects were classified into 4 categories according to their eGFR which included:

- Mild (eGFR=45-60 ml/min/1.73 m^2),
- Moderate (eGFR=25-44 ml/min/1.73 m^2),
- Severe (eGFR=10-24 ml/min/1.73 m^2) and
- End-stage renal diseases (eGFR<10 ml/min/1.73 m^2).

2-3. Data Collection

A trained physician gathered data from patients' files. Routinely, in the Children's Hospital Medical Center, data on demographic characteristics of the subjects including age, gender, height and weight were gathered on the patients' arrival. Then information on the past medical history of cardiac and other underlying diseases and the drug history of particularly anti-hypertensive medications were inquired through interview with the parents. Systolic and diastolic blood pressures of the children were measured via a mercury sphygmomanometer from the right arm of the children in a comfortable sitting position. Blood pressures were measured twice (with an interval of at least 30 seconds). Mean

value of the two recordings was used. Finally, 5 ml of venous blood was drawn from the cubital vein of the right arm for assessing the level of blood urea nitrogen (BUN), creatinine, parathyroid hormone and serum albumin.

2-4. Definition

Hypertension was considered as having a blood pressure higher than the 95th percentile plus 5 mmHg according to the guidelines provided by the Eighth Joint National Committee (JNC-8) (10).

In order to simplify assessment, patients were categorized into 7 groups regarding their etiologies for CKD, including: congenital anomalies of the kidney and urinary tract (CAKUT), glomerulopathies, cystic/hereditary/congenital disease, neoplasia/tumors, other renal disorders, miscellaneous conditions and unknown.

2-5. Outcome

Outcomes assessed in this survey included the death or living status, cause of death, their treatment (conservative, hemodialysis or peritoneal dialysis) and final results of their kidney transplant (with normal or abnormal renal function).

2-6. Statistical Analysis

The study sample size was estimated to be approximately 329 subjects according to a 69% prevalence of need for dialysis (11) in children with CKD (P=0.69), for α=0.05 and a precision of 5%. Eventually, information gathered from 372 children with CKD was included in the survey.

Descriptive analyses were performed using STATA 11.0 statistical software. Quantitative data were reported as means and standard deviations and the qualitative information were presented as frequencies and percentages.

3- RESULTS

A total of 372 children with CKD were included during 1991-2014. The proportion of males and females were equal with 186 subjects in each gender. The final outcome of 9 patients was not clear; therefore, data on 363 patients are presented in the final outcome reports. The mean age of the study population was 7.71±3.94 years with a range of 0.42 to 16.56 years.

There were 74 (19.9%) patients below 2 years of age, 72 (19. 35%) were within the age range 3–6 years, 113(30.37%) patients were within the age range 7-10 and 113(30.37%) patients were within the age range 11-18 years of age, of whom 106 (28.49%) were aged between 11 years and 15 years.

Table.1 presents the baseline characteristics of the subjects. The etiology was CAKUT in 125 (33.60%), cystic/ hereditary/ congenital diseases in 91 (24.46%), glomerulopathies in 73 (19.62%), and cause unknown in 71 (19.09%) patients (**Figure.1**).

Detailed etiology of chronic kidney diseases in children aged 0-18 years is presented in **Table.2**.

Of the 372 children, 48 (13.22%) were on conservative treatment, 174 (47.93%) had end-stage renal disease (ESRD) with chronic hemodialysis, 24 (6.61%), were on continuous ambulatory peritoneal dialysis. Sixty-eight (18.74%) underwent on renal transplant which was successful in 52 (14.33%) patients and was associated with abnormal renal function in 16 (4.41%).

Finally, 49 (13.50%) patients died, the etiology of which was cardiovascular in 20 (20.81%), infection in 5 (10.20%) and it was unknown in 11 (22.45%) patients (**Figure. 2**).

Table1: Baseline characteristics of in children aged 0-18 years with chronic kidney diseases

Variable	Mean ± SD
Age	8.3±4.0
Height (cm)	105.3±34.4
Wright (kg)	22.8 ±10.9
BUN (mg/dl)	76.8±44.4
Creatinine	9.3±49.3
Albumin	6.5±30.2
Parathyroid hormone	393.1±353.9
Gender (n, %)	
Boy	186 (50.0)
Girls	186 (50.0)
Hypertension (n, %)	
BP> 95th centile with treatment	152 (42.70)
BP> 95th centile without treatment	6 (1.64)
BP< 95th centile with treatment	101 (28.37)
BP< 95th centile without treatment	97 (27.25)
Cardiac diseases (n, %)	
Left ventricular hypertrophy	43 (11.84)
Heart failure	21 (5.78)
Arrhythmia	9 (2.48)
Other	58 (15.98)

