



EPIDEMIOLOGY OF RENAL REPLACEMENT THERAPY IN MACEDONIA

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ABSTRACT

The purpose of the study is to give an overview of end-stage renal disease (ESRD) and renal replacement therapy (RRT) in the Republic of Macedonia in a period of 6 years (2002-2007). Data are collected by questionnaires for individual patients that are distributed to 18 haemodialysis centres in the country. Incidence, prevalence, mean and median age, primary renal disease, established therapy, number of renal transplants per year and mortality are assessed and elaborated. There is an increase of incident patients on RRT over the years, from 75,5 in 2002 to 99,5 per million population in 2007, on day 91, adjusted for age and gender. Mean age of incident patients is also increasing, from $55,2 \pm 14,0$ at day 91 in 2002, to $57,5 \pm 14,2$ in 2007. Hypertension and diabetes are increasing and have become the leading cause of renal failure in incident patients at day 91, unadjusted, in 2007 (26,8 and 21,4% respectively). Prevalent counts on RRT are also increasing, from 559,2 per million population in 2002, adjusted for age and gender, to 767,4 in 2007. Glomerulonephritis and unknown cause of renal failure are the leading cause of ESRD in prevalent patients. Haemodialysis is the predominant RRT modality in Macedonia either for incident, or prevalent patients, and is around 90%. The crude death rate on dialysis is relatively low, 12,5% in 2006. Incidence and prevalence on RRT are continuously increasing, and hypertension and diabetes are becoming the leading cause of ESRD. Kidney transplantation is underrepresented and efforts should be undertaken for its increase.

KEY WORDS: RRT, epidemiology, ESRD, hemodialysis.

INTRODUCTION

The incidence and prevalence of End-stage-renal disease (ESRD) are continuously increasing in the United States, Canada, Australia and Europe, but recently, as a result of changes in life style, they also increase in many countries in transition. ESRD is of substantial public health importance, not only for its high mortality rate and impaired quality of life, but also for its high cost of Renal Replacement Therapy (RRT) (1). The epidemiology data of patients on RRT are of great interest to health care planners and providers to forecast equipment, facility, and other resources. These data are collected by renal registries, but the extent and accuracy vary widely. There are national, regional and international renal registries. In 1997 the International Federation of Renal Registries (IFFR) was founded for international comparison and improvement and standardization of different renal databases (2). The Macedonian Renal Registry was established in the nineties, but collecting and elaborating data was sporadically (3). It started collecting data in an organized and systematic manner since 2002 and is contributing data to the ERA-EDTA (European Renal Association-European Dialysis and Transplant Association) Renal Registry on an aggregated basis (B-section). There are 18 public in-hospital dialysis centres in the Republic of Macedonia distributed evenly throughout the country. Since 2002, responsible physicians in each dialysis centre are extending collected data for individual patients to the key-person of the national registry, and

after elaborating all the collected data, the aggregated data are extended to the European Renal Registry. The purpose of this study is to give an overview of some epidemiologic data of ESRD in the Republic of Macedonia, as well as the renal replacement therapy in a period of 6 years (2002-2007).

MATERIALS AND METHODS

According to the population census in 2002, the general population in the Republic of Macedonia is 2,023,000 inhabitants (1,015,000 men and 1,007,000 women). This number is used for adjustment of incident and prevalent counts of ESRD patients for age and gender to the European population of 1995 (adjustment for the registry data of 2002-2004) and to the general population of EU25 of the year 2000 (adjustment for the registry data of 2005-2007). The percent coverage of the general population by the renal registry is 100%, and all the 18 haemodialysis centres are extending complete data for individual patients. Data on start of RRT, age, gender, primary renal disease, vascular access, type of established therapy, number of renal transplants and mortality are collected for individual patients in all the dialysis centres in the country, and extended to the national registry. The summarized data are elaborated, and incident counts on day 1 and 91, unadjusted and adjusted for age and gender, as well as prevalent counts on 31st December, unadjusted and adjusted for age and gender are established. Mean and median age of incident and prevalent patients, primary renal disease, established therapy

