Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2025;50(1):1-10
DOI: 10.17826/cumj.1548878

RESEARCH

Antibiotic susceptibilities and microorganisms isolated from blood cultures of inpatients in a secondary state hospital in Türkiye

Türkiye'de ikinci basamak bir devlet hastanesinde yatan hastaların kan kültürlerinden izole edilen mikroorganizmalar ve antibiyotik duyarlılıkları

Eyyüp Kaya[1], Hamide Kaya[2], Candan Öztürk[2]

[1]Toros State Hospital, Mersin, Türkiye
[2]Mersin University, Mersin, Türkiye

Abstract

Purpose: The aim of this study was to evaluate the bacterial species distribution and antibiotic susceptibility in blood cultures obtained from patients in a secondary care center in Mersin, Türkiye.

Materials and Methods: Blood culture specimens of inpatients sent to the microbiology laboratory between January 2022 and December 2023 were retrospectively analyzed to determine the etiologic agents of bloodstream infections and to evaluate their antimicrobial susceptibility. Samples were processed using the BD Bactec FX40 automated blood culture system (BD, USA), which allows continuous monitoring and rapid detection of microbial growth. Typing of causative agents in positive cultures and antimicrobial susceptibility testing were performed using conventional methods and the Vitek2 Compact automated system.

Results: Microbial growth was observed in 369 (42.7%) of 864 patients. Of the microorganisms isolated, 79.4% (293) were Gram-positive bacteria, 18.2% (67) were Gram-negative bacteria and 2.4% (9) were yeasts. *Escherichia coli* (26.9%) was the most frequently isolated Gram-negative bacterium followed by *Acinetobacter baumannii* (20.9%), *Enterobacter cloacae* (13.4%), *Klebsiella pneumoniae* (13.4%) and *Pseudomonas aeruginosa* (13.4%). Among Gram-positive bacteria, coagulase-negative staphylococci (81.2%) and *Staphylococcus aureus* (10.2%) were most frequently isolated. Methicillin resistance was found in 30.0% of *S. aureus* and 71.8% of coagulase-negative staphylococci. No resistance to vancomycin, tigecycline or daptomycin was observed. Extended-spectrum β-lactamase production was detected in 44.4% of *E. coli* and 55.5% of *Klebsiella* spp.

Conclusion: This study highlights the local prevalence of bacterial isolates in bloodstream infections and emphasizes the need for routine monitoring of etiologic agents and

Öz

Amaç: Bu çalışmanın amacı Mersin, Türkiye'de bulunan bir ikinci basamak merkezindeki hastalardan alınan kan kültürlerinde bakteri tür dağılımını ve antibiyotik duyarlılığını değerlendirmektir.

Gereç ve Yöntem: Ocak 2022 ve Aralık 2023 tarihleri arasında yatan hastalardan mikrobiyoloji laboratuvarına gönderilen kan kültürü örnekleri, kan dolaşımı enfeksiyonlarının etiyolojik ajanlarını belirlemek ve antimikrobiyal duyarlılıklarını değerlendirmek için retrospektif olarak analiz edilmiştir. Örnekler, sürekli izleme ve mikrobiyal üremenin hızlı bir şekilde tespit edilmesini sağlayan BD Bactec FX40 otomatik kan kültürü sistemi (BD, ABD) kullanılarak işlenmiştir. Pozitif kültürlerde etkenlerin tiplendirilmesi ve antimikrobiyal duyarlılık testleri konvansiyonel yöntemler ve Vitek2 Compact otomatize sistemi kullanılarak gerçekleştirilmiştir.

Bulgular: 864 hastanın 369'unda (%42,7) mikrobiyal üreme görüldü. İzole edilen mikroorganizmaların %79,4'ü (293) Gram-pozitif bakteriler, %18,2'si (67) Gram-negatif bakteriler ve %2,4'ü (9) mayalardan oluşuyordu. Gram negatif bakteriler arasında en sık izole edilen bakteri *Escherichia coli* (%26,9) olup sırasıyla *Acinetobacter baumannii* (%20,9), *Enterobacter cloacae* (%13,4), *Klebsiella pneumoniae* (%13,4), *Pseudomonas aeruginosa* (%13,4) izledi. Gram pozitif bakteriler arasında ise en sık CoNS (%81,2) ve *Staphylococcus aureus* (%10,2) izole edildi. Metisilin direnci *S. aureus*'un %30,0'unda ve koagülaz-negatif stafilokokların %71,8'inde bulundu. Vankomisin, tigesiklin veya daptomisine karşı direnç gözlenmedi. *E. coli*'nin %44,4'ünde ve *Klebsiella* spp'nin %55,5'inde genişlemiş spektrumlu β-laktamaz üretimi tespit edildi.

Sonuç: Bu çalışma, kan dolaşımı enfeksiyonlarında bakteriyel izolatların yerel yaygınlığını belirtmekte ve

Address for Correspondence: Hamide Kaya, Mersin University Faculty of Medicine, Department of Medical Microbiology, Mersin, Türkiye. E-mail: hamidekirac@gmail.com
Received: 19.09.2024 Accepted: 29.12.2024

antibiotic susceptibility to prevent resistance and aid rational antibiotic use.

Keywords:. Blood culture, bloodstream infections, antimicrobial susceptibility, multidrug resistance, sepsis.

direnci önlemek ve akılcı antibiyotik kullanımına yardımcı olmak için etiyolojik ajanların ve antibiyotik duyarlılığının rutin olarak izlenmesi gerektiğini vurgulamaktadır.

Anahtar kelimeler: Kan kültürü, kan dolaşımı enfeksiyonları, antimikrobiyal duyarlılık, çoklu ilaç direnci, sepsis.

