Geography of peritoneal dialysis in Brazil: analysis of a cohort of 5,819 patients (BRAZPD)

Authors

Natália Maria da Silva Fernandes[1]
Alfredo Chaoubah[2]
Kleyton Bastos[3]
Antônio Alberto Lopes[4]
José Carolino Divino-Filho[5]
Roberto Pecoits-Filho[6]
Marcus Gomes Bastos[1]

[1]Universidade Federal de Juiz de Fora – UFJF
[2]Department of Statistics of UFJF
[3]Universidade Federal de Sergipe – UFSE
[4]Universidade Federal da Bahia – UFBA
[5]Baxter Renal Division, Baxter Health Care, Belgium
[6]PUC do Paraná

Submitted on: 05/27/2010
Approved on: 07/08/2010

Correspondence to:
Natália Fernandes. Universidade Federal de Juiz de Fora Rua Jamil Altaff, 132. Vale do Ipê – Juiz de Fora – Minas Gerais
CEP-36035-380
E-mail: nataliafernandes02@gmail.com

We declare no conflict of interest.

Abstract

Introduction: Brazil is a continental country with great diversity of population, social and cultural. This factor may determine different demographic, clinical and outcome presented by patients with chronic kidney disease on peritoneal dialysis (PD). **Objective:** To evaluate the clinical characteristics and outcomes presented by PD patients in different regions of Brazil, analyzing a cohort of patients (BRAZPD) from December 2004 until October 2007. **Patients and Methods:** Data were collected monthly and patients were followed until the outcome (death, renal transplantation, renal function recovery, transfer to hemodialysis or loss of follow-up). **Results:** We evaluated 5.819 patients incident and prevalent. Most patients performed renal replacement therapy (RRT) in the Southeast, where the average follow up time was longer (12.3 months) and there is a higher percentage of elderly (36.4%). The prevalence of diabetes is higher in Southeast and South (38.1% and 37%, respectively). Most patients in the North region had previously hemodialysis (66.2%). The mortality was higher in the Northern region (30.1%), as well as failure of the technique (22.3%). **Conclusion:** The data shows different demographic, clinical, mortality and technique failure of PD reflecting the demographic and social peculiarities of Brazil. The geography of the DP in Brazil proves to be a mirror of the geography of Brazil. So health policies should take into account the characteristics of each region so we can improve patient survival and technique on peritoneal dialysis.

Keywords: peritoneal dialysis, geography, epidemiology, Brazil.

[J Bras Nefrol 2010;32(3):265-271]©Elsevier Editora Ltda.

Introduction

According to the *Pesquisa Nacional de Amostras por Domicílio* (National Research per Sample of Domicile) – PNAD/2006,[1] Brazil has a land area of 8,514,215.3 km^2 and 187 million inhabitants. It is divided in five large regions (North, Northeast, South, Southeast and Midwest). A trend towards a change in the demographic pyramid has been observed in all regions of the country, being less evident in the North region, which also has a larger male elderly population (> 60 years) in relation to the female population, in contrast with the rest of the country, where women predominate at this age range. This region also has a higher fertility rate and has a higher number of individuals per household.

The level of schooling varies according to the analyzed region, with the Northeast region presenting the highest rate of illiteracy (18.9%), followed by the North region (10.3%). Regarding the mean income, the Northeast region presents the lowest mean monthly income, both for women (R$ 460.00) and men (R$ 519.00), followed by the North region (women: R$ 519.00; men: R$ 809.00).

Regarding the differences observed in the different regions, data from DATASUS (Brazilian Public Health System Database) show that cardiovascular diseases are the main cause of death in all regions; however, the North region presents the lowest rate of cardiovascular mortality when compared to the other regions.[2] The reason for this fact is probably multifactorial; one of the factors is the low life expectancy in this region, which decreases the prevalence of chronic-degenerative diseases.

Data from the *Sociedade Brasileira de Nefrologia* (Brazilian Society of Nephrology - SBN)[3] show that there are 87,044 patients undergoing renal replacement therapy (RRT) in Brazil, of which 10.6% undergo peritoneal dialysis (PD).

