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**Research Article**

# Evaluation of Blood Culture Results in Catheter Associated Bloodstream Infections in Hemodialysis Patients

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**Abstract**

***Purpose:****Arteriovenous fistula or catheter-related bloodstream infection may develop due to catheter use in patients receiving hemodialysis treatment. This study aims to contribute to epidemiological data by evaluating blood cultures in patients receiving hemodialysis treatment and developing catheter-related bloodstream infection.*
***Methods:****In the present study, hemodialysis patients who were admitted to the hemodialysis unit, nephrology service and intensive care units of Dr. Ersin Arslan Training and Research Hospital between January 1, 2021 and February 29, 2024 and Gaziantep City Hospital between October 6, 2023 and February 29, 2024, who were over 18 years of age and who had microorganism growth in blood culture and/or catheter culture were included in the study. A total of 160 catheter-associated bloodstream infection episodes from 102 patients were retrospectively evaluated.*
***Results:****Of the 160 infection episodes included in this study, Gram-positive bacteria were isolated in 61.2%, Gram-negative bacteria in 33.8% and Candida spp. in 5%. Distribution of causative microorganisms was as follows; Staphylococcus aureus in 45 (28.1%), Coagulase Negative Staphylococcus (CNS) in 38(23.8%), Klebsiella pneumoniae in 18 (11.3%), Acinetobacter baumannii in 11 (6.9%), Escherichia coli in 9 (5.6%). Methicillin resistance was 37.2% in Staphylococcus aureus and 42.1% in CNS. Carbapenem resistance was 54.5% in Acinetobacter baumannii, 33.3% in Klebsiella pneumoniae and 22.2% in Escherichia coli, respectively.*
***Conclusions:*** *Determining the causative microorganisms of catheter-related bloodstream infections in hemodialysis patients and monitoring antibiotic resistance rates may guide empirical treatment selection and contribute to the development of more effective strategies for infection management.*

***Key Words:*** *Antibiotic resistance, Catheter-related bloodstream infection, Hemodialysis*

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## Introduction

Hemodialysis is the most common type of renal replacement therapy for the treatment of individuals with chronic renal failure (CRF). Infections are the second most common cause of morbidity and mortality in hemodialysis patients (1). The risk of infection increases in hemodialysis patients due to many reasons including impaired immune system, catheter use, disruption of the skin barrier system, comorbid diseases and malnutrition (2, 3). The risk of infection is high in these patients, especially bloodstream infections are frequently observed (1). Catheter-related bacteremia due to central venous catheter (CVC) or peripheral catheter use causes healthcare-associated infections in intensive care units (4). The most serious complication of catheter and bloodstream infection is sepsis and septic shock. It is one of the life-threatening complications in chronic hemodialysis patients. In patients who develop sepsis, the odds of dying were nearly three-fold higher vs hemodialysis patients with no sepsis (5).

Temporary or tunneled hemodialysis catheters are frequently used in patients requiring renal replacement therapy (6). In Turkey, the majority of patients undergo dialysis with temporary catheters which is associated with an increased risk of complications.

The gold standard in the diagnosis of infection in hemodialysis patients is the collection of a blood culture sample. The growth of the causative microorganism in culture samples is a pathfinder for diagnosis. Infections related to catheter use are frequently observed. In recent studies, the most common pathogens are Gram-positive bacteria. Gram-negative bacteria are observed less frequently and response rates to treatment are lower (7, 8). Gram-positive bacteria are usually found on the skin around the hemodialysis catheter site. Colonization creates a suitable microbiological environment for biofilm formation and growth of pathogenic bacteria (9, 10). Infection control measures lead to a decrease in the number of infections caused by Gram-positive microorganisms. In infections caused by Gram-negative microorganisms, the urinary system and gastrointestinal tract are significantly more likely to be the source (11) and the risk of infection with Gram-negative bacteria increases.. When the distribution of bloodstream infection pathogens in hemodialysis patients is examined, the most frequently observed pathogens are *Staphylococcus aureus*, coagulase negative staphylococci (CNS) and other Gram-positive pathogens. *Staphylococcal species* are usually resistant