INTRODUCTION

Bloodstream infections (BSIs) in hospitalized patients can manifest with a wide range of clinical symptoms, varying from asymptomatic cases to fatal sepsis[1]. These infections represent a significant cause of morbidity and mortality, with BSIs and sepsis being among the leading causes of death following hospital admission. In developed countries, hospital-acquired infections account for approximately 40% of hospital-related deaths[2]. Particularly concerning are antimicrobial-resistant (AMR) bacterial infections, which pose significant health challenges in developing nations, with their global impact becoming increasingly evident. The misuse of antibiotics has contributed to the proliferation of these resistant bacteria, limiting available antimicrobial treatment options[3].

The Surviving Sepsis Campaign International Guidelines published in 2021 recommend the collection of blood cultures prior to the initiation of antimicrobial therapy in septic patients. This approach highlights the importance of blood cultures in accurately identifying infectious agents and guiding appropriate treatment[4]. Blood cultures play a critical role in identifying pathogens responsible for both community-acquired and hospital-associated BSIs, and the results are essential for selecting tailored antibiotic therapies for individual patients[5]. However, the epidemiology of central line-associated bloodstream infections (CLABSI) is influenced by various factors, including age group, infection source, healthcare context, and the clonal distribution of pathogenic strains. These variables significantly determine the type and spread of BSIs. Recent years have witnessed an increase in Gram-negative bacterial infections, revealing the growing prevalence of resistance mechanisms in hospital settings[6].

The study conducted over two years at a secondary public hospital in Mersin Province provides critical insights into the prevalence of BSIs and the antimicrobial susceptibility profiles of the pathogens responsible for these infections. This research adds to the existing literature by highlighting specific regional data on BSIs, which is essential for tailoring infection management strategies and antibiotic stewardship programs in clinical practice. The hypothesis of the study posits that understanding the prevalence and resistance patterns of pathogens responsible for BSIs will facilitate the development of effective infection control measures and enhance the judicious use of antibiotics. The study's results are expected to contribute to a better understanding of the local epidemiology of BSIs, which is crucial for healthcare providers in making informed decisions regarding empirical therapy and for developing targeted interventions to mitigate the impact of antimicrobial resistance.

MATERIALS AND METHODS

Study design and sample

The study was conducted retrospectively at a secondary state hospital located in Mersin, Turkiye, utilizing the medical records of patients with suspected BSIs admitted to the microbiology laboratory between January 2022 and December 2023. This institution is equipped with a microbiology laboratory that adheres to national standards for laboratory practices, ensuring the reliability and accuracy of the medical records utilized in this research. The laboratory employs qualified personnel who follow established protocols for the collection, processing, and analysis of microbiological samples, thereby enhancing the credibility of the data obtained from patient records.

The study focused on adult patients with suspected BSIs admitted. The criteria for inclusion were clearly defined: only adult patients presenting with clinical signs indicative of BSIs, such as fever, hypotension, or other systemic infection symptoms, were considered for inclusion. Blood cultures were collected based on these clinical indications to ensure that the samples were relevant to the diagnosis of BSIs.

Exclusion criteria were also rigorously applied to maintain the integrity of the study's findings. Specifically, patients who had received prior antibiotic therapy within the last 24 hours were excluded, as such treatment could significantly impact the results of blood cultures by suppressing bacterial growth or altering the microbial flora. Additionally, blood cultures from patients with known immunosuppression or those with chronic infections were excluded based on clinical judgment, as these conditions could confound the interpretation of culture results and complicate the identification of the causative pathogens.

Procedure

This study was approved by the Ethical Committee for Clinical Research of the Rectorate of Mersin University with decision number 2023/688 on 18.10.2023.

A blood sample of 5 ml was aseptically collected from each adult patient using 70% alcohol and 2% povidone-iodine for skin disinfection, following national and international guidelines on blood culture collection[7].

Blood cultures were obtained at appropriate times, considering the patient's clinical condition and symptoms, and in accordance with standard protocols. Blood culture collection was timed to ensure proper diagnostic yield, typically at the onset of fever or other systemic symptoms, with samples taken from different sites if clinically indicated.

Identification of positive blood cultures

Blood cultures were incubated in BacTAlert3D (Biomerieux, France), a fully automated system designed to detect microbial growth. Cultures were incubated for a standard duration of 7 days. In cases of suspected slow-growing pathogens, such as *Brucella* spp., incubation was extended. Vials showing no significant growth by day 7 were considered negative for culture. When a positive alarm was received, Gram staining was performed, and cultures were inoculated onto sheep blood agar, eosin methylen blue agar, and chocolate agar, followed by evaluation after 18-24 hours of incubation at 37°C.

A positive blood culture was defined as the growth of the same microorganism in both blood culture bottles taken simultaneously and clinical signs or symptoms consistent with a bloodstream infection. In our study, only one of the simultaneous growths was included in the study. In cases where more than one organism was detected, the possibility of contamination was carefully considered and further clinical correlation was required. Blood cultures containing skin flora organisms (e.g. Coagulase-negative Staphylococci (CoNS) or *Staphylococcus epidermidis*) in the absence of systemic infection were classified as contamination. Results considered to be contamination were excluded.

The identification of bacterial isolates was performed using an automated Vitek 2 Compact system (Biomerieux, France) with the aid of Gram-positive, Gram-negative, and yeast identification cards. Antimicrobial susceptibility testing was also conducted using the Vitek 2 Compact system (Biomerieux, France). Resistance to methicillin was identified based on cefoxitin screening tests or oxacillin MIC, which were used to classify methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant coagulase-negative staphylococci (MRCoNS). The antimicrobial susceptibility test results were interpreted according to the guidelines of the European Committee on Antimicrobial Susceptibility Testing (EUCAST), version 13.0[8].

Extended-spectrum β-lactamase (ESBL) screening was performed using double disk synergy test. Carbapenemase screening was not performed for gram negative bacteria with carbapenem resistance.

Two reference strains, *Escherichia coli* (ATCC 25922) and *Staphylococcus aureus* (ATCC 25923), were used as controls for the identification and antimicrobial susceptibility testing to ensure the reliability and accuracy of the laboratory procedures.

