Original Article

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Clinical Characteristics, Microbiological Profile and Antimicrobial Resistance Pattern of Bloodstream Infections in Critically Ill Patients: A Cross-sectional Study

Microbiology Section

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ABSTRACT

Introduction: Bloodstream Infections (BSIs) often complicate the outcomes of critically ill patients and are typically associated with high morbidity and mortality rates. There is marked variation reported in the prevalence and antimicrobial resistance patterns of pathogens causing BSIs. Updated and comprehensive data, integrating the microbiological profile and clinical characteristics, may serve as a promising framework for planning and executing management strategies for BSIs in critically ill patients.

Aim: To investigate the clinical characteristics, microbiological profile, and antimicrobial resistance patterns of BSIs in critically ill patients.

Materials and Methods: This cross-sectional study was conducted over a period of four years (June 2021 to May 2025) in a tertiary care academic hospital. Blood cultures from adult patients (>18 years) with a strong clinical suspicion of sepsis were included. Sepsis was diagnosed based on the criteria for Systemic Inflammatory Response Syndrome (SIRS). Bacterial pathogens isolated from blood cultures were identified, and antimicrobial susceptibility testing was performed using the Kirby-Bauer disc diffusion test on Mueller-Hinton agar. The clinical characteristics of patients were recorded and analysed. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 24.0 (IBM, USA). A p-value <0.05 was considered significant.

Results: Out of 15,894 blood cultures received, a total of 2,764 (17.4%) were positive. Risk factors such as the use of corticosteroids and the presence of invasive medical devices were significantly associated with BSIs. Bacterial pathogens were isolated from 2,481 (89.8%) samples, while *Candida* was isolated from 283 (10.2%) samples. Coagulase-negative Staphylococci 411 (59.1%) were the most common Gram-positive cocci (GPC). *Klebsiella pneumoniae* 642 (50.1%) was the most common Gram-negative bacilli (GNB). Both GPC and GNB demonstrated high resistance to commonly used first- and second-line antimicrobial agents.

Conclusion: The overall prevalence of bacterial pathogens was high in BSIs among critically ill patients, with GNB—particularly *Klebsiella pneumoniae*—being the most prevalent pathogen. The significant antimicrobial resistance demonstrated by both Gram-positive and Gram-negative pathogens is alarming and emphasises the importance of strengthening infection prevention and control practices, along with the effective implementation of enhanced antimicrobial stewardship programs.

Keywords: Blood culture, Gram-negative bacilli, Sepsis

INTRODUCTION

The Bloodstream Infections (BSI) remain a significant cause of morbidity and mortality in critically ill patients, despite advances in therapy and supportive care [1]. These infections often complicate patient outcomes and are significantly associated with increased use of broad-spectrum antibacterial agents and prolonged hospitalisation [2]. Factors such as the presence of invasive medical devices, surgical interventions, extended hospitalisation—particularly in the Intensive Care Unit (ICU)—increased use of immunosuppressive agents, and alterations in antimicrobial therapy contribute to the higher incidence of BSIs in critically ill patients. BSIs can lead to life-threatening conditions like sepsis, septic shock, and multiorgan failure [3]. Although the aetiological spectrum of BSIs is broad, involving bacteria, fungi, and viruses, bacterial BSIs are most commonly noted in routine practice. Studies have reported considerable variation in the pathogen profile, epidemiology, and outcomes of BSIs based on geographical area, patient population, and the type of healthcare setting. *Escherichia coli, Staphylococcus aureus*, and *Streptococcus pneumoniae* are significant causes of BSIs in countries such as Australia, Canada, Denmark, Finland, Iceland, New Zealand, Sweden, and the United States, whereas *Salmonella enterica* is commonly isolated from BSIs in African and Asian countries [4].

