

Epidemiological study of end-stage renal disease in western Paraná. An experience of 878 cases in 25 years

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Submitted on: 08/18/2009

Accepted on: 12/07/2009

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We declare no conflict of interest.

ABSTRACT

Introduction: The incidence and prevalence of treated end-stage chronic kidney disease (CKD) patients continue to grow throughout the world. Renal transplantation remains the preferred form of renal substitutive therapy, but given the limited number of donors, dialytic therapies are the most common modalities. **Objectives:** To assess a registry of patients admitted for renal substitutive therapy at a single centre from 1984 to 2009. **Methods:** This is a retrospective epidemiological study. The following were analyzed: demographic and clinical characteristics; incidence of CKD; underlying renal disease; dialysis modalities; mortality; and causes of death. The variables were compared by using the chi-square test, Student *t* test, ANOVA, and Tukey test. Kaplan-Meier curves were used to estimate patient's survival. A *p* value < 0.05 was considered statistically significant. **Results:** In the period studied, 878 patients were admitted to dialysis. Their mean age was 47.0 ± 16.2 years, 549 (62.5%) were males, and 712 (81.1%) were white. The major cause of CKD was hypertension in 351 (40.0%) patients, diabetic nephropathy in 174 (19.8%), and chronic glomerulonephritis in 180 (20.5%) patients. The main dialytic modality was hemodialysis. The one-year mortality rate was 10.4%. The most common cause of death was cardiovascular, affecting 126 (34.6%) patients. **Conclusions:** The cohort of patients studied had a low mortality rate. Cardiovascular disease remains the most common cause of death in end-stage chronic renal disease. Screening for cardiovascular disease is highly recommended for those patients.

Keywords: chronic kidney disease, renal substitutive therapy, hemodialysis

[J Bras Nefrol 2010;32(1):49-54]©Elsevier Editora Ltda.

INTRODUCTION

Chronic kidney disease (CKD) relates to a syndromic diagnosis of progressive and irreversible loss of renal function. It is characterized by deterioration of the biochemical and physiological functions of all body systems secondary to the accumulation of catabolites (uremic toxins), alterations in the hydroelectrolytic and acid-base balances, hypervolemia, hyperkalemia, hyperphosphatemia, anemia, hyperparathyroidism, etc.¹

Chronic kidney disease is a problem of public health and its incidence and prevalence significantly increase in the population on dialysis programs.² The modalities of renal replacement therapy (RRT) available are as follows: hemodialysis (HD); continuous ambulatory peritoneal dialysis (CAPD); and renal transplantation. In Brazil, the prevalence of patients on dialysis programs has considerably increased in the past years, since the number of renal transplantations does not accompany that growth.^{2,3} Recent data have shown an overall prevalence of patients on RRT, including transplantations, of 518 patients per million inhabitants. Approximately 90% of the patients on dialysis programs in Brazil undergo HD, and the remaining undergo CAPD.⁴

The major causes of CKD are as follows: hypertension (AH); chronic glomerulonephritis (CGN); and diabetes mellitus (DM).^{5,6,7} In recent years, DM has become the major cause of end-stage CKD, mainly due to the increase in the incidence of type 2 DM.⁸

The annual mortality of patients on dialysis programs in Brazil has been estimated as approximately 15%.³ The major cause of mortality of patients with CKD is that of cardiovascular origin, being 10 to

20 times greater when compared to that of the general population, even when adjusting for other risk factors, such as age, ethnicity, sex, and presence of DM.⁹

This study aimed at assessing the profile of patients with end-stage CKD, incidence of CKD, etiology of the underlying disease, dialysis modality, survival in dialytic treatment, and the causes of death in western Paraná, comprising 25 municipalities and an estimated population of approximately 500,000 inhabitants, in the past 25 years.

METHODS

We reviewed the medical records of all patients undergoing dialysis (HD or peritoneal dialysis) in the past 25 years, in the city of Cascavel, State of Paraná, Brazil, available at the dialysis center Renalclin Oeste Ltda, which serves patients of an area of the State of Paraná comprising 25 municipalities. The population estimated in 2007 was approximately 500,000 inhabitants. The following data were collected: sex; ethnicity; age; dates of entering and exiting the dialysis program; dialysis modality; reason for exiting; and, in case of death, cause of death. The present study was approved by the Committee on Ethics and Research in Human Beings of the Universidade Estadual do Oeste do Paraná (157/2009-CEP).