Statistical analysis

The Statistical Package for Social Sciences (IBM SPSS Software, USA) 24.0 was used to analyze the data. Categorical measurements were calculated as numbers and percentages, and continuous measurements were calculated as mean and standard deviation (median and minimum-maximum where necessary). Chi-Square Test (χ^2) was used to compare the rates of different microorganism species or resistance profiles between groups. T-tests were used to compare the mean values of continuous variables between different groups (e.g. resistant and susceptible isolates, different patient demographics). Statistical significance was accepted as 0.05 in all tests.

RESULTS

Growth was detected in 369 (42.7%) of the total 864 patients. Of the patients, 506 (58.6%) were male and 358 (41.4%) were female. Of those with growth, 201 (54.5%) were male and 168 (44.5%) were female. The mean age of males was 58.6±19.5 years and the mean age of females was 68.6±17.9 years ($p<0.05$). The age range of the patients was 19-101 years and the number of culture-positive patients was 58 (15.7%) in the 19-40 age range, 87 (23.7%) in the 41-60 age range, 152 (41.2%) in the 61-80 age range, and 72 (19.5%) in the 81-101 age range. When the patients with positive blood cultures were evaluated according to the distribution of age groups, a significant difference was observed in patients over the age of 60 ($p<0.05$).

Among the isolated microorganisms, Gram-positive bacteria were 79.4% (293), Gram-negative bacteria 18.2% (67), and yeasts 2.4% (9). Microorganisms isolated from blood samples were most frequently obtained from intensive care units 73.2% (270), and second most frequently from hemodialysis units 12.4% (46) (Table 1). The culture positivity rate was found to be higher in the intensive care unit ($p<0,05$).

Among the Gram-positive bacteria isolated, CoNS isolates were in the first place with 81.2% (238), followed by *S. aureus* 10.2% (30), *Enterococcus faecalis* 3.8% (11), *Enterococcus faecium* 2.4% (7), *Streptococcus (Group A/B)* 2.4% (7) (Table 2). Among the Gram-negative bacteria isolated, *E. coli* was the first isolate with 26.9% (18), followed by *Acinetobacter baumannii* 20.9% (14), *Klebsiella pneumoniae* 13.4% (9), *Enterobacter cloacae* 13.4% (9), *Pseudomonas aeruginosa* 13.4% (9), *Proteus mirabilis* 7.5% (5), *Serratia marcescens* 4.5% (3) (Table 2).

Table 1. Distribution of patients according to wards

Services	(n)	%
Intensive care unit	270	73.2
Hemodialysis unit	46	12.4
Infectious diseases service	32	8.7
Urology service	14	3.8
Palliative care service	7	1.9
Total	369	100.0

Table 2. Distribution of microorganisms isolated from blood samples

Gram-positive	(n)	%	Gram-negative	(n)	%
Enterococcus faecalis	11	3.8	*Acinetobacter baumannii*	14	20.9
Enterococcus faecium	7	2.4	*Enterobacter cloacae*	9	13.4
CoNS	238	81.2	*Escherichia coli*	18	26.9
Staphylococcus aureus	30	10.2	*Klebsiella pneumoniae*	9	13.4
Streptococcus (Group A/ B)	7	2.4	*Proteus mirabilis*	5	7.5
			Pseudomonas aeruginosa	9	13.4
			Serratia marcescens	3	4.5
Total	293	100	Total	67	100.0

CoNS: Coagulase-negative staphylococci

Methicillin resistance was detected in 30.0% (9) of *S. aureus* isolates and 71.8% (171) of CoNS isolates. However, no resistance was observed to vancomycin, tigecycline or daptomycin in these isolates. *E. faecalis* was 9% (1) and *E. faecium* was 14.3% (1) resistant to vancomycin. While linezolid resistance was not observed in *E. faecalis, E. faecium, S. aureus*, linezolid resistance was detected in 5.9% (14) of CoNS isolates (Table 3). ESBL positivity was determined in 44.4% (8/18) isolates of *E. coli*, and 55.5% (5/9) isolates of *Klebsiella spp. E. cloacae, E. coli, K. pneumoniae* were not resistant to colistin. *A. baumanii 21.4% (3), P. mirabilis 100% (5), P. aeruginosa 33.3% (3)* were resistant to colistin. No meropenem resistance was observed in *E. cloacae, E. coli* and *P. mirabilis*. However, 100% (14) of *A. baumanii,* 44.4% (4) of *K. pneumoniae* and 33.3% (3) *of P. aeruginosa* were resistant to meropenem (Table 4).

Table 3. Antibiotic susceptibility of Gram-positive bacteria

	Enterococcus faecalis (n=11)	*Enterococcus faecium* (n=7)	*Staphylococcus aureus* (n=30)	*CoNS* (n=238)	*Group A/B Streptococcus* (n=7)
AMC	-	-	-	-	62.5% (5)
AMP	100% (11)	14.2% (1)	-	-	-
CIP	72.7% (8)	28.5% (2)	3.3% (1)	0% (0)	-
DA	-	-	70.0% (21)	40. %3 (96)	87.5% (7)
DAP	-	-	100% (30)	100% (238)	87.5% (7)
E	-	-	73.3% (22)	19.7% (47)	87.5% (7)
FA	-	-	86.7% (26)	19.3% (46)	-
FOX	-	-	70% (21)	28.1% (67)	-
FS	-	-	100% (30)	68.1% (162)	-
GEN	72.7% (8)	0% (0)	86.7% (26)	68.9% (164)	87.5% (7)
LEV	72.7% (8)	28.5% (2)	3.3% (1)	0% (0)	87.5% (7)
LNZ	100% (11)	100% (7)	100% (30)	94.1% (224)	87.5% (7)
NIT	82.0% (9)	71.4% (5)	-	-	-
OX	-	-	66.7% (20)	26.9% (64)	-
PEN	-	-	20% (6)	0% (0)	62.5% (5)
SXT	63.6% (7)	14.2% (1)	86.7% (26)	76. %4 (182)	87.5% (7)
TEC	100% (11)	85.7% (6)	100% (30)	92.4% (220)	87.5% (7)
TET	-	-	83.3% (25)	61.3% (146)	62.5% (5)
TGC	100% (11)	100% (7)	100% (30)	100% (238)	-
VA	91.0% (10)	85.7% (6)	100% (30)	100% (238)	87.5% (7)

