ORIGINAL ARTICLE

Microbiological Analysis of Sepsis in the Intensive Care Unit of a Tertiary Care Hospital in Chennai

Nivaedhitha Mohan Kumar[1], Aruna Jebaraj[1], Jayakumar Subramaniam[1], Thangasamy Selvankumar[2]

[1]Department of Microbiology, Saveetha Medical College and Hospital, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India, [2]Department of General Medicine, Saveetha Medical College and Hospital, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India

Abstract

Hospital-acquired bloodstream infections are a prominent source of morbidity and mortality in intensive care units (ICUs), with important clinical implications for patient length of stay and medical costs. A retrospective study was undertaken from August 2023 to July 2024, with blood samples collected from sepsis patients in the ICU and cultivated using the BacT/ALERT 3D Automated Microbial Detection system. The VITEK2 Automated Bacteriological Identification system was used to identify organisms and determine their antimicrobial susceptibility patterns. Out of a total of 2031 isolates, 429 were blood isolates from patients with sepsis in the ICU. 63.3% of specimens were from males and 36.7% were from females. Age was divided into newborns (11.4%), 1–20 years (4.6%), 21–30 years (10.7%), 31–40 years (6.99%), 41–50 years (20.3%), 51–60 years (23.5%), 61–70 years (13.5%), 71–80 years (7.5%), and 81–90 years (1.4%). Departments were divided into respiratory ICU (36.1%), medical ICU (31.3%), neonatal ICU (13.5%), surgical ICU (11.6%), and pediatric ICU (6.9%). Most common organisms isolated were *Klebsiella pneumoniae* (29.8%), *Acinetobacter baumannii* (18.1%), *Escherichia coli* (17.5%), and *Staphylococcus aureus* (11%). Antimicrobial susceptibility patterns were analyzed. Highest susceptibility on average among Gram-positive cocci: Teicoplanin (91%), linezolid (100%), and vancomycin (100%). Highest susceptibility on average among Gram-negative bacilli: Amikacin (52.1%), imipenem (51.73%), and meropenem (51.73%). Much of the current understanding of the burden, causative pathogens, and clinical outcomes of sepsis is based on clinico-epidemiological studies from developed countries. However, statistics on the microbiological landscape and resistance patterns of sepsis in intensive care settings in Asian countries, including India, remain limited and underexplored. Multiple studies within India and globally were analyzed for this study to identify the significance of each microbiological parameter in relation to sepsis. This study shows the distribution of frequently encountered bacteria and their antibiotic susceptibility in different ICUs in a tertiary care hospital in Chennai. To limit the spread of multidrug-resistant diseases, different antibiotic regimens should be explored for different wards and age groups.

Key words: Bloodstream infections, intensive care unit, sepsis

INTRODUCTION

The term sepsis describes a complex, diverse, deadly emergency that progresses due to the body's dysfunctional response to an infection and is linked with tissue and organ damage. In simpler terms, it is a life-threatening condition caused by the body's response to an infection harming its own tissues and organs. Septic shock is an aspect of sepsis in which the root cause of circulatory and cellular/metabolic irregularities is sufficiently significant to increase fatality rates radically.[1] Sepsis is a leading cause of substantial mortality in the world, affecting both wealthy and resource-poor developing countries significantly.

Address for correspondence:
Thangasamy Selvankumar, Department of General Medicine, Saveetha Medical College and Hospital, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India.
E-mail: nivutti@gmail.com

Received: 15-11-2025
Revised: 22-12-2025
Accepted: 30-12-2025

Every year, it is projected that over 20–30 million patients worldwide are impacted. Every hour, sepsis kills over 1000 individuals and 24,000 people worldwide. Sepsis is also one of the few diseases wherein the pathogenesis is least understood, despite countless studies to identify the same, and even though it claims nearly 8 million lives every year. Sepsis causes 60–80% of pediatric fatalities in underdeveloped nations, affecting up to 6 million newborns and children each year. More than 100,000 cases of maternal sepsis occur each year owing to sepsis alone, which in some countries is now considered a greater concern during pregnancy than even thromboembolism or hemorrhage.[2,3]

Providing pathogen-specific antimicrobial therapy to patients with sepsis can be difficult due to their numerous infectious etiologies (viral, bacterial, and parasitic) and the high incidence of multidrug-resistant (MDR) bacteria in developing and tropical countries like India.[4,5] It is still challenging to determine the true impact, epidemiology, and risk factors for mortality associated with sepsis patients across India due to the country's large population, inadequate healthcare facilities, disparities in national and international organizations' guidelines regarding healthcare practices, and variations in the quality of care provided nationally.[6] In the last several years, there has been a rising number of consistent reports from different areas of India of rising trends in the occurrence of MDR pathogens that cause infection. Nevertheless, it is uncertain how MDR bacteria affect the clinical results of sepsis patients in India.[7]

Among the most common causes of sepsis in patients in the intensive care unit (ICU) are hospital-acquired bloodstream infections, particularly those brought on by drug-resistant Gram-positive (GP) cocci such as methicillin-resistant *Staphylococcus aureus* (MRSA), and Gram-negative (GN) bacilli such as *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Escherichia coli*. To start early targeted therapy and enhance results, prompt pathogen identification and antimicrobial susceptibility profile are crucial.[8] This study focuses on the microbiological profile and antimicrobial susceptibility of sepsis-causing organisms taken from ICU patients in a tertiary care hospital in Chennai.