The dialysis modality chosen was conventional HD, three sessions per week, each session lasting three to four hours. Continuous ambulatory peritoneal dialysis was indicated when vascular access lacked or when patients had better socioeconomic conditions and a profile adequate for the procedure.

Data were stored in a Microsoft Excel database and were analyzed by use of descriptive statistics as follows: arithmetic mean; standard deviation; minimum and maximum values; and gross and percentage frequency. The differences between continuous variables with parametric distribution were analyzed by using the Student *t* test. Categorical variables were analyzed by use of the *Chi*-square test or Fisher exact test, according to the size of the sample. The mean ages at the different periods studied were compared by using analysis of variance (ANOVA) and Tukey test.

Annual mortality was calculated and the Kaplan Meier survival curve was built (overall analysis and analysis divided into two periods, 1983 to 1999 and 2000 to 2009). The curves were compared by using the log-rank test. A *p* value < 0.05 was considered statistically significant. For including in the survival curve, the patients censored were those who died within 30 days of treatment, who were transferred, and who were transplanted.

RESULTS

From 1984 to 2009, 878 patients were admitted for dialytic treatment, 549 (62.5%) of whom were males, and their ages ranged from 2 to 90 years (mean of 47.0 ± 16.2 years). Regarding ethnicity, 712 (81.1%) patients were white. The predominant dialysis modality at admission was HD (752 patients, representing 85.6%). Regarding the etiology of the CKD, AH was the most frequent, affecting 351 (40.0%) patients. Table 1 shows the demographic characteristics, types of dialytic treatments used, and etiology of CKD. When assessing the etiologies of CKD over time, an increase in the incidence of DM and AH and a decrease in the incidence of CGN were observed. Figure 1 shows the evolution of the three main causes of CKD (DM, CGN and AH) over 25 years, divided into five subperiods (1984 to 1990, 1991 to 1995, 1996 to 2000, 2001 to 2005, and 2006 to 2009).

A progressive increase in the incidence of patients admitted to RRT has been observed. When dividing the time period analyzed into the above-mentioned five subperiods, the number of patients admitted per year was, on average, 18.6, 23.4, 35.2, 42.2, and 44.6, respectively. The current prevalence of patients on dialysis program is 344 per million inhabitants.

In the time periods of 1984 to 1990, 1991 to 1995, 1996 to 2000, 2001 to 2006, and 2007 to 2009, the mean ages at admission were 40.9, 43.9, 45.7, 50.3, and 52.6 years, respectively, which shows an increase over time and a statistically significant difference.

Regarding the reasons for exiting the program, death prevailed in 364 (41.5%) patients, followed by renal transplantation in 203 (23.1%) patients. Regarding the causes of death, the cardiovascular was the most frequent, affecting 126 (34.6%) patients. Table 2 shows the reasons for exiting the program and the causes of death in that population.

When comparing the patients who died with the survivors, no statistically significant difference was observed in regard to sex and ethnicity between both groups (*p* > 0.05). However, in regard to the type of treatment, patients on CAPD died more than those on HD (*p* < 0.0001). Regarding the other variables, the statistical analysis could not be performed because of the small number of patients in the subgroups.

The current situation of the patients on RRT is as follows: 133 transplanted patients with functioning kidneys; 172 patients on dialysis, 12 (7%) on CAPD and 160 (93%) on HD.

Figure 2 depicts Kaplan-Meier survival curve of the overall analysis of all patients in the period studied.

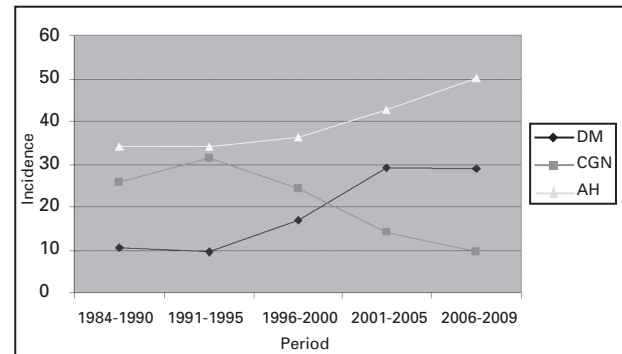
Annual mortality was 10.4%. When dividing the period studied into two subperiods, no statistically significant difference was observed between both curves ($p > 0.05$) (Figure 3).