AMC: Amoxicillin clavulanic acid, AMP: Ampicillin, CIP: Ciprofloxacin, DA: Clindamycin, DAP: Daptomycin, E: Erythromycin, FA: Fusidic asite, FOX: Cefoxitin, FS: Phosphomycin, GEN: Gentamicin, LEV: Levofloxacin, LNZ: Linezolid, NIT: Nitrofrantoin, OX: Oxacillin, PEN: Penicillin, SXT: Trimethporim sulfamethaxazole, TEC: Teikoplanin, TET: Tetracycline, TGC: Tigicycline, VA: Vancomycin.

Table 4. Antibiotic susceptibility of Gram-negative bacteria

	Acinetobacter baumannii (n=14)	*Enterobacter cloacae* (n=9)	*Escherichia coli* (n=18)	*Klebsiella pneumoniae* (n=9)	*Proteus mirabilis* (n=5)	*Pseudomonas aeruginosa* (n=9)	*Serratia marcescens* (n=3)
AK	0% (0)	100% (9)	88.9% (16)	77.8% (7)	80% (4)	77.8% (7)	100% (3)
AMC	-	0% (0)	50% (9)	0% (0)	60% (3)	-	0% (0)
AMP	-	0% (0)	33.3% (6)	%0 (0)	20% (1)	-	0% (0)
CAZ	0% (0)	89.0% (8)	61.1% (11)	33.3% (3)	100% (5)	0% (0)	100% (3)
CIP	0% (0)	89% (8)	39.0% (7)	22.2% (2)	20% (1)	0% (0)	100% (3)
COL	78.6% (11)	100% (9)	100% (18)	100% (9)	0% (0)	66.7% (6)	0% (0)
CRO	0% (0)	100% (9)	55.6% (10)	33.3% (3)	100% (5)	-	100% (3)
CXM	-	-	39.0% (7)	0% (0)	-	-	0% (0)
CXM AX	-	-	55.6% (10)	33.3% (3)	-	-	0% (0)
ETP	0% (0)	100% (9)	100% (18)	44.4% (4)	100% (5)	-	100% (3)
FEP	0% (0)	100% (9)	55.6% (10)	33.3% (3)	100% (5)	0% (0)	100% (3)
FOX	-	0% (0)	5.6 % (1)	44.4% (4)	-	-	0% (0)
GEN	0% (0)	100% (9)	77.8% (14)	66.7% (6)	20% (1)	88.9% (8)	100% (3)
IMP	0% (0)	100% (9)	100% (18)	55.6% (5)	0% (0)	0% (0)	100% (3)
LEV	0% (0)	89.0% (8)	39.0% (7)	22.2% (2)	40% (2)	0% (0)	100% (3)
MEM	0% (0)	100% (9)	100% (18)	55.6% (5)	100% (5)	66.7% (6)	100% (3)
SXT	0% (0)	89.0% (8)	50% (9)	77.8% (7)	20%0 (1)	-	100% (3)
TOB	78.6% (11)	-	-	-	-	88.9% (8)	-
TZP	0% (0)	89.0 % (8)	88.9% (16)	55.6% (5)	100% (5)	0% (0)	100% (3)

AK: Amikacin, AMC: Amoxicillin clavulanic acid, AMP: Ampicillin, CAZ: Ceftazidim, CIP: Ciprofloxacin, COL: Colistin, CRO: Ceftriaxone, CXM: Cefuroxime, CXM AX: Cefuroxime acetyl, ETP: Ertapenem, FEP: Cefepim, FOX: Cefoxitin, GEN: Gentamicin, IMP: Imipenem, LEV: Levofloxacin, MEM: Meropenem, SXT: Trimethporim sulfamethaxazole, TOB: Tobramycin, TZP: Piperacillin tazobactam.

Candida albicans was the most common yeast fungus with a frequency of 66.6% (6/9), *Candida guilliermondii* 11.1% (1/9), *Candida parapsilosis* 11.1% (1/9), *Candida tropicalis* 11.1% (1/9). While *C. guilliermondii* was found to be intermediate resistant to fluconazole, fluconazole resistance was not detected in other *Candida* species.

DISCUSSION

Gram-negative bacteria, such as *E. coli, P. aeruginosa, K. pneumoniae, S. marcescens, Salmonella* spp, and *E. cloacae*, are the most common cause of BSIs. Gram-positive bacteria, such as *Staphylococcus, Streptococcus*, and *Enterococcus* species, can also enter the bloodstream[9]. Hospital-acquired BSIs can significantly increase the risk of morbidity and mortality, worsening the condition of hospitalized patients. Therefore, prompt identification and antibiotic treatment are necessary[10]. BSIs account for 9-11% of hospital-acquired infections in Europe and the US, with higher prevalences of up to 19% recorded in undeveloped and developing countries[11]. In developing countries, the rate of culture positivity in patients with BSIs ranged from 9.2 to 44.0%[12]. In a European study, it was reported that patients with BSIs spent an extra 6.0-11.5 days in hospital than other patients and the expenditure of this time ranged from 8000-56,000 US Dollars (USD)[13]. In studies conducted in different geographical regions and even in different centers in the same geographical region, the distribution of bacteria produced in blood cultures has been reported at different rates.

