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Original Article

A six-year experience of catheter-related bloodstream infections in hemodialysis patients

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Abstract

Introduction: This study investigated the clinical characteristics, causative microorganisms, and antibiotic resistance patterns of catheter-related bloodstream infections (CRBSIs) in hemodialysis patients at a tertiary healthcare institution.

Methodology: A retrospective analysis of 300 patients treated for CRBSIs between January 2018 and December 2023 was conducted. Patients were divided into two groups: those with less than 1 year of hemodialysis (Group 1) and those with more than 1 year of hemodialysis (Group 2). Risk factors for intensive care unit (ICU) transfer and 28-day mortality were analyzed.

Results: The median age was 68 years. Gram-positive bacteria were the predominant pathogens (69%), with Staphylococcus aureus being the most frequent. Group 1 had significantly higher rates of recent hospitalization ($p = 0.014$) and a history of previous ICU admission ($p = 0.001$). However, no significant differences were found in causative microorganisms or antimicrobial resistance between the two groups. Risk factors for ICU transfer included carbapenem resistance (OR: 7.657, $p = 0.013$), history of catheter revision (OR: 4.632, $p = 0.022$), and leukocytosis (OR: 1.150, $p = 0.004$). The 28-day mortality rate was 8%. Significant risk factors for mortality were ICU transfer (OR: 17.29; $p = 0.001$) and Vancomycin-Resistant Enterococcus (VRE) infection (OR: 14.10; $p = 0.002$).

Conclusions: Despite shorter-term dialysis patients having more frequent hospitalizations, the distribution and resistance of pathogens remain similar regardless of hemodialysis duration. Empirical therapy should prioritize broad anti-staphylococcal coverage and be tailored to specific risk factors such as VRE or carbapenem resistance rather than hemodialysis duration.

Key words: catheter-related bloodstream infection; hemodialysis; mortality; hemodialysis duration; Gram-positive bacteria.

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Introduction

Bloodstream infections (BSIs) are among the most significant complications in patients with chronic kidney disease (CKD) undergoing hemodialysis. Systemic infections, sepsis, and subsequent hospitalization and mortality rates increase following BSIs [1,2]. The risk of infectious complications may vary depending on factors such as catheter duration, catheter location, prior infections, prior antibiotic use, and comorbidities [3-6]. Infectious complications associated with tunneled catheters are more common, particularly during the initial period of catheter use [7]. Prospective studies have reported infection rates for tunneled central venous catheters to range from 0.51 to 1.59 per 1000 catheter-days [8,9]. The most frequently isolated microorganism in catheter-related bloodstream infections (CRBSIs) is Staphylococcus aureus. Methicillin resistance in this patient population is a significant concern and should not be overlooked [10]. In non-staphylococcal CRBSIs, enterococci and Gram-negative bacilli are also common pathogens [11].

There are no specific symptoms in CRBSIs. Patients usually present with complaints such as high fever, hypotension, and tachycardia that begin during hemodialysis. In the absence of local signs of infection at the catheter site (e.g., redness, warmth, tenderness, or discharge), a diagnosis is made by excluding other potential sources of infection [12]. Initiating empirical anti-staphylococcal therapy is a crucial component of treatment recommendations for patients with these infections. However, decisions regarding coverage for methicillin-resistant strains and Gram-negative organisms should be guided by local resistance rates and patient-specific risk factors [13].

The first year of treatment for patients new to hemodialysis is an adaptation period, during which they become accustomed to catheter care, and their overall health may be more vulnerable. During this period, the risk of infection, along with other complications, and mortality rates is higher [14,15]. Our study aimed to

investigate whether there are differences in microbiological and resistance profiles, as well as prognosis, between patients in this initial, high-risk period and those in the more stable, longer-term period.

Methodology

This retrospective study included patients who underwent hemodialysis and were treated for CRBSI at a 90-bed Nephrology Clinic between January 2018 and December 2023. Only the first episode was included for patients hospitalized with CRBSI on more than one occasion.

Case Definition, Inclusion and Exclusion Criteria

Patients aged 18 and older who were diagnosed with CRBSI and treated in the Nephrology Department during the specified period were included in the study.