DISCUSSION

We assessed a retrospective cohort of patients with CKD on dialysis, admitted at a single dialysis center over 25 years. The study assessed the profile of those patients, incidence of CKD, etiology of the underlying disease, survival of patients on dialysis, and causes of death.

A progressive increase in the incidence of patients admitted for RRT was observed and was disproportional to the population increase, probably due to the better structuration of the health system. The incidence in the literature varies from 18 per million inhabitants in Ukraine to 213 per million inhabitants in Germany. The prevalence of patients on RRT in this study was 344 per million inhabitants, while in 2006, in Europe, that prevalence was 630 per million inhabitants.¹⁰ We hypothesize whether the elevated number of renal transplantations performed in our region has contributed to that lower prevalence. Data referring to renal transplantation at our service were assessed

Figure 1. Evolution of the three major causes (DM, AH, and CGN) over 25 years, divided into five subperiods (1984 to 1990, 1991 to 1995, 1996 to 2000, 2001 to 2005, and 2006 to 2009).



in another publication.¹¹ In our study, the male sex prevailed, which is in accordance with the literature, where some series have reported a predominance of up to 70%.⁶

When assessing the etiology of the underlying disease, a progressive increase in DM has been observed, as previously reported by our group.¹² Those data are in accordance with those of other studies, which show

Table 1

DEMOGRAPHIC CHARACTERISTICS, TYPES OF DIALYSIS TREATMENT, AND CAUSES OF CKD

Variable	Frequency	Percentage
Sex		
Male	549	62.5%
Female	329	37.5%
Ethnicity		
White	712	81.1%
Black	154	17.5%
Yellow	12	1.4%
Treatment		
HD	755	86.0%
CAPD	123	14.0%
Causes of CKD		
AH	351	40.0%
CGN	180	20.5%
DM	174	19.8%
UND	79	9.0%
TIN	50	5.7%
PKD	32	3.6%
NEO	10	1.1%
HUS	2	0.2%

AH: hypertension; DM: diabetes mellitus; CGN: chronic glomerulonephritis; UND: undetermined; TIN: tubulointerstitial nephropathy; PKD: polycystic kidney disease; NEO: neoplasia, HUS: hemolytic-uremic syndrome.

Table 2 CAUSES OF EXITING THE PROGRAM AND OF DEATH IN THE POPULATION STUDIED

Variable	Frequency	Percentage
Causes of exiting		
Death	364	41.5%
Transplantation	203	23.1%
Transference	76	8.7%
Recovery	7	0.8%
Drop-out	4	0.5%
Total	654	100.0%
Causes of death		
UND	164	45.1%
CVD	126	34.6%
SEPSIS	62	17.0%
NEO	5	1.4%
UGB	3	0.8%
MALN	2	0.5%
CET	2	0.5%
Total	364	100.0%

UND = undetermined; CVD = cardiovascular disease; NEO = neoplasia; UGB = upper gastrointestinal bleeding; MALN = malnutrition; CET = cranioccephalic trauma

that diabetic nephropathy is currently the major cause of starting RRT.¹³ A limitation regarding the assessment of the diagnosis of the underlying disease is the late presentation of patients at services of nephrology, usually already at an advanced stage of renal disease.

The most frequently used modality of dialysis has been conventional HD, three times per week. The CAPD has been reserved for patients with better

Figure 2. Kaplan-Meier survival curve of the overall analysis of all patients in the period studied.