A study conducted in Colombia reported the isolation of 43.9% Gram-negative bacteria, 40.7% Gram-positive bacteria, and 2.8% *Candida* species from blood cultures[14]. Data reported from India show that the total culture positivity was 10.8% (156), of which 52.56% (82) were Gram-positive and 47.4% (74) Gram-negative[15]. 21.0% (13882) of 66004 blood culture results were culture positive in an analysis conducted in Turkiye over a five-year period[16]. In our study, culture positivity was 42.7% (369) and among the isolated microorganisms, Gram-positive bacteria were 79.4% (293), Gram-negative bacteria were 18.2% (67), yeasts were 2.4% (9). Our study shows higher rates of blood culture positivity compared to the literature. The fact that the majority of the samples were taken from the intensive care unit (ICU) may affect this result. Also variations in premorbid conditions such as age, gender, hospitalization history, use of peripheral and central venous catheters, diabetes mellitus, malignancy, and the presence of chronic conditions such as renal failure, antibiotic use, and burns may explain the differences between the studies.

In the majority of studies, the organisms most frequently isolated were CoNS*, Klebsiella spp., S. aureus, E. coli,* and *Acinetobacter spp*[16-18]. A recent research found that *S. aureus* (20.7%) was the most frequently isolated bacteria from bloodstream infections (BSIs) globally, followed by *E. coli* (20.5%), *K. pneumoniae* (7.7%), *P. aeruginosa* (5.3%), and *E. faecalis* (5.2%)[6]. In the investigation by Robledo et al., *E. coli* was the most often isolated microbe (20.38%), followed by *S. aureus* (14.84%), *S. epidermidis* (11.70%), and *K. pneumoniae* (10.65%)[14]. In our study, the most frequently isolated microorganism was CoNS (81.2%), followed by *E. coli* (26.9%), *A. baumannii* (20.9%), *E. cloacae* (13.4%), *K. pneumoniae* (13.4%), *S. aureus* (10.2%), *E. faecalis* (3.8%), *E. faecium* (2.4%) (Table 2). Only known CoNS isolates were evaluated in our study. Compared to other studies, CoNS rates were higher. In our study, the most frequently isolated Gram-positive bacterium was CoNS (81.2%). It was followed by *S. aureus* (10.2%). With the increasing number of immunosuppressed patients, especially in the ICU, CoNS is considered to be one of the important causes of BSIs. These bacteria can easily colonize the skin and mucosal surfaces as part of the normal flora and may act as opportunistic pathogens. In addition, this wide spectrum of bacterial distribution may be closely related to the number of samples received from the ICU.

The emergence and spread of Multi-drug resistant (MDR) microorganisms such as methicillin-resistant *S. aureus* (MRSA) and carbapenem-resistant *Enterobacteriaceae* significantly limit the use of antimicrobial therapies and have adverse effects on survival, especially in patients with BSIs hospitalized in ICU[19]. Antimicrobial resistance is a major global problem, causing more than 2 million illnesses and 23,000 deaths in the United States every year. It's estimated that 10 million people will die worldwide by 2050, with almost 90% of these expected to occur in developing countries such as Asia and Africa[20]. India uses 3rd or 4th generation antibiotics in treatments, while Europe and America prefer to use 1st or 2nd generation antibiotics[21]. This suggests that stronger antibiotics are being used due to high rates of antibiotic resistance, necessitating the use of broader spectrum and stronger antibiotics to

effectively treat infections. Therefore, it is very important for each hospital to closely monitor the data on causative microorganisms and antibiotic susceptibilities.

The World Health Organization (WHO) has included a few of these bacteria on its priority list of microorganisms to help direct the development of new antibiotics[22]. The latest WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS) report shows that the prevalence of *E. coli* resistant to third-generation cephalosporins is 36%, while the prevalence of methicillin-resistant *S. aureus*, which causes bloodstream infections, is 24.9%[23]. A 2020 study found that carbapenems and 4th generation cephalosporins are highly effective against both gram-positive and gram-negative bacteria, while increased resistance was observed against 3rd generation cephalosporins, such as ceftazidime, ceftriaxone, and cefixime. The study found that *E. coli* showed the highest resistance to cefuroxime sodium and ceftriaxone, *P. aeruginosa* to aztreonam and colistin sulfate, *K. pneumoniae* to ceftriaxone and ciprofloxacin, *S. aureus* to azithromycin and linezolid, *S. epidermidis* to gentamicin, and *S. viridans* to cloxacillin[24]. In our study, clindamycin, linezolid, teicoplanin, tigecycline, and vancomycin were found to be the most effective antibiotics against Gram-positive bacteria, while amikacin, colistin, carbapenems (meropenem, imipenem, ertapenem) and piperacillin-tazobactam were effective against Gram-negative bacteria (Table 3, Table 4). In our study, all *S. aureus* (including 9 MRSAs) and CoNS were 100% susceptible to vancomycin. Teicoplanin susceptibility was 100% for *S. aureus* and 92.4% for CoNS (Table 3). In our study, not all isolates were tested for susceptibility to all antibiotics, making it difficult to compare the resistance status. However, self-treatment without diagnosis, easy access to antibiotics, unnecessary and irregular antibiotic use or discontinuation of antibiotic use before completion of treatment may be responsible for different antibiotic resistance rates. The resistance of CoNS and MRSA to vancomycin presents a significant challenge, as it can lead to treatment failure and poor clinical outcomes[25].