Most of the patients undergoing RRT (57.4%) are in the Southeast region, the most populous one according to the *Instituto Brasileiro de Geografia e Estatística* (The Brazilian Institute of Geography and Statistics - IBGE). Only 19.1% of them are in the Northeast region, the second most populous region of the country, which demonstrates the differences regarding access to RRT in this region. The aforementioned data disclose a continental country with broad demographic, economic and cultural diversity.

Studies carried out in other countries, such as Canada, where native Canadians have lower access to PD[4] and studies that show multiple difficulties related to RRT access, vascular access procedures, access to medication and kidney transplantation due to ethnicity, economic status and geographic location[5-9] demonstrate that differences can occur in clinical conditions and outcomes of patients undergoing dialysis according to the geographic area assessed, even within the same country.

With the objective of assessing the clinical characteristics and outcomes presented by patients undergoing PD in different regions of Brazil, we evaluated a cohort of patients (BRAZPD) from December 2004 to October 2007.

Patients and Methods

This analysis was performed with the data from BRAZPD,[10] a multicentric, prospective, observational study of patients undergoing PD, from December 2004 to October 2007. A total of 5,819 prevalent and incident patients from Brazilian clinics were included, with more than ten patients using the Baxter peritoneal dialysis system. The study was approved by the Ethics Committee in National Research and the Ethics Committee in Local Researches. After approval, the nurses and physicians were trained to fill out and send the data. Demographic, clinical and laboratory data were collected monthly, and the patients were followed up to the outcome (death, kidney transplantation, kidney function recovery, transference to hemodialysis or loss of follow-up). The variable definitions are the ones described by Fernandes *et al.* in 2008.[10]

We evaluated patients undergoing PD in each one of the five regions of the country regarding the described variables and outcomes. Initially, a descriptive analysis was performed of the general characteristics of the population undergoing PD in each region, and then, a survival analysis (Kaplan Meier) was carried out for each region. Subsequently, a Cox regression (corrected for age, sex, cardiovascular diseases and presence of diabetes mellitus) was performed. The outcome variables for survival analysis were: death (censoring the losses of follow-up due to other causes) and technique failure (censoring the losses of follow-up due to other causes). The data are presented as means ± standard deviation or percentages. A p value ≤ 0.05 was considered significant. The software package SPSS 13.0 was used for the statistical calculations.

Results

A total of 5,819 patients were assessed from December 2004 to October 2007. Most patients underwent RRT in the Southeast region, followed by the South, Northeast, Midwest and North regions. The mean follow-up period was shortest in the Midwest (8.9 months) and longest in the Southeast region (12.3 months). The mean age was higher in the Southeast (57 ± 19.9) and South (55.5 ± 19.5) regions. The Southeast region also had the highest percentage of elderly individuals (36.4%).

As for level of schooling, the Northeast region had the highest number of illiterate individuals (15.2%) and the highest percentage of patients with an income of up to 2 minimum wages (45.2%). In all regions, most of the patients (70%) lived up to 50 km away from the dialysis center. Regarding the prevalence of comorbidities, it is noteworthy the fact that the prevalence of diabetes mellitus was higher in the Southeast and South regions (38.1% and 37%, respectively). The highest body mass index (BMI) is also seen in these regions (24.6 ± 5 and 25.5 ± 5, Southeast and South regions, respectively – Table 1). The main cause of CKD was diabetes mellitus (33.2%), followed by nephropathy associated to hypertension (21.4%).

The indication of PD was medical and it was the only option available in 64.5% of the cases in the Southeast region, 65.4% in the South, 56.5% in the Northeast, 84.9% in the North and 41.3% in the Midwest. Regarding the pre-dialytic follow-up carried out by a nephrologist, 48.5% were followed in the Southeast, 52.6% in the South, 34.89% in the Northeast, 29% in the North and 39.3% in the Midwest regions. Most patients from the North region (66.2%) had previously undergone hemodialysis, followed by the ones from

Table 1 Demographic, clinical and laboratory characteristics of the patients undergoing peritoneal dialysis in several regions of Brazil