to methicillin. Treatment and management of multidrug-resistant microorganisms is more difficult in hemodialysis patients (12, 13). The frequent use of central venous catheters in hemodialysis patients can lead to life-threatening complications such as catheter entry site infection, septic thrombophlebitis, endocarditis, metastatic infections, bacteremia and sepsis, and this effect increases mortality (14, 15). Therefore, early identification of infectious microorganisms and determination of their antibiotic susceptibility profiles will aid in early diagnosis and initiation of appropriate empirical treatment. With the effective communication and coordination of clinicians and medical laboratory staff, the antibiotic susceptibility profile of isolated strains can be evaluated and the surveillance data of each center can be documented. The causative microorganisms and antibiotic susceptibilities in hemodialysis patients should be monitored periodically.

The aim of this study was to analyze and evaluate the microbiologic results of blood cultures in patients receiving hemodialysis treatment for chronic renal failure (CRF) who developed catheter-related bloodstream infection (CRBSI). It is also aimed to guide treatment practice by determining epidemiologic data.

## Material and Methods

The This study complied with the standards of medical ethics as endorsed by decision 2024/06, dated 20.03.2024, of the Ethics Committee of Gaziantep City Hospital. The study population included hemodialysis patients over 18 years of age who were admitted to the hemodialysis unit, nephrology service and intensive care units of Dr. Ersin Arslan Training and Research Hospital between January 1, 2021 and February 29, 2024 and Gaziantep City Hospital between October 6, 2023 and February 29, 2024, and who were found to have microorganism growth in blood culture and/or catheter culture. Catheter-related infection was determined according to the Infectious Diseases Society of America (IDSA) criteria (16). Catheter tip colonization was defined as the production of >15 CFU microorganisms from the catheter tip. A catheter-related local infection was defined as local findings (induration, edema, increased temperature, purulent discharge) and growth of microorganisms in catheter tip culture. A catheter-related bloodstream infection was defined as presence of positive blood cultures from peripheral veins and signs of systemic infection, the absence of any other source of bacteremia other than the catheter,

and the presence of the same microorganism in the catheter tip colonization. Polymicrobial catheter cultures samples were not included in the present study. 160 episodes of CRBSIs from a total of 102 patients who fulfilled the criteria were retrospectively evaluated in this study.

**Sample processing and microbiologic diagnosis**

The blood culture samples obtained from patients with CRF who had received hemodialysis treatment and admitted to the hemodialysis unit, nephrology service and intensive care units of Dr. Ersin Arslan Training and Research Hospital between January 1, 2021 and February 29, 2024 and Gaziantep City Hospital between October 6, 2023 and February 29, 2024 were analyzed. The samples were collected in blood culture bottles (Render-China and bioMerieux-France) and transferred to the microbiology laboratory. Blood culture vials were incubated in a hemoculture device (Render-China and Bact/Alert 3D, BioMerieux France) for up to seven days for growth control. When a positive signal was obtained from the hemoculture device indicating growth in the culture, the slides were prepared from the relevant bottles and processed by Gram staining method. The slides were subcultured on 5% sheep blood agar, chocolate agar and eosin methylene blue (EMB) agar (GBL, RTA, Turkey) and incubated at 37°C for 18-24 hours. At the end of incubation, colonies on the media with growth were identified at the species level using a completely automated system (VITEK® 2 AST , bioMerieux, France). Antibiotic susceptibility tests were performed in accordance with European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria.

