Chronic Kidney Disease in Iran: First Report of the National Registry in Children and Adolescences

Neamatollah Ataei[1]*, Abbas Madani[1], Seyed Taher Esfahani[1], Hasan Otoukesh[2], Nakysa Hooman[2], Rozita Hoseini[2], Mojtaba Fazel[3], Ali Derakhshan[4], Alaleh Gheissari[5], Hadi Sorkhi[6], Arash Abbasi[1], Daryoosh Fahimi[7], Fatemeh Ghane Sharbaf[8], Fakhrossadat Mortazavi[9], Behnaz Falakaflaki[10], Ahmad Ali Nikibakhsh[11], Simin Sadeghi Bojd[12], Seyyed Mohammad Taghi Hosseini Tabatabaei[12], Kambiz Ghasemi[13], Ali Ahmadzadeh[14], Parsa Yousefichaijan[15], Afshin Safaei Asl[16], Baranak Safaeian[17], Salman Khazaei[18], Leila Hejazipour[1], Abolhassan Seyed Zadeh[19], and Fatemeh Ataei[1,20]

Purpose: Knowing the epidemiological aspects of chronic kidney disease (CKD) in children is crucial for early recognition, identification of reversible causes, and prognosis. Here, we report the epidemiological characteristics of childhood CKD in Iran.

Materials and Methods: This cross-sectional study was conducted during 1991 - 2009. The data were collected using the information in the Iranian Pediatric Registry of Chronic Kidney Disease (IPRCKD) core dataset.

Results: A total of 1247 children were registered. The mean age of the children at registration was 0.69 ± 4.72 years (range, 0.25 –18 years), 7.79 ± 3.18 years for hemodialysis (HD), 4.24 ± 1.86 years for continuous ambulatory peritoneal dialysis (CAPD), and 3.4±1.95 years for the children who underwent the renal transplantation (RT) ($P < .001$). The mean year of follow-up was 7.19 ± 4.65 years. The mean annual incidence of CKD 2–5 stages was 3.34 per million age-related population (pmarp). The mean prevalence of CKD 2–5 stages was 21.95 (pmarp). The cumulative 1-, 5-, and 10-year patients' survival rates were 98.3%, 90.7%, and 84.8%, respectively.
The etiology of the CKD included the congenital anomalies of the kidney and urinary tract (CAKUT) (40.01%), glomerulopathy (19.00%), unknown cause (18.28%), and cystic/hereditary/congenital disease (11.14%).

Conclusion: The incidence and prevalence rate of pediatric CKD in Iran is relatively lower than those reported in Europe and other similar studies. CAKUT was the main cause of the CKD. Appropriate management of CAKUT including early urological intervention is required to preserve the renal function. Herein, the long-term survival rate was higher among the children with CKD than the literature.

Keywords: chronic kidney disease; children; epidemiology; etiology; end-stage renal disease; Iran

INTRODUCTION

Chronic Kidney Disease (CKD) is a condition characterized by a gradual loss of renal function. It can be progressive and may ultimately lead to the irreversible nephron loss and scarring[1]. Extensive research has focused on the epidemiology of CKD in the adult population[2,3]. In contrast, there is limited knowledge about

[1]Pediatric Chronic Kidney Disease Research Center, Department of Pediatric Nephrology, Children's Medical Center, Tehran. University of Medical Sciences, Tehran, Iran.
[2]Ali-Asghar Children's Hospital, Iran University of Medical Sciences, Tehran, Iran.
[3]Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.
[4]Shiraz Nephro-Urology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.
[5]Al-Zahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran.
[6]Non-Communicable Pediatric Diseases Research Center, Department of Pediatric Nephrology, Amirkola Children Hospital, Babol University of Medical Sciences, Babol, Iran.
[7]Bahrami Children's Hospital, Tehran University of Medical Sciences, Tehran, Iran.
[8]Sheikh Children's Hospital, Mashhad University of Medical Sciences, Mashhad, Iran.
[9]Department of Pediatrics, Tabriz University of Medical Sciences Tabriz, Iran.
[10]Mousavi Hospital, Zanjan University of Medical Sciences, Zanjan, Iran.
[11]Urmia University of Medical Sciences, Urmia, Iran.
[12]Department of Pediatrics, Zahedan University of Medical Sciences, Zahedan, Iran.
[13]Department of Pediatrics Nephrology, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
[14]Abozar Hospital, Ahvaz Jondishapour University of Medical Sciences, Ahvaz, Iran.
[15]Amirkabir Hospital, Arak University of Medical Sciences, Arak, Iran.
[16]Department of Pediatrics, Guilan University of Medical Sciences, Guilan, Iran.
[17]Taleghani Pediatric Hospital, Golestan University of Medical Sciences, Gorgan, Iran.
[18]Research Center for Health Sciences, Hamadan University of Medical Sciences, Hamadan, Iran.
[19]Razi Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran.
[20]Department of Nuclear Medicine, Valiasr Hospital, Zanjan University of Medical Sciences, Zanjan, Iran.
*Correspondence: Pediatric Chronic Kidney Disease Research Center, Department of Pediatric Nephrology, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran. Tel : +98 21 66929234, E-mail: ataiinem@tums.ac.ir.
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Table 1. Distribution of the children with respect to different stages of CKD in the studied patients