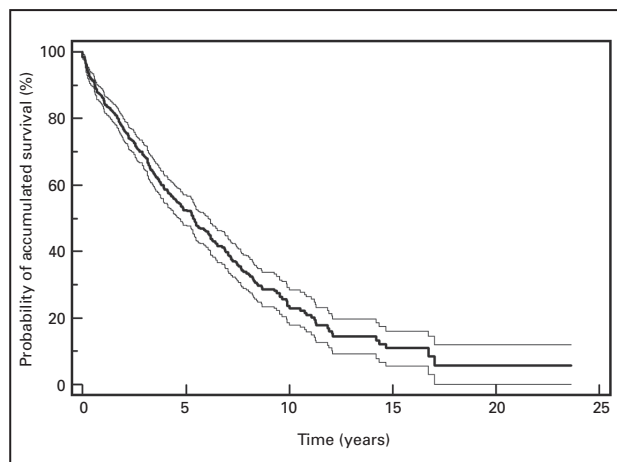
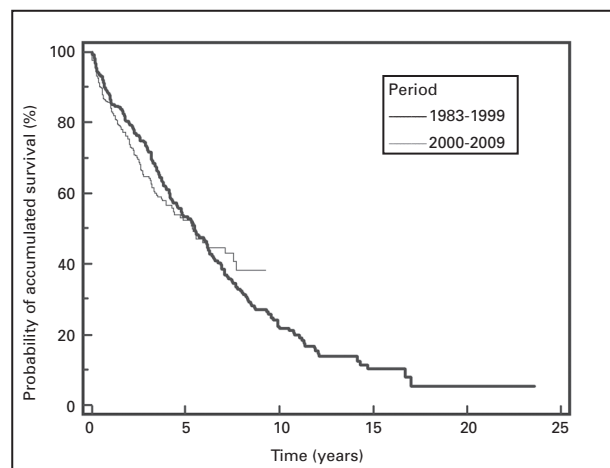


Figure 3. Kaplan-Meier survival curve dividing the period studied into two subperiods.



socioeconomic conditions, or for those with no vascular access.^{14,15} Thus, it is difficult to compare evolution data of patients treated with those modalities. Renal transplantation has better results in selected populations, such as those lacking significant comorbidities, and at some age ranges.^{16,17} In our study, HD was the initial treatment in most patients, who had access to renal transplantation in 23.1% of the cases. There are several studies indicating a greater cardiovascular risk

for patients on peritoneal dialysis,^{18,19,20} and our data have shown an increase in mortality for those patients. Nevertheless, a study showed no difference in survival between both methods.²¹

The age of entering the dialytic program has been increasing over time. Jager *et al.*²² have shown that the percentage of elderly patients (≥ 65 years) on RRT was 22% in 1985 and 48% in 1999. Rayner *et al.*²³ have reported that approximately 50% of the patients admitted for dialysis are over the age of 65 years. Those are preoccupying data, because with the increase in prevalence in the elderly, comorbidities and the cardiovascular risk also increase.²⁴

The annual mortality in that group of patients was 10.4%. When assessing if an alteration in survival has occurred over the years, no difference was observed. In our interpretation, this is positive, because, despite the increase in the diabetic population, with lower survival as already shown by our group¹², and an increase in the age of patients at admission, a decrease in survival would be expected. However, an improvement in the quality of dialysis and availability of new medications (erythropoietin, sevelamer) has occurred in the last period studied, as shown in Figure 3. The annual mortality in patients on HD in other studies has varied from approximately 10% in Japan,²⁵ 16.3% in Italy²⁶ to over 20% in Mexico.²⁷

Regarding the causes of death in patients on RRT, the cardiovascular cause has been the most common.²⁸ When assessing the causes of death in the elderly, no difference exists as compared with the general population on dialysis.²² Mechanisms have been proposed to explain that elevated cardiovascular mortality in individuals on dialysis, such as accelerated atherogenesis, dyslipidemia, endothelial dysfunction, and inflammation.^{29,30} Patients over the age of 75 years have an increased risk of death due to cardiovascular cause of up to five times, and it may reach 375 times for patients aged from 25 to 35 years.²⁴ Those data are preoccupying and may be even more alarming, considering that undetermined causes may comprise cases of cardiovascular cause.

One limitation of this study is its retrospective characteristic, but data were collected by the same team caring for the patients for over 25 years. As in any epidemiological study, in regard to the etiology of CKD, AH may be overestimated and CGN may be underestimated as its cause, because of the admission of many end-stage renal disease patients for dialysis, many of whom without undergoing renal biopsy.

CONCLUSIONS

In this study, this cohort of patients showed low mortality. Cardiovascular disease remains the major cause of death in the population with end-stage CKD. Screening for cardiovascular disease is highly recommended for those patients.

We hope to have contributed to the better understanding of end-stage CKD and of RRT among us. Despite all difficulties found in approaching those patients, we conclude that we provide quality health care with satisfactory survival rates in all dialysis modalities available for patients with chronic disease. New strategies have been implemented to enable early diagnosis and referral to a nephrologist at earlier stages of the disease.

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