BANTAO Journal 2007: 5 (2); 32–36

BJ
BANTAO Journal

Original Article

Serbian Pediatric Chronic Kidney Disease Registry - SPEKID

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Abstract

Background. The SPEKID Registry is a prospective, population-based registry formed in Serbia in 2000 to provide current and reliable information concerning pediatric chronic kidney disease (CKD) stage 2 to 5 for planning pediatric renal replacement treatment and devising and monitoring strategies for prevention of chronic renal failure (CRF) in Serbia.
Methods. The index cases were defined using the following criteria: 1) decreased GFR for at least 3 months; for children aged ≥ 1 year less than 90 ml/min/1,73m² and for younger ones as serum creatinine > mean +2SD; 2) age below 19 years at the time of registration, and 3) written informed consent for data collection, reporting and storage. The estimated numbers of people "at risk" for the morbidity analysis, derived from the 2002 state census were 7,5 millions of general total population and 1,7 million of those younger than 19 years. All of the Serbian centres potentially involved in caring for children and adolescents with CRF were invited to report index cases. The children were reported on a prospective basis, but retrospective check-up was also performed.
Results. From January 2000 to December 2006, 205 children were registered. An average age of patients at the time of the registration was 8.4 years; boys were about 2 years younger than girls. Ratio of male to female was 1.97:1. A median follow-up of the patients after being registered was 5 years, while 25% of the patients were followed for 7 years. The mean annual incidence of CKD stage 2 to 5 was 10.04 per million child population (pmcp), ranging from 6.5 to 19.4 pmcp. The prevalence increased significantly during the study period, reaching 100.7 pmcp in December 2006. The mean annual incidence of terminal renal failure was 6.0 pmcp, while average point prevalence was 3 times greater. **Conclusion.** Congenital disorders contributed to more than two third of all causes of CRF. Eight children died during 7 years of the study period, 4 patients in non-terminal group and 4 patients on renal replacement therapy. The most common cause of the death was due to cardiovascular complications. The probability of survival was 92.9% at 7 years of the follow-up.

Keywords: Chronic kidney disease, children, chronic renal failure, renal replacement therapy, epidemiology

Introduction

The epidemiological reports on non-terminal stages of the progressive forms of pediatric chronic kidney disese (CKD) from well-defined populations are rare [1]. The existing data from literature are mainly concentrated on renal replacement tharapy (RRT) and the incidence of pediatric end-stage renal disease (ESRD) is approximated by determing the numer of children accepted into dialysis/transplant programs [2-4]. On that way, the considerable number of children with renal impairment is not included as they reach ESRD in adulthood. Furthermore, ESRD epidemiological data are not sufficient when the emphasis is on ESRD prevention. Although pediatric RRT dramaticaly improved during the last decade, it can be difficult for pediatric patients with ESRD to acheive normal cognitive, psychological, and physical development and normal lifestyle. In addition, pediatric RRT is very costly and kidney transplantation as the treatment of choice is not within the reach of the majority of the patients. Recent research results make it clear that appropriate therapeuthic intervention at the less advanced stages of renal impairment can change the course of CKD to avoid ESRD. With this in mind, prevention should be directed at limiting the progression of the disease after the existing progressive renal disease is discovered. Therefore, the Serbian Pediatric Nephrology Working Group (SPNWG), founded in January 2000, established in June 2000 Serbian Pediatric Kidney Disease registry (SPEKID) as a prospective, population-based registry to provide current and reliable information concerning CKD for devising and monitoring strategies for prevention of chronic renal failure (CRF) and planning RRT in Serbia. Thus, the secondary objectives were to examine the epidemiological characteristics, modalities of treatment and survival of the children with CRF treated in Serbia. Here we report the basic epidemiologic results of the first 7 years of SPEKID activity.