CKD stage No (%)	Study period																		
CKD 2	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
	0	0	2(5.8)	2(8)	2(5.2)	1(2)	2(2.8)	3(4.5)	5(6.3)	2(2.5)	1(1.35)	3(3.75)	2(2.35)	2 (2.2)	1(1.35)	4(4.4)	2(2.3)	3(4.3)	4(6.1)
CKD 3	0	0	1(2.9)	1(4)	1(2.6)	1(2)	6(8.3)	6(9)	7(8.8)	7(8.8)	2(2.7)	7(8.75)	6(7)	9(9.8)	9(9.7)	6(6.5)	14(15.9)	2(2.9)	9(13.6)
CKD 4	1(3)	1(3.6)	2(5.8)	2(8)	2(5.2)	8(16.3)	4(5.6)	10(14.9)	12(15)	17(21.2)	7(9.5)	7(8.75)	10(11.75)	13(14.1)	12(12.9)	19(20.4)	17(19.3)	17(22.5)	15(27.7)
CKD 5	32(97)	27(96.4)	29(85.3)	20(80)	33(86.8)	39(79.6)	60(83.3)	48(71.6)	56(70)	54(67.5)	64(86.5)	63(78.75)	67(78.8)	68(76.1)	71(81.7)	64(68.8)	55(62.5)	48(68.6)	38(57.6)
Total	33	28	34	25	38	49	72	67	80	80	74	80	85	92	93	93	88	70	66

the epidemiology of CKD in the pediatric population[4]. Understanding the epidemiology of CKD in children is crucial for early detection and precise diagnosis, as well as identification of preventable causes of progression, prognosis, and treatment decisions including treatment of reversible causes. Etiology, the progression of the disease, and treatment modality in the children with CKD are different from those observed in the adult patients[5,6].

In children, CKD not only may progress to end-stage renal disease (ESRD) but also influences on the longitudinal bone growth through alterations in the nutrition and mineral metabolism[7]. It can also negatively influence the life quality of the patients and family members [8,9].

Despite few recent studies on the epidemiological and clinical features of the pediatric CKD[10], there is insufficient knowledge about the risk factors leading to disease progression in the children[11].

There is much less information available on the epidemiological and clinical manifestations of the Iranian children with CKD because of the lack of a central reporting registry[12,13]. Therefore, in 1991, the Iranian Pediatric Nephrology Working Group established the Iranian Pediatric Registry of Chronic Kidney Disease (IPRCKD) aimed at providing a comprehensive national data warehouse for studying various aspects of CKD in the pediatric population.

Thus, the present study is conducted to report the basic epidemiological information for analysis of the IPRCKD activity in which 1247 patients with CKD were registered from January 1991 to December 2009.

PATIENTS AND METHODS

Study Design, Setting, and Sampling

The data were collected using the IPRCKD core dataset including name, date of birth, gender, primary renal diagnosis and associated diseases, residence, height, serum creatinine (Cr), treatment modality, changes in the therapy, death and its cause at the time of registration.

The inclusion criteria of the study were: (1) estimated Creatinine Clearance (eCCI) of $\leq$ 75 mL/min/1.73m^2 body surface area according to the Schwartz's formula [14,15,16] for at least 3 months and (2) having less than 19 years of age at the time of registration.

There were 31 large and small provinces, at the time of registration in Iran, all of which were covered by 19 pediatric nephrology centers. In other words, all the centers in Iran were potentially involved in the care of children and adolescents with CKD, accounting for a total population base of 21.3 million children, and a general population of 75 million inhabitants[17] was considered to report the index cases. Herein, the children with CKD were not evaluated in each province separately. On the other hand, some provinces lacked the pediatric nephrology center(s) thus; their patients referred to neighboring or non-adjacent provinces with pediatric nephrology center(s) for follow-up treatment. All the 19 pediatric nephrology centers were asked to voluntarily register the characteristics of their children with CKD in the questionnaire. There was mandatory request to register CKD patients in this database.

The children with CKD were detected using a standardized registration form containing a predefined list of diagnoses classified into eight groups: Congenital anomalies of the kidney and urinary tract (CAKUT) in the forms of hypodysplasia ± reflux nephropathy and obstructive uropathy, glomerular diseases, cystic/hereditary/congenital diseases, vascular nephropathies, neoplasia/tumors, other renal disorders, miscellaneous causes, and unknown causes.

After developing a software program at the following website: "http://www.tums.ac.ir" entitled "http://iprcrf.tums.ac.ir" and including identification code for regional principal investigators (pediatric nephrologists), they were asked to record their own patient's data electronically in the questionnaires and send them via e-mail to the executive director.