		2002	2003	2004	2005	2006	2007
Day 1 unadjusted	m	89,6	101,4	97,4	111,3	110,3	111,3
	f	55,6	64,5	71,5	84,4	86,4	72,5
	all	72,7	83	84,5	97,9	98,4	92,0
Day 1 adjusted	m	101,8	121,8	113,2	133,8	133,1	134,4
	f	60,5	70,5	85,4	99,2	104,8	84,4
	all	80,1	96,1	99,8	117,4	119,7	110,8
Day 1 Mean age	m	53,7±13,6	55,2±14,8	55,8±14,5	58,2±14,8	58,4±14,1	57,9±14,7
	f	58,6±13,5	59±14,4	58,7±13,7	56±16,9	61±13,5	58,2±12,6
	all	55,6±13,8	56,7±14,7	57,0±14,2	57,3±15,7	59,5±13,9	58,0±13,8
Day 91 unadjusted	m	83,7	89,6	84,6	97,5	97,5	104,4
	f	50,6	55,6	54,4	74,5	82,4	61,6
	all	67,2	72,7	69,7	86,1	90,0	83,1
Day 91 adjusted	m	94,2	104,2	97,9	117	115	125,4
	f	54,9	60,6	64,0	85,1	100,2	71,2
	all	75,5	82,4	81,6	102,2	107,3	99,5
Day 91 mean age	m	53,1±13,6	53,7±14,2	54,9±14,8	57,6±15,3	57,9±13,7	57,3±14,8
	f	58,9±14,0	58,2±14,8	59,1±13,2	54,6±16,5	60,9±13,5	57,9±13,1
	all	55,2±14,0	55,4±14,5	56,5±14,3	56,3±15,9	58,8±13,7	57,5±14,2

m- male f- female

TABLE 1. Incident counts per million population at day 1 and 91, unadjusted and adjusted for age and gender, mean age of incident patients at day 1 and 91.

		2002	2003	2004	2005	2006	2007
Day 1 unadjusted % cause of renal failure	GN	14,3	11,3	9,9	13,1	11,6	8,1
	PN	15,6	17,3	15,2	16,2	8,5	8,6
	PKD	5,4	4,2	7,0	3,5	5,0	7,5
	DM	19	17,3	9,9	21,2	19,6	22,6
	HT	20,4	21,4	24,6	19,2	28,1	25,8
	RVD	2,7	1,2	0,6	1,0	1,0	0,5
	Misc	9,5	14,9	14,0	5,6	8,5	6,5
	Unkn	10,9	10,7	18,7	20,2	17,1	20,4
	Missing	2	1,8	0,0	0,0	0,5	0,0
Day 91 unadjusted % cause of renal failure	GN	11,8	12,2	10,6	16,1	11,5	8,9
	PN	16,2	17	15,6	16,7	8,8	9,5
	PKD	5,9	4,8	7,8	1,7	5,5	7,7
	DM	18,4	16,3	9,2	21,8	18,1	21,4
	HT	21,3	21,1	26,2	19,0	30,2	26,8
	RVD	2,9	1,4	0,7	0,6	1,1	0,6
	Misc	10,3	15,6	12,8	6,3	7,1	6,5
	Unkn	11,8	10,2	17,0	17,8	17,0	18,5
Missing	1,5	1,4	0,0	0,0	0,5	0,0	
Day 91; % of established therapy	HD	100	99,3	98,6	96	98,4	92,9
	PD	0	0,7	1,4	2,3	4,1	4,2
	Tx	0	0	0	0	0,5	3,0

GN-glomerulonephritis, PN-pyelonephritis, PKD-polycystic kidney disease, DM- diabetes mellitus, HT-hypertension, RVD-renovascular disease, Misc-miscellaneous, Unkn-unknown renal disease

TABLE 2. Incident counts by primary renal disease at day 1 and 91 and by established therapy

in percentage and per million population are also established, and number of renal transplants per year. The crude death rate for a certain year is calculated by dividing the number of patients who died that year with the average number of prevalent RRT patients at the end of that year and the previous year.

