Mortality in patients with chronic kidney disease undergoing hemodialysis in a public hospital of Peru

Authors
Percy Herrera-Añazco[1]
Vicente Benites-Zapata[2]
Adrian V. Hernandez[3]
Edward Mezones-Holguin[3]
Manuela Silveira-Chau[4]

[1] Universidade Nacional de Piura.
[2] Universidade de San Martín de Porres.
[3] Universidade Peruana de Ciencias Aplicadas.
[4] Universidade Nacional Federico Villarreal.

Submitted on: 09/04/2014.
Approved on: 12/04/2014.

Correspondence to:
Percy Herrera-Añazco.
Hospital Nacional 2 de Mayo.
Olavegoya 1879 dpto 701. Distrito de Jesus Maria. Lima-Perú.
E-mail: silamud@gmail.com

DOI: 10.5935/0101-2800.20150031

Abstract

Introduction: The Peruvian Ministry of Health does not have a national program of hemodialysis and hospitals that offer it have coverage problems, which may result in increased mortality. **Objective:** We evaluated mortality of a population with incident hemodialysis in a Peruvian public hospital as well as its associated factors. **Methods:** Retrospective and descriptive study of a population over 18 years-old who started treatment between January 1, 2012 and December 31, 2013 with the final follow-up day on31 March 2014. We used bivariate and multivariate logistic regression models to evaluate factors associated with mortality and Kaplan Meier curves were used to determine the probability of survival. **Results:** We included 235 patients with a mean age of 56.4 ± 15.8 years. Median follow-up was 0.6 years (IQR 0.3 to 1.5). 50% of years withdrew from therapy during the study for lack of financial resources or space available. The third month mortality was 37.7% (95% CI 4.7 to 48.5) and 49.5% (95% CI 5.8 to 61.4) at 7 months. There was a trend towards lower mortality when patients had more than 6 months with a diagnosis of chronic kidney disease (CKD) (OR = 0.39 [95% CI 0.12 to 1.27]) and when the patient was admitted with scheduled dialysis (OR = 0.28 [95% CI 0.01 to 2.28]). **Conclusion:** Half of patients died within seven months of follow-up. Scheduled dialysis and having longer time with CKD diagnosis tend to be associated with lower mortality

Keywords: hemodialysis units; hospital; mortality; renal dialysis.

Introduction

The number of dialysis centers made available by the Peruvian Ministry of Health (MOH) is insufficient. Seventy percent of the Peruvian population is covered by the country's national health insurance, but in many regions patients do not have access to nephrologists or renal care centers.[1] Kidney care options are mostly concentrated in Lima. However, many of the city's inhabitants are still underserved, with patients not receiving the treatment they need and others being forced to discontinue dialysis.[1,2]

Despite the advances in the treatment of individuals with chronic kidney disease (CKD), death rates are reportedly high among hemodialysis (HD) patients.[3,4] Among other factors, mortality has been associated with the treatment they are administered before starting dialysis.[5-9] Therefore, dialysis candidates should undergo proper assessment by a nephrologist in order to mitigate patient morbidity and mortality.[9-12]

In Argentina, the mortality rate reported for prevalent patients on maintenance hemodialysis was 15.65 deaths per 100 patient-years.[13] In Brazil, an annual mortality rate of 19.9% has been described.[14] In Peru, studies have reported mortality rates for dialysis patients covered by public health insurance[15] and individuals treated at national MOH-managed

reference centers.[16] However, the association between death and patient health status before the start of dialysis has not been studied.

The *Hospital Nacional 2 de Mayo* (HN2M) - a national reference center - and the *Hospital Nacional Cayetano Heredia* (HNCH) are the largest MOH-managed dialysis centers in Peru. Assessing their dialysis programs may shed light on the country's actual patient mortality rates. This study aims to present the mortality rates and the factors associated with the death of patients starting dialysis at the *Hospital Nacional 2 de Mayo*.