This phase of the registry has been completed with the participation of nearly 120 pediatric nephrologists working in 19 pediatric nephrology centers in the country.

All pediatric nephrologists followed a single protocol and, considering the comprehensiveness of the registration system that covered the whole country, as well as the full justification of pediatric nephrologist, the validity, and reliability of the results can be confirmed. The data set used and analyzed during the study is available from the corresponding author upon request.

In this phase of registry (first phase), we did not invite primary care physician or pediatrician to register and participate in sharing CKD patients. However, we intended to include primary care physicians in the upcoming second phase of registry.

The incidence was calculated using the number of newly detected cases in each year, while the point prevalence rate included all the living children followed in the registry on 31 December 2009. Both incidence and prevalence were expressed as per million age-related population (pmarp). Hypertension was defined as the blood pressure above the 95th percentile with respect to age, gender, and height as reported in the Task Force percentile reference[18].

The children were categorized into the patients with CKD stages 2–5 according to the classification described by the Clinical Practice Guidelines of the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI guidelines)[19].

Stages 2 - 4 were considered as preterminal chronic

Table 2. Primary causes of CKD in all the registered patients

Groups of Diseases		No	%		N	%
CAKUT	Obstructive	190	15.23	Posterior urethral valve	73	5.85
				Anterior urethral valve	1	0.08
				Bilateral ureteral stenosis	5	0.4
				Ureteropelvic junction stenosis	22	1.76
				Ureterovesical junction stenosis	9	0.72
				Other obstructive malformation	9	0.72
				Prune belly syndrome	2	0.16
				Neurogenic bladder	69	5.53
	Hypodysplasia	79	6.33	Renal aplasia / hypo/dysplasia	79	6.33
				Interstitial nephritis	14	1.12
	Reflux Nephropathy/ Pyelonephritis	230	18.44	Reflux nephropathy	105	8.42
				Pyelonephritis	26	2.08
				VUR with associated neurogenic bladder	60	4.81
				VUR without associated neurogenic bladder	25	2
Glomerulopathies		237	19.00	Focal segmental glomerulosclerosis	82	6.57
				GN with advanced diffuse sclerosis	4	0.32
				Focal segmental proliferative GN	2	0.16
				Post infectious GN	21	1.68
				Crescentic GN	38	3.04
				Membranous GN	3	0.24
				Membranoproliferative GN type1	20	1.6
				Membranoproliferative GN type2	4	0.32
				Non- classified GN	9	0.72
				Idiopathic nephrotic syndrome	20	1.6
				SLE nephritis	28	2.24
				Henoch-Schonlein nephritis	5	0.4
				Other systemic immunologic disease	1	0.08
Cystic / Hereditary /Congenital Diseases		159	12.72	Juvenile nephronophthisis	25	2
				Infantile polycystic kidney disease	29	2.32
				Adult-type polycystic kidney disease	1	0.08
				Undetermined polycystic kidney	7	0.56
				Medullary cystic disease	6	0.48
				Primary hyperoxaluria	3	0.24
				Laurence Moon Biedl syndrome	10	0.8
				Congentital nephrotic syndrome	22	1.76
				Alport syndrome	21	1.68
				Cystinosis	34	2.72
				Cystinuria	1	0.08
Vascular Nephropathies		47	3.76	Hemolytic uremic syndrome	40	3.2
				Sepsis-induced renal ischemia	4	0.32
				Polyarteritis nodosa	2	0.16
				Renal artery stenosis	1	0.08
Neoplasia / Tumors		6	0.48	Wagner syndrome	1	0.08
				Wilms' tumor	4	0.32
				Others	1	0.08
Other Renal Disorders		24	1.92	Sickle cell nephropathy	1	0.08
				Diabetic glomerulonephritis	6	0.48
				Nephropathy + mental retardation	6	0.48
				Fanconi syndrome	10	0.8
				Acute tubolar necrosis	1	0.08
Miscellaneous Conditions		47	3.76	Nephrolithiasis	25	2
				Hyperoxaluria	11	0.88
				Others	11	0.88
Unknown		228	18.28	-	228	18.28
Total				-	1247	100

renal failure, while CKD Stage 5 ESRD was defined as either having a Glomerular Filtration Rate (GFR) of <15 mL/min/1.73m^2 or being candidate for Renal Replacement Therapy (RRT) through dialysis or transplantation. For the children less than two years of age, the percentage of loss of renal function in each stage of the KDOQI guidelines was extrapolated considering the reference values of GFR in the children under than two years old[19]. The GFR was assessed according to the Schwartz's formula[14,15,16]. The estimated Glomerular Filtration Rate (eGFR) in all the children with CKD was calculated based on the Schwartz's formula modified for the children (Cystatin C-Based GFR Estimating Equation) using the fixed numbers of 48 and 38 for boys and girls, respectively according to the following equation[16].

$$\text{eGFR (using Cystatin C formula):} \quad \frac{\text{[48 (for boys) or 38 (for girls)] x Height (cm)}}{\text{Cr (mg/dL) x 88.4 (µmol/L)}} = \text{ml/min/1.73 m}^2$$

Creatinine was determined by the Jaffe method in all the centers. Descriptive statistics including the frequency tables, charts, and percentages were used for presenting the categorical variables.