**Results**

A total of 160 episodes of CRBSIs from 102 patients were analyzed in this study. The mean age of the patients was 58.96±14.59 years (23-86), 60 (58.8%) were female and 42 (41.2%) were male. Of the 160 episodes of CRBSIs, Gram-positive bacteria were isolated in 61.2%, Gram-negative bacteria in 33.8% and Candida species in 5%. Distribution of causative microorganisms; *Staphylococcus aureus* in 45 (28.1%), coagulase negative staphylococcus (CNS) in 38 (23.8%), *Klebsiella pneumoniae* in 18 (11.3%), *Acinetobacter baumannii* in 11 (6.9%), *Escherichia coli* in 9 (5.6%), *Candida spp*. in 8 (5%), *Enterobacter cloacae complex* in 7 (4.4%), *Enterococcus faecalis* in 6 (3.8%), *Enterococcus faecium* in 5 (3.1%), *Stenotrophomonas maltophilia* in 4 (2.5%), *Proteus mirabilis* in 3 (1.9%), *Serratia marcescens* in 2 (1.3%), *Enterococcus gallinarum* in 1 (0.6%), *Corynebacterium spp*. in 1 (0.6%), alpha

hemolytic Streptococcus in 1 (0.6%) and *Streptococcus sanguinis* in 1 (0.6%) (Table 1). Methicillin resistance was 37.2% in *Staphylococcus aureus* isolates and 42.1% in CNS isolates. Carbapenem resistance was 54.5% in *Acinetobacter baumannii*, 33.3% in *Klebsiella pneumoniae* and 22.2% in *Escherichia coli* (Table 2). There was no vancomycin resistance in Enterococcus strains and no azole resistance in Candida albicans and non-albicans Candida isolates.

**Table 1.** Bacteria isolate among patients undergoing hemodialysis**.**

| The causative microorganism | Total No | Frequency (%) |
|---|---|---|
| *Staphylococcus aureus* | 45 | 28.1 |
| CNS | 38 | 23.8 |
| *Klebsiella pneumoniae* | 18 | 11.3 |
| *Acinetobacter baumannii* | 11 | 6.9 |
| *Escherichia coli* | 9 | 5.6 |
| *Candida spp.* | 8 | 5.0 |
| *Enterobacter cloacae complex* | 7 | 4.4 |
| *Enterococcus faecalis* | 6 | 3.8 |
| *Enterococcus faecium* | 5 | 3.1 |
| *Stenotrophomonas maltophilia* | 4 | 2.5 |
| *Proteus mirabilis* | 3 | 1.9 |
| *Serratia marcescens* | 2 | 1.3 |
| *Enterococcus gallinarum* | 1 | 0.6 |
| *Corynebacterium spp.* | 1 | 0.6 |
| *Alpha-hemolytic Streptococcus* | 1 | 0.6 |
| *Streptococcus sanguinis* | 1 | 0.6 |

**Table 2.** The distribution of resistance of microorganisms.

| Microorganisms | Frequency (%) |
|---|---|
| **Meticillin resistance** | |
| MRSA | 37.2 |
| MRCNS | 42.1 |
| **Carbapenem resistance** | |
| *Acinetobacter baumannii* | 54.5 |
| *Klebsiella pneumoniae* | 33.3 |
| *Escherichia coli* | 22.2 |

MRSA: Meticillin resistant *Staphylococcus aureus*, MRCNS: Methicillin Resistant Coagulase Negative Staphylococcus

**Discussion**

Hemodialysis is the most frequently used type of renal replacement therapy in the treatment of individuals with chronic renal failure. It is the primarily used dialysis method with a frequency of 80% in 79% of countries (17). The increased risk of infection in hemodialysis patients is due to many reasons including impaired immune system, catheter use, disruption of the skin barrier system, comorbid diseases and malnutrition (2,3). It has been observed that 85% of healthcare-associated bloodstream infections are related to CVC (18). In patients undergoing hemodialysis treatment, CRBSIs and catheter colonization have been reported to occur at rates of 4.2%-4.8% (19). In Turkey, the majority of patients initially enter dialysis with temporary catheters and the frequency of infection increases with short-term use of CVCs (4.4%, 2.7 per 1000 catheter-days) (20).