Blood cultures are the mainstay of BSI diagnosis and are considered the gold standard investigation. Therefore, timely reporting of blood cultures is crucial for both the diagnosis and treatment of BSIs; any delay may result in improper and inadequate treatment, leading to poor outcomes in terms of increased morbidity and mortality [5,6]. In recent years, there has been a paradigm shift in the epidemiology of pathogens from more susceptible strains to drug-resistant ones. The development and emergence of drug resistance often worsen the outcomes of various infections, particularly BSIs [7]. Thus, understanding the antimicrobial susceptibility patterns of the infecting strains is of paramount importance. The changing patterns of pathogens and the emergence of more treatment-resistant strains underscore the necessity of institutional data on BSIs for implementing accurate therapeutic measures to facilitate better patient outcomes. Several factors, including patient population, geographical location, study design, and the increased threat of antimicrobial resistance, contribute to significant variations in the outcomes of studies on BSIs. This variability makes generalised findings more challenging and highlights the importance of institutional data [4].

The aim of the present study was to investigate the clinical characteristics, microbiology, and resistance patterns of BSIs in critically ill patients. The objectives of the study were to identify

organisms from BSIs, assess their antimicrobial susceptibility profiles, study risk factors associated with BSIs, and examine the clinical features and outcomes of patients with BSIs.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Microbiology at Byramjee Jeejeebhoy Medical College and Sassoon General Hospital, Pune, Maharashtra, India. Sassoon General Hospital is a 1,500-bed super specialty public teaching hospital. The study was conducted over a period of four years (June 2021 to May 2025). Approval from institutional ethics committee was taken.

Inclusion criteria: All blood cultures received in the laboratory from adult patients (>18 years of age) admitted to the intensive care units of the hospital. According to the inclusion criteria, blood cultures from patients with a strong clinical suspicion of sepsis were included in the study. Sepsis was diagnosed based on SIRS criteria [8].

Exclusion criteria: Blood cultures received from patients without clinical suspicion of sepsis and those on antimicrobial therapy upon admission were excluded from the study.

Sample collection and processing: Blood (10 mL) from clinically suspected cases of sepsis was collected following strict aseptic precautions and inoculated into blood culture bottles (prepared from Himedia Laboratories Pvt Ltd, Mumbai dehydrated BHI broth). These bottles were aerobically incubated in an incubator at 37°C and periodically subcultured onto blood agar and MacConkey's agar after overnight incubation on days 1 and 3 for pathogen isolation. Growth was identified based on Gram staining and biochemical reactions such as the catalase test, oxidase test, coagulase test, and IMViC test (indole, methyl red, Voges-Proskauer, and citrate). The antimicrobial susceptibility testing of bacterial pathogens was performed using the Kirby-Bauer disc diffusion method on Mueller-Hinton Agar. *Staphylococcus* spp. susceptibility to vancomycin was checked on vancomycin screen agar; if found resistant, it was tested further for Minimum Inhibitory Concentration (MIC). Colistin MIC was determined by broth microdilution. The antimicrobial discs were procured from Himedia Laboratories Pvt Ltd., Mumbai. The results of the antimicrobial susceptibility testing were interpreted according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI) 2022 [9].

Patients' demographic features, co-morbid conditions (such as diabetes mellitus, hypertension, malignancies, cardiovascular diseases, respiratory diseases, renal impairment, etc.), risk factors (including invasive medical devices, dialysis, surgical intervention, etc.) [3], history of corticosteroid therapy (within six months) [10], and clinical parameters at the time of admission were obtained from the case sheet. Outcome measurements, including length of hospitalisation and 30-day mortality, were also recorded and analysed.

If a blood culture was positive within 48 hours of hospital admission, it was considered a Community-Acquired Bloodstream Infection (CA-BSI). In contrast, a Hospital-Acquired Bloodstream Infection (HA-BSI) was considered when the blood culture was positive for cases developing after 48 hours of hospital admission.