Enterococci are known as opportunistic pathogens and are considered nosocomial infection agents. It has been reported that vancomycin resistance is directly related to the length of hospital stay and mortality in bacteremia caused by Enterococci. Vancomycin and teicoplanin are two glycopeptides that are effective against *E. faecium*. In a prospective study conducted in Korea between 2015 and 2016, 97 patients with *E. faecium* bacteremia were treated with either vancomycin (66%) or teicoplanin (34%). The study found that mortality rates were not significantly different between the two antibiotic treatments. The study authors noted that teicoplanin could be a viable alternative to vancomycin[26]. In a study conducted in Egypt with 200 clinical isolates, 53.8% of *E. faecalis* strains were resistant to vancomycin and 19.2% to teicoplanin[27]. Vancomycin resistance in *Enterococcus spp.* species has shown a significant increase over time[16]. In our study, *E. faecalis* showed a sensitivity of 100% to teicoplanin and 91.0% to vancomycin, whereas *E. faecium* showed a sensitivity of 85.7% to both teicoplanin and vancomycin (Table 3). Prevention and control strategies against vancomycin-resistant enterococci, which are extremely important in terms of hospital infections, include limiting the use of vancomycin and cephalosporins, reducing unnecessary hospitalizations, training hospital personnel, and contact isolation.

Enterobacteriaceae, especially *E. coli* and *K. pneumoniae*, are important nosocomial pathogens. In the treatment of infections caused by ESBL-producing Enterobacteriaceae isolates, carbapenems are the first choice. ESBL production is an important resistance mechanism for bacteria. It causes a global health burden and is a major cause of hospital costs. A study was conducted to evaluate carbapenem-resistant Enterobacteriaceae isolates in patients with bacteremia. The study found that the rate of carbapenem-susceptible isolates (imipenem, meropenem, and doripenem) ranged between 47-50%, while ertapenem susceptibility was 14% and colistin susceptibility was 87%[28]. In the study conducted in Turkiye, *E. coli* did not show any resistance to imipenem, meropenem, tigecycline or colistin[16]. In our study, *E. cloacae* and *E. coli* were found to be 100% susceptible to ertapenem, imipenem, and meropenem. However, *K. pneumoniae* showed susceptibility rates of only 44.4%, 55.6%, and 55.6% for ertapenem, imipenem, and meropenem, respectively (Table 4). These carbapenems are used as a last resort in antibiotic therapy, particularly for ESBL-producing Gram-negative bacteria in underdeveloped regions where access to new antibiotics is limited[29]. ESBL production rates were determined as 44.4% (8/18) in *E. coli* isolates and 55.5% (5/9) in *K. pneumoniae* isolates. The chances of curing Klebsiella infections are significantly reduced

by these high resistance rates. There are studies indicating that the combination of ceftazidime avibactam (CZA) and colistin (COL) and the combination of CZA and fosfomycin is an effective treatment protocol for carpapenem-resistant infections[30]. The resistance profile to combinations therapies was not explored in this study and further research on this topic is needed.

In a study that investigated the causative agents of BSIs, 46 isolates underwent agent identification and antibiotic susceptibility tests. The results showed that two of the isolates were identified as *P. mirabilis*, and both were found to be resistant to all drugs[31]. In our study, found that all *P. mirabilis* isolates were susceptible to ceftazidime, ceftriaxone, ertapenem, meropenem, and piperacillin-tazobactam. However, 20% of the isolates were resistant to ampicillin, ciprofloxacin, gentamycin, and trimethoprim-sulfamethoxazole (Table 4).

A. baumanii and *P. aeroginosa* are opportunistic pathogens and infections caused by these bacteria are usually associated with catheter/ventilator use[32,33]. *A. baumanii* bacteria are generally resistant to carbapenems and beta-lactams, aminoglycosides, rifampin, and fluoroquinolones. Therefore, they have limited treatment options. MDR isolates cause over 60% mortality. A study reported that colistin resistance in Acinetobacter isolates was 1.4%[34]. In our study, 21.4% of *A. baumannii* isolates were resistant to colistin and tobramycin and 100% resistant to many other antibiotics, including carbapenems (Table 4). The colistin resistance rate of 21.4% observed in *A. baumannii* indicates an increasingly worrying trend. The variability in resistance rates can be attributed to factors such as local antibiotic stewardship practices, prevalence of multidrug-resistant strains and methodologies used for resistance testing. In particular, the sensitivity and specificity of the widely used VITEK 2 system in detecting colistin resistance has been criticized; some studies suggest that the system may give false resistant results[35-36]. This raises concerns about the reliability of resistance data from automated systems compared to traditional methods such as microdilution, which is considered the gold standard.

In a study involving 3248 clinical isolates, *P. aeruginosa* was found to be the cause of 10-15% of nosocomial infections. The study reported that 15.53% of *P. aeruginosa* isolates were imipenem strains and 16.50% were MDR strains[37]. Studies have reported that up to 60% of *P. aer*uginosa isolates exhibit resistance to gentamicin, which is concerning given the pathogen's role in severe infections, particularly in immunocompromised patients[38]. *A. baumannii* has emerged as a significant pathogen in blood cultures, with resistance rates to carbapenems reaching as high as 95.5% in some studies conducted in Turkiye[39]. In a recent study, *Acinetobacter spp.* was found to be highly resistant to many antibiotics, with colistin being the most effective agent for *Acinetobacter spp.* and *Pseudomonas spp*[16]. In our study, *P. aeruginosa* isolates were susceptible to amikacin 77.8%, colistin 66.7%, gentamicin 88.9%, meropenem 66.7%, tobramycin 88.9% and 100% resistant to ceftazidime, ciprofloxacin, cefepime, imipenem, levofloxacin, trimethoprim-sulfamethoxazole (Table 4). Multidrug and widespread use of colistin led to the development of colistin resistance, which in turn led to the emergence of multidrug-resistant microorganisms[40]. Also, combined antimicrobial therapy reduces mortality in carbapenem-resistant Klebsiella infections. Recent studies have suggested that when the prevalence of carbapenem-resistant Klebsiella spp. among patients with BSIs is less than 50%, the use of carbapenem-based combination therapy may not provide a significant survival advantage over carbapenem monotherapy[41].