In this respect, microbiological analysis of blood culture results and evaluation of antibiotic resistance patterns are important for early diagnosis of infections in hemodialysis patients. A review of the literature revealed that Gram-positive microorganisms are the most common cause of CRBSIs. Berman et al. reported that the most common bloodstream infection pathogen in hemodialysis patients was CNS, followed by *Staphylococcus aureus* (21). Fram et al. reported that MRSA was isolated as the most prevalent resistant pathogen in hemodialysis patients and found that it was associated with increased morbidity and mortality (22). In the other study, it was reported that the most frequently isolated microorganism from blood cultures was staphylococci and the most common isolate was CNS (23). In the study in which 109 episodes of CRBSIs were analyzed, the distribution of pathogens isolated in blood cultures was as follows: 21.1% MRCNS, 21.1% methicillin-sensitive , 13.8% MRSA and 0.9% MSCNS (18). Quittnat Pelletier et al. reported that 75.4% of the microorganisms isolated from hemodialysis catheter cultures were Gram-positive and 24.6% of them were Gram-negative pathogens (24). In a study conducted in 2024, it was noted that the most common isolates seen in hemodialysis patients were Gram-positive microorganisms and the most common isolate was Staphylococcus aureus. It was additionally emphasized that the incidence of Gram-negative organisms has been gradually rising throughout the years (25). The findings of the present study were similar to those in the literature. 61.2% of the total isolates were Gram-positive pathogens. The most common Gram-positive pathogens were *Staphylococcus aureus* (28.1%) and CNS (23.8%).

The methicillin resistance of *Staphylococcus aureus* isolates was 37.2% and that of CNS isolates was 42.1%.

It has been demonstrated that Gram-negative bacterial isolates have increased over the years in CRBSIs in hemodialysis patients. In the study conducted by Sahli et al. in hemodialysis patients, the distribution of the causative microorganisms isolated in blood cultures was as follows; *Klebsiella pneumoniae* in 26.5%, CNS in 23.5% and *Staphylococcus aureus* in 23.5% and it was emphasized that the rate of Gram-negative pathogens increased (26). In a further study conducted between 2000 and 2004, 203 organisms were isolated from 153 positive blood cultures; the distribution of Gram-positive, Gram-negative and *Candida spp*. isolates was 55.7%, 43.3% and 1%, respectively. It was found that there was a tendency for a quantitative decrease in Gram-positive infections (64.3% vs. 34.8%, respectively) and a quantitative increase in Gram-negative and polymicrobial bacteremia (17.9 vs. 21.7 and 17.9 vs. 43.5, respectively) between 2000 and 2004, and it was documented that Enterobacter spp. was most frequently detected among Gram-negative bacterial isolates in hemodialysis patients (27). The studies conducted in the United States of America and Spain have shown that the rate of catheter-related bacteremia caused by Gram-negative organisms has increased (8,28). In a study published in 2023, an increase in the incidence of Gram-negative bacteria was observed in CRBSIs (29). In the other study in which Gram-negative microorganisms increased, *Klebsiella pneumoniae* (22.2%) was the most frequently isolated pathogen followed by *Staphylococcus aureus* (18.5%), CNS (14.8%) *E. coli* (14.8%) and *Pseudomonas aeruginosa* (9.6%) (30). In conclusion, it was emphasized that Gram-negative pathogens should be included in the empirical treatment protocol due to the increasing prevalence of Gram-negative pathogens in the etiology of bloodstream infections in chronic hemodialysis patients. In addition, it has been emphasized that epidemiologic data should be followed in order to initiate empirical antibiotic treatment (30, 31). Gram-negative bacteremia in hemodialysis patients occurs by endogenous or exogenous transmission. Exogenous transmission occurs from patient to patient via healthcare workers and the environment, endogenous transmission is a result of the passage of intestinal flora (13). The importance of multiple antibiotic resistance in Gram-negative isolates has been reported in these studies. In hemodialysis patients, antibiotic resistance rates of Gram-negative bacteria in CRBSIs are remarkable in terms of early diagnosis and mortality. In the present study, the prevalence of Gram-negative bacteria was