Methods

This study enrolled a cohort of patients with CKD on maintenance hemodialysis seen at the Nephrology Center of the HN2M. Patients aged 18 years or older were recruited between January 1, 2012 and December 31, 2013. They were followed up until March 31, 2014.

The date of the start of dialysis was considered as the date of patient enrollment in the study. The end date could be either the day the patient was last seen alive at the clinic, the verified day when the patient discontinued treatment, or the patient's date of death.

Patients on HD for acute kidney injury or poisoning, and individuals with CKD who started HD in other centers were excluded.

The following demographic and clinical data were recorded on a database: age, gender, whether the patient was seen regularly at the hospital, etiology of CKD, and whether the patient was started on planned or emergency HD.

The time for which the patient had been diagnosed with CKD, a minimum of two visits to a nephrologist the previous year, and the kind of vascular access used at the start of HD were also captured. Workup data such as hemoglobin, potassium, pH, bicarbonate, and creatinine levels before the first HD session were collected, along with patient glomerular filtration rates (GFR) calculated with the formula presented in the Modification of Diet in Renal Disease (MDRD) study.[17]

Nursing records were used to establish the dates of start of HD, discontinuation of treatment, and patient death.

In statistical analysis, mean values and standard deviations were calculated for continuous variables following a normal distribution, while medians and interquartile ranges were calculated for variables with asymmetric distributions. Percent frequencies were used to describe categorical variables. Student's *t*-test was used to analyze continuous variables associated with death following a normal distribution and the Mann-Whitney U test was applied to asymmetric variables. Categorical variables were analyzed with the chi-square test or Fisher's exact test, depending on the expected values. Survival was estimated using the Kaplan-Meier curves. The following variables were treated using univariate and multivariate logistic regressions: age, glomerular filtration rate, time for which the patient had been diagnosed with CKD, previous assessment by a nephrologist, and planned dialysis. Associations were estimated by the calculation of odds ratios (OR) with a 95% confidence interval. Statistical significance was attributed to findings with a $p < 0.05$.

Statistical analysis was carried out with the aid of software package STATA™ version 11.0 (Stata Corp LP, College Station, TX).

The data sets used in this study were obtained from the epidemiologic surveillance service of the nephrology clinic at the HN2M. Therefore, approval from the Hospital's Research Ethics Committee was not required.

Results

The study enrolled 235 patients with a mean age of 56.4 years. Nearly 60% were males (Table 1). Most patients had been diagnosed with diabetic nephropathy, while polycystic kidney disease (PKD) was the least frequent diagnosis. Roughly half of the patients had been diagnosed with CKD within less than a month of the start of hemodialysis. Only eight patients had arteriovenous fistulae. Just over a third of the patients were treated at the HN2M. Only 15 patients were started on planned dialysis and about one in four patients had been previously seen by a nephrologist.