MATERIALS AND METHODS

This retrospective study was carried out over 12 months, from August 2023 to July 2024, at a tertiary care hospital in Chennai, Tamil Nadu. Blood samples were taken and cultured from ICU patients exhibiting clinical indications of sepsis. Aseptic procedures were used to extract blood, which was then inoculated into blood culture bottles. Culture positive was determined using the BacT/ALERT 3D Automated Microbial Detection System. Throughout the study period, all blood-positive cultures identified as GP and GN bacterial pathogens were included; those identified as colonizers or skin contaminants were eliminated. The pathogen was then processed on blood agar, MacConkey agar, and chocolate agar after bottles with positive signals were subcultured. These plates were incubated for 18–24 h at 37°C in an aerobic environment.

The VITEK2 automated identification and antimicrobial susceptibility testing system was used to further process them after colonies grew. The GP ID and GN ID card identification panels were used for identification. On the other hand, the modified broth microdilution method was used to test for antimicrobial susceptibility using the minimum inhibitory concentration. The results were interpreted, and the susceptibility of each of the specimens was reported according to the Clinical and Laboratory Standards Institute guidelines for the given pathogen. Any blood culture bottle showing no sign of growth, i.e., showing no positive beep, was incubated in the BacT/ALERT 3D for 5 days, after which the sample was reported as no growth in blood. Demographic data (age and gender), ICU type, isolated organisms, and antibiotic susceptibility were analyzed using appropriate statistical tools, after the results were collected in terms of frequencies and percentages.

RESULTS

In the microbiology laboratory, 2031 isolates were acquired as blood cultures over the course of the 12-month study period. Of these, 429 isolates were particularly found in patients with sepsis who were admitted to the tertiary care hospital in Chennai's multiple ICUs. The importance of the numbers was indicated by the $P = 0.034$, which was found through data analysis using SPSS software.

Among the sepsis cases, a male predominance was observed, with 63.3% ($n = 272$) of the isolates derived from male patients, whereas 36.7% ($n = 157$) were from female patients [Figure 1]. The age distribution of patients showed that the highest number of sepsis cases occurred in the 51–60 years age group (23.5%, $n = 101$), followed by the 41–50 years (20.3%, $n = 87$) and 61–70 years (13.5%, $n = 58$) age

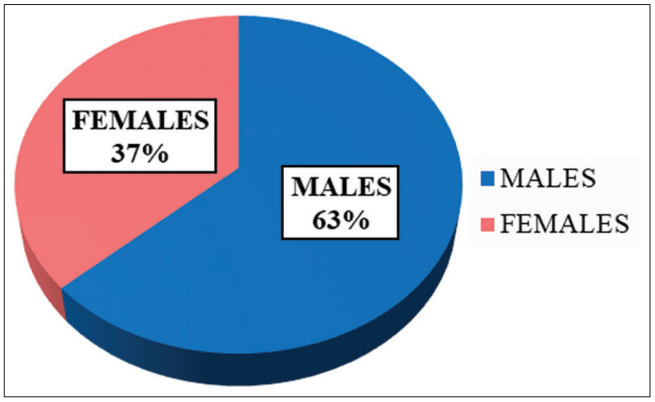

Figure 1: Gender distribution of intensive care units' blood culture isolates from sepsis patients (August 2023–July 2024)

groups. The remaining cases were distributed across other age brackets, including newborns (11.4%, *n* = 49), 21–30 years (10.7%, *n* = 46), 71–80 years (7.5%, *n* = 32), 31–40 years (6.99%, *n* = 30), 1–20 years (4.6%, *n* = 20), and 81–90 years (1.4%, *n* = 6) [Figure 2].

The ICU-wise distribution of cases revealed that the respiratory ICU (RICU) accounted for the largest proportion of sepsis isolates (36.1%, *n* = 155), followed by the medical ICU (MICU) with 31.3% (*n* = 134), the neonatal ICU with 13.5% (*n* = 58), the surgical ICU (SICU) with 11.6% (*n* = 50), and the pediatric ICU contributing the lowest count of 6.9% (*n* = 30) of the total isolates [Figure 3].

Mortality analysis revealed that 24% (*n* = 103) of patients succumbed to sepsis, whereas 76% (*n* = 326) survived their hospitalization in the ICU [Figure 4].