33.8% and the most frequent isolate was *Klebsiella pneumoniae* (11.3%) (Table 1). The literature contains case reports of *Candida spp*. infection in hemodialysis patients. Sahli et al. (26) reported that candida infection was observed in only two of 94 patients. It has been predicted that *Candida spp*. related infections may occur when with infection control measures decreases and inappropriate antibiotic use increases (8, 30). In the present study, *Candida spp*. were isolated in 5% of the patients. It was found in patients with prolonged intensive care unit hospitalization and long-term antibiotic use.

In hemodialysis patients, the increasing rate of antibiotic resistance in bloodstream infections affects prognosis and mortality. Multidrug resistance complicates the treatment pathway. In the current study, methicillin resistance was found to be 37.2% in *Staphylococcus aureus* isolates and 42.1% in CNS isolates (Table 2). Carbapenem resistance of Gram-negative bacteria was 54.5% in *Acinetobacter baumannii*, 33.3% in *Klebsiella pneumoniae* and 22.2% in *Escherichia coli*, respectively. It was observed that multiple drug resistance is gradually increasing in studies in the literature (5, 22, 23, 25-28, 30). Catheters are being used for hemodialysis treatment, medical treatment and nutritional support in hospitals (29). Prevention of catheter-related infections in hemodialysis patients is a critical issue. The distinction between colonization, infection and contamination should be ensured in CRBSIs. The differentiation should be made easily with the cooperation and coordination of clinicians and medical laboratory physicians. Culture results should be monitored in terms of infectious pathogens and antimicrobial resistance and precautions should be planned when necessary.

Treatment options for CRBSIs include catheter removal, catheter exchange or systemic antibiotic administration (32). Prevention package of catheter infections includes rules such as catheter insertion by trained personnel, ensuring compliance with disinfection and asepsis rules (hand hygiene, wearing sterile gloves, hand disinfection and use of masks, etc.), and insertion of the catheter with imaging if possible. The infection rate can be reduced by using disposable catheters, closing the catheter tip after the procedure and not using the catheter for other purposes. In addition, if it is necessary to use a catheter for more than four weeks, the use of tunneled catheters should be recommended (33). It is attempted to decrease the rates of CRBSIs with methods such as topical antibiotic use, antibiotic locking method, use of antimicrobial coated catheters,

application of fibrinolytic agent to remove the biofilm formed in the catheter and catheter replacement over a guide wire (33, 34).

## Conclusion

In conclusion, early diagnosis and treatment of catheter-related bloodstream infections (CRBSIs), which affect mortality and morbidity in hemodialysis patients, are of great importance. Whenever feasible, active screening of hemodialysis patients is recommended. Identification of microorganisms isolated from blood cultures, monitoring of antibiotic resistance rates, and analysis of epidemiological data may guide the selection of empirical therapy and contribute to the development of more effective strategies for infection management and treatment optimization..

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## Author Contribution

H. B.: Study hypothesis, design, management, data collection and writing.

M. T.: Data collection/ processing/ analysis/ interpretation.

S. A.: Provision of facts/equipment and reviewing.

A. S.: Data collection, provision of equipment and reviewing.

## Conflict of Interest

The authors declare no conflict of interest.

## Ethics Committee Approval

This study was conducted in accordance with the principles of the Declaration of Helsinki. This study complied with the standards of medical ethics as endorsed by decision 2024/06, dated 20.03.2024, of the Non-invasive Clinical Trials Ethics Committee of Gaziantep City Hospital.

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