Table 1 Demographic and clinical variables of the studied population

Variables	Total N = 236	Deceased N = 68	Living N = 168	*p-value*
Age (years)	56.40 ± 15.76	59.35 ± 14.80	55.20 ± 16.02	0.07
Males	149 (63.14)	41 (60.29)	108 (64.29)	0.57
Etiology of CKD				0.34
Diabetic nephropathy	78 (44.07)	28 (51.85)	50 (40.65)	
Chronic glomerulonephritis	41 (23.16)	13 (24.07)	28 (22.76)	
Obstructive uropathy	27 (15.25)	5 (9.26)	22 (17.82)	
Hypertensive nephropathy	22 (12.43)	7 (12.96)	15 (12.20)	
Polycystic kidney disease	9 (5.08)	1 (1.85)	8 (6.50)	
Time for which the patient had been diagnosed with CKD				0.55
< 1 month	107 (45.34)	31 (45.59)	76 (45.24)	
1-6 months	53 (22.46)	18 (26.47)	35 (20.83)	
> 6 months	76 (32.20)	19 (27.94)	57 (33.93)	
Type of Vascular Access				0.11
Arteriovenous fistula	8 (3.43)	0 (0)	8 (4.82)	
Non-tunneled catheter	225 (95.18)	67 (100)	158 (95.18)	
HN2M patient	79 (33.91)	27 (40.91)	52 (31.14)	0.15
Planned dialysis	15 (6.36)	1 (1.47)	14 (8.33)	0.07
Follow-up by a nephrologist	57 (24.15)	19 (27.94)	38 (22.62)	0.38
Workup				
Glomerular filtration rate	4.94 ± 3.08	5.39 ± 3.06	4.76 ± 3.08	0.16
Hemoglobin	7.18 ± 2.52	7.13 ± 2.52	7.19 ± 2.53	0.85
pH	7.29 (7.20- 7.36)	7.29 (7.17-7.36)	7.29 (7.21-7.36)	0.54
HCO3	11.11 ± 4.76	11.13 ± 5.31	11.10 ± 4.52	0.97
Potassium	6.11 ± 1.49	5.94 ± 1.57	6.18 ± 1.45	0.25
Calcium	7.70 (6.90-8.40)	7.90 (7.00-8.40)	7.65 (6.70-8.40)	0.35
Phosphorus	7.27 ± 2.84	7.33 ± 2.55	7.24 ± 2.95	0.85

Mean ± standard deviation; median (interquartile range); number (percentage). CKD: chronic kidney disease; H2M: Hospital Dos de Mayo.

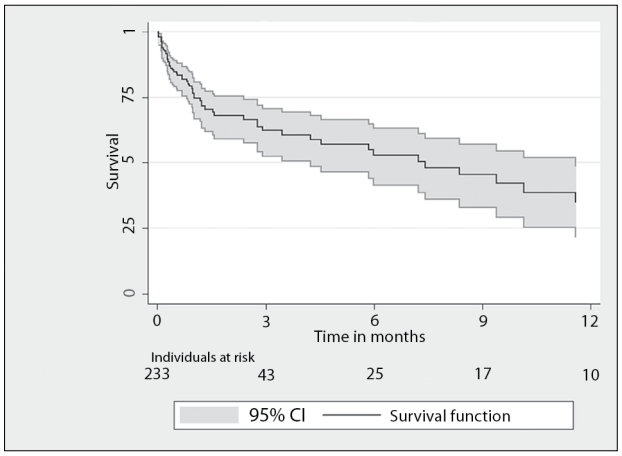
The median follow-up was 0.6 years (IQR 9-45). Eighty-two percent of the participants were followed for less than three months. Sixty-eight patients died and 118 (50.2%) dropped out of treatment during follow-up.

The mean mortality rate in the third month was 37.7% (95% CI; 29.3 to 48.5), while in the seventh month the mean death rate was close to 50% (49.5%; 95% CI 38.8 to 61.4). See the Kaplan-Meier curve in Figure 1 for the patient survival distribution pattern.

Table 1 shows the distribution of patient demographic and clinical variables according to their health statuses at discharge. Patient GFR, hemoglobin, bicarbonate, potassium, calcium, and phosphorus levels were also captured. No statistically significant differences were observed when the values found for survivors *versus* deceased patients were compared.

The multivariate analysis results are shown in Table 2. The following factors were not associated with death: age, etiology of CKD, time for which the patient had been diagnosed with CKD, monitoring by a nephrologist, GFR, and dialysis (Table 2). However, a tendency for better outcomes was seen in patients diagnosed for over six months, diagnosed with CKD (OR = 0.39 [95% CI 0.12 to 1.27]) and in individuals starting dialysis in non-emergency situations (OR = 0.28 [95% CI 0.01 to 2.28]).

Figure 1. Kaplan-Meier curves of patients with chronic kidney disease on hemodialysis.



Discussion

High death rates were seen among incident patients, with values reaching 50% in the seventh month of follow-up. Death rates were lower among patients diagnosed with CKD for over six months and individuals on planned *versus* emergency dialysis.

