Abstract

Introduction: approximately 50% of the annual health care expenditure of patients with chronic kidney disease on dialysis is related to hospitalizations. Infections represent the second reason for consultation, with a high morbidity and mortality. There are no studies comparing hospitalization time due to infectious causes between the different dialysis options.

Objective: to determine the difference in hospitalization time for treatment of infectious diseases in patients with chronic kidney disease on dialysis, comparing patients on hemodialysis vs. peritoneal dialysis.

Materials and methods: a retrospective, dynamic cohort study of patients on hemodialysis and peritoneal dialysis who were admitted to the emergency department at the Hospital Universitario Mayor due to infectious diseases. The study patients were included using nonprobabilistic methods. The sample size was calculated by comparison of means. A total of 172 hemodialysis patients and 85 peritoneal dialysis patients were included for statistical analysis.

Results: hospitalization time is greater in patients on hemodialysis than in patients on peritoneal dialysis; 12 (IQR 8-21) vs. 10 (IQR 6.5-13) days, respectively, p= 0.004.

Conclusions: hospitalization time due to infectious causes is greater in patients on hemodialysis than in patients on peritoneal dialysis. In addition, the incidence of treatment-related infections in our population is lower than the globally reported incidence. (Acta Med Colomb 2020; 45. DOI: https://doi.org/10.36104/amc.2020.1222).

Key words: chronic kidney failure; chronic kidney disease; dialysis, infectious diseases; hospital admission. enfermedad renal crónica; enfermedad crónica renal.
Methods

This is an observational, analytical, dynamic, historical cohort study. Clinical records were reviewed of patients with end stage renal disease on hemodialysis (cohort 1) and peritoneal dialysis (cohort 2) renal replacement therapy who were admitted to Hospital Universitario Mayor between June 1, 2015 and December 31, 2016. Only those who had been treated for infectious diseases were selected. To evaluate the inpatient stay needed to treat this group of diseases, two dates were taken into account, namely: 1) the date of admission to the emergency room and 2) the date of hospital discharge.

The inclusion criteria were: a) patients with advanced chronic kidney disease on hemodialysis or peritoneal dialysis renal replacement therapy for three or more months, b) 18 years old or older, and c) a chief complaint and current illness compatible with an infectious process, regardless of the site of origin. The exclusion criteria were: a) pregnant women, b) patients for whom an infectious reason for admission was ruled out during the course of hospitalization.

The Epidat statistical program was used to calculate the sample size. This process involved hypothesis testing and comparison of means. This technique was used since differences were sought in the average number of inpatient days needed to treat infectious diseases in patients on hemodialysis and peritoneal dialysis. A confidence level of 95% and power of 80% were selected, yielding a sample size of 242 patients distributed as follows: 172 on hemodialysis and 69 on peritoneal dialysis. The patients who entered the study were included through non-probabilistic methods.

Statistical analysis of the data

The whole sample was characterized using descriptive statistical methods. Categorical variables were reported using absolute frequency and relative frequency. For quantitative variables, normality was proven using the Kolmogorov-Smirnov statistical test. For quantitative variables with a normal distribution, the data were reported using mean as the measure of central tendency and standard deviation as the measure of dispersion. For quantitative variables with a non-normal distribution, the data were reported using the median as the measure of central tendency and interquartile range as the measure of dispersion.

The Chi square test for two independent samples was used to detect differences between the patients on hemodialysis and those on peritoneal dialysis, when evaluating a quantitative variable.

This study was submitted to and approved by the RTS-Baxter human research ethics committee and the research committee of the Hospital Universitario Mayor.

Results

During the 18 months from June 1, 2015 to December 31, 2016, 994 patients with chronic kidney disease on renal replacement therapy were admitted to the emergency room at the Hospital Universitario Mayor (H.U.M.). After evaluating the inclusion and exclusion criteria, 257 patients were obtained and included in the statistical analysis. The patient selection flowchart is shown in Figure 1.

The baseline characteristics of all the patients included in the statistical analysis, including demographic, hospital admission and infection site characteristics, as well as those evaluated during the hospital stay, are shown in Tables 1 and 4.

The quantitative variables of hemoglobin g/dL, serum calcium mg/dL, serum albumin g/dL and serum sodium mmol/L were converted to categorical variables in order to determine which patients had the following on admission: anemia, hypocalcemia, hypoalbuminemia or hyponatremia, respectively. Furthermore, the infectious diseases were categorized in six large groups, namely: 1: soft tissue and musculoskeletal infections (including diabetic foot); 2: dialysis-related infections (including therapy-induced complications such as infectious endocarditis); 3: respiratory tract infections; 4: gastrointestinal and abdominal infections not related to dialysis; 5: genitourinary system infections; and 6: central nervous system infections (including spondylodiscitis).