In our study, not all isolates could be tested for susceptibility to all antibiotics, making it difficult to compare susceptibility or resistance patterns. The majority of isolates showed resistance to three or more antibiotics, which is particularly concerning. In a previous study, over 90% of isolates were resistant to three or more drugs[25]. To prevent bacterial resistance to antibiotics and preserve patient life, it is critical to adopt an antibiotic policy and follow treatment recommendations for bacterial BSIs.

The limitations of this study are that clinical data on patients could not be accessed. Susceptibilities to all antibiotics and combinations were not analyzed. Blood cultures of all hospitalized patients were included in the study. However, growths within 48 hours of hospitalization also reflect community-acquired infections. In our study, no distinction was made between community-acquired and nosocomial infections. Carbapenemase detection was not possible for carbapenem-resistant Enterobacter. Furthermore, COL susceptibility was only screened by automated system and not confirmed by microdilution plate method.

Monitoring antibiotic susceptibility patterns of pathogens is crucial for the diagnosis, treatment, and management of BSIs. Local, regional and national antimicrobial susceptibility surveillance is essential to discover resistant microorganisms, monitor resistance over time and evaluate the effectiveness of control measures. Continuously updating existing antibiotic policies based on local surveillance data and identifying the best empirical antibiotic treatment alternatives for various BSIs conditions in each hospital setting may help slow the rate of increase in antibiotic resistance.

Author Contributions: Concept/Design : EK; Data acquisition: EK; Data analysis and interpretation: EK, HK; Drafting manuscript: EK, HK; Critical revision of manuscript: EK, HK, CÖ; Final approval and accountability: EK, HK, CÖ; Technical or material support: EK; Supervision: EK, HK, CÖ; Securing funding (if available): n/a.
Ethical Approval: Ethical approval was obtained from the Clinical Research Ethics Committee of the Mersin University Rectorate by its decision dated 18.10.2023 and numbered 20/688.
Peer-review: Externally peer-reviewed.
Conflict of Interest: The authors declare that there is no conflict of interest..
Financial Disclosure: This research did not receive support from any funding agency/industry.
Informed Consent: Since the study was retrospective, patient files were analysed. Therefore, written and/or verbal consent was not obtained.

REFERENCES

1. Martinez RM, Wolk DM. Bloodstream infections. Microbiol Spectr. 2016;4:10.1128/microbiolspec.dmih2-0031-2016.
2. Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR et al. Global, regional, and national sepsis incidence and mortality, 1990–2017:analysis for the global burden of disease study. Lancet. 2020;395:200–11.
3. Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. 2022;399:629–55.
4. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Crit Care Med. 2021;49:e1063–143.
5. WHO. Global Action Plan on Antimicrobial Resistance. Geneva, World Health Organization. 2015.
6. Diekema DJ, Hsueh PR, Mendes RE, Pfaller MA, Rolston KV, Sader HS et al. The microbiology of bloodstream infection: 20-year trends from the SENTRY antimicrobial surveillance program. Antimicrob Agents Chemother. 2019;63:e00355-19.
7. Basustaoglu A. Kan kültürü uygulama klavuzu. Ankara, Türk Mikrobiyoloji Cemiyeti. 2013.
8. EUCAST. The European Committee on Antimicrobial Susceptibility Testing version 13.0, 2023. Copnhagen, EUCAST. 2023.
9. Mia A, Zerin T. Antibiogram of blood culture isolates of patients from a hospital in Dhaka, Bangladesh. Matrix Science Medica. 2020;4:1−5.
10. Totad Rd, Ganganahalli P. Bacteriological profile and antibiotic sensitivity pattern of blood culture ısolates from tertiary care level teaching hospital of vijaya pura district. Int J Res Med Sci. 2020;8:3974-8.
11. Suetens C, Latour K, Karki T, Ricchizzi E, Kinross P, Moro ML et al. Prevalence of healthcare-associated infections, estimated incidence and composite antimicrobial resistance index in acute care hospitals and long-term care facilities: results from two European point prevalence surveys 2016 to 2017. Euro Surveill. 2018;23:1800516.
12. Oyekale OT, Ojo BO, Olajide AT, Oyekale OI. Bacteriological profile and antibiogram of blood culture isolates from bloodstream infections in a rural tertiary hospital in Nigeria. Afr J Lab Med. 2022;11:1807.
13. Cassini A, Colzani E, Pini A, Mangen MJJ, Plass D, McDonald SA et al. Impact of infectious diseases on population health using incidence-based disability-adjusted life years (DALYs): Results from the burden of communicable diseases in Europe study. European union and European economic area countries, 2009 to 2013. Euro Surveill. 2018;23:17- 00454.
14. Robledo J, Maldonado N, Robledo C, Ceballos Naranjo L, Hernández Galeano V, Pino JJ. Changes in antimicrobial resistance and etiology of blood culture ısolates: results of a decade (2010–2019) of surveillance in a Northern Region of Colombia. Infect Drug Resist. 2022;15:6067–79.
15. Nishanthy M, Saikumar C. Bacteriological profile and antibiotic susceptibility of blood culture ısolates in ıntensive care units of a tertiary care hospital. Int J Life Sci Pharma Res. 2022;12:112-9.
16. Arabacı Ç, Kutlu O. Evaluation of microorganisms isolated from blood cultures and their susceptibility profiles to antibiotics in five years period. J Surg Med. 2019;3:729-33.
17. Tian L, Sun Z, Zhang Z. Antimicrobial resistance of pathogens causing nosocomial bloodstream infection in Hubei Province, China, from 2014 to 2016: a multicenter retrospective study. BMC Public Health. 2018;18:1121.
18. Banik A, Bhat SH, Kumar A, Palit A, Snehaa K. Bloodstream infections and trends of antimicrobial sensitivity patterns at Port Blair. J Lab Physicians. 2018;10:332-7.
19. Stewardson AJ, Allignol A, Beyersmann J, Graves N, Schumacher M, Meyer R. et al. The health and economic burden of bloodstream infections caused by antimicrobial–susceptible and non–susceptible Enterobacteriaceae and Staphylococcus aureus in European hospitals, 2010 and 2011: a multicentre retrospective cohort study. Euro Surveill. 2016;21:30319.

