

## Survival of hemodialysis patients at a university hospital

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## ABSTRACT

**Introduction:** Chronic Kidney Disease (CKD) is associated with high rates of morbidity and mortality, especially in dialyses population. **Objective:** To determine the overall survival rate; the epidemiological and clinical profiles; the comorbidities and the variables associated with survival of the patients undergoing hemodialysis. **Methods:** This is a longitudinal and descriptive study with 162 patients undergoing hemodialysis, at the University Hospital. The categorical variables were described by frequency and percentage; numerical variables by mean and standard-deviation. The analysis by Cox Regression model was used to study the influence of several clinical and demographic variables in survival rates. Kaplan Meyer model was used to construct the survival curves of the significant variables. **Results:** The mean age was 48.09 years, and the monthly family income and level of education were reduced in most of the patients studied. Hypertension was the main comorbidity associated with CKD in this population, followed by *Diabetes Mellitus*. The variables that negatively influenced the survival rates were advanced age at the beginning of therapy and low hemoglobin and albumin levels. The overall survival was 84.41% and 63.32% in one and five years, respectively. **Conclusion:** The rate of survival was considered low compared others studies and was decreasing over the years, not representing improvements despite technological advances in diagnostic and therapeutic approaches. Advanced age, hypoalbuminemia and anemia are strong predictors of mortality.

**Keywords:** mortality; renal dialysis; survival rate.

## INTRODUCTION

Chronic kidney disease (CKD) consists of kidney damage and/or slow, progressive and irreversible loss of renal function.<sup>1</sup> It carries high morbidity and mortality.<sup>2,3</sup>

The number of patients with end-stage kidney disease (ESRD) treated with renal replacement therapy (RRT) grows globally at a rate of approximately 7% per year. This rate exceeds the population growth rate.<sup>4</sup>

The three treatment modalities for patients with ESRD are hemodialysis (HD), peritoneal dialysis or kidney transplantation. HD is the most used in the majority of countries.<sup>5</sup>

Between the years of 2000 and 2006 in Brazil, the number of patients in dialysis grew at a rate of about 9% a year; and the Public Healthcare System (SUS) funded 89% of that treatment.<sup>4</sup> According to the census data collected from dialysis units in Brazil, held in July 2010, the number of patients undergoing dialysis was 92,091; 90.6% in HD.<sup>6</sup> Epidemiological surveys estimate that there are over 2 million Brazilians having some degree of renal dysfunction and, of these, about 70% are unaware of the condition.<sup>7</sup>

The risk factors that most influence the mortality of dialysis patients are advanced age and *diabetes mellitus* as causes of chronic renal failure (CRF), and additional comorbidities to the kidney condition.<sup>8</sup>

Azevedo *et al.*,<sup>9</sup> published a study from Barbacena, Minas Gerais, in which they report that the main causes of death were cardiovascular disease, infections and neoplasms. The overall survival rate found was 86.2% and 60%, in one and five years, respectively.

In a meta-analysis, Mailloux & Henrich, cited by Azevedo *et al.*,<sup>9</sup> reported that HD patient survival time depends on factors such as gender, age, dialysis adequacy ratio (Kt/V), hemoglobin (Hb), albumin, calcium x phosphorus product (CaxP) and parathyroid hormone (PTH), among others.

In the study by Barbosa *et al.*,<sup>10</sup> held in Sao Paulo, high mortality rates were reported, and mortality by CKD was 10 to 20 times higher than in the general population.

The importance of determining survival for renal patients on HD favors the improvement of care, since it enables the early identification of patients at high risk, which improves their survival and quality of life. Besides contributing to the strategic planning of health actions - as evidence suggests that the increase in spending on HD is due to the increased survival of patients and not specifically to the growing demand for treatment.<sup>11</sup>

In São Luís, Maranhão, we did not find studies depicting data correlated with patient survival, we felt motivated to do this study, which aims to determine the survival rate, characterize the clinical and epidemiological profile and identify the comorbidities and the variables associated with survival of patients on hemodialysis.

## METHOD

This is a descriptive cohort study. We carried out a retrospective and longitudinal study involving

162 CKD patients undergoing HD at the Nephrology Department of the Presidente Dutra University Hospital at the Federal University of Maranhão - UFMA.