Finally, a table was constructed, summarizing various events documented throughout the hospital stay which were related to the various infectious diseases that led to the emergency room consult. These include the proportion of patients who required intensive care unit (ICU) management, the proportion of patients who required surgery to control the infectious process, or the number of patients who had hospital stays longer than 14 days.

Blood cultures were taken from 113 (44%) patients; 80 (70.6%) were reported as negative. *Staphylococcus aureus* (*S. aureus*) was isolated in 12 (10.6%), *Escherichia coli* (*E. coli*) was isolated in five (4.4%), *Klebsiella pneumoniae* (*K. pneumoniae*) was isolated in three (2.7%), and *Enterobacter cloacae* (*E. cloacae*) was isolated in two (1.8%). Finally, in the last 9% of cultures, the following microorganisms were found, evenly distributed (one each, 0.9%): *Enterococcus faecalis* (*E. faecalis*), *Serratia marcescens* (*S. marcescens*), *Staphylococcus epidermidis* (*S. epidermidis*), *Staphylococcus hominis* (*S. hominis*), *Staphylococcus lugdunensis* (*S. lugdunensis*), *Staphylococcus spp*, *Streptococcus agalactiae* (*S. agalactiae*), *Streptococcus pneumoniae* (*S. pneumoniae*),
Aeromona hydrophila, and S. aureus + S. epidermidis, S. aureus + E. coli.

Urine cultures were also taken from 41 patients (16%); 14 (31.1%) were reported as negative, E. coli was isolated in nine (22%), K. pneumoniae was isolated in three (7.3%), Proteus mirabilis was isolated in two (4.9%), S. aureus was isolated in two (4.9%) and, finally, in the last 26.4%, the following microorganisms was found equally distributed, one (2.4%) each: E. faecalis, E. faecium, E. cloacae, Pseudomonas aeruginosa, S. marcescens, S. agalactiae, Citrobacter amalonaticus, Candida tropicalis, Candida glabrata, E. coli + E. faecalis, and Pseudomonas aeruginosa + Aeromona hydrophila.

Secretion cultures were also taken from 17 patients (6.6%): from a lower limb in six (35.3%), an abscess in three (17.7%), oral-tracheal secretion in two (11.8%), and the urethra in one (5.8%). Of these samples, the following reports were obtained: S. aureus was isolated in six (35.3%), E. coli was isolated in two (11.6%) and, finally, in the last 53.1%, the following microorganisms were evenly distributed, one each (5.9%): Proteus mirabilis, Morganella morganii, K. pneumoniae, Haemophilus influenzae, E. faecium, E. cloacae, E. cloacae + Citrobacter freudii, E. coli + K. pneumoniae, and Pseudomonas aeruginosa + Proteus mirabilis.

**Discussion**

This study describes the characteristics of infectious disease hospitalizations in a population of patients with Stage 5 chronic kidney disease receiving renal replacement therapy through either hemodialysis or peritoneal dialysis who were admitted to the emergency room at the Hospital Universitario Mayor (Mederi). A literature review of the average hospital stay in this group of patients showed that this epidemiological indicator is presented as an average obtained from the inclusion of various groups of unrelated diseases (such as infections, cardiovascular diseases, cancers and gastrointestinal diseases, among others), making hospitalization a data point which sum-

**Table 1. Medical history and length of hospitalization, by type of dialysis.**

| Characteristics | Hemodialysis (172) | Peritoneal Dialysis (69) | P |
|-----------------|--------------------|------------------------|---|
|                 | n  | %       | n  | %       |     |
| Male            | 125 | 72.7    | 52 | 61.2    | 0.061 |
| Diabetes mellitus | 95  | 55.2    | 52 | 75.3    | 0.413 |
| Arterial hypertension | 152 | 88.4    | 77 | 90.6    | 0.592 |
| Mortality       | 29  | 16.9    | 15 | 17.6    | 0.875 |
| Median          |     | P 25    | P 75 |        |     |
| Age (Years)     | 66  | 57.3    | 75  |         | 0.569 |
| Inpatient Days  | 12  | 8       | 21  |         | 0.004 |