STATISTICAL ANALYSIS

The data obtained from the study were entered into Microsoft® Excel spreadsheet for initial organisation and analysed using SPSS version 24.0, IBM, USA. Categorical variables were analysed using descriptive statistics and presented in the form of percentages and frequencies. The Chi-square test was employed to assess the risk factors associated with BSI, with a p-value <0.05 considered significant.

RESULTS

During the study period, a total of 15,894 blood cultures were received in the Microbiology laboratory. Of these, 2,764 (17.4%) blood cultures from patients satisfying the inclusion criteria were positive. A total of 968 (35%) positive blood cultures were from patients who were admitted to the hospital for less than 48 hours, classified as having CA-BSIs. Conversely, 1,796 (65%) positive blood cultures were from patients whose cultures were positive after 48 hours of hospital admission, classified as HA-BSIs.

Demographic and clinical characteristics of patients with positive blood cultures are shown in [Table/Fig-1]. Risk factors such as the use of corticosteroids (p-value <0.0001, Chi-square test) and the presence of invasive medical devices (p-value <0.0001, Chi-square test) were significantly associated with BSI.

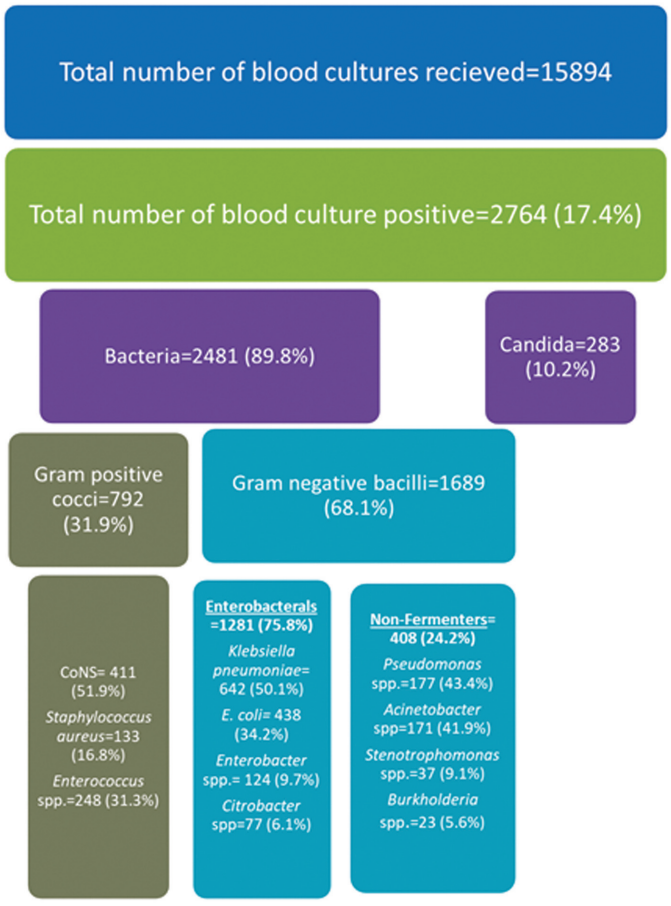
Parameters	N=2764	p-value
Demographic features		
Age in years, (median, IQR)	59.9 (19-71)	-
Male gender	1863 (67.4%)	-
Risk factors		
Diabetes mellitus	932 (33.4%)	>0.05
History of corticosteroid therapy (within six months)	1121 (40.6%)	<0.0001*
Neutropenia	631 (22.8%)	>0.05
Malignancy	392 (14.2%)	>0.05
Recent surgical intervention	116 (4.2%)	>0.05
Invasive medical devices	1248 (45.2%)	<0.0001*
Dialysis	105 (3.8%)	>0.05
Clinical characteristics		
Fever (temperature>38.5°C)	1689 (61.1%)	-
Systolic blood pressure (mmHg) (median, IQR)	130 (110-150)	-
Pulse (bpm) (median, IQR)	102 (89-116)	-
Outcome		
ICU stay after positive blood culture (days) (median, IQR)	10.5 (4.5-21)	-
Total hospital days after positive blood culture (days) (median, IQR)	17.5 (6.8-31.5)	-
30-day mortality	496 (17.9)	-

[Table/Fig-1]: Demographic and clinical features of patients with positive blood cultures.