The inclusion criteria were: having started treatment between January 2007 and December 2011; be chronically enrolled in a regular HD program for at least three months, undergoing three sessions per week for 4 hours.

We collected our data from the computerized registration system of the Hemodialysis Service (NEFRODATA-ACD, version 4.5.4.268); information pertaining to gender, age, race, education, family income, CKD cause, length of stay in treatment, comorbidity, destination, cause of death and the results from the following variables - Kt/V, albumin, calcium x phosphorus, Hb and PTH. The quality parameters used were: Kt/V > 1.2; Albumin > 3.5 g/dl; calcium x phosphorus < 55 mg<sup>2</sup>/DL<sup>2</sup>; Hb ≥ 11 g/dl and PTH = 150-300 pg/ml. The data concerned the period from January 2007 to December 2012.

Categorical variables were described by frequencies and percentages, and the numerical variables by using the mean ± standard deviation. We used the Cox regression analysis to study the influence of various clinical and demographic variables on patient survival. Those variables with *p*-value < 0.10 were eligible for the multivariate model, a *p* value < 0.05 was considered statistically significant.

We used the Kaplan Meyer method to build the survival curves of the significant variables. Statistical analyzes were performed using the Data Analysis and Statistical Software (STATA), version 12.0.

This study was preceded by the approval from the Ethics Committee of the Federal University of Maranhão, protocol No. 123.351.

## RESULTS

We assessed the medical records from 162 patients, of whom 72 (44.44%) were females and 90 (55.56%) were males. Their average

age was 48.09 years, with a standard deviation (SD) of 19.88.

The sociodemographic and clinical characteristics of the patients studied upon dialysis onset, are presented on Table 1.

Regarding treatment duration, considering follow up losses, it was 31.13 months, with SD  $\pm$  42.22. Losses were computed for 68 patients, of whom 14 (8.64%) were transferred to other units; 14 (8.64%) were transplanted; and 40 (24.69%) died. At the end of the study period, 94 (58.02%) patients were receiving regular HD.

As to monthly family income and educational level, of the 162 patients, 83 (51.23%) received up to two minimum wages and 140 (86.42%) had up to 8 years of study.

Regarding comorbidities, hypertension and *diabetes mellitus* were the main causes of comorbidity that prevailed in patients starting dialysis in this study, and 60 (37.04%) patients had more than one associated disease.

Considering the underlying disease, we found that diabetic nephropathy was the prevalent underlying disease (33.33%), followed by chronic glomerulonephritis (22.22%) and hypertensive nephropathy (17.28%).

Table 2 shows data on the survival of patients by year. Importantly, three patients died before reaching one year of study and the survival rate decreased over the years on hemodialysis.

Table 3 depicts the Cox regression univariate analysis results, analyzing the impact of clinical and demographical variables on patient survival. The variables that showed statistically significant influence on survival were: age when starting HD, serum albumin and Hb. Variables such as gender, skin color, educational level, income, *diabetes mellitus*, cardiovascular disease, Kt/V, calcium-phosphorus product and PTH did not affect patient survival.

In the multivariate analysis (Table 4), the factors associated with patient survival were the same that were significant in the Cox univariate regression analysis. There was a significantly increased hazard ratio (HR) for each additional

**TABLE 1** SOCIODEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS IN HEMODIALYSIS CARE IN A UNIVERSITY HOSPITAL AT TREATMENT ONSET. SÃO LUÍS - MA, 2012

Characteristics	n	%
Age in years (mean $\pm$ SD)		48.09 $\pm$ 19.88
Treatment time - months (mean $\pm$ SD)		31.13 $\pm$ 42.22
Gender		
Female	72	44.44
Male	90	55.56
Skin color		
Not white	155	95.68
White	7	4.32
Family income		
Up to 2 minimum wages	83	51.23
2 to 4 Minimum wages	9	5.56
> 4 Minimum wages	70	43.21
Schooling		
$\leq$ 8 years	140	86.42
> 8 years	22	13.58
Comorbidities		
Arterial hypertension	67	41.36
Arterial hypertension and <i>Diabetes Mellitus</i>	42	25.93
Arterial hypertension and <i>Diabetes Mellitus</i> and Cardiovascular	12	7.41
Others	22	13.58
Underlying disease		
Hypertensive nephropathy	28	17.28
Chronic glomerulonephritis	36	22.22
Diabetic nephropathy	54	33.33
Others	44	27.17
Outcome		
Transferred	14	8.64
Death	40	24.69
Transplant	14	8.64
Remained in the program	94	58.02

year in age upon HD onset. Moreover, considering serum albumin and Hb, we found a significantly lower HR for the higher rates; thus being inversely associated with the risk of mortality. In the set of