RESULTS

Incident counts on RRT per million population at day 1 and 91, unadjusted for age and gender, as well as adjusted numbers and the mean age of patients at day 1 and 91 are presented in Table 1. The data show a continuous gradual increase in incident counts on RRT over the years. Incident patients are relatively young, females are older than males, but the mean age is also increasing over the years.

The primary renal disease of incident patients in percentage, at day 1 and 91, unadjusted for age and gender, and the percentage of established therapy are presented in Table 2. The leading cause of ESRD in patients who start RRT in The Republic of Macedonia is hypertension, followed by diabetes and unknown cause. There is a decrease in glomerulonephritis and pyelonephritis as primary renal diseases for RRT over the years, which is accounted for by the increase of hypertension and diabetes. Haemodialysis is almost unique initial RRT, and peritoneal di-

alysis and kidney grafts are rarely used to initiate RRT for ESRD, but there is a slight change in the last years.

The prevalent counts per million population, unadjusted and adjusted for age and gender, the mean age of prevalent patients, the cause of renal failure in percentage and the established therapy in percentage are presented in Table 3. The data also show a continuous and gradual increase in prevalent counts over the years. Prevalent patients are younger than incident patients, females are older than males, and the prevalent population is growing older over the years. The leading cause of renal failure in prevalent patients is glomerulonephritis and pyelonephritis, although the picture is changing over the years, and hypertension in 2007 is the third leading cause for ESRD (after glomerulonephritis and unknown renal failure). Haemodialysis (HD) is the preferred renal treatment practice in the country; more than 92% of patients are treated with HD in 2002. But, there is a slight increase in the number of patients treated by peritoneal dialysis and with transplanted kidneys over the years (Table 3).

The number of renal transplants per year (Macedonian residents only) is shown in Table 4. It is very low and shows no increase. Cadaveric transplantation is lacking in the country. The established therapy in percentages is shown in Figure 1.

		2002	2003	2004	2005	2006	2007
Prevalent counts pmp 31 Dec unadjusted	m	615,5	642,7	656,5	719,2	755,7	787,2
	f	427,9	436,9	437,9	482,6	529,3	547,2
	all	522,1	540,3	547,7	601,4	642,9	667,7
Mean age of prevalent pts	m	50,5±13,4	51±13,1	51,5±13,3	52,4±14,3	53,4±14,1	54,1±14,1
	f	52,4±14,0	52,7±14	52,8±14,2	52,5±14,4	54,4±14,1	55,4±14,1
	all	51,3±13,7	51,7±13,5	52,0±13,7	52,4±14,3	53,8±14,1	54,6±14,1
Prev. counts pmp 31 Dec adjusted for age & gender	m	670,4	701,6	730,0	801,4	859,3	902,8
	f	448,0	458,7	483,5	539,6	597,4	628,4
	all	559,2	580,1	606,1	672,0	728,3	767,4
Prevalent counts by cause of renal failure (%) 31 Dec	GN	27,1	26,3	25,2	23,8	22,2	20,4
	PN	15,3	15,5	14,7	15,9	15,5	15,1
	PKD	9,5	8,9	8,8	8,2	8,0	8,0
	DM	8,6	7,9	7,9	8,8	9,4	10,3
	HT	9,3	11,5	12,5	14,1	16,1	16,4
	RVD	1,9	1,5	1,6	1,4	1,4	2,0
	Misc	10,1	10,8	10,5	9,2	8,5	8,3
	Unkn	13,9	13,7	18,7	18,4	18,7	19,3
	Miss	4,3	4,0	0,2	0,2	0,2	0,2
	HD	92,1	91,0	89,4	88,6	88,6	87,8
% of established therapy 31 Dec	PD	0,5	0,4	0,9	1,5	1,1	1,9
	Tx	7,4	8,6	9,7	10,0	10,3	10,4