The most affected age group among deceased patients was the age group between 41 and 50 years, accounting for 30.5% (*n* = 31) of total deaths. Among the deceased, 67.8% (*n* = 70) were male, and 32.2% (*n* = 33) were female, indicating a male predominance in sepsis-related mortality. The leading cause of death was septic shock (56%, *n* = 58), followed by urosepsis (25.4%, *n* = 26), with the most common comorbidities observed in these deceased patients being chronic kidney diseases, i.e., patients on hemodialysis (16.9%, *n* = 17) and road traffic accidents (15.2%, *n* = 16). The most common ICU stay duration was 6 days (18.6%, *n* = 19) among all the ICU deceased patients. Maximum deaths were recorded in the MICU (45.8%, *n* = 47), followed by SICU (39%, *n* = 40). The most commonly isolated organisms in deceased patients were *K. pneumoniae*, accounting for 25.4% (*n* = 26) of isolates, followed by *A. baumannii* (22%, *n* = 22) [Figure 5].

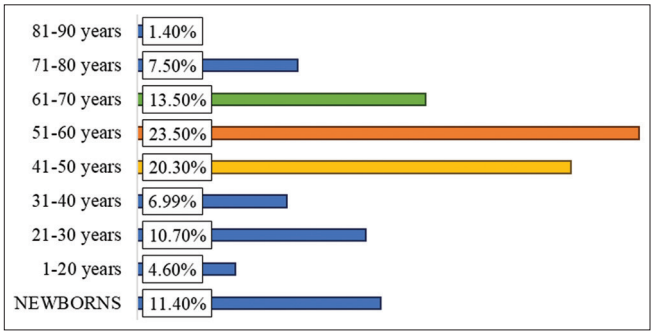

Figure 2: Age-wise distribution of intensive care units' blood culture isolates from sepsis patients (August 2023–July 2024)

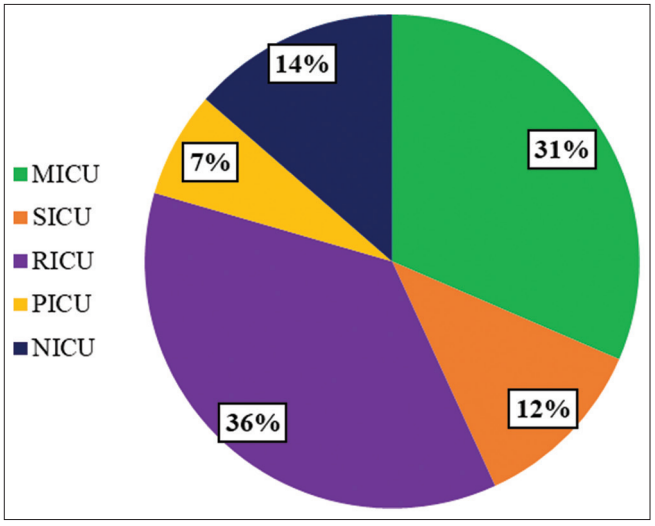

Figure 3: Department-wise distribution of intensive care units' blood culture isolates from sepsis patients (August 2023–July 2024)

Microbiological analysis showed that GN bacilli were the predominant pathogens in ICU sepsis cases. The most frequently isolated organism was *K. pneumoniae*, accounting for 29.8% (*n* = 128) of all the isolates. This was succeeded by *A. baumannii* (18.1%, *n* = 78), *E. coli* (17.5%, *n* = 75), and *S. aureus* (11%, *n* = 47), which was the most common GP cocci among the analyzed isolates. This pattern mirrors regional studies that in recent years have consistently reported GN organisms – particularly *K. pneumoniae* and *A. baumannii* – as leading pathogens in ICU-associated sepsis, often linked to high levels of multi-drug resistance and increased mortality risk.[9] The notable isolation of *Serratia marcescens* (8.5%, *n* = 36) and *Pseudomonas species* (5.9%, *n* = 25) highlights the diversity of non-fermenters contributing to nosocomial sepsis in ICU settings [Figure 6].

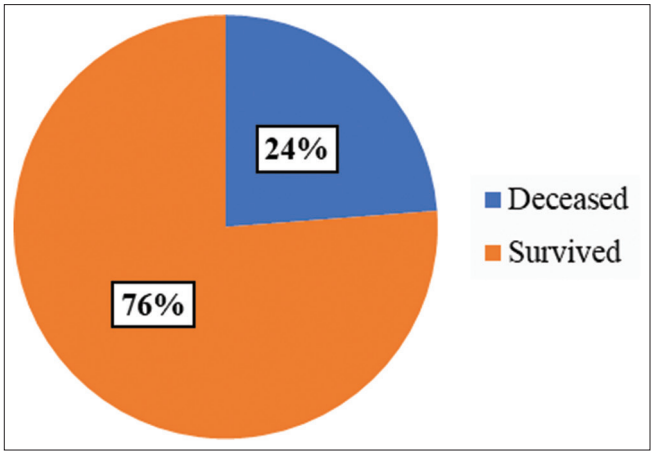

Figure 4: Mortality outcome of intensive care units sepsis cases – survived versus deceased (August 2023–July 2024)

