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Morbimortality study of infection in patients undergoing different types of dialysis in a renal replacement therapy center

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ABSTRACT

Introduction: Renal replacement therapy is the treatment of end-stage chronic kidney disease and can be performed through dialysis catheters, arteriovenous fistulas/grafts, and peritoneal dialysis. Patients are usually immunocompromised and exposed to invasive procedures, leading to high rates of infection and increased mortality.
Objectives: To compare the prevalence of infection and related deaths, as well as the sensitivity profile of the putative bacteria in patients treated with peritoneal dialysis, arteriovenous fistula hemodialysis and catheter hemodialysis.
Methods: This is case–control study. Six hundred forty-four patients undergoing renal replacement therapy were selected. Patients were divided into three groups according to the modality of dialysis treatment: peritoneal dialysis (126 patients), arteriovenous fistula hemodialysis (326 patients), and catheter hemodialysis (192 patients).
Results: One hundred sixteen patients (18.01%) developed infection. There was a higher incidence of infection in the peritoneal dialysis group (44 patients; 34.92%; OR: 3.32; CI 95% = 2.13–5.17; $p = 0.0001$). In the catheter hemodialysis group, 48 patients (25%) had infection (OR: 1.88; CI 95%: 1.24–2.85; $p = 0.0035$). In the arteriovenous fistula hemodialysis group, 24 patients (7.36%) developed infection (OR: 0.19; CI 95%: 0.12–0.31; $p = 0.0001$). Five patients (4.31%) died due to infection (four in the peritoneal dialysis group and one in the catheter hemodialysis group). There were no deaths due to infection in the arteriovenous fistula hemodialysis group.
Conclusions: Peritoneal dialysis is the treatment with greater risk of infection and mortality, followed by catheter hemodialysis. The lowest risk of infection and mortality was observed in arteriovenous fistula hemodialysis group.

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Introduction

Chronic kidney disease (CKD) has high prevalence and incidence worldwide, particularly in Brazil.[1] Although the National Kidney Foundation (NKF)[2] in 2002 has proposed staging CKD in order to slow the advance toward the functional failure of the kidneys, difficulties such as lack of early diagnosis, inadequate treatment in the early stages, delayed specialized monitoring, and the complexity of the disease lead many people to need renal replacement therapy (RRT).[1–3] RRT can be implemented through hemodialysis (HD), peritoneal dialysis (PD), and renal transplantation. Each treatment has its own characteristics, advantages, disadvantages, and complications.[4] Peritoneal dialysis allows the patient home treatment decreasing outpatient visits. Hemodialysis can be performed through a central catheter (CH) inserted in the internal jugular or subclavian vein or through an arteriovenous fistula (AVF) preferably in the upper limbs whose optimal functionality delay varies from one to three months.[5,6] Nosocomial infection is one of the most serious complications and the second cause of death in dialysis patients.[7] The risk factors that predispose to nosocomial infection in RRT may be influenced by patient characteristics, site of dialysis access, and disorders of the skin and mucous membranes[8]; and comorbidities such as diabetes mellitus, anemia, cardiovascular disease, immunosuppression, and metabolic imbalances.[4,5] Peritonitis is the most frequent infection in patients undergoing PD, and septicemia is the most frequent complication among patients on HD, especially when conducted through a central venous catheter. The kind of vascular access for HD has significant influence on patient survival. Catheters are associated with substantially greater risk of septicemia, hospitalization, and mortality compared to AVF.[9] There are few studies in Brazil evaluating infection rates, the prevalent microorganisms and the susceptibility profile of bacterial infections associated with RRT. These data may be useful for empirical anti-infective therapy in these patients, as well as to better evaluate the choice of dialysis treatment aiming at preventing infections. The objective of the present study was to compare the prevalence of infection and related deaths, as well as the sensitivity profile of the putative bacteria in RRT treated patients.

Methods

This is a case–control study. The study sample consisted of 644 patients treated in the RRT outpatient center at Santa Casa de Misericordia de Ponta Grossa Hospital during a 29-month period. Patients on RRT who developed nosocomial infection (116 patients) were considered as cases. Patients who did not develop infection (528 patients) were considered as controls. Nosocomial infections were considered when the Commission of Hospital Infection Control (CHIC) identified the case as such, based on clinical features, complementary blood tests, and culture results of biological material. Unconfirmed cases of infection by the CHIC were excluded. The patients were divided into three groups according to the type of dialysis treatment: PD (116 patients), CH (192 patients), and arteriovenous fistula hemodialysis (AVH) (326 patients). The study was approved by the local ethics committee.