**TABLE 2** SURVIVAL OF HEMODIALYSIS PATIENTS IN A UNIVERSITY HOSPITAL, BETWEEN 2007 AND 2011. SÃO LUÍS - MA, 2012

Follow up duration	Number of patients	Number of deaths	Survival likelihood	Death likelihood
1 year	157	24	0.8471	0.1529
2 years	97	4	0.8122	0.1878
3 years	65	2	0.7872	0.2128
4 years	42	5	0.6935	0.3065
5 years	23	2	0.6332	0.3668
6 years	4	0	0.6332	0.3668

**TABLE 3** INFLUENCE OF NUMEROUS VARIABLES ON THE SURVIVAL OF PATIENTS IN HEMODIALYSIS IN A UNIVERSITY HOSPITAL, FROM 2007 TO 2011 (COX REGRESSION - UNIVARIATE ANALYSIS). SÃO LUÍS - MA, 2012

VARIABLE	Hazard Ratio	CI 95%	p
Gender (Male x Female)	1.19	0.86 - 1.64	0.279
Skin color (White x Not white)	1.39	0.42 - 4.55	0.583
Schooling ( $\leq 8$ years x $> 8$ years)	1.97	0.93 - 4.15	0.074
Income ( $\leq 2$ wages x $> 2$ wages)	0.85	0.60 - 1.18	0.344
Arterial hypertension (Yes x No)	0.52	0.27 - 1.00	0.054
<i>Diabetes mellitus</i> (Yes x No)	1.48	0.79 - 2.77	0.213
Cardiovascular disease (Yes x No)	1.13	0.44 - 2.90	0.794
Age (Years)	1.02	1.01 - 1.04	0.001
Kt/V (ratio)	1.10	0.92 - 1.32	0.259
Serum albumin	0.35	0.21 - 0.58	$< 0.001$
Calcium x Phosphorus	0.99	0.97 - 1.01	0.727
Dosed hemoglobin	0.48	0.37 - 0.62	$< 0.001$
Parathyroid hormone	0.99	0.99 - 1.00	0.853

variables analyzed, the educational level factor had only marginally significant effect, with a higher survival rate from patients with more than eight years of schooling. The hypertension variable had no statistically significant influence on patient survival.

## DISCUSSION

As for the sociodemographic characteristics, it is noteworthy that the mean age was 48.09 years with SD = 19.88. This result represents a significant social data - as seen in other studies, because ESRD affects a population at full working age, causing spending in social areas due to early retirement, outpatient expenses and medications.<sup>10</sup>

Monthly family income and educational level were reduced in most of the patients investigated, 83 (51.23%) received up to two minimum wages and 140 (80.42%) had up to eight years of

schooling, which can affect treatment compliance and decrease the likelihood of an early diagnosis of chronic kidney disease and/or its treatment to slow the disease progression.<sup>12-14</sup>

Hypertension was found to be the major comorbidity associated with ESRD, being present in more than half (77.77%) of the patients analyzed, followed by *diabetes mellitus* (37.66%). Similar results were found in other studies.<sup>10,15</sup>

Diabetic nephropathy (33.33%) was the main underlying disease in the study group, followed by chronic glomerulonephritis (22.22%) and hypertensive nephropathy (17.28%), contrary to results from some studies,<sup>6,13,16</sup> i.e. the study from Calado *et al.*<sup>17</sup> conducted in São Luís, in 2009. However, these results were partially similar to those found in Rio Grande do Sul in 2007, where the diabetic nephropathy was the most common cause (24%) of underlying disease in patients under hemodialysis.<sup>18</sup>