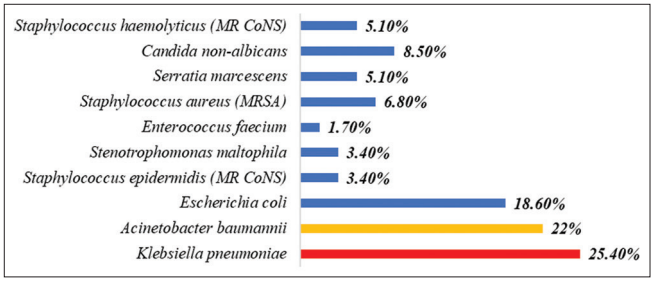

Figure 5: Distribution of isolates pathogens in intensive care units sepsis cases among the deceased (August 2023–July 2024)

Among GP cocci, coagulase-negative *Staphylococci* (CoNS) collectively represented the largest share at 28.1% (n = 121), with *Staphylococcus haemolyticus* (21.0%, n = 90) and *Staphylococcus hominis* (20.6%, n = 88) also prominent. The most clinically important GP cocci were also present in the isolates examined, namely *S. aureus* (including MRSA) at 11.0% (n = 47) and *Enterococcus* species at 9.0% (n = 39). While CoNS are frequently dismissed as contaminants, their high incidence in ICU blood cultures – particularly in patients with intravascular devices – highlights their genuine pathogenic potential in vulnerable hosts. The remaining 10% constituted non-pathogenic GP cocci, i.e., *Micrococci*, *Kocuria*, etc. [Figure 7].

A critical medical challenge is highlighted by the resistance patterns observed among the most prevalent GN bacilli cultured from bloodstream infections in ICUs. *A. baumannii* demonstrated uniformly raised resistance to all antibiotic classes tested, including β-actams/β-lactamase inhibitors (i.e., piperacillin–tazobactam [PIT] 76.5%, n = 60 resistant), cephalosporins (cefoperazone–sulbactam [CFS] 64.7%, n = 50 resistant), carbapenems (imipenem [IMI] and meropenem [MEM] 76.5%, n = 60 resistant), and aminoglycosides (amikacin [AK] and gentamicin [GEN] 76.5%, n = 60 resistant). Cephalosporins showed a mixed variety of resistance, with ceftriaxone [CTR] showing 59% (n = 46), whereas cefepime [CPM] demonstrated a higher count of resistance (76.5%, n = 60). It should be noted that ciprofloxacin [CIP] (94%, n = 73 resistant) and cotrimoxazole [COT] (67.7%, n = 53 resistant) also showed an alarming resistance pattern to the pathogen. Such pan-resistance is consistent with reports of >80% multi-drug resistance in ICU *A. baumannii* isolates worldwide, often linked to poor outcomes and limited treatment options.[8,9]

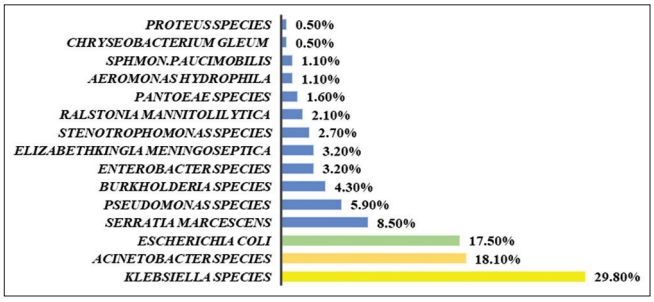

Figure 6: Distribution of Gram-negative bacilli in intensive care units' blood isolates (August 2023–July 2024)

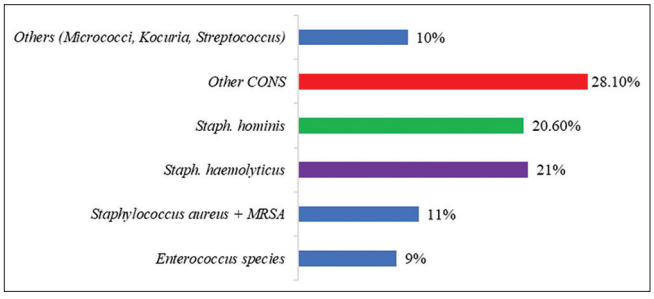

Figure 7: Distribution of Gram-positive cocci in intensive care units' blood isolates (August 2023–July 2024)

By contrast, *E. coli* retained moderate susceptibility to carbapenems and aminoglycosides, with IMI and MEM each 84.5%, n = 63, susceptible – and to ertapenem [ERT] 82%, n = 62 susceptible, whereas for AK 97%, n = 73 and GEN 75.6%, n = 57 was susceptible, but showed higher levels of resistance to the cephalosporins (cefuroxime [CU] 91%, n = 68 , CTR 85%, n = 64, and CPM 67%, n = 50 resistant) and fluoroquinolones (CIP 84.5%, n = 63 resistant). Moderate susceptibility was found in the β-lactams/β-lactamase inhibitors (amoxicillin–clavulanate [AMC], 60.6%, n = 45; PIT, 69.7%, n = 52, and CFS, 78.8%, n = 59 susceptible). COT demonstrated moderate susceptibility (54.5%, n = 41). ERT's preserved activity offers a potential targeted option for *E. coli* sepsis.