Pmp-per million population

TABLE 3. Prevalent counts per million population, unadjusted and adjusted for age and gender, by cause of renal failure and by established therapy

	2002	2003	2004	2005	2006	2007
Living related	15	16	17	12	10	12
Living unrelated	1	1	0	0	1	4
Cadaver	0	0	0	0	2	0
Total	16	17	17	12	13	16

Pmp-per million population

TABLE 4. Renal transplants per year

Average increase in incident patients Five-year period: 2002-2007	
Average increase in number of incident patients per year	3,86
Average percent increase in incident patients per year	5,17%

TABLE 5. Increase of incident patients per year: day 1, unadjusted

Average increase in prevalent patients Five-year period: 2002-2007	
Average increase in number of prevalent patients per year	29,1
Average percent increase in prevalent patients per year	5,1%

TABLE 6. Increase of prevalent patients per year, unadjusted

The average percent increase in incident and prevalent patients on RRT per year (Table 5 and 6) is approximately 5% (unadjusted counts, the period of 2002-2007). (Table 5, Table 6).

The crude death rate for 2006 and 2007 is shown in Table 7. The crude death rate for RRT is 10,7% in 2007

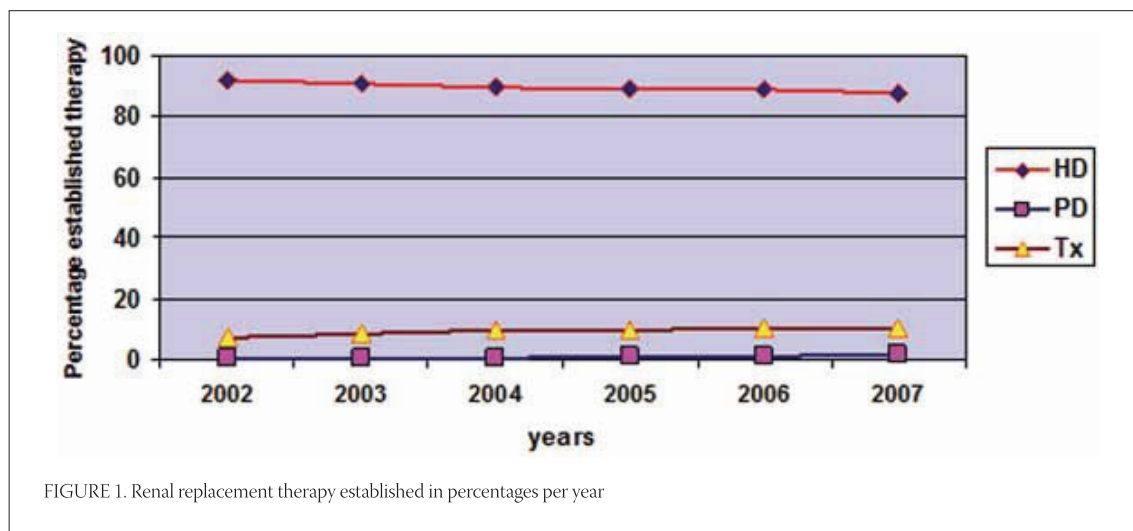


FIGURE 1. Renal replacement therapy established in percentages per year

year	HD Prev.	PD Prev.	Tx Prev.	RRT Prev.	Male Prev.	Female Prev.	HD Ex	PD Ex	Tx Ex	RRT Ex	Prev. RRT average	% mortality RRT
2007	1185	25	140	1350	799	551	140	1	1	142	1325	10,7 (5,13 –PD) (11,98-HD) (0,73-Tx) 11,9 (PD+HD)
2006	1152	14	134	1300	767	533	141	0	5	146	1258	11,6 (0 – PD) (12,65-HD) (3,92-Tx) 12,5 (PD+HD)
2005	1077	18	121	1216	730	486						
2005	1077	18	121	1216	730	486						

Prev.-prevalence PD-peritoneal dialysis HD-haemodialysis Tx-transplantation Ex-patients who died