Patients and methods

The index cases were defined using the following criteria: 1) decreased glomerular filtration rate (GFR) for at least 3 months, below 90 ml/min/1,73m² for children aged ≥ 1 year and for younger ones serum creatinine above mean +2SD; 2) age below 19 years at the time of registration, and 3) written informed consent for data collection, reporting and storage. The staging of registered population was done according to K/DOQI classification of. CKD [5]; stages from 2 to 4 were designated as non-terminal renal failure, while CKD stage 5, (ESRD) was defined as either GFR less than 15 ml/min/1.73 m2, or a need for the initiation of kidney replacement therapy by dialysis or transplantation. The estimated number of pediatric population "at risk" for the

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morbidity analysis derived from the 2002 state census: general total population of around 7,5 millions and 1,7 million of children [6]. All of the Serbian centres potentially involved in caring for children and adolescents with CRF were invited to report index cases. The children were reported on a prospective basis, but retrospective check-up was also performed. New cases were reported using a standardized registration form containing a predefined list of diagnosis. Updating of tha data were done every year.

Results

From January 2000 to December 2006, total of 205 children were registered. An average age of patients at the time of the registration was 8.4 years; mean age of boys as about 7 [8] years (7.8 ± 5.9; range 0-19), and girls were about 2 years older (9.5 ± 4.9; range 0-19). Pre registration mean follow-up of the patients was almost 5 years (4.7; range 0.5-16). Males predominated in all age groups; ratio of male to female was about 1.97:1. A median follow-up of the patients after being registered was 5 years, while 25% of the patients were followed for 7 years. The majority of the patients (91.5%) were from Serbia, 4.5% were form Republic of Srpska and 4% from Montenegro. The mean annual incidence of CKD stage 2-5 was 10.04 per million child population (pmcp), ranging from 6.5 to 19.4 pmcp. The prevalence increased significantly during the study period, reaching 100.7 pmcp in December 2006. Male predominated in incidence as well as in prevalence groups of patients. Linear trend of prevalence significantly increased, while the linear trend of incidence showed slight decrease (Figure 1). Regression analysis of age adjusted rates of incidence for boys showed slight decrease except in infants. The regression analysis of age adjusted rates of incidence for girls showed decrease in all age groups. On the contrary, regression analysis of prevalence of CKD stage 2 to 5 documented increases both in boys and in girls.

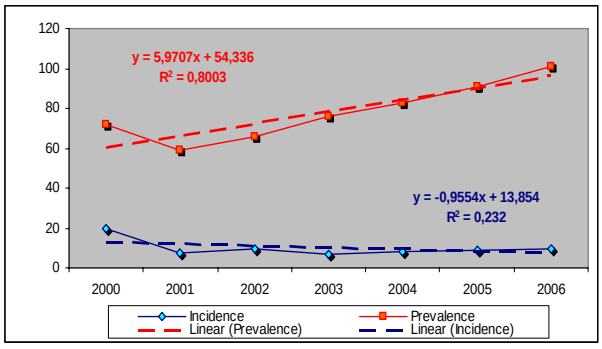


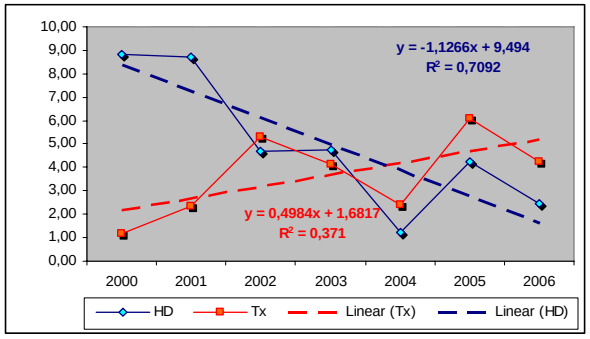
Fig. 1. Linear trend of incidence and prevalence of CKD stage 2-5

The mean annual incidence of terminal renal failure was 6 pmcp, while average point prevalence was 3 times greater. Male terminal renal failure patients were more numerous than female ones in incidence and in prevalence groups, although the difference was less prominent than in the non-terminal renal failure patients.