K. pneumoniae exhibited a more extensive pattern of resistance compared to the other major GN bacilli pathogens, with carbapenems (IMI and MEM both at 69.6%, n = 89 and ERT at 77%, n = 99 resistant), cephalosporins (CU 82%, n = 104, CTR 85.7%, n = 110 and CPM 78.6%, n = 101 resistant), β-lactams/β-lactamase inhibitors (AMC 80.3%, n = 103; PIT, 76.8%, n = 98 and CFS 71.4%, n = 91), aminoglycosides (AK and GEN 64%, n = 82 resistant), COT (62.5%, n = 80 resistant) fluoroquinolones (CIP 80.3%, n = 103) showing resistance [Table 1]. Overall, across all the isolates, the highest susceptibility on average was among Gram-negative Bacilli: AK (52.1%), IMI (51.73%), and MEM (51.73%).

Significant resistance to multiple types of antibiotics, especially β-lactams and fluoroquinolones, was found in the antimicrobial susceptibility profiles of the most prevalent GP cocci. Among MRSA – indicated by the presence of cefoxitin (CX) resistance – was noted in 72.7%, n = 34 of the isolates, whereas 27.3%, n = 13, remained susceptible. The susceptibility of *S. aureus* to glycopeptides and oxazolidinones showed 100% (n = 47) susceptibility to vancomycin (VA), teicoplanin (TEI), and linezolid (LZ). Resistance in *S. aureus* was highest among the macrolides (erythromycin [ERY] at 81.3%, n = 38) and lincosamides (clindamycin [CD] at 77.5%, n = 36), whereas good susceptibility was found in fluoroquinolones (CIP at 90.1%, n = 42 susceptible) and tetracycline (TETRA) (81.3%, n = 38). In terms of aminoglycoside susceptibility, GEN resistance was recorded at 77.5%, n = 36, in *S. aureus*. COT had better activity against *S. aureus*, with 68.2%, n = 32 resistance and 31.8%, n = 15 susceptibility.

For the CoNS isolates, the data are more alarming, with 84.2%, n = 102 of isolates showing resistance to CX, indicative of methicillin-resistant CoNS (MR-CoNS), leaving only 15.8%, n = 19 as methicillin-susceptible. CoNS also displayed 100%, n = 121 susceptibility to VA and LZ, demonstrating resistance to these agents slightly higher compared to *S. aureus*. CoNS

Table 1: Antibiotic resistance patterns among major Gram-negative bacilli from ICU blood isolates

Antibiotic	*Acinetobacter baumannii* (*n*=78) (%)	*Escherichia coli* (*n*=75) (%)	*Klebsiella pneumoniae* (*n*=128) (%)
Amoxicillin–clavulanate	-	39.4 (*n*=30)	80.3 (*n*=103)
Piperacillin–tazobactam	76.5 (*n*=60)	30.3 (*n*=23)	76.8 (*n*=98)
Cefoperazone–sulbactam	64.7 (*n*=50)	21.2 (*n*=16)	71.4 (*n*=91)
Cefuroxime	-	91 (*n*=68)	82 (*n*=104)
Ceftriaxone	59 (*n*=46)	85 (*n*=64)	85.7 (*n*=110)
Cefepime	76.5 (*n*=60)	67 (*n*=50)	78.6 (*n*=101)
Imipenem	76.5 (*n*=60)	15.1 (*n*=11)	69.6 (*n*=89)
Meropenem	76.5 (*n*=60)	15.1 (*n*=11)	69.6 (*n*=89)
Ertapenem	-	18.2 (*n*=14)	77 (*n*=99)
Amikacin	76.5 (*n*=60)	3.03 (*n*=2)	64 (*n*=82)
Gentamicin	76.5 (*n*=60)	24.4 (*n*=18)	64 (*n*=82)
Ciprofloxacin	94 (*n*=73)	84.5 (*n*=63)	80.3 (*n*=103)
Cotrimoxazole	67.7 (*n*=53)	45.4 (*n*=34)	62.5 (*n*=80)

also showed substantial resistance to macrolides (ERY 90%, *n* = 109) and lincosamides (CD 65.4%, *n* = 79 resistant), aminoglycosides (GEN 52.5%, *n* = 64 resistant), COT (59%, *n* = 71 resistant), and fluoroquinolones (CIP 77%, *n* = 93 resistant). TETRA retained robust activity against CONS (71%, *n* = 86 susceptible), whereas TEI also showed good activity in both groups, with 100% susceptibility in *S. aureus* and in CoNS.