The patient's survival was analyzed using the Kaplan–Meier method. The risk for progression to ESRD was assessed using the multiple Cox proportional hazards regression. P-value of $\leq .05$ was considered as statistically significant. Statistical analyses were performed using the Stata software, version 12 (Stata Corp, College Station, TX, USA).

Table 3. Patients' survival for all the registered children with CKD (1991-2009) using the life table

Survival time (year)	Total	Event	Censored	Survival probability	SE	95%CI
1	1247	21	1	0.983	0.004	0.97, 0.989
2	1225	25	68	0.962	0.005	0.95, 0.97
3	1132	18	120	0.946	0.007	0.93, 0.958
4	994	17	107	0.929	0.008	0.91, 0.94
5	870	19	110	0.907	0.009	0.89, 0.92
6	741	8	106	0.897	0.01	0.88, 0.91
7	627	12	114	0.878	0.011	0.84, 0.89
8	501	5	50	0.869	0.011	0.84, 0.88
9	444	3	4	0.863	0.012	0.82, 0.87
10	437	7	60	0.848	0.013	0.82, 0.87

RESULTS

General Characteristics of the Subjects

Totally, 1247 children were registered (662 boys, 585 girls, male/female ratio of 1.1) from January 1991 to December 2009. The mean age of the patients at the time of registration was 7.69 ± 4.72 years (range, 0.3-18). The mean follow-up duration was 7.19 ± 4.65 years. Concerning the gender of the patients, mean age of the patients at the time of registration was (6.27 ± 3.78) and (6.53 ± 3.82) years for boys and girls, respectively ($P = 0.22$). The mean annual incidence and prevalence of CKD 2–5 stages was 3.34 (pmarp) and 21.95 (pmarp), respectively.

The mean annual incidence of CKD 2–4 and CKD 5 stages was 0.83 (pmarp) (range, 0.06-1.57) and 2.53 (range, 1.11-3.62), respectively. The mean annual prevalence of CKD 2–4 and CKD 5 stages was 2.98 (pmarp) (range, 0.06-7.14) and 18.98 (range, 1.78-45.86), respectively.

CKD Classification

At the time of registration, 41(3.28%) children were in CKD Stage 2, 94 (7.54%) in CKD Stage 3, 176 (14.11%) in CKD Stage 4, and 936 (75.06%) were in CKD Stage 5. A high proportion (75.06%) of the patients was diagnosed with CKD Stage 5 at the first visit. During the study period, the number of the patients with CKD Stage 5 decreased from (97%) in 1991 to (57.6%) in 2009. At the same time, the frequencies of CKD in the early stages increased over the years. Table 1 shows the distribution of the children with respect to CKD stage during the whole registration period.

Incidence and Prevalence

The annual incidence of CKD was equal to 1.43 (pmarp) in 1991. It decreased to 1.21(pmarp) in 1992, while gradually increased to 4.03 (pmarp) in 2006, thereafter the incidence decreased to 2.86 (pmarp) (mean 2.84; range, 1.08-4.03). The prevalence rate had an increasing trend in this period so that, it reached from 1.43 (pmarp) in 1991 to 48.10 (pmarp) in 2009 (mean 19.41; range, 1.43-48.10) (**Figure 1**).

Causes of CKD

The etiology of CKD included the CAKUT in 499 cases (40.01%) [hypodysplasia ± reflux nephropathy in 309 cases (24.77%) ,and obstructive uropathy in 190 cases (15.23%)], glomerulopathy in 237 cases (19.00%), unknown cause in 228 cases (18.28%), cystic/hereditary/congenital diseases in 139 cases (11.14%), miscellaneous conditions in 47 cases (3.76%), vascular nephropathies in 47 cases (3.76%), other renal disorders in 44 cases (3.52%) ,and neoplasia /tumors in 6 cases (0.48%) as shown in (**Figure 2**). **Table 2** shows the primary causes of CKD in all the registered children. A significant decreasing trend was observed in the cases with unknown- etiology from 33% in 1991 to 13.6% in 2009 (P for trend=.01).