Table 2: Etiology of chronic kidney diseases in children aged 0-18 years

Etiology	N (%)
Congenital anomalies of kidney and urinary tract (CAKUT)	
A) Obstructive	
Posterior urethral valve	17 (4.57)
Anterior urethral valve	1 (0.27)
Bilateral ureteral stenosis	2 (0.54)
Ureteropelvic junction stenosis	6 (1.61)
Ureterovesical junction stenosis	3 (0.81)
Other Obstructive Malformation	4 (1.08)
Neurologic bladder	14 (3.76)
Reflux nephropathy/ pyelonephritis	
Interstitial nephritis	6 (1.61)
Reflux nephropathy	50 (13.44)
Pyelonephritis	6 (1.61)
Vesicoureteral reflux associated neurologic bladder	14 (3.76)
Vesicoureteral reflux without associated neurologic bladder	4 (1.08)
Glomerulopathies	
Focal segmental glomerulosclerosis	23 (6.18)
GN with advanced diffuse sclerosis	1 (0.27)
Idiopathic crescentic glomerulonephritis	1 (0.27)
Focal segmental proliferative glomerulonephritis	1 (0.27)
Post infectious glomerulonephritis	3 (0.81)
Rapidly progressive glomerulonephritis	16 (4.30)
Membranous glomerulonephritis	1 (0.27)
Membranoproliferative glomerulonephritis	6 (1.61)

Idiopathic nephrotic syndrome	11 (2.96)
Lupus nephritis	7 (1.88)
Henoch-Schoenlein purpura	3 (0.81)
Cystic/hereditary/congenital disease	
Renal aplasia / hypo/dysplasia	24 (6.45)
Juvenile nephronophthisis	7 (1.88)
Infantile polycystic kidney diseases	7 (1.88)
Undetermined polycystic kidney diseases	1 (0.27)
Primary hyperoxaluria	1 (0.27)
Laurence Moon Biedl syndrome	4 (1.08)
Congenital nephrotic syndrome	9 (2.42)
Alport syndrome	8 (2.15)
Cystinosis	12 (3.23)
Hemolytic-uremic syndrome	17 (4.57)
Renal infarct	1 (0.27)
Neoplasia / tumors	
Wilm's tumor	2 (0.54)
Other renal disorders	
Fanconi syndrome	1 (0.27)
Miscellaneous conditions	
Nephrolithiasis	3 (0.81)
Hyperoxaluria	6 (1.61)
Unknown	71 (19.09)

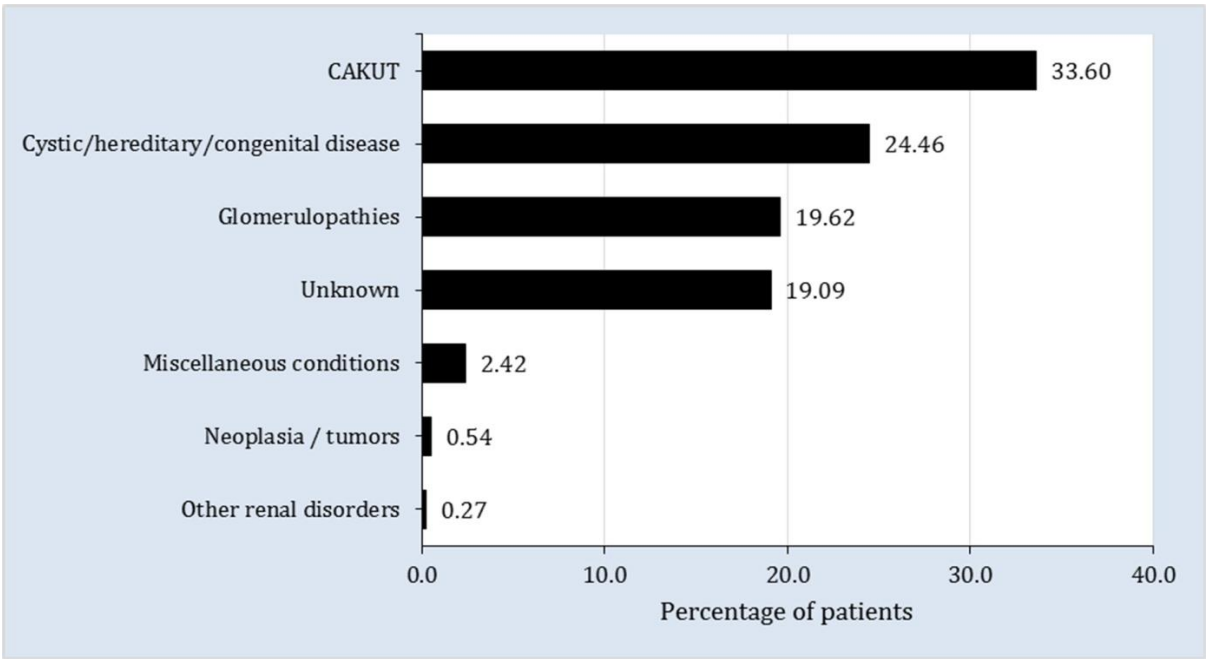

Fig.1: Etiology of chronic kidney diseases in children aged 0-18 years.

CAKUT: Congenital anomalies of the kidney and urinary tract.