20. Islam S, Aldstadt J, Aga D. Global antimicrobial resistance: a complex and dire threat with few definite answers. Trop Med Int Health. 2019;24:658−62.
21. Farooqui HH, Selvaraj S, Mehta A, Heymann DL. Community level antibiotic utilization in India and its comparison vis-à-vis European countries: evidence from pharmaceutical sales data. PloS One. 2018;13:e0204805.
22. WHO. WHO Global Priority List of Antibiotic-Resistant Bacteria yo Guide Research, Discovery, And Development of New Antibiotics; 2017. Geneva, World Health Organization. 2017.
23. Agnew E, Dolecek C, Hasan R, Mahra M, Merk H, Perovic O et al. Global Antimicrobial Resistance and Use Surveillance System (GLASS) Report; 2021. Geneva, World Health Organization. 2021.
24. Zerin T, Islam A, Gulnahar S, Farjana NE, Begum MA, Sadia HE. Identification and antibiotic susceptibility of blood culture ısolates from Rajshahi, Bangladesh. J Sci Res Med Bio Sci. 2021;2:1-10.
25. Onelum O, Odetoyin B, Onipede A, Oyelese A. The role of methicillin-resistant Staphylococcus aureus in clinical infections in Obafemi Awolowo university teaching hospitals complex, Ile-Ife, South Western Nigeria. J Microbiol Exp. 2015;2:59-64.
26. Haa S, Huha K, Chunga DR, Koa JH, Cho SY, Huh HJ et all. Efficacy of teicoplanin in bloodstream infections caused by Enterococcus faecium: posthoc analysis of a nationwide surveillance. Int J Infect Dis. 2022;122:506-513.
27. Esmail MAM, Abdulghany HM, Khairy RMM. Prevalence of multidrug-resistant Enterococcus faecalis in hospital-acquired surgical wound infections and bacteremia: concomitant analysis of antimicrobial resistance genes. Infect Dis. 2019; 12:1178633719882929.
28. Perovic O, Ismail H, Quan V, Bamford C, Nana T, Chibabhai V et al. Carbapenem-resistant Enterobacteriaceae in patients with bacteraemia at tertiary hospitals in South Africa, 2015 to 2018. Eur J Clin Microbiol Infect Dis. 2020;39:1287-94.
29. Fawzy R, Gad G, Mohamed H. Phenotypic and genotypic detection of resistance mechanisms in carbapenem-resistant gram-negative bacteria isolated from egyptian icu patients with first emergence of ndm-1 producing klebsiella oxytoca. Iran J Microbiol. 2022;14:832-40.
30. Tüzemen NÜ, Önal U, Merdan O, Akca B, Ener B, Özakın C et al. Synergistic antibacterial activity of ceftazidime–avibactam in combination with colistin, gentamicin, amikacin, and fosfomycin against carbapenem-resistant Klebsiella pneumoniae. Sci Rep. 2024;14:17567.
31. Manyahi J, Kibwana U, Mgimba E, Majigo M. Multi-drug resistant bacteria predict mortality in bloodstream infection in a tertiary setting in Tanzania. PLoS One. 2020;15:e0220424.
32. Whiteway C, Breine A, Philippe C, Van der Henst C. Acinetobacter baumannii. Trends Microbiol. 2022;30:199-200.
33. Casale R, Boattini M, Comini S, Bastos P, Corcione S, De Rosa FG et al. Clinical and microbiological features of positive blood culture episodes caused by non-fermenting gram-negative bacilli other than Pseudomonas and Acinetobacter species (2020–2023). Infection. 2024.
34. Russo A, Bassetti M, Ceccarelli G, Carannante N, Losito AR, Bartoletti M et all. Bloodstream infections caused by carbapenem-resistant Acinetobacter baumannii: clinical features, therapy and outcome from a multicenter study. J Infect. 2019;79:130-8.
35. Pfennigwerth N, Kaminski A, Korte-Berwanger M, Pfeifer Y, Simon M, Werner G et al. Evaluation of six commercial products for colistin susceptibility testing in enterobacterales. Clin Microbiol Infect. 2019;25:1385-9.
36. Chauhan S, Kaur N, Saini A, Aman S, Chauhan J, Kumar H. Colistin resistant gram-negative bacteria isolated from various clinical samples in north indian tertiary care center. IJPQA. 2022;13:15-23.
37. Mirzaei B, Bazgir ZN, Goli HR, Iranpour F, Mohammadi F, Babaei R. Prevalence of multi-drug resistant (MDR) and extensively drug-resistant (XDR) phenotypes of Pseudomonas aeruginosa and Acinetobacter baumannii isolated in clinical samples from Northeast of Iran. BMC Res Notes. 2020;13:380.
38. Sezener M, Ergüden V, Findik A, Akgöz S, Gülhan T, Moţco O et al. Türkiye ve romanya kökenli Pseudomonas aeruginosa izolatlarının antibiyotik dirençlerinin, biyofilm oluşumu ve genotiplerinin araştırılması. J Etlik Vet Microbiol. 2022;33:1-6.
39. Çaşkurlu H, Davarcı İ, Koçoğlu M, Çağ, Y. Examination of blood and tracheal aspirate culture results in intensive care patients: 5-year analysis. Medeniyet Med J. 2020;35:128-35.
40. Mondal AH, Khare K, Saxena P, Debnath P, Mukhopadhyay K, Yadav, D. A review on colistin resistance: an antibiotic of last resort. Microorganisms. 2024;12:772.
41. Li D, Rao H, Xu Y, Zhang M, Zhang J, Luo J. Monotherapy vs combination therapy in patients with Klebsiella pneumoniae bloodstream infection: a systematic review and meta-analysis. J Infect Chemother. 2024;30:372-8.