The literature indicates death rates are high among dialysis patients,[3,4] and in Peru they appear to be as high as the rates reported in African countries, a region in which the costs and death rates associated with renal replacement therapy (RRT) are considered in the decision of whether a patient should start treatment at all.[18] This finding shows that Peru's economic growth has not been associated with improved health status of patients with CKD or enhanced coverage by the MOH.[1,2]

The issues around the cost of RRT reported in other developing nations[19,20] have led the Kidney Disease Improving Global Outcomes (KDIGO) initiative to consider the publication of a guide on palliative care for patients with stage-5 CKD after it was found that in many parts of the world RRT was not available.[21]

Two studies on the mortality of HD patients have been carried out in Peru. Meneses *et al.*[15] compared the death rates of incident patients on dialysis from 1982 to 1995 and from 1995 to 2007 seen at a private clinic and public health insurance patients and found no significant differences between the two time periods. The authors reported a first-year overall survival rate of 87% (n = 236). Cieza *et al.*[16] discussed the survival rates of patients on three RRT modes (hemodialysis, peritoneal dialysis, and kidney transplant) seen at the HNCH between January 1, 2008 and December 31, 2011. The first-year survival rate for patients on HD was 95.1% ± 0.21 (n = 90). Lower survival rates in the three modes of RRT were observed for female patients and patients aged 60 years or older.

The type of patients enrolled in these studies explains the discrepancy in mortality when compared to our study. The studies cited above enrolled only prevalent patients and did not include subjects who dropped out of treatment. Additionally, the study by Meneses *et al.* was carried out at a private care unit, while Cieza *et al.* did not include patients on emergency dialysis or individuals who died on the first hospitalization. These studies form only a partial picture of the issues previously reported[1] for patients on dialysis at the MOH care centers, which also explains the higher death rates seen in our study.

Table 2 Multivariate logistic regression for death rates of patients with chronic kidney disease on hemodialysis

Variable	Odds Ratio (95% CI)	*p-value*
Age*	1.03 (0.99-1.07)	0.08
Etiology		
Diabetic nephropathy	1	--
Chronic glomerulonephritis	0.92 (0.25-3.38)	0.90
Obstructive uropathy	0.28 (0.76-1.06)	0.06
Hypertensive nephropathy	0.64 (0.14-3.01)	0.57
Polycystic kidney disease	0.41 (0.40-4.31)	0.46
Time for which the patient had been diagnosed with CKD		
< 1 month	1	--
1-6 months	0.55 (0.18-1.71)	0.30
> 6 months	0.39 (0.12-1.27)	0.11
Follow-up by a nephrologist	2.29 (0.89-5.91)	0.09
Glomerular filtration rate	1.00 (0.88-1.13)	0.99
Planned dialysis	0.28 (0.01-2.28)	0.18

* Odds ratio for each year of age.

Our study found a trend toward lower death rates among patients on planned dialysis and individuals diagnosed earlier with CKD. However, efforts to implement changes in the direction of these findings may be hampered, as only a third of the patients had been previously seen at the hospital. This finding and the fact that almost half of our patients were diagnosed only a month before they were started on dialysis, show the inexistence of a comprehensive care program sponsored by the MOH for patients with CKD.

Adequate renal monitoring has been associated with better outcomes in patients on hemodialysis.[9-12] Among other things, renal monitoring includes having patients on planned dialysis, having a nephrologist to follow them up,[9,11] and offering patients an arteriovenous fistula as a permanent vascular access.[22] However, despite these recommendations, reported outcomes vary. Eighty-three percent of the incident patients on dialysis in Germany have arteriovenous fistulae, against 69% in Spain and 15% in the United States.[6] Follow-up by a nephrologist before the start of HD was reported for 56.6% of the patients in the United States[7] and 63% in Spain.[8] Most of the patients in this study started HD with a transitional venous catheter, and only one in four had consulted with a nephrologist prior to starting dialysis.