**TABLE 4** INFLUENCE OF NUMEROUS VARIABLES ON THE SURVIVAL OF PATIENTS UNDER HEMODIALYSIS IN A UNIVERSITY HOSPITAL, BETWEEN 2007 AND 2011 (COX REGRESSION - MULTIVARIATE ANALYSIS). SÃO LUÍS - MA, 2012

VARIABLES	Hazard Ratio	CI 95%	p
Age (Years)	1.04	1.02 - 1.06	< 0.001
Schooling ( $\leq 8$ years x $> 8$ years)	2.32	0.98 - 5.52	0.055
Hemoglobin	0.40	0.28 - 0.57	< 0.001
Serum albumin	0.47	0.24 - 0.92	0.029
Arterial hypertension (Yes x No)	0.49	0.22 - 1.07	0.074

In this study, the factors that significantly compromised survival of HD patients were older age at treatment onset, Hb and serum albumin. Other variables, which in previous studies<sup>10,19</sup> had an association with patient survival, in this study were not associated with mortality, such as gender, skin color, schooling, income, high blood pressure, *diabetes mellitus*, cardiovascular diseases, Kt/V, calcium-phosphorus product and parathyroid hormone.

Several studies have suggested that DM is a predictor of mortality, especially due to cardiovascular causes arising from accelerated atherosclerosis.<sup>20</sup> Similar results have been found in several studies,<sup>18,21-23</sup> although this study did not prove such association. One of the limitations of our study, as well as in the study of Angelo *et al.*,<sup>20</sup> is not to be able to include and evaluate all the variables needed to assess survival in diabetic patients, as the type of DM, smoking, BMI, physical exercise, dyslipidemia. Such information was not possible because of missing data in the records.

The overall mortality rate was 24.69%, with an overall survival of 84.71% and 63.32% in one and five years, respectively. This rate is similar to the one reported by Azevedo *et al.*<sup>9</sup> and Silva *et al.*<sup>18</sup>, in which they found 86.2% in a year and 60% in five years; 91% in one year and 64% in five years, respectively. Large studies show 89% survival rates at one year and 57% in five years, respectively, in the countries of the European Dialysis and Transplant Association.<sup>24</sup>

According to the census data from dialysis units in Brazil,<sup>6</sup> held in July 2010, the gross mortality rate (with the dialysis population on July 1 in the denominator) was 17.9% during the year. This rate was reduced to 14.9, when the denominator

included patients at risk in the year (who were submitted to dialysis during the year). Studies reported by Dialysis Outcomes and Practice Patterns Study (DOPPS)<sup>25</sup> consistently showed a marked difference in gross mortality between countries, with mortality in the United States being one of the highest. In 2003, DOPPS reported gross mortality rates at one year being 6.6% in Japan, 15.6% in Europe and 21.7% in the United States. These results show that the overall mortality rate in this study - 24.69%, is above the rates of the Brazilian record as well as those from Japan, Europe and the United States in the studies cited above.

This mortality rate has remained high despite technological advances; which may be explained by the greater severity and age of patients starting treatment, offsetting these data.

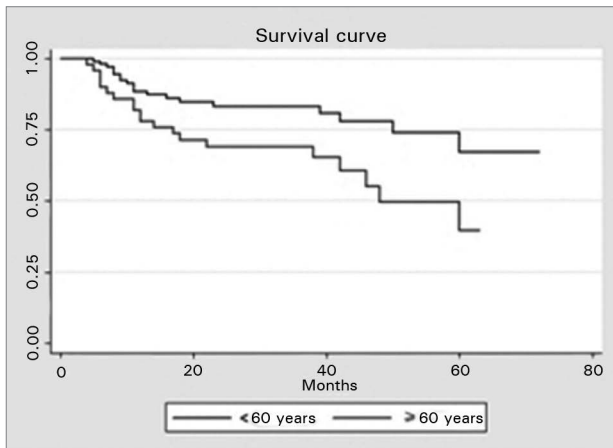
Age had a statistically significant impact on patient survival, with an increased HR for each year in the age of hemodialysis onset. This effect strengthens the evidence that mortality rates rise with increasing age. The survival rate was higher in patients who started HD with less than 60 years of age and has remained higher over the months when compared to the survival of patients with 61 years or more (Figure 1). Similar data was also found in other studies.<sup>8</sup>

Regarding Hb, Cox regression univariate and multivariate analyses showed that it had a 52% 60% protection factor, respectively, at each increased level, reflecting the current knowledge that patients with higher levels of Hb have lower mortality.<sup>9,26,27</sup> However, Hb was not statistically significant when categorized for the Kaplan Meyer method.