The positive blood cultures comprised bacterial pathogens isolated from 2,481 (89.8%) samples and *Candida* isolates from 283 (10.2%) samples. Out of the 2,481 bacterial isolates, GPC were isolated from 792 (31.9%) samples, while 1,689 (68.1%) were GNB. Coagulase-negative Staphylococci (CoNS) were the most common GPC, and the isolation of CoNS was considered significant only when it was isolated from paired blood cultures. Enterobacterales were the most common GNB, with *Klebsiella pneumoniae* being the most frequently isolated GNB [Table/Fig-2].

The antimicrobial susceptibility pattern of Gram-positive isolates from BSI is shown in [Table/Fig-3]. Among Gram-positive isolates, susceptibility was high to antimicrobial agents such as linezolid, daptomycin, teicoplanin, and vancomycin. A total of 8 (3.2%) of the enterococcal isolates were resistant to vancomycin.

The antimicrobial susceptibility profile of Gram-negative isolates from BSI is shown in [Table/Fig-4]. Gram-negative isolates tested for colistin showed 100% susceptibility. Among Enterobacterales, *Klebsiella pneumoniae* exhibited significantly high resistance to antimicrobial agents, whereas among non fermenters, antimicrobial resistance was notably high in *Acinetobacter* spp. (Chi-square p-value <0.00001).



[Table/Fig-2]: Microbiological profile of blood cultures.

Antimicrobial agent	Coagulase negative Staphylococci (N=411) S (%)	*Staphylococcus aureus* (N=133) S (%)	*Enterococcus* spp. (N=248) S (%)
Penicillin	06 (1.5)	15 (11.3)	28 (11.3)
Oxacillin	71 (17.3)	64 (48.1)	Not tested
Gentamicin	23 (5.6)	82 (61.7)	Intrinsically resistant
High-level-gentamicin	Not tested	Not tested	41 (16.5)
Ciprofloxacin	48 (11.7)	12 (9.1)	11 (4.4)
Levofloxacin	50 (12.2)	14 (10.5)	16 (6.5)
Tetracycline	226 (54.9)	115 (86.5)	21 (8.5)
Cotrimoxazole	117 (28.5)	111 (83.5)	Intrinsically resistant
Erythromycin	52 (12.6)	06 (4.5)	08 (3.2)
Clindamycin	91 (22.1)	52 (39.1)	Intrinsically resistant
Vancomycin	411 (100)	133 (100)	240 (96.8)
Teicoplanin	389 (94.6)	128 (96.2)	242 (97.6)
Linezolid	411 (100)	133 (100)	246 (99.2)
Daptomycin	411 (100)	133 (100)	248 (100)

[Table/Fig-3]: Antimicrobial susceptibility of Gram-positive isolates from Blood stream infections.
S: Susceptible

DISCUSSION

BSIs present significant challenges in managing critically ill patients. Their management necessitates a multidimensional approach involving high clinical acumen, optimal laboratory support, and accurate treatment. BSIs can be acquired in hospitals or in the community [10]. This condition manifests upon the entry of pathogenic microorganisms via lymphatic drainage or directly through blood vessels [11]. Clinical symptoms of BSIs include fever, Disseminated Intravascular Coagulation (DIC), hypotension, hyperventilation, excessive sweating, endocarditis, and septic shock [6]. Various studies have reported significant variations in the prevalence and resistance patterns of pathogens associated with BSIs in critically ill patients. Therefore, monitoring trends in pathogens along with their antimicrobial susceptibility patterns is a crucial aspect for understanding the epidemiology of BSIs and managing patients effectively.