Statistical analysis

To compare categorical variables, two-tailed *Fisher*'s exact test with *Bonferroni* correction for multiple comparisons was used. To evaluate the effect size *Odds Ratio* (OR) was calculated with 95% confidence interval (CI) and its transformation in probability (p). The samples were properly tested for normality by *Anderson–Darling* test. The presence of *outliers* was checked by the *Grubbs* test. The statistical power of the sample was computed in each comparison. Results are presented as mean ± standard deviation (SD). Analyses, including descriptive statistics, were performed using EPI INFO program. $p < 0.05$ was considered statistically significant.

Results

Of the 644 patients who underwent dialysis during the study period, 116 (18.1%) developed some infection (63 male; 57.22 ± 12.76 years). One hundred fifty-six infections were reported. Seventy-one (45.51%) infections (56.14 ± 11.22 years) were in patients on PD, 60 (38.46%) infections (59.82 ± 13.33 years) in patients on CH, and 25 (16.2%) infections in patients on AVH (53.8 ± 14.7 years) (Table 1).

Comparison between groups

Of the 126 patients undergoing PD, 44 (34.92%) had at least one infection during the study period, which was significantly higher than that in the other two groups (OR: 3.32; CI 95%: 2.13–5.17; $p = 0.0001$). CH also showed up as a risk factor for the development of infection with 48 (25%) of the 192 infected patients (OR: 1.8824; CI 95%: 1.24–2.85; $p = 0.0035$). The lowest incidence of infection was observed in AVH group: 24 (7.36%) of 326 patients (OR: 0.19; CI 95%: 0.12–0.35; $p = 0.0001$). For all comparisons made, the statistical power was greater than 99%, with a consequent error – beta less than 1% (Table 2).

Individual comparison between groups

Comparing the groups individually, AVH turned out to be the safest method with less infections, resulting in lower incidence of morbidity when compared with CH (OR: 0.23; CI 95%: 0.14–0.40; $p = 0.0001$) and PD (OR: 0.14; CI 95%: 0.08–0.25; $p = 0.0001$). There was no statistically significant difference between the incidence of infections in the PD group and the CH group (OR: 0.62; CI 95%: 0.38–1.01; $p = 0.0593$). The statistical power to detect these differences was 100% in both cases, therefore no beta error (Table 3).

Deaths

Of patients infected (116), five died due to infection, with an overall mortality rate of 4.31%. There were four deaths (9.09%)

Table 1 – Patient characteristics by age and sex.

	PD		CH		AVH		Total		
	n	%	*n*	%	*n*	%	*n*	%	
Sex									
Male	21	47.72	29	60.41	13	54.16	63	54.31	
Female	23	52.27	19	39.58	11	45.83	53	45.68	
Total	44	37.93	48	41.37	24	20.68	116	100	
Age	56.14 ± 11.22		59.82 ± 13.33		53.8 ± 14.70		57.22 ± 12.76		$p = 0.84$

PD, peritoneal dialysis; CH, central catheter hemodialysis; AVH, arteriovenous fistula hemodialysis.

Table 2 – Rate of infection in patients on renal replacement therapy according to the type of dialysis.

Type of dialysis	Patients with infection *n* (%)	Patients without infection *n* (%)	OR (CI 95%)[b]	P[c]	*p*[a]	Statistical power (%)
AVF	24 (7.36)	302 (92.63)	0.19 (0.12–0.31)	6.12	0.0001[1]	100
Catheter	48 (25)	144 (75)	1.88 (1.24–2.85)	1.53	0.0035[2]	99.2
Peritoneal	44 (34.92)	82 (65.07)	3.32 (2.13–5.17)	1.30	0.0001[3]	99.8
Total	116	528	–	–	–	–

[a] Fisher's exact test with correction for Bonferroni multiple comparisons. Considering a significant $p < 0.017$.
[b] Odds Ratio (OR) with Confidence Interval (CI) of 95%.
[c] Probability (P). 1 hemodialysis by arteriovenous fistula (AVH) versus hemodialysis by catheter (CH) + peritoneal dialysis (PD). 2 CH versus AVH + DP. 3 DP versus AVH + CH. RRT = renal replace therapy. AVF = arteriovenous fistula.