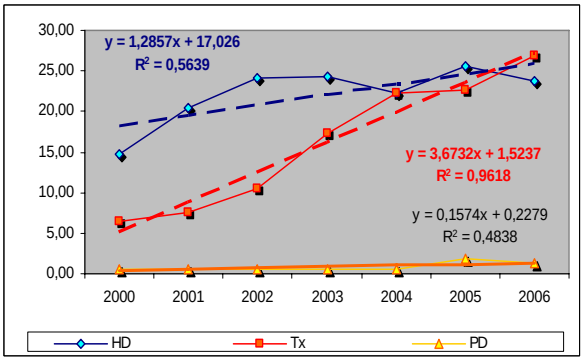
The majority of the patients with CKD stage 5 (57.9%) were from the central part of Serbia, 21% were from Vojvodina, 8.8% from Kosovo, 7% from Republic of Srpska and 5.3% from Montenegro. Single specialized pediatric RRT centre at University Children's Hospital, Belgrade, covered all needs for chronic hemodialysis and kidney transplantation, while peritoneal dialysis was also done at Institute for Mother and Child Health Care, Belgrade and in the Institute for Children and Youth, Novi Sad.

Congenital anomalies of kidney and urinary tract (CAKUT) accounted for 64.5 % of all cases and hereditary renal conditions for 16.5%. Therefore, congenital disorders contributed to more than three fourth of all causes of CRF. Primary glomerular disease was the cause of CRF in 13.5%. Non obstructive pyelonephritis as the cause of CRF was not found in any of the children. Congenital disorders were more common in male than in female patients. When compared the causes of non terminal renal failure, to those of terminal renal failure one can notice that rate of CAKUT occurrence, although still remaining on the first place, decreased while the frequency of the primary glomerular diseases increased. Age at the diagnosis of primary renal disorder was the highest for the patients with primary glomerular disease, while that for the CAKUT was about 4 years.

The prevalence of the kidney transplantation has been clearly expanded from 2000; the chronic hemodialysis has been slowly decreases in the recent years, while the prevalence rate of peritoneal dialysis was constantly low (Figure 2).



a)



b)

Fig. 2. Linear trend of incident (a) and prevalent RRT* (b)

***Legend:** HD-hemodialysis; Tx - transplantation; PD - periotoneal dialysis

From 2000 to 2006 linear trend of incidence of dialysis treatment decreased while that of kidney transplantation increased. However, the prevalence of both of these treatments, chronic hemodialysis and transplantation, showed significant increase, especially transplantation, while peritoneal dialysis remained in stable low position.

Eight children died during 7 years of the study period, 4 patients in non-terminal group and 4 patients on renal replacement therapy, mostly occuring early after starting RRT (3/4). The most common cause of the death was due to cardiovascular complications. The probability of survival was 92.9% at 7 years of the follow-up (Figure 3).