Inclusion criteria were as follows:

- Receiving hemodialysis via a central catheter
- Being diagnosed with a catheter-associated bloodstream infection
- Having the causative microorganism isolated by the same hospital microbiology unit

Exclusion criteria were as follows:

- Patients who completed their treatment at another center
- Patients whose causative microorganisms were isolated at another center
- Patients whose data were unavailable
- Patients with tunnel infections
- Patients with contamination

Data Collection

Patient characteristics, including age, gender, underlying diseases, and the duration, location, and type of hemodialysis catheter, were recorded. Outcomes such as catheter replacement or removal, transition to other hemodialysis methods, the presence of septic embolic complications, and 28-day mortality were also documented. The distribution of causative microorganisms, their antibiotic resistance profiles, the appropriateness of empirical treatment, and patient prognosis were analyzed. Patients were divided into two groups based on their duration of hemodialysis. Group 1 included patients with less than 1 year of hemodialysis, while Group 2 included those with more than 1 year of hemodialysis. We compared demographic data, comorbidities, risk factors for CKD, laboratory findings, causative microorganisms, resistance profiles, and prognoses between the two groups.

Definitions

- Catheter-Related Bloodstream Infection: Defined as the presence of fever or systemic signs of infection in a patient with a tunneled catheter, with no other evident source of infection, and the isolation of identical microorganisms from blood cultures obtained from both a peripheral vein and the catheter.
- Appropriate Empirical Antibiotic Therapy: Defined as the in vitro effectiveness of the empirically administered antibiotic(s) against the subsequently isolated microorganism.
- Contamination: Results with a single positive coagulase-negative staphylococcus growth, for which the clinician considered contamination and did not initiate antibiotic treatment, were considered contamination and were not included in the microorganism and antibiogram results.
- Tunnel Infection: Tenderness, erythema, or induration (without accompanying bacteremia or sepsis) in an area greater than 2 cm along the catheter from the catheter exit site was accepted as a tunnel infection and excluded from the study.
- Polymicrobial CRBSI: Infections that met the definition of CRBSI and in which more than one microorganism was isolated were included. Susceptibility of microorganisms was determined based on whether they were Gram-positive or Gram-negative.
- Recent hospitalization: Having received at least 48 hours of hospital inpatient treatment for any reason within the last 90 days before applying to the hospital with a diagnosis of CRBSI.

Microbiological Analysis

Following clinical suspicion of CRBSI, paired blood cultures were aseptically collected from both a peripheral vein and the catheter lumen. Samples were incubated in a BACTEC™ FX automated blood culture system (Becton Dickinson, USA) until a positive result was obtained or for up to five days. Positive cultures were subjected to Gram staining and sub-cultured onto standard media.

From January 2018 to March 2020, bacterial identification (ID) and antimicrobial susceptibility testing (AST) were performed using the Vitek 2 (bioMérieux, France) and Phoenix M50 (Becton

Dickinson, USA) automated systems. From April 2020 to December 2023, species-level ID was enhanced by the implementation of MALDI-TOF Mass Spectrometry systems (Vitek MS Prime, bioMérieux; BD Sirius, Bruker).

Antimicrobial susceptibility tests were conducted to determine Minimum Inhibitory Concentration (MIC) values. The results were interpreted according to the clinical breakpoint tables provided by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for the year in which the isolate was tested. Methicillin resistance in *Staphylococcus aureus* was confirmed using the cefoxitin screen test. Phenotypic confirmatory tests, such as the combination disk test, were used to detect Extended-Spectrum Beta-Lactamase (ESBL) production in *Enterobacterales,* where appropriate.

Statistical Analysis

Data were analyzed using SPSS 27. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess the normality of data distribution. Data were presented as mean ± standard deviation or percentages, as appropriate. The Student's t-test or Mann-Whitney U-test was used for the analysis of continuous variables, while the chi-square or Fisher's exact test was used for categorical variables. To identify independent risk factors for ICU transfer and 28-day mortality, multivariate logistic regression analysis was performed. Results from the regression analysis were presented as Odds Ratios (OR) with 95% Confidence Intervals (CI). A $p < 0.05$ was considered statistically significant.

Results

Three hundred patients were included in the study. The median age was 68 years, and 134 patients (44.7%) were male. The median duration of CKD was 5 years, and the median duration of hemodialysis was 18 months. The duration of hemodialysis was less than one year in 136 patients. The most common comorbidities were hypertension (73%), diabetes mellitus (48%), coronary artery disease (36%), and chronic lung diseases (21%). Three-quarters of the patients received hemodialysis three times a week.

Tunneled catheters were used in 291 patients (97%), while 51 individuals had previously used non-tunneled catheters. Before the index infection, catheters had been changed for various reasons in 141 patients; of these, 113 (37.7%) were due to previous CRBSI. Among previously isolated CRBSI agents, 65% were Gram-positive, and 34% were Gram-negative bacteria. A total of 128 patients had been hospitalized for any reason within the last three months, with 18 of these hospitalizations involving an intensive care unit (ICU).