Anemia affects almost all patients undergoing HD, worsens quality of life and is associated with a risk of early death.<sup>28-30</sup> However, the Hb



**Figure 1.** Survival of patients aged 60 or more vs. Patients younger than 60 ( $p = 0.0119$ ).



target range is still controversial in Nephrology, since most recent studies show that higher Hb targets can cause thrombolytic complications, uncontrolled hypertension and mortality.<sup>28,31</sup> Current recommendations suggest customized treatment for anemia, assigning more freedom to the Hb value for each patient - taking clinical status and risk factors into account, since some of them will benefit from higher levels of Hb, which will increase their quality of life and compensate for possible risks.<sup>31,32</sup>

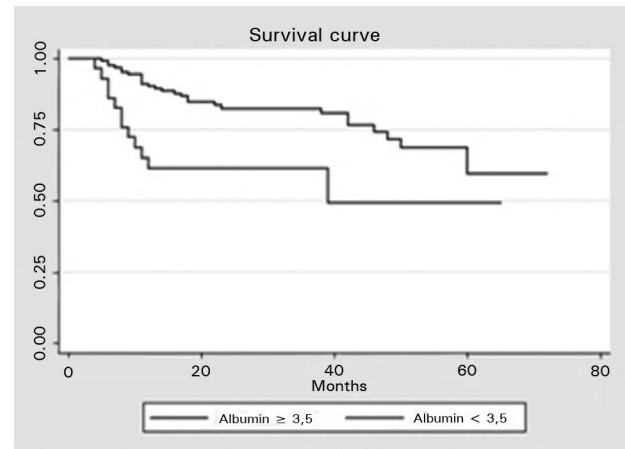
Albumin averaged 3,82 g/dL  $\pm$  0.71 in the patients investigated. Similar results were found in a study in Castelo Branco - Portugal,<sup>33</sup> in which albumin had mean values above 3.5 g/dL. It is noteworthy that some authors consider that desirable serum albumin for hemodialysis patients should be  $\geq 4.0$  g/dL and lower values are strongly linked to mortality.

Survival was significantly higher for patients who had albumin values  $\geq 3.5$  g/dL (Figure 2), especially in the first year of hemodialysis treatment, confirming that hypoalbuminemia at hemodialysis onset is a strong predictor of mortality.<sup>27,33,34</sup>

The causes of mortality of patients in this study could not be identified due to impaired information in the records thereof. This is partly due to the fact that many deaths occur in the patient's own home or in other institutions.

This study has its own retrospective-related limitations: 27 cases were excluded due to lack of adequate information.

**Figure 2.** Patient survival associated with serum albumin ( $p = 0.0015$ ).



We suggest greater concern for patient records and an active search for information about their deaths, when they do not happen in healthcare centers. This will help us identify the main causes of death of patients in HD and, therefore, seek the best results for their survival.

It is important to stress that several studies show that pre-dialysis nephrology monitoring and the type of vascular access directly influence mortality in the days of hospitalization and even total treatment cost. Thus, these factors represent another limitation to our study, because they were not associated to patient survival.

## CONCLUSIONS

This study showed that ESKD in this population affects mostly males, of working age, with low income and low level of education, in addition to confirming that hypertension and *diabetes mellitus* represent the most prevalent causes of comorbidities in patients in hemodialysis onset. Moreover, advanced age upon treatment onset, Hb and serum albumin were directly related to survival, with a significantly higher risk for each year in age when starting HD and a significantly lower risk for every increase in Hb levels and albumin, confirming that advanced age, hypoalbuminemia and anemia are strong predictors of mortality.

Survival rate was considered low and decreased over the years, not showing improvements despite advances in technology, diagnosis and treatment.

These findings enable the early identification of patients at risk, enabling improvements and adjustments in the care of patients on hemodialysis and, therefore, improvements in the survival and quality of life of such patients.

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