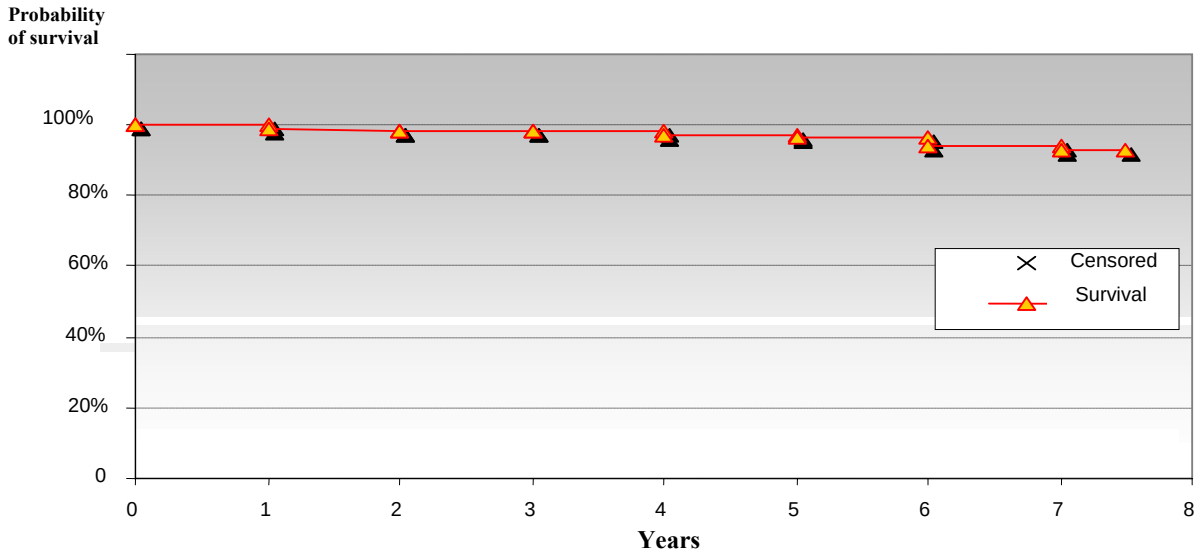


Fig. 3. Probability of survival of patients with CKD stage 2-5

Discussion

This is the first nation-wide prospective long-term study of incidence and etiology of pediatric CKD in Serbia. Having in mind the prevention of CRF at the first place, we defined our target pediatric population as those patients who have at least mild chronic reduction of the glomerular filtration rate. The limitation of this study, as well as with all epidemiological studies based on multicenter reporting data, must be acknowledged, including the possibility that all data might not have been reported or registered. Incomplete documentation may underestimate CKD due to both underdiagnosis, and under-referral. The former corresponds especially to children with CKD stage 2-3 as they might be unrecognased in time, while the later is possible for adolescent patients with CKD 5, as they could have been dialyzed in adult centers. Recently SPEKID has improved by on line reporting and verification the accuracy of the epidemiological data will be done using the capture-recapture method.

Data regarding the morbidity of CRF in children, commonly encountered in the literature are disappointingly different due to the un-uniform source of information, definition criteria for CRF and disease of selected classification. The incidence and prevalence of non-terminal CRF in children in some countries are shown in Table 1 [7-13].

Table 1. Incidence and prevalence of pediatric non-terminal CRF

Country (reference)	Time period	Age (years)	Definition of CRF	Incidence pmcp*	Point prevalence pmcp
Germany (7)	1972-1975	0-16	s. Cr >2 mg%	4.4	6.4
Swiss (8,9)	1972-1974	0.5-16	s. Cr >2 mg%	NA	1976-18,5 1991- 28
France (10)	1975-1990	0-16	s. Cr >2 mg%	10.05 (12.5-7.5)	29.0-54.0
Sweden (11)	1978-1985	0.5-16	CsCr<30 ml/min/1.73m2	6,9	14.1-26.1
Sweden (12)	1986-1994	0,5-16	CsCr<30 ml/min/1.73m2	7,7	21
Chile (13)	1996	0-18	CsCr<30 ml/min/1.73m2	5.7	42.5
Italy (1)	1990-2000	0-20	CsCr<75 ml/min/1.73m2	12.1	74.7
Serbia	2000-2006	0-19	CsCr<90 ml/min/1.73m2	10, 04	78.2 (59.3- 100.7)

*pmcp: per million child population; s: serum; CsCr: creatinine clearance; NA: not available