Among the *Enterococcus* species (*n* = 39) isolated in this study, high-level GEN resistance (HLG) was present in 50%, *n* = 20 of the isolates, indicating a significant threat in terms of treating synergistic bacteremia. Penicillin susceptibility testing revealed that 47% (*n* = 18) of the isolates were sensitive, whereas 53% (*n* = 21) exhibited resistance. Despite these resistance patterns, some agents retained good efficacy: LZ showed 100% susceptibility (*n* = 39), and TEI [TEICO] was also highly effective, with 100% susceptibility. VA demonstrated 73% susceptibility, *n* = 29, suggesting that VA-resistant *Enterococcus* (VRE) was present in 27%, *n* = 10, of the cases. [Table 2] Overall, across all the isolates, the highest susceptibility on average among GP cocci was observed for TEI (100%), LZ (100%), and VA (100%).

DISCUSSION

To better understand the epidemiology and factors influencing infection and outcomes in this critical care setting, the primary goal of this study was to examine the microbiological characteristics and antimicrobial resistance patterns among pathogens responsible for sepsis in ICU patients at a tertiary care hospital in Chennai. Clinico-epidemiological studies from high-income nations provide a large portion of the existing knowledge regarding the prevalence, responsible microorganisms, and clinical outcomes of sepsis. However, data on the microbiological landscape and resistance patterns of sepsis in intensive care settings in Asian countries, including India, remain limited and underexplored.[10] Hence, it is important to derive data from regional locations in order to analyze the epidemiological factors that influence the local population and revise treatment protocols accordingly.

Among the cases from the collected data, a male predominance was seen, at 63.3%, which is consistent with multiple studies, including in India,[6,11] and this factor holds true even globally.[12,13] Many studies, including experimental[14,15] and clinical studies,[16,17] have identified that the development of infectious problems following trauma, particularly sepsis, is likely to be associated with male gender. Only patients under 50 may exhibit this gender gap, suggesting that postmenopausal women are no longer in a favorable position. Research on gender-dimorphic reactions to sepsis has been cited; however, there have also been other research with conflicting findings. In this sense, no gender differences in patient outcomes were found in a sizable sample of trauma survivors.[18] Yet another study identified the presence of higher mortality in females than in males, contrary to the proposed hypothesis.[19] Hence, more studies are required to look into the various reasons for gender discrepancies in hospital mortality and care.

From the data collected regarding the various ages in the study, the age group with the highest number of sepsis cases was found in 51–60 years (23.5%), whereas the mean age group across the whole age distribution was 43.75 years. This data correlates with multiple studies, let it be in India[6,20] or worldwide,[21,22] with a well-known consensus across both clinical and research fields that elderly patients are more susceptible to the disease. Multiple risk factors help propagate the development of sepsis in elderly and middle-aged individuals, including prolonged institutionalization

Table 2: Antibiotic resistance patterns among major Gram-positive cocci from ICU blood isolates

Antibiotic	*Staphylococcus aureus* (*n*=47) (%)	Coagulase Negative *Staphylococci* CoNS (*n*=121) (%)	*Enterococcus* species (*n*=39) (%)
Penicillin	100 (*n*=47)	93.5 (113)	53 (*n*=21)
Cefoxitin	72.7 (*n*=34)	84.2 (*n*=102)	-
Erythromycin	81.3, (*n*=38)	90 (*n*=109)	-
Clindamycin	77.5 (*n*=36)	65.4 (*n*=79)	-
Vancomycin	0 (*n*=0)	0 (*n*=0)	27 (*n*=10)
Linezolid	0 (*n*=0)	0 (*n*=0)	0 (*n*=0)
Gentamicin	77.5 (*n*=36)	52.5 (*n*=64)	-
High-level gentamicin	-	-	50 (*n*=20)
Tetracycline	18.2 (*n*=9)	28.8 (*n*=35)	-
Ciprofloxacin	9 (*n*=4)	77 (*n*=93)	-
Cotrimoxazole	68.2 (*n*=32)	59 (*n*=71)	-
Teicoplanin	0 (*n*=0)	0 (*n*=0)	0 (*n*=0)

in hospitals, instrumentation (e.g., chronic indwelling urinary catheters), chronic diseases such as diabetes, chronic kidney diseases, malnutrition, and dementia.[23] Decreased immunological responses, such as compromised cytokine signaling and endothelial dysfunction during sepsis, are linked to aging. These changes may impair the body's capacity to fight infections, resulting in more serious consequences.[24,25]