Renal Replacement Therapy

Out of 1247 registered children, 310 (24.86%) of them were on the conservative treatment (188 boys, 122 girls mean age: 6.53 ± 4.77 years (range, 0.24-17.8), 537 (43.06%) of them had ESRD who were on the chronic hemodialysis (HD), (281boys and 256 girls; mean age: 8.85 ± 4.26 years (range, 0.24-17), 182 (14.6%) of them were on the continuous ambulatory peritoneal dialysis (CAPD) (98 boys, 84 girls mean age: 4.27 ± 4.41 years (range, 0.5-16.4), and 218 (17.48%) of them underwent the renal transplantation (RT) (104 boys,114 girls mean age: 9.41 ± 4.13 years (range, 1-15.2). The death occurred in 138 patients (11.06%), mainly due to the cardiovascular and infectious complications. HD was the most commonly used modality of RRT. Among 218 children who underwent the RT, 48 patients (22.01%) lost their first grafts. The majority (73.17%) of the transplanted children received their graft from the deceased donors. According to the results of Kaplan-Meier analysis, the 1-, 5 - and 10-year patients' survival rates were obtained as 98.3%, 90.7%, and 84.8%, respectively (**Table 3**). As shown in Figure 3, (A) the survival rate was lower in the boys than girls, there were no significant gender differences (HR= 1.14, $P = 0.42$) and (B) patients with ESRD had lower survival rate compared to those affected with other stages of CKD, but the difference was not statistically significant between the two groups (HR = 1.28, $P = 0.26$). Mean age of the patients at the time of death was 6.71 ± 4.52 years (range, 0.25-15). The percentage of death in the studied patients ranged from 20.43% in 2005 to 4.55% in 2009.

DISCUSSION

Currently, CKD is a public health issue due to the rapid rising trend of its prevalence [20]. To the best of our knowledge, this study is the first cross-sectional, nationwide report on the epidemiologic characteristics and etiology of the Iranian children and adolescents with CKD. Due to the asymptomatic nature of CKD, especially in the earlier stages, there are no accurate epidemiological data on the pediatric patients. According to the annual report by the European Renal Association – European Dialysis and Transplant Association (ERA-EDTA) registry in 2007, the overall CKD prevalence in the USA adult population was equal to 11% (Stage 1, 3.3%; Stage 2, 3.0%; Stage 3, 4.3%; Stage 4,

Table 4. Etiology of CKD in Iran compared to other similar studies

	Registry [reference]	NAPRTCS[6]	Italy[10]	Belgium[29]	Iran	ANZDATA[34]	ESPN/ERA-EDTA [37]	UK [36]	Japan [32]
	Inclusion criteria	CKD(eGFR <75)	CKD(eGFR <75)	CKD(eGFR <60)	CKD(eGFR <75)	ESRD (RRT)	ESRD (RRT)	ESRD (RRT)	ESRD (RRT)
	Age (years)	0-20	0-19	0-19	0-19	0-19	0-15	0-15	0-19
	Period	1994 - 2007	1990 - 2000	2001-2005	1991-2009	2003-2008	2008	2004-2008	1998
	Study sample size	7,037	1,197	143	1247	369	499	428	582
	CAKUT	3,361 (48%)	689 (58.0%)	84 (59%)	499 (40%)	127 (34%)	182 (36.0%)	184(43%)	208 (36%)
	Hypodyspalasia±	1,907(27%)	516(43.1%)	66 (46.1%)	309 (24.7%)	95 (25.7%)	-	135(31.5%)	198 (34%)
Etiology	reflux nephropathy								
	Obstructive uropathy	1,454(20.6%)	173 (14.4%)	18 (12.6%)	190 (15.2%)	32 (8.7%)	-	49(11.4%)	10 (1.7%)
	Glomerulopathies	993 (14%)	55 (5%)	10 (7%)	237 (19.0%)	108 (29%)	76 (15%)	78(18%)	130 (22%)
	HUS	141 (2.0%)	43 (4%)	9 (6%)	40 (3.2%)	9 (2.0%)	29 (6%)	-	13 (2%)
	Hereditary nephropathies	717 (10%)	186 (15%)	27 (19%)	21 (1.7%)	-	112 (22%)	-	69 (12%)
	Congenital NS	75 (1%)	13 (1%)	5 (3.5%)	22 (1.8%)	7 (1.9%)	-	15(3.5%)	34 (5.8%)
	Metabolic disease	-	-	5 (3.5%)	-	-	17 (3.4%)	18(4.2%)	-
	Cystinosis	104 (1.5%)	22 (1.8%)	2 (1.4%)	34 (2.7%)	4 (1%)	-	-	2 (0.3%)
	Cystic kidney disease	368 (5.2%)	101 (8.4%)	13 (9%)	43 (3.4%)	25 (6.7%)	59 (11.8%)	49(11.4%)	35 (6%)
	Ischemic renal failure	158 (2%)	49 (4%)	3 (2%)	4 (0.3%)	8 (2%)	11 (2%)	-	11(1.9%)
	Miscellaneous conditions	1,485 (21.1%)	122 (10.2%)	10 (7%)	47 (3.8%)	65 (17.6%)	52 (10.4%)	19(4.4%)	83 (14.3%)
	Missing / unknown	182 (2.6%)	40 (3.3%)	-	228 (18.3%)	16 (4.3%)	37 (7.4%)	65 (15.2%)	34 (5.8%)