Region / n	Southeast 3,451	Northeast 809	South 1,025	Midwest 271	North 163
Age (mean ± SD)	57 ± 19.9	51.3 ± 21.2	55.5 ± 19.5	50.8 ± 23	50.5 ± 18.5
> 65 years (%)	36.4%	26.3%	33.4%	30.6%	21.5%
Sex (Female, %)	49.3%	51.8%	48.3%	45.4%	54.2%
Ethnicity (Caucasian, %)	64.6%	38.3%	76.5%	57.6%	9%
Level of schooling (%)					
Illiterate	11.7%	15.2%	10.4%	12.9%	9%
Elementary School	53.3%	48.5%	58%	46.1%	47%
High School	22.7%	23.6%	19.9%	26.1%	29.5%
College/University	7.8%	6.9%	6.3%	8.5%	14.5%
Income up to 2 minimum wages (%)	30.7%	45.2%	32.8%	30.8%	35.5%
Distance from dialysis center (up to 50 km, %	74.8%	57%	71.8%	56.6%	76.8%
Time of follow-up (mounths) (mean ± SD)	12.13 ± 8.8 (1 a 34 m)	10,5 ± 7,4 (1 a 27 m)	10.3 ± 7.54 (1 a 28 m)	8.98 ± 6.4 (1 a 26 m)	12.67 ± 9.7 (1 a 31 m)
Creatinine (mg/dL) (mean ± SD)	7.15 ± 5.9	7.1 ± 4	6.5 ± 4.9	8.11 ± 3.67	7.59 ± 4.47
Urea (mg/dL, mean ± SD)	95.07 ± 34	171 ± 43	108 ± 36	97.3 ± 30.2	104.17 ± 42.2
Potassium (mEq/L, mean ± SD)	4.36 ± 1	4.3 ± 1.6	4.25 ± 1.15	4.2 ± 0.9	4.13 ± 0.84
Calcium (mg/dL, mean ± SD)	7.95 ± 3.54	8.7 ± 2	8.18 ± 2.57	8.99 ± 1.2	8.68 ± 0.96
Phosphorus (mg/dL, mean ± SD)	4.96 ± 2.32	4.58 ± 1.89	4.61 ± 1.8	4.4 ± 1.64	4.65 ± 1.5
Glycemia (mg/dL, mean ± SD)	120.7 ± 75.5	103.7 ± 68	112 ± 92	113.3 ± 67.57	125.5 ± 96
Hemoglobin (g/L, mean ± SD)	11.5 ± 3.9	12.7 ± 5.28	11.2 ± 3.37	10.93 ± 2.72	12.4 ± 2.4
Hematocrit (%, mean ± SD)	37.7 ± 17	33.7 ± 14.6	33.9 ± 16	32.14 ± 6.58	37.6 ± 7.36
GPT (mg/dL, mean ± SD)	21.3 ± 49	21 ± 19	22 ± 16	18.8 ± 13	24.49 ± 20.7
BMI (mean ± SD)	24.6 ± 5	23.8 ± 5	25.5 ± 5	22.9 ± 4.5	23.5 ± 5.5
Comorbidities (%)					
Neoplasia	3.3%	1.4%	1.9%	1.4%	0
Cardiovascular disease	25.6%	15,8%	24.8%	19%	1.2%
Vasculopathy	25.4%	20.1%	21.2%	14.6%	1.3%
Left ventricular hypertrophy	38.6%	42.6%	37%	29.2%	22%
Diabetes mellitus	38.1%	31.8%	37%	26.8%	31.3%
Collagenosis	1.4%	2.6%	2.1%	1.4%	1.8%
None	1.6%	3.5%	2.0%	5.4%	1.8%
Discharge (%)					
Death	23.3%	13.4%	20.7%	11.5%	30.1%
No	16.6%	16.8%	17.7%	10.8%	22.3%

the Northeast (51.6%), Southeast (35.4%), South (34.9%) and Midwest (26.1%) regions. Regarding the laboratory profile, the level of hemoglobin was lowest in the Midwest region (10.9 ± 2.7), whereas the other data were comparable.