Researchers have looked into how hospital departmental settings, especially various ICUs, affect sepsis outcomes. Some studies reveal no discernible changes in results, whereas others indicate variability depending on departmental practices and resources.[26] The samples collected from the RICU accounted for the largest proportion of sepsis isolates (36.1%), with many studies that support the hypothesis that pulmonary infections are linked with a higher risk of institutionalization in the hospital.[25,27] A study within the institution also identified the presence of specific pathogens among bronchoalveolar lavage samples, with the microbial growth identified from the data correlating with our study as well.[28] Multiple studies globally have found a correlation with other departments as well, including a study wherein CoNS were the main cause of surgical sepsis in infants <6 months of age.[29] Sepsis risk was raised by factors such as the use of central venous catheters and extended procedures. Despite the low death rate, the hospital stays of affected newborns were noticeably longer. Despite the correlation, it is well known that the management and outcomes of sepsis differ between wards and ICUs, wherein the former is equipped to handle cases of less severity, whereas ICUs are departments created to handle severe cases with advanced interventions.

Sepsis-related mortality in the ICU has been recognized as a major clinical burden, particularly in low- and middle-income countries, especially in India. In this study, the overall ICU mortality rate for patients with culture-positive bloodstream infections was 24%. This falls within the expected range seen in most studies (20–50%), as per regional statistics.[6] The mortality rate in this study is, however, somewhat lesser than in multiple other studies wherein the percentages were higher, including a multi-center prospective study called SEPSIS INDIA involving 1172 ICU patients with a mortality rate of ~50.8%,[30] a prospective observational study done across 5 years in a single centre, that identified the mortality rate at 56%,[6] and other global studies across multiple countries including in Asia, China (33%),[31] and Japan (23%),[32] South America in Brazil,[33] and Europe in Turkey (55.7%).[34] The most prevalent comorbidities have been linked to poor sepsis outcomes in the past, including diabetes mellitus and chronic renal disease.[35] These comorbid conditions exacerbate immune dysregulation and intensify the possibility of infection with resistant bacteria. Longer ICU stay has also been correlated with higher mortality, especially beyond 6 days, which may reflect complications from prolonged hospitalization, ventilator-associated infections, and secondary bloodstream infections, with the length of stay being considered a marker of cost-effectiveness and quality control for patients discharged alive from the hospital.[6,36] The MICU and SICU had the highest number of deaths, possibly due to the presence of more critically ill patients requiring mechanical ventilation or organ support.[37,38] Unit-specific infection control practices and staffing patterns may also contribute to this variability. The microbiological profile revealed that *K. pneumoniae*, *A. baumannii*, and *E. coli* were the predominant bacteria among deceased patients, many exhibiting resistance to carbapenems and aminoglycosides, with these trends being seen in multiple studies.[30,39] High rates of MDR isolates were seen, supporting findings from prior Indian ICU studies highlighting the growing burden of antimicrobial resistance (AMR) in nosocomial infections.

The findings of this study are consistent with existing literature that highlights *K. pneumoniae* (29.8%) and *A. baumannii* (18.1%) as dominant pathogens in ICU-related bloodstream infections. These GN organisms are notorious for their resistance profiles and their association with

hospital-acquired infections, including bloodstream infections.[9] The International Nosocomial Infection Control Consortium has also reported that these bacteria are among the most common isolated pathogens in ICU infections across multiple countries.[40] Some research contradicts these findings, stating that *K. pneumoniae* and *E. coli* are the most common pathogens.[41] In contrast to the presented study, where Pseudomonas was not that significant, another study examining the clinical effects of MDR GN bacilli in ICU settings found that infections brought about by MDR Pseudomonas or *Acinetobacter* species showed the association of significantly less favorable outcomes compared to other types of infections. The study highlighted that the likelihood of death in GN sepsis is significantly increased by multi-drug resistance.[42]

Multiple resistance mechanisms can cause resistance among these pathogens. *A. baumannii* exhibits high resistance rates to carbapenems, primarily caused by the release of carbapenem-hydrolyzing Class D β-lactamases, notably OXA-type enzymes such as OXA-23, OXA-24/40, and OXA-58. These enzymes hydrolyze carbapenems, making them ineffective.[43,44] The New Delhi metallo-β-lactamase-1 (NDM-1) is another significant contributor to carbapenem resistance in *A. baumannii*. NDM-1 confers resistance by hydrolyzing a broad spectrum of β-lactam antibiotics, including carbapenems.[45] The *bla*NDM-1 gene is frequently present on plasmids, facilitating horizontal gene transfer among bacteria. Studies have described the co-existence of *bla*OXA-23 and *bla*NDM-1 in clinical isolates, compounding the resistance challenge.[46] Other documented resistance mechanisms include the AdeABC efflux pump system, which reduces antibiotic intracellular concentrations and efficacy,[47] and the alterations in outer membrane porins, decreasing membrane permeability, thereby limiting antibiotic entry into the bacterial cell.[48]