In the present study, based on positive blood cultures, BSIs were confirmed in 17.4% of critically ill patients. Various contextual factors must be considered for the prevalence of BSIs in a particular healthcare setup, including study design, sample size, patient population, and healthcare practices, such as compliance with infection prevention and control (IPC) protocols and the use of antimicrobial drugs [12]. The rate of BSIs in a particular setup also depends on blood culture practices, including the use of automated blood culture systems, the volume of blood cultured, transportation time, concomitant antimicrobial therapy, and the type of sample obtained (venepuncture or through a catheter) [6].

When analysing the risk factors, it was noted that the use of corticosteroids and the presence of invasive medical devices were significantly associated with BSIs. Corticosteroid therapy is known to suppress the host immune system, rendering patients more susceptible to infections [13]. Indwelling medical devices, such as urinary catheters, ventilators, and central lines, can serve as portals of entry for several pathogens, leading to the development of infections [13].

Various pathogenic bacteria and fungi can cause BSIs, including GPC, GNB, and several yeast species. Common GNB isolates from BSIs include *K. pneumoniae, A. baumannii, E. coli*, and *Pseudomonas aeruginosa*, whereas *S. aureus, Streptococcus* spp., and *Enterococcus faecium* are common GPC reported from BSIs [14]. A similar finding was observed in this study, with GPC isolated from 792 (31.9%) samples, while GNB were isolated from 1,689 (68.1%) blood cultures.

Coagulase-negative Staphylococci (CoNS) were the predominant GPC from BSIs. *S. aureus* was the second most common GPC isolated from blood cultures obtained from critically ill patients. Several national and international studies have highlighted the emergence of CoNS in BSIs, particularly in hospital-acquired cases. In the study by Alpay Çağlar Y et al., CoNS was the most common Gram-positive pathogen isolated from hospital-acquired BSIs, accounting for 15.5% of total infections [15]. Anithas et al., reported CoNS in 42.5% of BSI cases. These authors emphasised that laboratories play a pivotal role in managing cases of BSI due to CoNS by correctly distinguishing between contaminants and true pathogens [16]. Researchers have concluded that 30-day mortality rates are high in hospital-acquired BSIs due to CoNS [17].

	Enterobacterales				Non fermenters			
Antimicrobial agent	*Klebsiella pneumoniae* (N=642) S (%)	*E. coli* (N=438) S (%)	*Enterobacter* spp. (N=124) S (%)	*Citrobacter* spp. (N=77) S (%)	*Pseudomonas aeruginosa* (N=177) S (%)	*Acinetobacter* spp. (N=171) S (%)	*Stenotrophomonas* spp. (N=37) S (%)	*Burkholderia* spp. (N=23) S (%)
Ceftazidime	Not tested	Not tested	Not tested	Not tested	79 (44.6)	11 (6.4)	Not tested	23 (100)
Cefepime	68 (10.6)	165 (37.7)	72 (58.1)	47 (61.1)	74 (41.8)	08 (4.7)	Not tested	Intrinsically resistant
Aztreonam	Not tested	Not tested	Not tested	Not tested	-	09 (5.3)	Intrinsically resistant	Intrinsically resistant
Meropenem	79 (12.3)	251 (57.3)	79 (63.7)	52 (67.5)	71 (40.1)	07 (4.1)	Intrinsically resistant	19 (82.6)