**Figure 1. Flow chart of the selection of patients for the study.**
Table 2. Characteristics on hospital admission. Ca: Calcium, Na: Sodium, Hb: Hemoglobin, P: Phosphorus, Hb A1c: Glycated hemoglobin.

| Characteristics                                    | Hemodialysis (172) | Peritoneal Dialysis (69) | P   |
|----------------------------------------------------|--------------------|-------------------------|-----|
| Repeat consultation within the last 30 days        | 66 38.4            | 26 30.6                 | 0.221|
| Hemoglobin < 10 mg/dL                              | 60 34.9            | 25 29.4                 | 0.45 |
| Albumin < 3 gr/dL                                  | 54 31.4            | 59 69.4                 | 0.000|
| Ca < 10 mg/dL                                      | 35 20.3            | 48 56.5                 | 0.000|
| Na < 136 mmol/L                                    | 112 65.1           | 49 57.6                 | 0.149|
| **Mean SD**                                        | 11 2.19            | 10.8 1.9                | 0.137|
| Hb (g/dL)                                          | 8.7 2.19           | 7.8 7.1                 | 0.000|
| Albumin (gr/dL)                                    | 3.6 0.74           | 2.6 0.6                  | 0.039|
| Ca (mg/dL)                                         | 8.7 8.1            | 9.5 7.8                 | 0.000|
| P (mg/dL)                                          | 3.6 2.9            | 4.6 3.9                 | 0.000|
| Na (mmol/L)                                        | 137 134            | 139 137                 | 0.718|
| Hb A1c (%)                                         | 6.9 5.9            | 7.5 6.9                 | 0.573|

Table 3. Infection site, by type of dialysis.

| Infection Site                             | Hemodialysis (172) | Peritoneal Dialysis (69) | P   |
|--------------------------------------------|--------------------|-------------------------|-----|
| Soft tissue and musculoskeletal            | 53 30.8            | 9 10.6                  | 0.000|
| Related to dialysis                        | 25 14.5            | 33 38.8                 | 0.000|
| Respiratory                                | 44 25.6            | 14 15.6                 | 0.1  |
| Gastrointestinal                           | 21 12.2            | 18 21.2                 | 0.059|
| Urinary tract                              | 24 14              | 11 12.9                 | 0.824|
| Central nervous system                     | 5 2.9              | 0 0                     | 0.174|

Table 4. Characteristics during hospitalization, by type of dialysis therapy. ICU: Intensive care unit, UPRBCs: Units of packed red blood cells.

| Characteristic                              | Hemodialysis (172) | Peritoneal Dialysis (69) | P   |
|---------------------------------------------|--------------------|-------------------------|-----|
| # of antibiotics used                       |                    |                         |     |
| 1                                           | 58 33.7            | 20 23.5                 | 0.095|
| 2                                           | 60 34.9            | 34 40                   | 0.423|
| 3                                           | 28 16.3            | 15 17.6                 | 0.782|
| 4                                           | 8 4.7              | 10 11.8                 | 0.036|
| 5                                           | 7 4.1              | 3 3.5                   | 0.566|
| 6                                           | 3 1.7              | 0 0                     | 0.298|
| Required surgery                            | 37 21.5            | 18 21.2                 | 0.951|
| Required ICU                                | 37 21.7            | 23 27.1                 | 0.323|
| Required transfusion                        | 39 22.7            | 16 18.8                 | 0.521|
| Inpatient stay of 14 days or more           | 75 43.6            | 20 23.5                 | 0.005|
| **Median P 25 P 75**                        | 7 3.5              | 13 11                   | 0.801|
| # of UPRBCs                                 | 2 2                | 4 1.5                   | 0.386|
marizes entities that are hard to compare and which could result in incorrect therapeutic objectives (5-7, 10).

In our opinion, this is one of the few existing studies which seeks to evaluate the length of hospital stay required to treat infectious diseases. Thus, it was found that hemodialysis patients require longer hospital stays than peritoneal dialysis patients, a similar finding to that of Sanabria et al. (4). This may be due to the fact that peritoneal dialysis patients are more likely to have a home hospitalization plan and therefore have fewer inpatient days.

In addition, the proportion of respiratory, central nervous system and urinary tract infections in both types of renal replacement therapy were found to be very similar to those reported by other authors (11, 12). On the other hand, contrary to what other studies report, the proportion of infections related to renal replacement therapy was lower, which could be secondary to the high quality standards (in matters related to the type of dialysis access) required of dialysis providers in the country, due to its high cost. Furthermore, the percentage of soft tissue infections was found to be greater than that reported by the same authors, which indicates the need to reinforce the management of diseases such as diabetic foot within the patients’ outpatient care.