Patient mortality rate during the 34-month period was highest in the North region (30.1%), followed by the Southeast (23.3%), South (20.7%) and Northeast (13.4%) regions and lowest in the Midwest (11.5%) region (Figure 1, log rank p = 0.001). The mean patient survival time was, respectively, 8.2 ± 5 months, 8.6 ± 6 months, 9.2 ± 5.2 months, 9.6 ± 7 months and 9.6 ± 7.8 months, for the North, Southeast, South, Northeast and Midwest regions. It is worth mentioning that the mean follow-up time for each region was different, as shown in Table 1. The technique

failure rate was highest in the North region (22.3%), followed by the South (17.7%), Northeast (16.8%), Southeast (16.6%) and Midwest (10.8%) regions (Figure 2, log rank p = 0.02, respectively) and the mean technique failure time was 8.3 ± 4 months, 9.1 ± 6.1 months, 9.5 ± 7 months, 9.7 ± 6 months and 10 ± 7.5 months, respectively, for the aforementioned regions. At the patient survival analysis (Cox proportional hazard, Table 3), when analyzing incident and prevalent patients in a same model, the variables that correlated with worse survival were the Midwest region (HR = 1.66; CI = 1.2 to 2.3); age: 65 to 75 years (HR = 3.11, CI = 2.39 to 4.04), > 75 years (HR = 4.29; CI = 3.31 to 5.57), presence of diabetes mellitus (HR = 1.23; CI = 1.03 to 1.46) and cardiovascular disease (HR = 1.31; CI = 1.12 to 1.54). When evaluating technique survival (Cox proportional hazard, Table 4), age from 65 to 75 years had a HR = 0.77, CI = 0.61 to 0.97 and age > 75 years HR = 0.55, CI = O.41 to 0.72 and female sex had a HR = 1.21, CI = 1.03 to 1.43.

Discussion

The demographic, clinical and laboratory characteristics of patients undergoing PD in Brazil reflect the characteristics of each geographic region. This information demonstrates that there is no bias selection regarding the geographic region; however, the bias of PD indication for patients with a higher prevalence of comorbidities persists.

Studies on RRT survival in general and on PD have shown that age, cardiovascular diseases and diabetes mellitus are the main determinants of survival. The cardiovascular diseases are the main cause of death in the general population; however, in the population with CKD, mainly those undergoing RRT, this mortality increases exponentially.[11] This is due to the fact that patients with CKD, in addition to suffering the influence of traditional cardiovascular risk factors (age, male sex, genetic predisposition, systemic arterial hypertension, obesity, hypercholesterolemia, diabetes mellitus, sedentary lifestyle), with the decline in kidney function also start to suffer the influence of new risk factors related to the CKD (anemia, hypervolemia, calcium x phosphorus metabolism alterations, albuminuria, oxidative stress increase, chronic inflammation, accumulation of ADMA - in asymmetrical dimethylarginine, decrease in serum levels of fetuin A and adiponectin).[12] Moreover, the alterations present in the CKD are considered risk factors for cardiovascular diseases.[13]

Figure 1. Analysis of patient survival per region. Kaplan-Meier curve (Log rank p = 0.001).

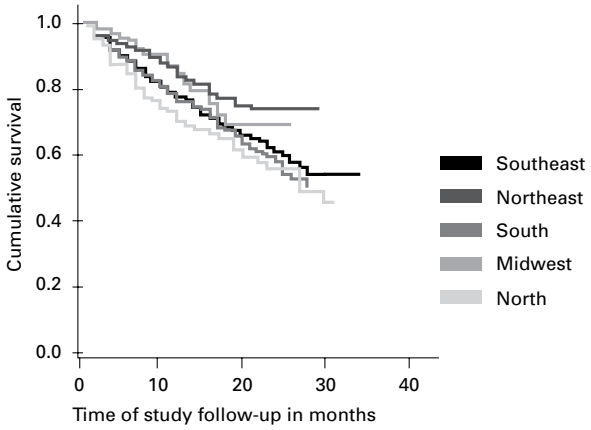
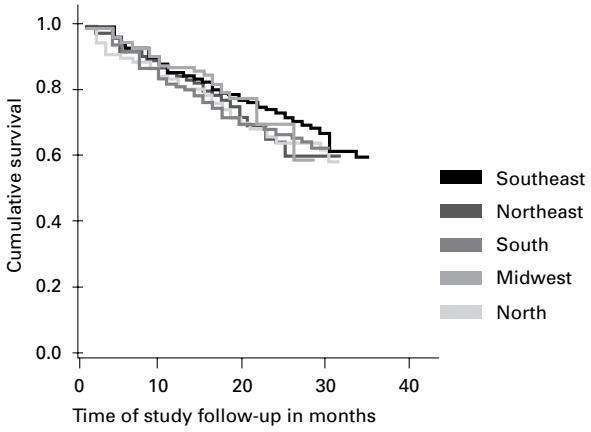