Empirically initiated antibiotic therapy was appropriate for the isolated microorganism in 200 patients; empirical treatment was changed in 155 patients; and most subsequent treatment changes were for de-escalation (in 72 patients). Following treatment, infected catheters were removed in 173 patients. Of these, 86 had a new catheter placed in a different location, 45 in the same area, and 42 transitioned to an arteriovenous (A-V) fistula. The time to catheter removal after an index positive culture was 11 days (Table 1). Complications included abscesses in nine patients, endocarditis in ten, and metastatic infections

Table 1. General characteristics of patients.

Characteristics	Total (n = 300)
Age (years), median (min-max)	68 (18-93)
Male sex	134 (44.7)
Living in rural areas	100 (33.3)
Duration of CKD (months), median (min-max)	60 (1-360)
Duration of hemodialysis (months), median (min-max)	18 (1-348)
Hypertension	218 (72.7)
Diabetes Mellitus	144 (48.0)
Coronary Artery Diseases	108 (36.0)
Chronic Lung Diseases	65 (21.7)
Malignancy	39 (13.0)
Corticosteroid Use	29 (9.7)
History of Renal Transplantation	28 (9.3)
Hypothyroidism	23 (7.7)
Hemodialysis session	
2/7	75 (25.0)
3/7	225 (75.0)
History of peritoneal dialysis	22 (7.3)
History of arteriovenous fistula	74 (24.7)
Non-tunneled catheter	51 (17.0)
Tunneled catheter	291 (97.0)
History of any catheter revision	141 (47.0)
History of catheter revision after CRBSI	113 (37.7)
The median number of the CRBSI attacks median (min-max)	2 (1-11)
Previous CRBSI history	113 (37.7)
Previous Causes of CRBSI Attacks	n = 113
Gram Positive Bacteria	74 (65.4)
Gram Negative Bacteria	38 (33.6)
Yeast	1 (0.8)
Hospitalization in the last 3 months	128 (42.7)
ICU Hospitalization in the last 3 months	18 (6.0)
Appropriate empirical treatment rate	200 (66.6)
Change in empirical treatment	155 (51.7)
De-escalation	72 (46.5)
Side effect	13 (8.4)
Prognosis of the catheter	
Catheter removal	173 (57.6)
Catheter removal and replacement with another region	86 (28.0)
Catheter removal and replacement in the same region	45 (15.0)
Transition of arteriovenous fistula	42 (14.0)
Time to catheter removal (n = 173) (days median min-max)	11 (2-28)
Mortality (28-day)	24 (8.0)

CKD: chronic kidney disease; CRBSI: Catheter-related bloodstream infection; ICU: intensive care unit.

in fifteen. Catheters were removed in all patients who developed complications. A total of 45 patients were transferred to the ICU, and 24 patients died within 28 days of treatment. The annual distribution of cases showed that the highest number of admissions occurred in 2021 and 2022 (Figure 1). This increase in the number of cases during the pandemic period was statistically significant ($p < 0.001$).

Comparison of patients according to hemodialysis duration is shown in Table 2. Patients with a hemodialysis duration of 1 year or less were categorized as Group 1; those with a duration of hemodialysis longer than 1 year were categorized as Group 2. Accordingly, the median age was higher in Group 1 than in Group 2 (69 years vs. 67 years; $p = 0.043$). The rate of coronary artery disease among chronic diseases was significantly higher in Group 1 compared to Group 2 (42.6% vs. 30.5%; $p = 0.03$). The rate of three-times-weekly hemodialysis sessions was higher in Group 2. Among the tunneled catheter hemodialysis patients, the rates were 94% in Group 1 and 99.4% in Group 2 ($p = 0.013$). The history of catheter changes for any reason, as well as catheter changes due to CRBSI, was significantly higher in Group 2 ($p = 0.001$). However, the history of hospitalization in the previous 3 months ($p = 0.014$) and history of treatment in the intensive care unit (ICU) ($p = 0.001$) were higher in Group 1. No significant differences were observed between the two groups in terms of suitability for empirical treatment, treatment change rates, need for ICU, and mortality.

When laboratory findings were compared, the median platelet count ($p = 0.005$) and creatinine ($p = 0.001$) were lower in Group 1 than in Group 2 (Table 3).

Table 4 presents the isolated microorganisms and their comparison by hemodialysis duration. Accordingly, 69% of the organisms were Gram-positive and 30% were Gram-negative, and 1% were yeasts. Among Gram-positive bacteria, *Staphylococcus aureus* was the most frequently isolated, with the majority methicillin-susceptible (92 MSSA and 41 MRSA). *Enterococcus spp.* was isolated in 30 patients.