From a microbiological isolation standpoint, the main microorganisms isolated from blood cultures were Staphylococcus aureus in the group of Gram positives and E. coli in the group of Gram negatives, which is very similar to what is described in the literature (13, 14). However, it is noteworthy that in 70% of cases, the blood culture was negative, which could be interpreted as a greater performance of this test in infections which do not cause bacteremia. Nonetheless, it opens the door to continued research related to infectious events associated with patients with chronic kidney disease.

In conclusion, we believe that more detailed knowledge of the causes and characteristics of hospital admissions for patients with Stage 5 CKD who are on hemodialysis and peritoneal dialysis is essential to direct the clinical measures needed to improve the clinical outcomes of outpatient treatment, avoid hospital admissions and optimize their management. In our particular case, we observed that patients on peritoneal dialysis require fewer inpatient days to resolve infectious diseases and that therapy-related infections have a lower incidence than reported globally; however, diabetic foot soft tissue infections are a problem which needs to be given special attention in our country’s renal units.

References
1. Readmission O. Chapter 3: Morbidity and Mortality in Patients with CKD. 2018:1:45–78.
2. White N, American A, ESRD A. Chapter 4: Hospitalizations, Readmissions, Emergency Department Visits, and Observation Stays. Am J Kidney Dis. 2019;73(3):S387–410.
3. XXXIII Cuenta de Hemodialisis cronica (HDC) en Chile (Al 31 de agosto de 2013). Soc Chil Nefrol. 2013;3(2):1–134.
4. Rodríguez MS, Sánchez KR, Astudillo K, Camargo D, Bunch A. frecuencia y costos de hospitalización en una población de pacientes en diálisis en colombia. 2012;60(4):293–301.
5. United States Renal Data System. USRDS 2018 Annual Data Report: Atlas of End-Stage Renal Disease in the United States, Chapter 5: Mortality. 2019;2:411–26.
6. San EC, Rosa G, San D. Registro Argentino de Diálisis Crónica 2013. 2014.
7. Pattern P. Current Status of Dialysis Therapy and Related Clinical Guidelines in Japan. Japanese Soc Dial Ther. 2010;53(3):185–7.
8. Ramos A, Gonza MC, Martí AL, Francisco D, Lo M, Arias M. Nephrology Dialysis Transplantation B lymphopenia in uremia is related to an accelerated in vitro apoptosis and dysregulation of Bcl-2. 2000;502–10.
9. Vaziri ND; Pahl MV; Crum A; Norris K; Effect of uremia on structure and function of immune system. J Ren Nutr. 2013;23(1):149–56.
10. Ao ROM. End-stage renal disease in Brazil : Epidemiology , prevention , and treatment. J R , and R OBERTO Z ATZ. 2005:68:82–6.
11. Dalrymple LS, Johansen KL, Chertow GM. Infection-Related Hospitalizations in Older Patients With ESRD. Am J Kidney Dis [Internet]. 2010;56(3):222–30. Available from: http://dx.doi.org/10.1053/j.ajkd.2010.04.016
12. Dalrymple LS, Mu Y, Romano PS, Nguyen D V, Chertow GM, Delgado C, et al. Original Investigation Outcomes of Infection-Related Hospitalization in Medicare Beneficiaries Receiving In-Center Hemodialysis. Am J Kidney Dis. 2015;65(5):754–62.
13. Fream D, Fernanda M, Okuno P, Taminato M, Ponizio V, Manfredi SR, et al. Risk factors for bloodstream infection in patients at a Brazilian hemodialysis center : a case – control study. 2015;1–9.
14. Fysaraki M, Samonis G, Valachis A, Daphnis E, Karageorgopoulous DE. Incidence , Clinical , Microbiological Features and Out- come of Bloodstream Infections in Patients Undergoing Hemodialysis. 2013;10.
15. KDIGO. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl. 2013;1:150.
16. Eustace JA, Coresh J. Chronic Kidney Disease: Definition and Epidemiology. Chronic Kidney Dis Dial Transplant A Companion to Brenner Rector’s Kidney, Elsevier Inc. Philadelphia, Pennsylvania, 2004.
17. United States renal data system. Chapter 1: Incidence, Prevalence, Patient Characteristics, and Treatment Modalities. United States Renal Data Syst 2015.
18. Pippias M, Stel VS, Diez JMA, Afentakis N, Herrero-Calvo VA, Arias M, et al. Renal replacement therapy in Europe: A summary of the 2012 ERA-EDTA Registry Annual Report. Clin Kidney J. 2013;6(3):248–61.
19. Costa C de alto. Enfermedad renal crónica, hipertensión arterial y diabetes mellitus. Cuenta Alto-Costo. 2015;1:152.
20. United States Renal Data System. Chapter 11: Medicare Expenditures for Persons With ESRD. United States Renal Data Syst 2015.
21. Griveas I, Visvardis G, Flyva A, Papadopoulou D, Mitsopoulou E, Kyrkildou P, et al. Comparative analysis of immunophenotypic abnormalities in cellular immunity of uremic patients undergoing either hemodialysis or continuous ambulatory peritoneal dialysis. Ren Fail. 2005;27:279–82.
22. Nitta K, Akiba T, Kawashima A, Klmata N, Mifwa N, Nishida E. Characterization of Th1 / Th2 profile in uremic patients. Nephron. 2002;91:14.
23. Mocchegiani E, Malavolta N, and NK and NKT cell functions in immunosenescence. Aging Cell. 2004;3(4):177–84.
24. Vacher-Cooponat H, Brunet C, Lyonnet L, Bonnet E, Loundou A, Sampol J, et al. Natural killer cell alterations correlate with loss of renal function and dialysis duration in uremic patients. Nephrol Dial Transplant. 2008;23(4):1406–14.
25. Pahl M V, Gollapudi S, Sepass , L Gollapudi P, Elahimreh E, Vaziri ND. Effect of end-stage renal disease on B-lymphocyte subpopulations, IL-7, BAFF and BAFF receptor expression. Nephrol Dial Transplant. 2010;25(1):205–12.
26. He Q, Johnston J, Zeitlinger J, City K, City K. Outcomes of Infection Related Hospitalization in Medicare Beneficiaries Receiving In Center Hemodialysis. Am J Kidney Dis. 2015;33(4):395–401.
27. Laurin LP, Harrak H, ElRouf N, Ounied M, Vallée M, Lafrance JP. Outcomes of infection-related hospitalization according to dialysis modality. Clin J Am Soc Nephrol. 2015;10(5):817–24.
28. Ng LJ, Chen F, Pisoni RL, Krishnan M, Mapes D, Keen M, et al. Hospitalization risks related to vascular access type among incident US hemodialysis patients. Nephrol Dial Transplant. 2011;26(11):3659–66.
29. Róa Curty NF, da Silva Martins LF, Sanches Itto CA, Schafranski M,
30. Brites DA, Busato CR. Mortimortality study of infection in patients undergoing different types of dialysis in a renal replacement therapy center. Brazilian J Infect Dis. Elsevier Editora Ltda; 2014;18(3):281–6.