The outcomes reported in this study were similar to those described in a Brazilian study, in which nearly half of the patients started on dialysis did not know they had CKD, and approximately one in four had been seen by a nephrologist before being prescribed HD.[23]

An alarming number of patients dropped out of dialysis. The reasons leading patients to drop out of treatment were not studied, as the subjects who decided to leave our dialysis center were not followed. However, the reduced number of seats for chronic dialysis in the hospital - only a hundred - and poverty are the most likely reasons for patients to drop out of treatment.[2]

This study has important limitations, namely: (1) the outcomes reported herein reflect the reality of one institution, and may not be used to describe other Peruvian MOH-managed public hospitals. However, as the study was held at a national reference hospital, it may be used to discuss issues not considered in past reports of death rates of patients on dialysis in Peru; (2) the significant number of patients dropping out of treatment may cause an underestimation of the reported death rates; (3) the small number of patients included and events -58- may also limit the analysis of associated factors; and (4) the elevated frequency of factors attributable to poor prior disease management, both in living and deceased patients, impedes the identification of statistically significant associations.

In conclusion, elevated death rates were observed for the dialysis patients included in this study. Patients diagnosed earlier with CKD and individuals started on planned dialysis tended to have lower mortality rates.

Acknowledgements

The authors would like to thank Dr. Marcus Tolentino Silva, Adjunct Professor at the School of Medicine, Federal University of Amazonas.

References

1. Herrera-Anazco P, Mezones-Holguín E, Hernandez AV. Global kidney disease. Lancet 2013;382:1243-4. PMID: 24120193 DOI: http://dx.doi.org/10.1016/S0140-6736(13)62087-5
2. Herrera-Añazco P, Palacios-Gillén M, Hernandez AV. Alta tasa de interrupcion de hemodiálisis en pacientes del hospital nacional 2 de mayo de Perú. Rev Nefrol Dial Transpl 2014;34:94-8.
3. Nordio M, Limido A, Maggiore U, Nichelatti M, Postorino M, Quintaliani G; Italian Dialysis and Transplantation Registry. Survival in patients treated by long-term dialysis compared with the general population. Am J Kidney Dis 2012;59:819-28. DOI:http://dx.doi.org/10.1053/j.ajkd.2011.12.023
4. Goodkin DA, Bragg-Gresham JL, Koenig KG, Wolfe RA, Akiba T, Andreucci VE, et al. Association of comorbid conditions and mortality in hemodialysis patients in Europe, Japan, and the United States: the Dialysis Outcomes and Practice Patterns Study (DOPPS). J Am Soc Nephrol 2003;14:3270-7. DOI: http://dx.doi.org/10.1097/01.ASN.0000100127.54107.57
5. Bradbury BD, Fissell RB, Albert JM, Anthony MS, Critchlow CW, Pisoni RL, et al. Predictors of early mortality among incident US hemodialysis patients in the Dialysis Outcomes and Practice Patterns Study (DOPPS). Clin J Am Soc Nephrol 2007;2:89-99. DOI:http://dx.doi.org/10.2215/CJN.01170905
6. Rayner HC, Pisoni RL, Gillespie BW, Goodkin DA, Akiba T, Akizawa T, et al.; Dialysis Outcomes and Practice Patterns Study. Creation, cannulation and survival of arteriovenous fistulae: data from the Dialysis Outcomes and Practice Patterns Study. Kidney Int 2003;63:323-30. PMID:12472799 DOI: http://dx.doi.org/10.1046/j.1523-1755.2003.00724.x
7. US Department of Public Health and Human Services, Public Health Service, National Institutes of Health, Bethesda. United States Renal Data System [Acesso 8 Ago 2014]. Disponível em: http://www.usrds.org/atlas.aspx