Figure 1. Distribution of the number of patients treated over the years.

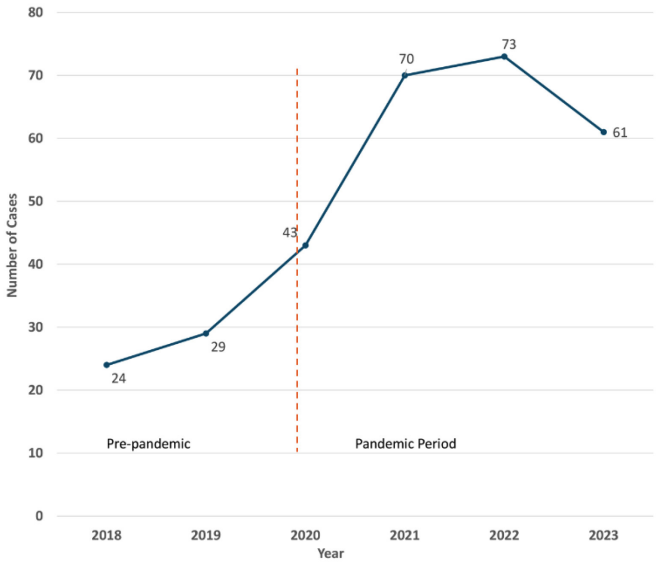

Table 2. Comparison of patients' demographic data, infection risk factors and prognosis according to hemodialysis duration.

	Group 1 HD year ≤ 1 Year (n = 136)	Group 2 HD year > 1 Year (n = 164)	*p*
Age median (min-max)	69 (18-93)	67 (23-92)	0.043
Male gender	60 (20.0)	74 (24.7)	0.907
Duration of CKD (months) median (min-max)	34 (1-300)	108 (13-360)	0.001
Hypertension	105 (77.2)	113 (68.9)	0.119
Diabetes Mellitus	70 (51.5)	74 (45.1)	0.297
Coronary Artery Diseases	58 (42.6)	50 (30.5)	0.030
Chronic Lung Diseases	35 (25.7)	30 (18.3)	0.124
Malignancy	23 (16.9)	16 (9.8)	0.084
HD session			
2/7	49 (36.0)	26 (15.9)	0.001
3/7	87 (64.0)	138 (84.1)	
History of peritoneal dialysis	5 (3.7)	17 (10.4)	0.043
History of A-V fistula	14 (10.3)	60 (36.6)	0.001
Non-tunneled catheter	25 (18.4)	26 (15.9)	0.644
Tunneled catheter	128 (94.1)	163 (99.4)	0.013
History of any catheter revision	34 (25.0)	107 (65.2)	0.001
History of catheter revision after CRBSI	33 (24.3)	80 (48.8)	0.001
Hospitalization in the last 3 months	69 (50.7)	59 (36.0)	0.014
ICU Hospitalization in the last 3 months	15 (11.0)	3 (1.8)	0.001
Appropriate empirical treatment rate	73 (53.7)	99 (60.4)	0.291
Change in empirical treatment	62 (45.6)	93 (56.7)	0.064
Transferring to the ICU	24 (17.6)	21 (12.8)	0.259
Mortality (28-day)	13 (9.6)	11 (6.7)	0.398

HD: hemodialysis; CKD: Chronic Kidney Diseases; CRBSI: Catheter-related bloodstream infection; ICU: intensive care unit.

No significant difference was observed between Groups 1 and 2 regarding ampicillin-resistant and vancomycin-resistant enterococci. Among Gram-negative bacteria, *Escherichia coli* was the most frequently isolated (6.6%). *Klebsiella pneumoniae* (5%) and *Enterobacter cloacae* (5%) were then isolated, respectively. Among non-fermenting bacteria, the frequencies of Pseudomonas aeruginosa and Acinetobacter baumannii were 4.3% and 3.6%, respectively. In Gram-negative bacteria, fluoroquinolone resistance was 17.3%, piperacillin-tazobactam resistance was 18.3%, and carbapenem resistance was 10.6%. No difference in antimicrobial resistance was observed among Gram-negative microorganisms (Figure 2).