31. Brookhart MA, Freburger JK, Ellis AR, Wang L, Winkelmayer WC, Kshirsagar AV. Infection risk with bolus versus maintenance iron supplementation in hemodialysis patients. J Am Soc Nephrol. 2013;24:1151–8.

32. Ribeiro SC, Figueiredo AE, Barretti P, Pecoits-Filho R, de Moraes TP. Low Serum Potassium Levels Increase the Infectious-Caused Mortality in Peritoneal Dialysis Patients: A Propensity-Matched Score Study. PLoS One. 2015;10(6):e0127453.

33. Kumar PS, Mauriello CT, Hair PS, Rister NS, Lawrence C, Raafat RH, et al. Glucose-based dialysis fluids inhibit innate defense against Staphylococcus aureus. Mol Immunol. Elsevier Ltd; 2015;67(2):575–83.

34. Allon M, Radeva M, Bailey J, Bedihu S, Butterfly D, Coyne DW, et al. The spectrum of infection-related morbidity in hospitalized haemodialysis patients. Nephrol Dial Transplant. 2005;20(March):1180–6.

35. Yun G, Norris KC, Greene T, Yu AJ, Ma JZ, Yu W, et al. Race/ethnicity, age, and risk of hospital admission and length of stay during the first year of maintenance hemodialysis. Clin J Am Soc Nephrol. 2014;9(8):1402–9.

36. Dalgard LS, Norgaard M, Povlsen J V., Jespersen B, Jensen-Fangel S, Ellermann-Eriksen S, et al. Risk and Prognosis of Bacteremia and Fungemia Among Peritoneal Dialysis Patients: A Population-Based Cohort Study. Perit Dial Int. 2016;36(6):647–54.