Table 3 – Comparison of the infection frequency in the different groups of dialysis.

Groups	Patients with infection *n* (%)	Patients without infection *n* (%)	OR (CI 95%)[b]	P[c]	*p*[a]	Statistical power (%)
AVF	24 (7.36)	302 (92.63)	0.23 (0.14–0.40)	3.19	0.0001[1]	100
Catheter	48 (25)	144 (75)	0.62 (0.38–1.01)	0.60	0.0593[2]	100
Peritoneal	44 (34.92)	82 (65.07)	0.14 (0.08–0.25)	5.75	0.0001[3]	100
Total	116	528	–	–	–	–

[a] Fisher's exact test with Bonferroni correction for multiple comparisons. Considering significant $p < 0{,}017$.
[b] Odds Ratio (OR) with Confidence Interval (CI) of 95%.
[c] Probability (P). 1 hemodialysis by arteriovenous fistula (FAVH) versus hemodialysis by catheter (CH). 2 hemodialysis by catheter (CH) versus peritoneal dialysis (PD). 3 PD versus hemodialysis by arteriovenous fistula (AVH). AVF = arteriovenous fistula.

in PD group and one (8.2%) in CH group. No death was observed in AVH group.

Sites of infection and bacterial etiology

Microbiological tests were carried out in 151 (96.78%) patients, with infections turning out positive in 126 (80.76%). CH group was the group with the highest positivity rate (93.33%; 56/58 cultures), followed by the PD group (81.28%; 59/71 cultures) and the AVH group (52%; 13/22 cultures). The biological samples used for culture were peritoneal fluid in 46.47% of infections of PD group, blood culture in 72.41% of infections of CH group and 40.9% of infections of AVH group. Other samples used for culture were catheter secretion, dialysate fluid, cardiac valve secretion, sputum, and urine (Table 4). The most common infection in the PD group was peritonitis in 55 (77.46%) patients. In CH group, bloodstream infection was the most frequent infection occurring in 44 (73.33%) patients. Vascular access was the commonest site of infection in AVH group occurring in 12 (48%) patients (Table 5). *Staphylococcus aureus* was the most commonly recovered bacteria present in 44 (32.59%) cases (24 in PD group, 16 in CH group, and 4 in AVH group). Coagulase-negative *Staphylococcus* spp. (SNPC) was recovered from 47 (34.81%) cases (13 in PD group, 29 in CH group, and 5 in AVH group). *Escherichia coli* was isolated in 18 (13.33%) cases (10 in PD group, 6 in CH group, and 2 in AVH group). Other less frequent bacteria are shown in Table 6.

Sensitivity profile of etiologic agents

The sensitivity profiles of the main isolated bacteria are shown in Table 7. Among the most important findings, 5 (11.4%)

Table 4 – Microbiological culture results from patients on different types of dialysis.

Culture	PD		CH		AVH		Total
	n	%	*n*	%	*n*	%	*n*
Positive	57	81.28	56	93.33	13	52	126
Negative	14	19.71	2	3.33	9	36	25
Not done	0	0	2	3.33	3	12	5
Total	71	45.51	60	38.46	25	16.02	156

PD, peritoneal dialysis; CH, central catheter hemodialysis; AVH, arteriovenous fistula hemodialysis.

Table 5 – Site of infection in patients on different types of dialysis.

	PD		CH		AVH		Total	
	n	%	*n*	%	*n*	%	*n*	%
Site								
Peritonitis	55	77.46	0	0	0	0	55	35.25
Blood stream (BS)	3	4.22	44	73.33	4	16	51	32.69
Related to vascular access/catheter	12	16.90	14	23.33	12	48	38	24.35
Urinary tract infection (UTI)	0	0	2	3.33	2	8	4	2.5
Respiratory tract infection	0	0	0	0	4	16	4	2.5
Endocarditis	0	0	0	0	3	12	3	1.92
Peritonitis + BS + UTI	1	1.40	0	0	0	0	1	0.64
Total	71	45.51	60	38.46	25	16.02	156	100

PD, peritoneal dialysis; CH, central catheter hemodialysis; AVH, arteriovenous fistula hemodialysis.