In empirical therapy, combination treatments (n = 173) were more frequently preferred than monotherapy (n = 127). The most common empirical combination was piperacillin-tazobactam + vancomycin, which was used in 100 (57.8%) of all combination regimens, followed by a carbapenem + vancomycin (26.5%). Among empirical monotherapies, vancomycin was the most selected agent (35.4%). After the causative agent was identified and susceptibility results were available, a shift towards monotherapy was observed: 197 patients received single-agent therapy compared with 103 receiving combination therapy. In agent-specific monotherapy, cefazolin (19.2%), carbapenems (16.2%), and piperacillin-tazobactam (15.7%) were the most used antibiotics. When combination therapy was

Figure 2. Antimicrobial susceptibilities of Gram-negative bacteria and comparison of susceptibilities.

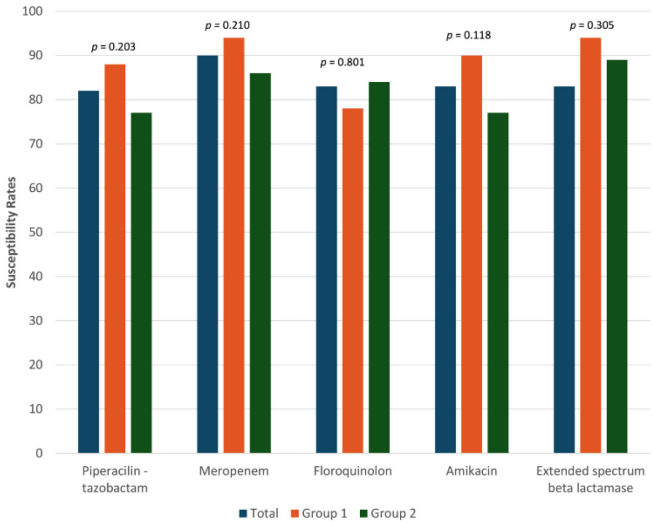

Table 3. Comparison of the laboratory findings of the groups.

	Total (n = 300)	Group 1HD year ≤ 1 Year (n = 136)	Group 2 HD year > 1 Year (n = 164)	*p*
White Blood Cell (10^3/µL), median (min-max)	9.2 (1.9-34.4)	9.2 (1.9-32.3)	9.3 (2.2-34.4)	0.781
Hemoglobin (g/dL), median (min-max)	10.0 (4.6-16.3)	10.0 (4.6-15.0)	10.1 (4.6-16.3)	0.893
Platelet (10^3/µL), median (min-max)	183 (8-524)	169 (8-514)	190 (62-524)	0.005
C-Reactive Protein (mg/L), median (min-max)	122 (2-413)	121 (3-413)	124 (2-380)	0.976
Procalcitonin (ng/mL), median (min-max)	4.5 (0.11-100)	4.9 (0.1-100.0)	3.7 (0.1-100.0)	0.430
Alanine aminotransferase (u/L), median (min-max)	12 (1-456)	13 (2-456)	11 (1-139)	0.056
Sedimentation, median (min-max)	63 (3-140)	59 (3-140)	64 (13-133)	0.300
Blood Urea Nitrogen (mg/dL) (min-max)	43 (8-130)	41 (8-118)	45 (9-130)	0.503
Creatinine (mg/dL), median (min-max)	4.5 (0.7-14.0)	3.9 (0.7-12.5)	5.4 (1.1-14.0)	0.001

HD: hemodialysis.

Table 4. Causative microorganisms, antimicrobial susceptibilities, and comparison according to hemodialysis duration.

	Total	Group 1 HD year ≤ 1 Year (n = 136)	Group 2 HD year > 1 Year (n = 164)	*p*
Gram-positive bacteria	207 (69)	85 (62.5)	122 (74.3)	0.095
Coagulase negative staphylococci	31 (14.9)	13 (15.2)	18 (14.7)	0.658
Methicillin Resistant Staphylococcus aureus	41(19.8)	18 (21.1)	23 (18.8)	0.853
Methicillin Susceptible Staphylococcus aureus	92 (44.5)	41 (48.2)	51 (41.8)	0.798
Enterococcus spp.	30 (14.5)	12 (14.1)	18 (14.7)	0.185
Vancomycin Resistant *Enterococcus*	13 (6.2)	6 (4.4)	7 (4.2)	0.999
Gram negative bacteria	89 (30)	44 (32.0)	45 (33.5)	0.715
Escherichia coli	19 (21.3)	7 (15.9)	12 (26.6)	0.38
Klebsiella pneumoniae	15 (16.8)	9 (20.4)	6 (13.3)	0.25
Enterobacter cloacae	15 (16.8)	8(18.2)	7 (15.5)	0.516
Pseudomonas aeruginosa	13 (14.6)	7 (15.9)	6 (13.3)	0.523
Acinetobacter baumannii	10 (11.2)	5 (12.2)	5 (11.1)	0.74
Ralstonia pickettii	5 (5.6)	3 (6.8)	2 (4.4)	0.999
Stenotrophomonas maltophilia	6 (6.7)	2 (4.5)	4 (8.8)	0.3
Other	6 (6.7)	3 (6.8)	3 (6.6)	0.99
Yeast	4 (1.0)	3 (1.5)	1 (0.6)	0.592

HD: hemodialysis.