As expected, both the incidence and prevalence are largely dependent on the definition criteria used in the specific investigation. Our data seems more comparable to those from the Italian study [1]. Comparing our data of ESRD to those from literature [7-14,15,16] (Table 2) we can conclude that the incidence of terminal renal failure in Serbia of 6 pmcp is close to those reported in Sweden [11], Swis [8,9] and Germany [7], but less than those reported for USA [14] and France [15]. The mean prevalence of terminal renal failure of 31.6 pmcp is similar to that reported in Sweden [11] and France [10]. All investigators confirmed the male predominance in CRF pediatric

patients. Also there is agreement in our data and those from literature concerning the causes of CRF in children [17]. Hypo/dysplasia with or without associated urological malformations accounts for the majority of CRF in our patients as well as in others (41% in Sweeden, 53% in France and 57% in Italy), whereas glomerular disease are by far less common (14.5, 22.5 and 6.8%, respectively), than reported in the past [11,18,19]. Overall survival rate of our patients was quite well. In children younger than two years the mortality occured due to comorbid states and/or early after starting RRT. The survival of transplanted patients was better than that of dialysis patiens.

Table 2. Incidence and prevalence of ESRD pediatric patients

Country (reference)	Time period	Age (years)	Incidence pmcp*	Point prevalence pmcp*
Germany (7)	1972-1977	0-16	4.4-5.4	11.9-22.0
Swiss (8,9)	1967-1974	0.5-16	5.6	NA
France (10)	1975-1990	0-16	5.6-9.1	15.5-37.0
Sweden (11)	1978-1985	0.5-16	6.9	12.4-16
Sweden (12)	1986-1994	0.5-16	6.4	38
USA (14)	1989-1991	0-19	11.0	53.0
France (15)	1998	0-17	14.0	NA
Yugoslavia (16)	1980-1999	0-19	1.6	NA
Serbia	2000-2006	0-19	6 (1.3-10)	31.6

*pmcp, per million child population; NA, not available

Conclusion

SPEKID data demonstrated an increase in annual incidence of CRF in infants and increase in the prevalence of CRF in all age groups. Congenital renal malformations were the main cause of CRF in Serbian children. Survival of non-terminal and terminal CRF patients is comparable to those in the developed countries. Single specialized pediatric RRT centre can meet all needs the Republic of Serbia. Transplantation is the best modality of RRT. Future efforts should be directed to extend peritoneal dialysis and to improve pediatric renal transplantation to meet individual needs of children with ESRD in Serbia.

Primary prevention should be directed at avoiding renal injury through improved and increased prenatal diagnosis and early postnatal care in targeted groups. Secondary prevention should be aimed at limiting disease progression after discovering renal injury. Early detection interventions (urine protein annual screenings, blood pressure control, dietary counselling, renoprotective therapy) may delay renal deterioration and/or reduce the incidence of renal-related deaths in pediatric patients

Conflict of interest statement. None declared.

Acknowledgements. This article was written on behalf of all the members of the Serbian Pediatric Nephrology Working Group – SPNWG whose contribution has been essential.
Blagojevic Lj (Cacak), Bubalo J (Novi Sad), Danojlic S (Kraljevo), Golubovic E (Nis), Gostovic S (Beograd), Karaklajic D (Pancevo), Kasza Meszaros M (Subotica), Kojic-Maletkovic D (Gornji Milanovac), Kostic M (Beograd), Kovacevic B (Zrenjanin), Kruscic D (Beograd), Malbasic Lj (Zemun), Milosevic-Rudic B (Novi Sad), Milosevski G (Beograd), Milcanovic B (Uzice), Miljkovic P (Nis), Nikolic R (Cuprija), Paripovic D (Beograd), Pavicevic M (Kragujevac), Pejovic B (Beograd), Pejcic I (Beograd), Poznan A (Subotica), Putnik J (Novi Beograd), Radisavljevic S (Cuprija), Ristic N (Smederevska Palanka), Spasojevic B (Beograd), Stajic N (Novi Beograd), Stanic M (Beograd), Stojanovic V (Novi Sad), Djapic M (Novi Sad), Virijevic V (Krusevac), Vujic-Janic A (Kragujevac), Serer V (Valjevo), Scekic G (Zemun).

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