Abbreviations: CKD, chronic kidney disease; ESRD, end-stage renal disease; RRT, renal replacement therapy; eGFR, estimated glomerular filtration rate (mL/min/1.73 m^2);
CAKUT, congenital anomalies of the kidney and urinary tract; NS, nephrotic syndrome; HUS, hemolytic uremic syndrome; NAPRTCS, North American Pediatric Renal Trials and Collaborative Studies; ANZDATA, Australia and New Zealand Dialysis and Transplant Registry; ESPN/ERA-EDTA Registry, European Registry for Children on Renal Replacement Therapy

0.2%, and Stage 5, 0.2%)[21]. The prevalence rate for the early stages of CKD was about 50 times higher than that of advanced stages. Unfortunately, there is no comparable information regarding the CKD in a pediatric population, especially for early-stages of the disease.
In the present study, the prevalence of CKD stages 2-5 was lower than that reported in the studies conducted in Italy[10] and Serbia[22].
The prevalence rate of CKD Stage 5 decreased over the study period. In the same period, an increase occurred in the frequency of the early stages of CKD (**Table1**) attributing to the routine antenatal ultrasound screening, early detection of renal and urinary tract anomalies, early urological interventions, and treatment.

The mean incidence and prevalence rate of CKD among the Iranian children was relatively lower compared to those reported from the European countries, such as Serbia[22], Italy[10], as well as Chile[23] and Nigeria[24] (**Figure 4**).
However, it is difficult to make a direct comparison regarding the incidence and prevalence of CKD in different pediatric populations due to the methodological differences in the case definitions and disease classifications both within and between the countries. It has been reported that, pediatric patients with ESRD account for a very small proportion of the total ESRD population[21]. There are considerable variations in the incidence and prevalence of ESRD in the pediatric pop-