Table 5. Risk factors for intensive care transfer and mortality.

Transferring to the ICU	**Multivariate analysis OR (95% CI)**	***p***
Carbapenem resistance	7.657 (1.525-38.452)	0.013
History of any catheter revision	4.632 (1.248-17.199)	0.022
Leukocytosis (> 10 × 10^3/μL)	1.150 (1.046-1.266)	0.004
28-Day Mortality	**Multivariate analysis OR (95% CI)**	***p***
Transferring to the ICU	17.29 (2.54-139.39)	0.001
VRE infection	14.10 (1.67-32.64)	0.002

VRE: vancomycin-resistant enterococcus.

required for a specific agent, carbapenem + vancomycin was the most frequent choice (25.2%). A comparison between the two groups based on hemodialysis duration did not reveal significant differences in the selection of empirical or agent-specific antibiotic regimens (Supplementary Table 1).

A multivariate analysis was conducted to identify risk factors for poor outcomes (Table 5). The analysis identified carbapenem resistance (OR: 7.657, 95% CI: 1.525-38.452, p = 0.013), a history of any catheter revision (OR: 4.632, 95% CI: 1.248-17.199, p = 0.022), and leukocytosis (> 10 × 10^3/μL) (OR: 1.150, 95% CI: 1.046-1.266, p = 0.004) as significant risk factors for being transferred to the intensive care unit (ICU). For 28-day mortality, significant risk factors were transfer to the ICU (OR: 17.29, 95% CI: 2.54-139.39, p = 0.001) and infection with Vancomycin-Resistant Enterococcus (VRE) (OR: 14.10, 95% CI: 1.67-32.64, p = 0.002).

Discussion

This study was conducted at a university hospital with a capacity of 90 beds. It accepts complicated patients referred from peripheral health institutions and hemodialysis centers. All patients included in this study did not have their catheters placed in the same center. Therefore, the CRBSI rate was not calculated. The higher median patient age, longer hemodialysis duration, and greater comorbidities were attributed to the center's treatment of more complex cases. The median age of patients in this study was 68 years. In a study examining the incidence of CRBSI among hemodialysis patients in Spain between 2010 and 2014, the median age was reported as 54.9 years. In that study, the Aboriginal and Torres Strait Islander rate was reported as 60% and the CRBSI rate was reported to be higher in this patient group [10]. In a study examining 1-year CRBSIs at the largest tertiary health care facility in Ghana, the mean age was reported as 45 years [16]. The high number of geriatric patients in the study group suggested deficiencies in catheter care at home and in hemodialysis centers. Inadequate home catheter care and hygiene practices have been identified as significant contributors to catheter-related bloodstream infections in hemodialysis patients. Several studies have demonstrated that patients' or caregivers' insufficient training on aseptic techniques during home-based catheter maintenance increases the risk of infection and readmission rates [7,14].

In 37% of patients with a history of catheter revision due to CRBSI, 65% of the isolated microorganisms were Gram-positive. A study investigating risk factors for recurrent CRBSI in a pediatric intensive care unit found a 1.7-fold increased risk associated with an interval of less than 4 days between negative blood culture and the reinsertion of the second central venous catheter [17]. The duration of antimicrobial treatment, severity score, and advanced age were identified as risk factors for recurrent CRBSI in a study conducted in an adult ICU [18]. In a retrospective analysis of hemodialysis patients' tunneled catheter-associated bacteremia, 13 of 17 recurrences involved Gram-positive bacteria in the second instance, and Gram-positive bacteria were found in all recurrences after three [13]. Inadequate therapies, particularly in cases of *Staphylococcus aureus* bacteremia, may potentially contribute to recurrent CRBSI, even if the predominance of Gram-positive bacteria in the skin flora is the most relevant determinant [19].