Table 6 – Etiology of infections from patients on different types of dialysis.

Bacterium	PD		CH		AVH		Total
	n	%	*n*	%	*n*	%	*n*
Staphylococcus aureus	24	40.67	16	25.39	4	30.76	44
SNPC	13	22.03	29	46.03	5	38.46	47
Enterococcus faecalis	1	1.69	1	1.58	1	7.69	3
Streptococcus sp.	1	1.69	0	0	0	0	1
Escherichia coli	10	16.94	6	9.52	2	15.38	18
Klebsiella pneumoniae	3	5.08	2	3.17	0	0	5
Serratia spp.	2	3.38	3	4.76	0	0	5
Enterobacter spp.	0	0	2	3.17	1	7.69	3
Proteus vulgaris	0	0	1	1.58	0	0	1
Pseudomonas aeruginosa	3	5.08	3	4.76	0	0	6
Acinetobacter baumannii	2	3.38	0	0	0	0	2
Total	59	43.70	63	46.66	13	9.62	135
Polymicrobial infection	2	3.50	6	10.71	0	0	8
Monomicrobial infection	55	96.49	50	89.28	13	100	118

PD, peritoneal dialysis; CH, central catheter hemodialysis; AVH, arteriovenous fistula hemodialysis.

methicillin-resistant *S. aureus* (MRSA) isolates, all observed in PD group, and 7 (15.2%) methicillin-resistant SNPC infections (6 in CH group) stand out. There was no reported resistance to neither vancomycin nor rifampicin. One (5.5%) *E. coli* isolate from PD group was extended-spectrum β-lactamase producer (ESBL) and multidrug resistant to antimicrobials. Multidrug resistant *Klebsiella pneumoniae* was recovered from two isolates (40%), one from PD group and another from CH group. Isolates of *Serratia* spp. (5) were susceptible to most antimicrobials tested. Resistant *Pseudomonas aeruginosa* was observed in only one isolate (16.7%) from CH group. Carbapenem resistance was not detected. The remaining isolates were susceptible to most antibiotics tested. Overall, multidrug resistant bacterial infections were recovered from 16 (10.26%) patients: 9 (56.25%) from CH group and 7 (43.75%) from PD group, representing 14.28% and 11.86% infections, respectively, with no statistical difference (OR: 1.23; CI 95%: 0.42–3.5; $p = 0.7914$; statistical power of 100%). No multidrug resistant isolate was recovered from AVH group.

Discussion

As previously reported, PD patients had higher rate of infection compared to CH and AVH patients.[9–12] Likewise, a high mortality rate (9.9%) of infected patients was observed in PD

Table 7 – Sensitivity profile of the main isolated bacteria.

Antimicrobial	*S. aureus*			SNPC			*E. coli*			*K. pneumoniae*			*P. aeroginosa*		
	n	*s*	%	*n*	*s*	%	*n*	*s*	%	*n*	*s*	%	*n*	*s*	%
Azithromycin	44	32	72.72	46	19	41.30									
Ampicillin (Amp)							18	3	16.66	5	0	0			
Amp/Sulbactam							18	11	61.11	5	2	40			
Cefazolin							18	12	66.66	5	2	40			
Cefalotin	44	39	88.63	46	38	82.60	18	12	66.66	5	2	40			
Ceftazidime							18	14	77.77	5	3	60	6	5	83.33
SMT + TMT	44	40	90.90	46	31	67.39									
Gentamicin	44	39	88.63	46	31	67.39	18	12	66.66	5	3	60	6	5	83.33
Ciprofloxacin	44	39	88.63	46	34	73.91	18	10	55.55	5	4	80	6	5	83.33
Amikacin							18	16	88.88	5	3	60	6	5	83.33
Ceftriaxone							18	17	94.44	5	4	80			
Meropenem							18	18	100	5	5	100	6	6	100
Penicillin	44	8	18.18	46	5	10.86									
Oxacillin	44	39	88.63	46	39	84.78									
Vancomycin	44	44	100	46	46	100									
Cefepime							16	16	100	5	4	80	6	5	83.33
Aztreonam							16	16	100	5	4	80	6	5	83.33
Erithromycin	44	32	7272	46	33	71.73									
Clindamycin	44	37	84.09	46	32	69.56									
Chloramphenicol	44	40	90.90	46	44	95.65									
PIP + TZB							16	16	100	5	5	100	6	5	83.33
Rifampin	44	44	100	46	46	100									
Tobramycin													6	6	100