Imipenem	137 (21.3)	268 (61.2)	84 (67.7)	61 (79.2)	69 (38.9)	10 (5.8)	Intrinsically resistant	Intrinsically resistant
Piperacillin-tazobactam	135 (21.1)	185 (42.2)	96 (77.4)	69 (89.6)	23 (12.9)	09 (5.3)	Intrinsically resistant	Intrinsically resistant
Cefoperazone sulbactam	139 (21.7)	242 (55.3)	107 (86.3)	63 (81.8)	43 (24.3)	11 (6.4)	Not tested	04 (17.4)
Gentamicin	172 (26.8)	279 (63.7)	85 (68.5)	61 (79.2)	Not tested	12 (7.1)	Intrinsically resistant	Intrinsically resistant
Amikacin	189 (29.4)	334 (76.3)	105 (84.7)	63 (81.8)	Not tested	09 (5.3)	Intrinsically resistant	Intrinsically resistant
Ciprofloxacin	78 (12.1)	19 (4.3)	76 (61.3)	56 (72.7)	32 (18.1)	08 (4.7)	Not tested	08 (34.8)
Levofloxacin	Not tested	Not tested	Not tested	Not tested	28 (15.8)	09 (5.3)	29 (78.4)	06 (26.1)
Minocycline	Not tested	Not tested	Not tested	Not tested	Intrinsically resistant	08 (4.7)	31 (83.8)	17 (73.9)
Colistin	642 (100)	438 (100)	124 (100)	77 (100)	177 (100)	171 (100)	Intrinsically resistant	Intrinsically resistant
Cotrimoxazole	172 (26.8)	165 (37.7)	51 (41.1)	40 (51.9)	Intrinsically resistant	07 (4.1)	31 (83.8)	23 (100)
Cefuroxime	156 (24.3)	56 (12.8)	68 (54.8)	31 (40.3)	Intrinsically resistant	Intrinsically resistant	Intrinsically resistant	Not tested
Ceftriaxone	207 (32.2)	134 (30.6)	93 (75)	35 (45.5)	Intrinsically resistant	Intrinsically resistant	Intrinsically resistant	Intrinsically resistant
Ertapenem	199 (30.9)	248 (56.6)	98 (79.1)	38 (49.4)	Intrinsically resistant	Intrinsically resistant	Intrinsically resistant	Intrinsically resistant
Amoxicillin clavulanate	178 (27.7)	112 (25.6)	24 (19.4)	33 (42.9)	Intrinsically resistant	Intrinsically resistant	Intrinsically resistant	Intrinsically resistant

[Table/Fig-4]: Antimicrobial susceptibility profile of Gram-negative isolates from blood stream infections.
S: Susceptible

K. pneumoniae was the predominant GNB from BSIs. A similar observation was noted by Fostervold A [18]. This finding was consistent with several studies. BSI due to *K. pneumoniae* is one of the important causes of mortality in critically ill patients, accounting for nearly 67.6% of deaths in ICU patients [19].

Accurate and rapid diagnosis, along with timely initiation of the most appropriate antimicrobial agent, is crucial for the effective management of BSIs in critically ill patients. Antimicrobial therapy is the cornerstone of managing BSI cases. Antimicrobial susceptibility testing provides a tailored solution for selecting the most suitable antimicrobial drug for managing BSI cases.

In the present study, the results of antimicrobial susceptibility testing of Gram-positive and Gram-negative isolates from BSIs in critically ill patients raise major concerns, as these isolates demonstrated significant resistance to commonly used first- and second-line antimicrobial agents.

Limitation(s)

Fungal BSIs are on the rise. However, Antifungal susceptibility testing could not be done in present study due to resource constraints. Also, the present study was a single centric study so data will be useful for developing antimicrobial resistance data for institute and local area and cannot be used directly for larger scale.

CONCLUSION(S)

From the results of the present study, it can be concluded that the overall prevalence of bacterial pathogens is high in BSIs among critically ill patients, with GNB, particularly *Klebsiella pneumoniae*, being the most prevalent pathogen. The significant antimicrobial resistance demonstrated by both Gram-positive and Gram-negative pathogens is alarming and underscores the importance of strengthening infection prevention and control practices, along with effectively implementing an enhanced Antimicrobial Stewardship Program (AMSP). Continuous monitoring of pathogen trends and the emergence of drug-resistant strains remain essential cornerstones for managing BSIs in critically ill patients.

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