Figure 2. Analysis of technique survival per region. Kaplan-Meier curve (Log rank p = 0.02).



When evaluating the survival of patients during the period in the Southeast (76.7%), South (79.3%), Northeast (86.6%), Midwest (88.5%) and North (69.9%) regions, we can observe that it is similar and comparable to the studies published in developed countries. The technique survival is also satisfactory in the period in the Southeast (83.4%), South (82.3%), Northeast (83.2%), Midwest (89.2%) and North (77.7%) regions and comparable to large studies published in the literature[14-18,19] (Table 1, Figures 1 and 2).

The distance to the nearest center of dialysis was up to 50 km for the Southeast, South and North regions for more than 70% of the patients. However, in the North region, as there were few dialysis centers, which were concentrated in the great region of the capital city, Manaus, a high percentage of the patients does not have access to RRT or change domicile so that they can have access to treatment. In the

Table 2 Analysis of patient survival (Cox proportional hazard, censoring loss of follow-up caused by death, kidney function recovery and transplantation)

			Confidence interval	
	p	HR	Lower limit	Upper limit
Region				
Southeast	0.076	0.80	0.64	1.22
Northeast	0.22	1.13	0.92	1.37
South	0.50	0.85	0.54	1.35
Midwest	0.002	1.66	1.20	2.3
Age < 65 years	1			
65-75 years	0.00	3.11	2.39	4.04
> 75 years	0.00	4.29	3.31	5.57
Female sex	0.51	0.95	0.82	1.10
Diabetes mellitus	0.007	1.23	1.03	1.46
Cardiovascular disease	0.001	1.31	1.12	1.54
Type of therapy APD: CAPD	0.68	1.03	0.88	1.19

APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis.

Northeast and Midwest regions, almost 40% of the patients live more than 50 km away from the nearest RRT center. PD is a therapy that is carried out in the patient's domicile, even when the distance from the domicile to the RRT center is a long one and thus, it must be considered for patients with difficulty to have access to the dialysis centers. Ritt *et al.* (2007) carried out a study that evaluated the distance from the domicile to the RRT center in the state of Bahia, Brazil and concluded that most patients needed to leave their towns or cities and travel long distances to have access to hemodialysis (HD), which is excessively time-consuming and has socioeconomic implications.[20]

A very similar demographic, economic and clinical profile can be observed between the South and Southeast regions, when the regions are evaluated separately. The largest number of patients undergoing RRT in the two most developed regions of the country is in accordance with Sesso *et al.*[3] who demonstrated an estimated prevalence of 467/million inhabitants in the South and 583/million inhabitants in the Southeast with CKD undergoing RRT. These regions concentrate the largest number of clinics, as well as of nephrologists, which facilitates patients' access to treatment. Therefore, we observe a larger number of patients undergoing pre-dialytic follow-up in the South (52.6%) and Southeast (48.5%) regions, which decreases the percentage of patients with late referral to specialized nephrology services. The longer life expectancy (Southeast – 74.0 years, and South – 74.7 years)[21] increases the prevalence of elderly individuals with chronic-degenerative diseases, notably cardiovascular diseases and diabetes mellitus. These are important causes of dialytic CKD and factors that correlate with worse survival in patients with CKD undergoing RRT.