TABLE 7. Crude death rate per year (2006/2007)

and 11,6% in 2006. It is the highest in haemodialysis patients, 11,98% in 2007, and 12.65% in 2006. (Table 7)

DISCUSSION

Over the past years, an increase in the prevalence of RRT has been observed in almost all Western European countries, which was partly explained by the decreased mortality, and mainly by the increased incidence rate of ESRD which was mainly accounted for by the increased acceptance rate of diabetics and older patients (4). In most of the post-communistic countries of Central and Eastern Europe, as well as the Former Yugoslav countries, the incidence and prevalence rates of ESRD patients have increased after the fall of the communistic regime (5). The data presented above show that the incidence rate of ESRD patients in Macedonia is relatively low, when compared to Western European countries. In 2007, although it has increased substantially since 2002, the incidence rate of RRT per million population, at day 91, adjusted for age and gender, was 99,5. Most of the Western European countries had much higher incidence rates, for example, Belgium, French speaking, had incidence rate of 164,7 per million population, but on the other hand, Finland and Iceland had much lower rates, 82,9 and 81,5 respectively. Greece, although being a Balkan country, had very high incidence rate of RRT in 2007, 145,8 per million population, most probably due to the high number of diabetics with ESRD (6). The mean age of incident and prevalent patients in Macedonia is below 60 years of age, thus being rather different than most of the Western European countries where the mean age is above 60, up to 69 years (6). This is not surprising, when having in mind that the European population is older, and the acceptance rate

for older ESRD patients and diabetics is much higher. Regarding cause of renal failure, the incident rates of patients with diabetes and hypertension were continuously increasing over the past years and hypertension and diabetes have become the leading cause of ESRD. The incident counts of diabetics at day 1, unadjusted, have increased from 11,3% in 1997 (7) to 22,6% in 2007 (6). This change affects the prevalence rates, as well. The prevalence counts of diabetes and hypertension are increasing, too, but, still, the leading cause of ESRD in prevalent patients is glomerulonephritis and unknown cause of renal failure.

Although there is an increase in the percentage of prevalent renal transplanted patients and patients on peritoneal dialysis, still, the percentage of haemodialysis as treatment modality is very high, slightly below 90% in 2007, unlike most Western European countries where it ranges between 28 and 61% (6). Renal transplants per year are very low and not sufficient. Only 16 were performed in 2007. Peritoneal dialysis, too, is not adequately presented in the country, the reason being the lower cost of haemodialysis compared to peritoneal dialysis due to the underpayment of medical personnel.

The crude mortality rate on RRT in Macedonia is not high. In 2006 it was 11,6 %, and the mortality rate on dialysis (haemo and peritoneal dialysis) was 12,5%. The crude mortality annual rate in Baltic countries varies between 12,5 and 15% (5). When compared to the data of the Slovenian Renal Registry (8), the crude death rate in Macedonia is relatively low, which is mainly due to the much lower number of prevalent diabetic patients on RRT in Macedonia and younger age of patients. In 2006, in Slovenia, the crude death rate for dialysis patients was 14,7% (15,56% for HD and 4,58% for PD patients).

CONCLUSION

Incident and prevalent rates of patients on RRT are continuously increasing. There is a changing picture regarding age of patients on RRT (older patients are accepted for RRT) as well as cause of renal failure. Diabetes and hypertension are becoming the leading cause of ESRD as in Western European countries. Higher number of older patients and diabetics will impact RRT mortality in future. This imposes efforts to be undertaken for planning prevention strategies towards diabetic complications and diabetes mellitus itself.

Kidney transplantation is underrepresented as RRT in Macedonia compared to Western Europe, and efforts should be made for its increase, particularly the cadaveric one.

List of Abbreviations

m	-	male
f	-	female
GN	-	glomerulonephritis
PN	-	pyelonephritis
HT	-	hypertension
RVD	-	renovascular disease
PKD	-	polycystic kidney disease
Misc	-	miscellaneous
DM	-	diabetes mellitus
Unkn	-	unknown renal disease

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