group when compared to CH patients (2.08%). Johnson et al.[13] reported a mortality rate of 7.6% and 4.2%, respectively, also showing an increased risk of death in infected PD patients. Lower rates (3.5%) of mortality in PD were reported by Barretti et al.[14] Peritonitis is the main limitation of PD and is very frequent.[11,13–15] In CH group, bloodstream infection is the most common site of infection. In the present study, bloodstream infection was presented in 73.33% of patients in CH group, compared to 16% in AVH group and 4.22% in PD group. These results are similar to several studies reporting 50–80% of bloodstream infections[16] mostly related to the use of catheters.[11,12,16] Couto et al.[15] describe aseptic peritonitis, an entity found in about 10% of cases, where there is no identified etiological agent. In the present study 19.71% of negative cultures were found in PD group with clinically diagnosed peritonitis. Furthermore, culture was made in all cases with no possibility of underreporting. The most frequent infectious agents isolated were Gram positive bacteria responsible for 70.36% of all infections. Similar values are found in the study by Silva et al.[6] with 60% of cases, in Aslan et al.[11] with 62%, and in Couto et al.[15] with 67% of cases. Other studies show that the proportion of Gram positive and Gram negative bacteria is similar.[17,18] *S. aureus* and SNPC were the most frequent pathogens isolated, as in other studies.[14,15,19–21] Methicillin resistant SNPC was found in 15.2% of infections, a lower rate of resistance than the 58.4% and 100% reported by Barretti et al.[14] and Britta et al.,[20] respectively. The incidence of MRSA in the present study was 11.4% compared to rates of 14.3%,[14] 22%,[22] 23%,[20] and 43.4%[17] found in other studies. Gram negative organisms were responsible for 23.69% of all infections in the present study. *E. coli* was the most frequent with 13.33%. Seventeen of 18 cultures (94.45%) were sensitive to ceftriaxone, whereas 66.7% and 55.6% were sensitive to ciprofloxacin and cefalotin. Britta et al.[20] reported a study in which *E. coli* had 100% resistance to these antibiotics. An isolate of *E. coli* was ESBL producer (5.55%), multidrug resistant, and sensitive to meropenem. As in the study by Sader et al.[23] no resistance to this antibiotic was found in the present study. For *K. pneumoniae* 80% was sensitive to ceftriaxone and 60% to ceftazidime. Nogueira et al.[24] showed 53.3% and 80% sensitivity, respectively, and Almeida et al.[25] reported 34% sensitivity for both antibiotics. *Serratia*, *Enterobacter*, and *Proteus* were also isolated (Table 6). Non-fermentative bacilli were isolated in eight (5.92%) cultures, *P. aeruginosa* in six (4.44%) of which only one (16.7%) was multidrug resistant, and *Acinetobacter baumannii* was recovered in two cultures. Britta et al.[20] showed multidrug resistance in 50% of cases. Polymicrobial infections were observed in 3.5% of cases of PD group, a rate much lower than the 30%,[15] 10.7%,[18] and 9.09%[25] reported by other studies. In CH group polymicrobial infections were more frequently isolated (10.71%). The lower rate of resistance of the isolates in the present study translates into reduced morbidity and hospital costs.[26] This finding could be attributed to the antimicrobial control policy implemented by the CHIC, which is based on quarterly updates of clinical sensitivity of local microbiota and prescription supervision of electronic medical records.

Conclusions

The present study provides evidence that the type of vascular access in RRT is an important predisposing factor for infection which, in turn, increases comorbidity and hospital costs. The AVF for hemodialysis is the safest access for RRT. These results emphasize the need for early referral program for patients with CKD regarding the indication and maturation of the dialysis method. This policy decreases morbidity, mortality, and

hospital costs. More studies are needed, especially those that are prospective and adequately powered.

Conflicts of interest

The authors declare no conflicts of interest.

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