The Northeast region presents some geographic peculiarities. The life expectancy is the lowest in the country, 69.7 years.[21] The patients are younger and present fewer comorbidities, notably with a smaller number of diabetic patients. The region has the worst social indicators, RRT centers are concentrated in large cities, and therefore many patients have no access to this type of treatment. This fact becomes clear when we observe that the Northeast is the second most populous region in the country and its population undergoing RRT is smaller than the population in the South region and that it presents an estimated prevalence of individuals with CKD undergoing RRT of 347/million.[3]

There is also a lower percentage of patients receiving pre-dialytic care (34.8%), which reflects a late referral to the nephrologist. The survival of the patient undergoing PD in this region is higher than in the South and Southeast regions; however, the loss of follow-up rate due to other causes (such as technique failure) is higher.

The North of the country has the lowest population concentration, the lowest general cardiovascular mortality and the second lowest life expectancy (71.5 years),[21] which reflects a lower prevalence of chronic degenerative diseases. Its social indicators are also among the worst in the country. The mortality rate of patients undergoing PD is higher than in other

Table 3 Analysis of technique survival (Cox proportional hazard, censoring loss of follow-up due to death, kidney function recovery and transplantation)

			Confidence interval	
	p	HR	Lower limit	Upper limit
Region				
Southeast	0.56	1.07	0.85	1.34
Northeast	0.41	1.10	0.87	1.39
South	056	0.85	0.50	1.46
Midwest	0.38	1.18	0.80	1.74
Age < 65 years	1			
65-75 years	0.004	0.77	0.61	0.97
> 75 years	0.02	0.55	0.41	0.72
Female sex	0.02	1.21	1.03	1.43
Diabetes mellitus	0.6	1.23	0.78	1.14
Cardiovascular disease	0.058	0.95	0.64	1.00
Type of therapy APD: CAPD	0.08	085	0.72	1.01

APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis.

regions. The estimated prevalence of individuals with CKD undergoing RRT is 236/million.[3] In this region, we also observe a concentration of RRT centers in the capital and great difficulty in having access to specialized services. The number of patients that receive pre-dialytic follow-up is low and there is a large number of patients submitted to PD that used to undergo hemodialysis (66.2%) and that have PD as the only possibility of RRT (84.9%). The technique survival rate is also lower than in other regions, probably reflecting the worse clinical condition of the patient with CKD when admitted to undergo PD in this region.

The Midwest region has characteristics that make it quite heterogeneous. It is the region with a proportionally larger number of inhabitants that come from other areas. And although its social indicators are, on average, better than those in the North and Northeast regions, its population is a heterogeneous one. For instance, its general illiteracy rate is not high, but it has the highest number of children out of school. The estimated prevalence of individuals with CKD undergoing RRT is 455/million.[3] The number of patients undergoing RRT is low and the number of patients undergoing PD is the lowest in the country. Life expectancy is 73.3 years[21]. It has a good survival, both of the technique and the patient. The characteristics of patients undergoing PD in this region are of younger patients, with the lowest number of patients with diabetes and cardiovascular diseases of the country and a higher number of patients without other comorbidities in addition to CKD undergoing PD. The pre-dialytic follow-up was carried out in 39.3% of the patients and the indication of PD in this region was mainly medical and the only option of RRT (41.3%).

When evaluating the Cox proportional hazard model for survival of the patients, it is worth mentioning that this analysis included incident and prevalent patients. The variables that classically correlate with higher mortality, older age, presence of diabetes mellitus and cardiovascular diseases also show significance in the model. However, concerning the technique survival, older age showed to be a protective factor and the female sex a risk factor for lower technique survival rates, findings that are not in accordance with most studies. It is probable that analyzing together incident and prevalent patients was responsible for these findings

The study describes important clinical and outcome differences in patients with CKD undergoing PD in different regions of Brazil. Some of the differences observed apparently reflect the sociodemographic diversity of the country. These regional differences must be considered by health management professionals and the professionals that treat the patients, aiming at improving the technique survival and the survival of patients undergoing maintenance peritoneal dialysis in the country.

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