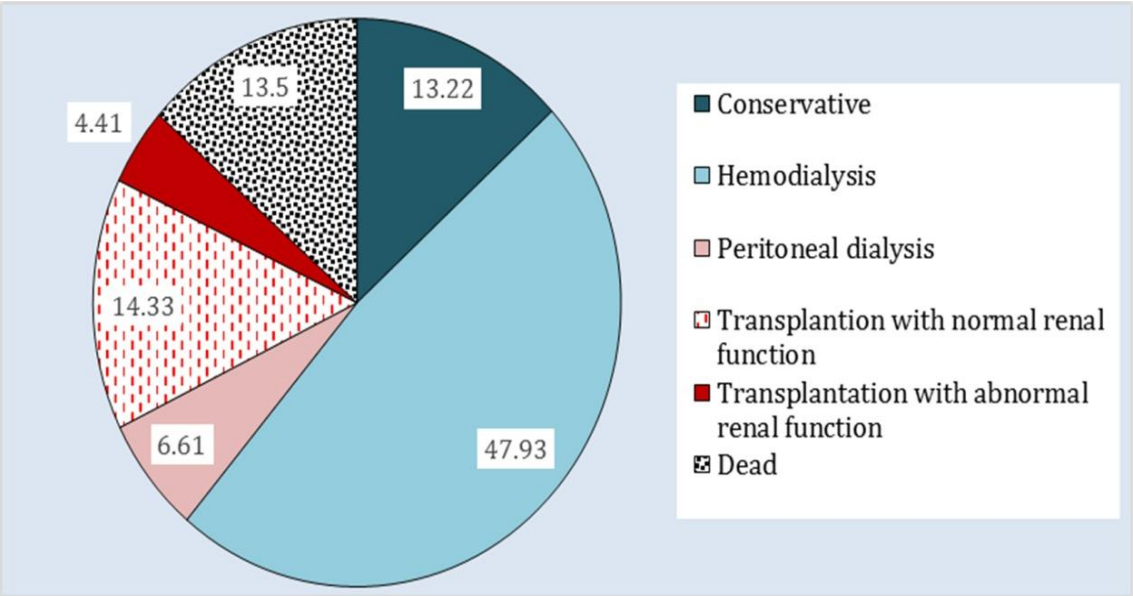

Fig.2: Outcome of chronic kidney diseases in children aged 0-18 years. Data was presented as percentage of patients.

4- DISCUSSION

The results of the present study showed that CAKUT and cystic/ hereditary/ congenital diseases were the most prevalent etiologies of CKD among Iranian children. Mortality rate was reported to be 13.50% in these patients, the most prevalent cause of which was cardiovascular diseases.

Congruent with the results of the present survey, Madani et al., reported CAKUT as the most common etiology of kidney disease in Iran (12). Moreover, Gheissari et al. reported that the most prevalent cause of CKD in Iranian children is CAKUT (13). So, the early detection and treatment may be helpful in reducing the burden of CKD. In this regards, many of the congenital abnormalities of kidney and urinary tract can be diagnosed through imaging studies and appropriate prenatal and postnatal measures may prevent or decrease the progression of the disease into the ESRD (14). Laparoscopic polar nephrectomy with ureteropyeloanastomosis and other fetal surgeries are of the recommended treatments for these conditions (15).

Mortality rate among our study was estimated to be approximately 13.5%. This figure varied in different geographical regions and ethnicities. For example in Sudanese population, Ali et al. (16) reported a 23.4% mortality rate in children with CKD while it was reported to be 8.3% in Saudi Arabia (17).

The mortality rate and final outcome of CKD is closely related to the economical situation of the studied population and their access to health care resources. More than 90% of the treated ESRD patients are from developed countries while most CKD-related mortalities are reported in countries with lower incomes. This might be due to the fact that economical problems force the patients to cease from renal replacement therapies (18-21). Therefore, special attention needs to be paid to this matter. Supportive and insurance systems in low income countries should cover children with CKD in order to decrease its mortality rate.

4-1. Limitations of the study

Although to the best of our knowledge the present study includes the highest number of Iranian children with CKD, but

it being a single center survey restrains us from generalizing our results to the whole country. However, Children's Hospital Medical Center, as the main pediatric referral center in Iran, not only has patients from Tehran, but also has referrals from all over the country. In fact, 50.6% of the children in the present study were coming from provinces other than Tehran. On another note, despite the consecutive sampling method executed in this survey, the results might be subject to selection, information and measurement biases.

5. CONCLUSION

A large number of children developed CKD secondary to congenital anomalies of the kidney and urinary tract. Cystic/ hereditary/ congenital diseases, glomerulopathies, and unknown causes also were common etiology of CKD in our series. Planning for screening, early detection and instituting timely treatment of preventable causes could lead to a lower incidence of CKD in this group of children.

6- CONFLICT OF INTEREST

All the authors declare that they have no conflict of interest.

7- ACKNOWLEDGMENTS

This research has been supported by Tehran University of Medical Sciences & health Services grant (Number: 94-02-184-26097).

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