It was demonstrated that the coronavirus disease 2019 (COVID-19) pandemic seasons of 2020, 2021, and 2022 were associated with higher case counts. In many studies evaluating the impact of the COVID-19 pandemic on healthcare-associated infections, significant increases were expressed, especially in CRBSI and *S. aureus* bacteremia [20,21]. In a meta-analysis of 21 clinical studies, primarily using national health registration system data, a statistically significant increase in the incidence of CRBSI was observed in 17 clinical studies compared to the pre-pandemic period [22]. The CLABSI rate decreased from 0.82 per 1,000 catheter days between February and May 2019 to 0.20 per 1,000 catheter days between February and May 2020 in a retrospective observational study comparing CRBSI rates seen in 71 hemodialysis patients [23].

This discrepancy in the literature likely reflects the variable impact of the pandemic on different healthcare settings. While some well-controlled outpatient units may have successfully enhanced their preventive

measures due to heightened awareness, the increased workload and patient density in a tertiary referral hospital such as ours likely overshadowed any potential benefits from universal precautions, contributing to the rise in infections observed in our cohort. When the groups were compared according to the duration of hemodialysis, it was seen that the average age, chronic diseases, and hospital and ICU stays were higher in patients whose HD duration was shorter than one year. It was thought that these results might be due to the treatment the patient group received during the COVID-19 pandemic period. A review examining the effect of the COVID-19 pandemic on the prognosis of chronic kidney disease emphasized that chronic kidney disease worsened COVID-19 severity, and severe COVID-19 was associated with increased acute kidney injury and the need for hemodialysis [24]. When 3697 patients with COVID-19 disease in Japan were divided into 3 groups according to their kidney functions as normal, acute kidney failure (AKF) without a history of CKD, and AKF with a history of CKD, it was seen that the rate of progression to critical findings was highest in AKF with a history of CKD [25].

The most frequently isolated microorganism in both groups, regardless of the duration of hemodialysis, was Gram-positive bacteria, particularly methicillin-susceptible *Staphylococcus aureus* (MSSA). Phillips *et al.* [26] reported that 66% of bloodstream infections among 99 patients treated between 2005 and 2018 were caused by Gram-positive bacteria, mostly *Staphylococcus aureus*. In the same study, patients with Gram-positive and Gram-negative causative agents were compared, and no difference in hemodialysis duration was observed between the groups [26].

One of the most significant findings of our study is the lack of difference in pathogen distribution and antimicrobial resistance between the groups, despite patients with shorter hemodialysis duration (Group 1) having a significantly higher frequency of recent hospitalizations and ICU stays—well-established risk factors for acquiring multi-drug resistant (MDR) organisms. This seemingly paradoxical result is best explained by the unique and dominant pathogenesis of CRBSI in the outpatient hemodialysis population.

The primary mechanism of CRBSI is colonization of the catheter by the patient's endogenous skin flora, which leads to the formation of a biofilm that serves as a reservoir for infection [27]. As Soi *et al.* highlight in their review, this process typically involves microorganisms migrating from the skin at the catheter exit site (extraluminal colonization) or contamination of the catheter hub (intraluminal colonization). This constant microbiological pressure from the patient's own commensal bacteria, particularly *Staphylococcus aureus*, appears to override the intermittent risk of acquiring a different, nosocomial pathogen during a recent hospital stay [27]. Therefore, our results strongly suggest that for CRBSI in hemodialysis outpatients, the immediate and persistent risk posed by skin flora is a more powerful determinant of the causative pathogen than recent exposure to an inpatient hospital environment [27,28].

Our analysis identified key risk factors for ICU transfer, which in turn are major predictors of mortality. These factors included leukocytosis ($> 10 \times 10^3/\mu L$), a history of any catheter revision, and carbapenem resistance. Leukocytosis is a direct indicator of a severe systemic inflammatory response [29]. The association with a history of catheter revision may suggest that patients with recurrent catheter-related issues are more vulnerable to severe infections [30,31]. Most notably, carbapenem resistance as a risk factor for ICU admission, similar to the VRE finding for mortality, underscores the challenge of managing infections caused by MDROs. These infections can lead to delayed appropriate therapy and clinical deterioration, necessitating intensive care [32,33]. These findings underscore the critical need for robust infection control measures to prevent the spread of VRE and carbapenem-resistant organisms, and emphasize the importance of promptly identifying and effectively treating these high-risk infections.

Limitations

This study has several key limitations that should be acknowledged. First, its retrospective and single-center design may limit the generalizability of our findings to other healthcare settings with different patient populations or infection control practices. Furthermore, the lack of a catheter-day denominator prevented the calculation of standardized infection incidence rates, which makes direct comparisons of infection burden over time and with other studies challenging.