8. Pérez-García R, Martín-Malo A, Fort J, Cuevas X, Lladós F, Lozano J. Baseline characteristics of an incident haemodialysis population in Spain: results from ANSWER--a multicentre, prospective, observational cohort study. Nephrol Dial Transplant 2009;24:578-88. DOI:http://dx.doi.org/10.1093/ndt/gfn464
9. Saggi SJ, Allon M, Bernardini J, Kalantar-Zadeh K, Shaffer R, Mehrotra R; Dialysis Advisory Group of the American Society of Nephrology. Considerations in the optimal preparation of patients for dialysis. Nat Rev Nephrol 2012;8:381-9. DOI: http://dx.doi.org/10.1038/nrneph.2012.66
10. Moist LM, Trpeski L, Na Y, Lok CE. Increased hemodialysis catheter use in Canada and associated mortality risk: data from the Canadian Organ Replacement Registry 2001-2004. Clin J Am Soc Nephrol 2008;3:1726-32. DOI: http://dx.doi.org/10.2215/CJN.01240308
11. Frimat L, Loos-Ayav C, Panescu V, Cordebar N, Briançon S, Kessler M. Early referral to a nephrologist is associated with better outcomes in type 2 diabetes patients with end-stage renal disease. Diabetes Metab 2004;30:67-74. DOI: http://dx.doi.org/10.1016/S1262-3636(07)70091-5
12. Maynard C, Cordonnier D. The late referral of diabetic patients with kidney insufficiency to nephrologists has a high human and financial cost: interdisciplinary communication is urgently needed. Diabetes Metab 2001;27:517-21.
13. Marinovish S, Lavorato C, Celia E, Araujo J, Bisigniano L, Soratti M. Mortalidad según el registro de pacientes en diálisis crónica de Argentina 2004-2005. Nefrol Dial Trasplant 2009;29:13-48.
14. Sesso RCC, Lopes AA, Thomé FS, Lugon JR, Watanabe Y, Santos DR. Diálise crônica no Brasil - Relatório do Censo Brasileiro de Diálise, 2011. J Bras Nefrol 2012,34:272-7.
15. Meneses L, Leon C, Huapaya J, Cieza J. Sobrevida en hemodiálisis según el periodo de ingreso de pacientes entre 1982 y 2007, en Lima, Perú. Rev Med Hered 2011;22:157-61.
16. Cieza Zevallos J, Bernuy Hurtado J, Zegarra Montes L, Ortis Soriano V, León Rabanal C. Supervivencia en terapias de reemplazo renal dentro de un concepto integral de oferta de servicios públicos en el Perú, periodo 2008 y 2012. Acta Med Per 2013;30:80-5.
17. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002;39:S1-266.
18. Ekrikpo UE, Udo AI, Ikpeme EE, Effa EE. Haemodialysis in an emerging centre in a developing country: a two year review and predictors of mortality. BMC Nephrol 2011;12:50. DOI:http://dx.doi.org/10.1186/1471-2369-12-50
19. Sakhuja V, Sud K. End-stage renal disease in India and Pakistan: burden of disease and management issues. Kidney Int Suppl 2003;S115-8. DOI: http://dx.doi.org/10.1046/j.1523-1755.63.s83.24.x
20. Ranasinghe P, Perera YS, Makarim MF, Wijesinghe A, Wanigasuriya K. The costs in provision of haemodialysis in a developing country: a multi-centered study. BMC Nephrol 2011;12:42. DOI:http://dx.doi.org/10.1186/1471-2369-12-42
21. Kasiske B, Wheeler D. Kidney Disease: Improving Global Outcomes--an update. Nephrol Dial Transplant 2014;29:763-9. DOI: http://dx.doi.org/10.1093/ndt/gft441
22. Fluck R, Kumwenda M. Renal Association Clinical Practice Guideline on vascular access for haemodialysis. Nephron Clin Pract 2011;118:c225-40. PMID: 21555898 DOI:http://dx.doi.org/10.1159/000328071
23. Godinho TM, Lyra TG, Braga PS, Queiroz RA, Alves JA, Kraychete AC, et al. Perfil do paciente que inicia hemodiálise de manutenção em hospital público em Salvador, Bahia. J Bras Nefrol 2006;28:96-103.