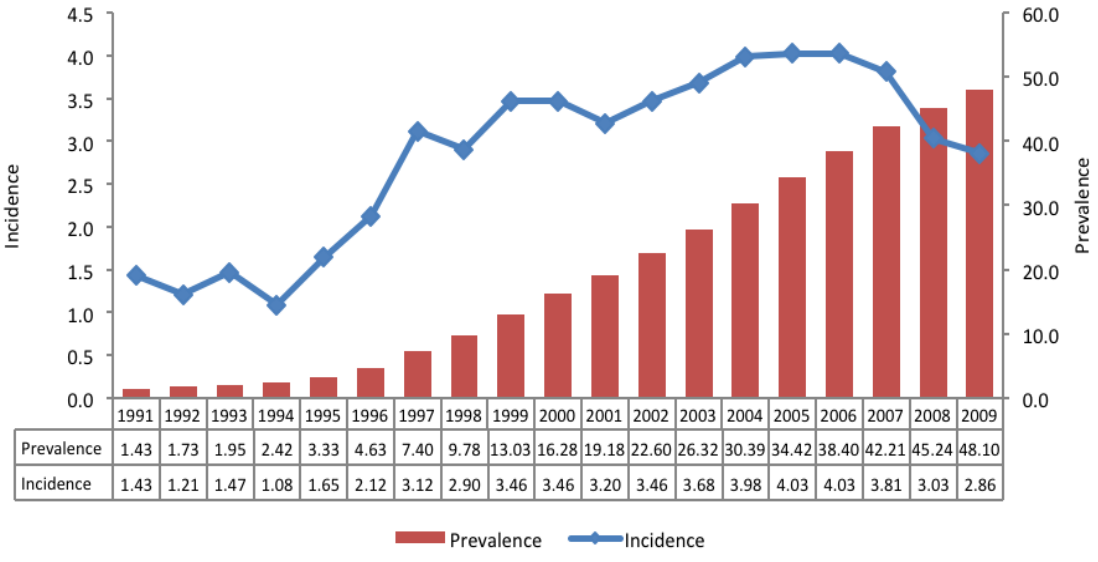

Figure 1. Incidence and prevalence rate of CKD during the study period

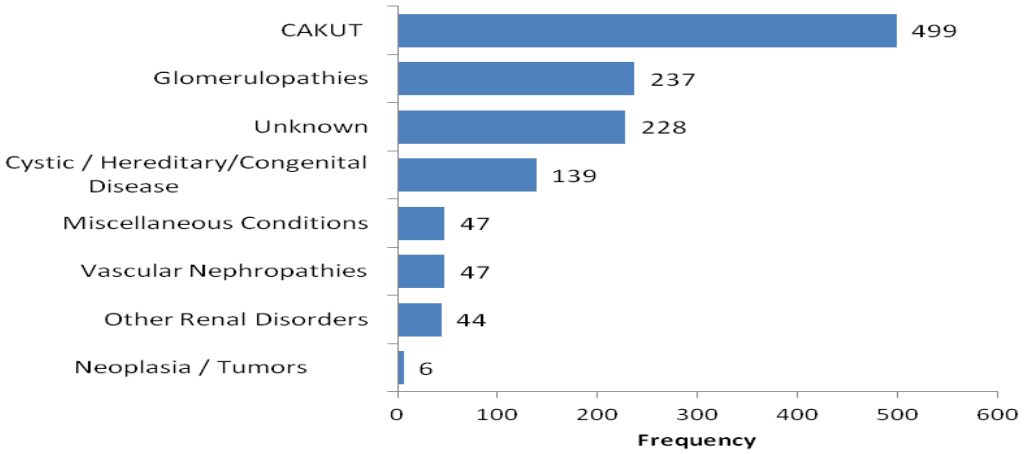

Figure 2. Primary causes of CKD stages 2–5 in the Iranian children

ulation across the regions of the world. In the present study, the mean annual incidence and prevalence rates of ESRD for children were equal to 2.53 and 18.98 (pmarp), respectively. The results of the study showed that the annual incidence of childhood CKD in Iran increased from 1.21 (pmarp) in 1992 to 4.46 (pmarp) in 2006, while at the end of three years of study, the trend became downward.

This increasing trend has been also observed in the USA from 1980 to 2008[25], as well as European countries during the 1980s[26] while, Australia and New Zealand have experienced a constant trend regarding the incidence of childhood CKD during the past 25 years [27]. Consistent with our findings, the above-mentioned studies have also reported an increasing trend for the prevalence of childhood CKD attributing to the improved survival rate of the patients. The annual incidence of RRT including the chronic HD, CAPD, and RT was less in the Iranian children 2.53 (pmarp) than that of other pediatric studies conducted in the countries such as Serbia 5.7 (pmarp)[22], Netherlands 5.8 (pmarp) [28], Belgium 6.2 (pmarp)[29], and Turkey10.9 (pmarp) [30]. The true proportion of CKD is expected to be higher than the value observed in the present study, as it is usually asymptomatic in its earliest stages and is often not diagnosed, and therefore, is not reported. Our results revealed a higher frequency of CKD in the boys than the girls (M/F=1.13), which is in accordance with other pediatric studies worldwide [24,29]. The highest reported incidence rate for ESRD in the children belonged to the USA, New Zealand, and Austria by 14.8, 13.6, and 12.4 per million populations, respectively[31] while, the lowest rate was reported in Japan[32]. In our study, the prevalence of CKD stage 5 was similar to the report from Sweden[33] but lower than that of other European countries, Australia, and the United States[10,22,31, 34,35] (**Figure 4**).

CAKUT is the most common cause of ESRD in the

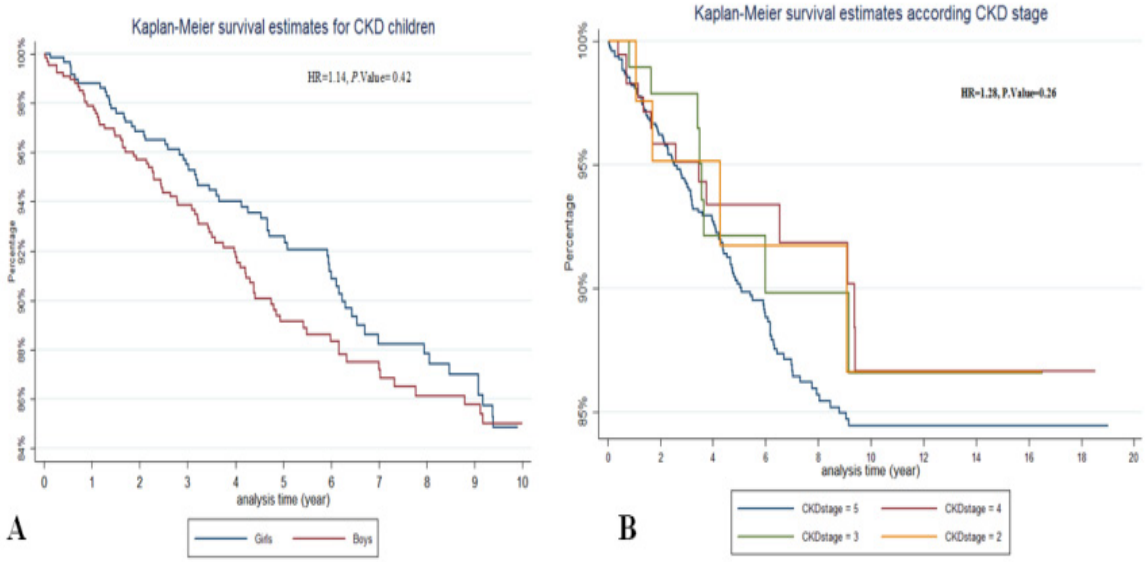

Figure 3. (A) Estimated patient's survival in the studied children with respect to the gender. **(B)** Estimated patient's survival in the studied children with respect to the CKD stage.