Conclusions

In conclusion, data from hemodialysis patients treated for CRBSI diagnoses at the Nephrology Department of a tertiary hospital over a 6-year period were retrospectively examined. It was observed that the number of cases increased significantly in 2021-2022. This increase was likely due to the increased workload of healthcare workers during the COVID-19 pandemic, inadequate catheter care, and higher inpatient admissions from peripheral hospitals.

There were no differences in the causative microorganisms or antibiotic resistance rates by hemodialysis duration. This study also identified specific risk factors for poor outcomes: ICU transfer and VRE infection were significant predictors of 28-day mortality. At the same time, carbapenem resistance and a history of catheter revision were associated with ICU transfer. Therefore, empirical treatment should prioritize anti-staphylococcal coverage and consider these identified risk factors (such as potential VRE infection or carbapenem resistance) rather than relying on the duration of hemodialysis.

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Ethics approval and consent to participate

This study was approved by the Erciyes University Non-Interventional Clinical Research Ethics Committee, 04.10.2023, No:2023/652.

Authors' contributions

Dr Zeynep Ture: Data curation, investigation, methodology, writing – original draft preparation. Dr. Alparslan Demiray, Dr. Kadir Demirkutlu, Dr. Beyza Hayırlıdağ: Conceptualization, project administration, supervision, validation. Dr. Fatma Cevahir: Visualization, formal analysis. Dr İsmail Koçyiğit: Writing, review, and editing.

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Conflict of interest

No conflict of interest is declared.

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Annex – Supplementary Items

Supplementary Table 1. Evaluation of empirical and agent-specific treatments.

	Total (n = 300)	**Group 1 HD year ≤ 1 Year (n = 136)**	**Group 2 HD year > 1 Year (n = 164)**
Empirical antibiotics			
Monotherapy	**n = 127**	**n = 51**	**n = 76**
Ampicillin sulbactam	20 (15.7)	10 (19.6)	10 (13.1)
Cefazolin	10 (7.8)	4 (7.8)	6 (7.8)
Piperacillin Tazobactam	25(19.6)	11 (21.5)	14 (18.4)
Carbapenem	12 (9.4)	5 (9.8)	7 (9.2)
Vancomycin	45 (35.4)	19 (37.2)	26 (34.2)
Daptomycin	9 (7)	-	9 (11.8)
Ceftriaxone	6 (4.7)	2 (3.9)	4 (5.2)
Combination Treatment	**n = 173**	**n = 86**	**n = 87**
Piperacillin-tazobactam + Vancomycin	100 (57.8)	51 (59.3)	49 (56.3)
Carbapenem + Vancomycin	46 (26.5)	25 (29)	21 (24.1)
Daptomycin + Carbapenem	12 (6.9)	5 (5.8)	7 (8)
Piperacillin Tazobactam + Daptomycin	9 (5.2)	3 (3.4)	6 (6.8)
Aminoglycoside + Vancomycin	6 (3.4)	2 (2.3)	4 (4.5)
Agent-specific treatment antibiotics			
Monotherapy	**n = 197**	**n = 95**	**n = 102**
Ampicillin sulbactam	18 (9.1)	8 (8.4)	10 (9.8)
Cefazolin	38 (19.2)	20 (21)	18 (17.6)
Piperacillin-tazobactam	31 (15.7)	15 (15.7)	16 (15.6)
Carbapenem	32 (16.2)	12 (12.6)	20 (19.6)
Vancomycin	28 (14.2)	18 (18.9)	10 (9.8)
Teicoplanin	11 (5.5)	3 (3.1)	8 (7.8)
Daptomycin	8 (4)	3 (3.1)	5 (4.9)
Ceftriaxone	6 (3)	2 (2.1)	4 (3.9)
Ciprofloxacin	12 (6)	8 (8.4)	4 (3.9)
Other	13 (6.5)	6 (6.3)	7 (6.8)
Combination Treatment	**n = 103**	**n = 35**	**n = 68**
Piperacillin-tazobactam +Vancomycin	10 (9.7)	10 (28.5)	0
Carbapenem + vancomycin	26 (25.2)	9 (25.7)	17 (25)
Daptomycin + carbapenem	14 (13.5)	5 (14.2)	9 (13.2)
Piperacillin tazobactam + daptomycin	8 (7.7)	3 (8.5)	5 (7.3)
Ampicillin-sulbactam + rifampicin	14 (13.5)	4 (11.4)	10 (14.7)
Daptomycin + rifampin	14 (13.5)	2 (5.7)	12 (17.6)
Cefazolin + linezolid	8 (7.7)	1 (2.8)	7 (10.2)
Other	9 (8.7)	1 (2.8)	8 (11.7)