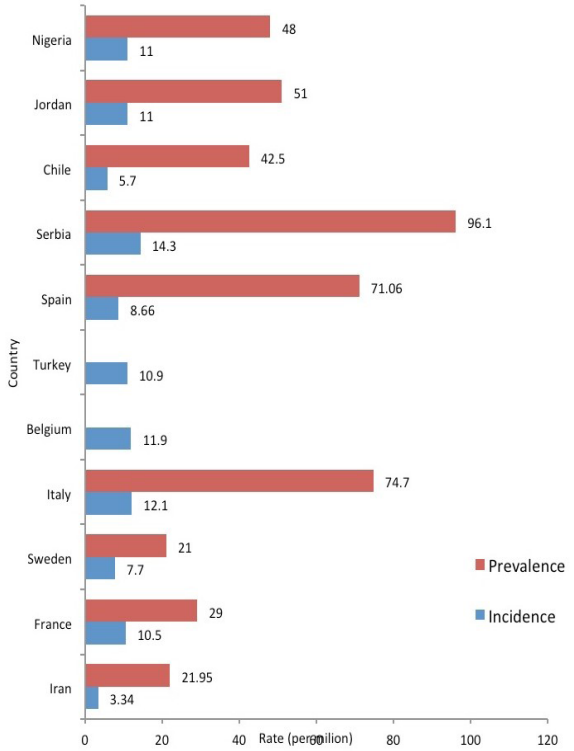

Figure 4. Incidence and prevalence rate of childhood CKD in different countries

pediatric patients undergoing the RRT[9,10,23]. In this study, CAKUT and glomerulopathies were leading causes of CKD in 40.01% and 19.00% of cases, respectively, which is consistent with the results reported by the ANZDATA[34], UK[36] and Japanese Registry[32], but hereditary nephropathies were the second cause of CKD in the ESPN/ERA-EDTA[37], Italian[10], and Belgian Registry[29] (**Table 4**). Higher frequency of CAKUT including renal hypodysplasia as well as obstructive uropathy in the males can justify more frequency of CKD in the boys than the girls[9]. HD was the first modality used for RRT in the majority of children with ESRD. The etiology of CKD remained unknown in 18.3% of the patients similar to the studies by Safouh et al., (20.6%)[38] and Lewis et al., (15.2%)[36] mostly due to late manifestation with small smooth kidneys, where tissue sampling (biopsy) would be of little or no benefit to the patients highlighting the need for further investigations in this regard to save many lives. In our study, more than 75% of the children were in the advanced stage of CKD at the time of presentation. Poor manifestation of CKD symptoms, delay in diagnosis, and late referral to the pediatric nephrologist makes it difficult to detect the CKD in early stages. Since 1976, the pediatric CKD registries revealed the reduction of unknown cause of etiology from 39% to 1.8% in the recent years [10,22,39,40]. However, the etiology of CKD is still unknown in 20 - 27% of the adult patients attributing to the multiple factors in the adults[41]. The mortality rate of 11.06% in the population under study was similar to that reported in the study by McDonald and Craig[42]. Among them, one patient died in the pre-terminal phase due to primary disease or serious coexisting morbidity; 81(15.08%) patients died during treatment with the HD; 54(29.67%) patients died during CAPD treatment, and 2 patients died after RT (1 died due to the cerebrovascular accident, the other died due to the sepsis). In our study, cardiovascular events (50%) and infections (11.11%) were the main causes of death as reported by other studies[43].

RT is associated with higher patients' survival rates, improving quality of life, and fewer public health costs compared to relying on the dialysis[44].

The 10–year patients' survival (84.8%) observed in our study is comparable to that reported in the studies by McDonald and Craig (79%)[42], Peco-Antic et al., (75%) [22] and ANZDATA registry (79%)[34]. On the other hand, these results are consistent with the findings reported in the studies by Mitsnefes et al.,[45] and Neild [41]. The improving trend in the survival rates among the patients in the present study is more likely to be related to RT rather than dialysis.

All the pediatric nephrologists followed a single protocol thus, the validity and reliability of the results can be confirmed considering the comprehensiveness of the registration system that covered the whole country, as well as the full justification by the pediatric nephrologists.

There were a number of limitations in this study. Firstly, the retrospective nature of the study and the lack of screening programs to identify the children with CKD in the early stages of the disease Secondly, incomplete or missing data within the medical records and finally, inter-laboratory variation in the calibration of serum Cr assay, which might have led to some variability, especially for estimating the GFR were among the limitations of this study. Despite these limitations, this study provided a comprehensive data source on the childhood CKD in Iran that can be used for healthcare planning and as a basis for further researches.

CONCLUSIONS

The IPRCKD provided valuable information about the epidemiological characteristics of the pediatric CKD in Iran. The incidence and prevalence rate of childhood CKD in Iran was found to be relatively lower than those reported from European countries and other similar studies. Most children had non-glomerular disease and CAKUT was the main cause of CKD similar to the studies reported from the European countries. However, the etiology of CKD was unknown in a significant number of children (18.3%) highlighting the need for further investigation on the etiologic factors associated with the progression of CKD. The long-term survival rate among the children with CKD in the present study was higher than the similar studies.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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