E. coli showed moderate susceptibility to carbapenems and aminoglycosides but high resistance to cephalosporins and fluoroquinolones. Resistance to cephalosporins is primarily due to the release of extended-spectrum β-lactamases (ESBLs), notably the CTX-M-15 type.[49] Mutations in the quinolone resistance-determining region (QRDR) of the gyrA and parC genes frequently cause fluoroquinolone resistance in *E. coli*. These alterations decrease medication affinity and efficacy by changing the fluoroquinolones' target enzymes.[50,51] While QRDRs are chromosomal changes, *E. coli* also exhibits plasmid-mediated mutations, or plasmid-mediated quinolone resistance (PMQR). PMQR genes, such as qnrA, qnrB, and qnrS, encode proteins that shield DNA gyrase and topoisomerase IV from fluoroquinolone inhibition.[52] The existence of efflux pumps, such as the AcrAB-TolC system, which actively remove a range of drugs from the bacterial cell and contribute to multi-drug resistance, is another mechanism observed in this organism. Drug efficacy may be decreased by overexpressing these pumps, which can lower intracellular antibiotic concentrations.[50]

K. pneumoniae exhibits resistance to cephalosporins and penicillin primarily due to the production of ESBLs, notably the CTX-M, TEM, and SHV types, particularly the CTX-M-15 variant, seen in other pathogens of the *Enterobacterales* group. These enzymes hydrolyze a broad range of β-lactam antibiotics, rendering them useless. Studies from Southern India have reported a high prevalence of these ESBL genes in *K. pneumoniae* isolates, highlighting their role in the pathogen's resistance profile.[53] Carbapenem resistance in *K. pneumoniae* is often mediated by carbapenemases such as NDM and OXA-48-like enzymes, including OXA-232. These enzymes degrade carbapenems, which are often used as last-resort antibiotics.[54] Reports from India have documented the co-existence of these carbapenemase genes in *K. pneumoniae* isolates, exacerbating the resistance challenge.[55] Alterations or loss of outer membrane porins, specifically OmpK35 and OmpK36, also contribute to carbapenem resistance by decreasing membrane permeability.[56]

Among the GP cocci, the notable occurrence of CoNS in ICU blood cultures, such as *S. haemolyticus* and *S. hominis*, highlights their growing significance as real pathogens, particularly in patients who have intravascular devices. This finding is corroborated by studies that show that CoNS are now known to induce nosocomial bloodstream infections rather than just being pollutants.[57] *S. haemolyticus* is the second most commonly isolated CoNS species after *S. epidermidis* in clinical settings. Its high level of antibiotic resistance and capacity to build biofilms on medical devices add to its pathogenicity, making infections challenging to cure. *S. hominis* has also emerged as a major pathogen in bloodstream infections, especially in immunocompromised people. *S. hominis* has been found as one of the three most frequently isolated CoNS species from blood cultures, with a particularly high incidence in ICU conditions.[58]

The acquisition of the *mecA* gene, which codes for a modified penicillin-binding protein (PBP2a) with low affinity for β-lactam antibiotics, such as CX and methicillin, is the main cause of resistance in MRSA strains. Between 13% and 47% of ICU patients in India have MRSA, which presents serious treatment problems.[59] Resistance to macrolides (e.g., ERY) and lincosamides (e.g., CD) in *S. aureus* is frequently caused by methylation of the 23S rRNA binding site, which is mediated by erm genes. This methylation inhibits antibiotic binding, resulting in resistance[60]. Despite high resistance to several antibiotics, *S. aureus* isolates showed 100% susceptibility to VA, TEI, and LZ, indicating these remain effective treatment options.[59]

CoNS, particularly *S. haemolyticus* and *Staphylococcus epidermidis*, are significant nosocomial pathogens. A study from an Indian tertiary care hospital reported that 57.6% of CoNS isolates were methicillin-resistant, with higher resistance rates to ERY (76%), CIP (64.7%), and COT (55.9%) compared to methicillin-sensitive strains. Methicillin resistance in CoNS is mediated by the *mecA* gene, causing

the production of PBP2a, which has a low affinity for β-lactam antibiotics. The presence of SCCmec type I was predominant among MR-CoNS isolates.[61] Similar to *S. aureus*, all CoNS isolates in the study were also susceptible to VA, TEI, and LZ.

A study from a tertiary care hospital in South India reported that 14.7% of *Enterococcus* isolates were VA-resistant. The majority of VA-resistant enterococci (VRE) cases were found in ICU patients.[62] VA resistance in *Enterococcus* species is chiefly facilitated by the vanA and vanB gene clusters, which alter the target site of VA, reducing its binding affinity. The vanA phenotype was the most common, producing high-level resistance to VA and TEI.[62] The presence of HLGR was present in 50% of *Enterococcus* isolates, indicating a significant threat in terms of treating synergistic bacteremia.[63] Despite resistance to several antibiotics, *Enterococcus* species showed high susceptibility to LZ and TEI, meaning that these remain effective treatment options.

This study provides a valuable understanding of the microbial landscape of ICU-acquired bloodstream infections. However, several limitations must be acknowledged to contextualize its findings. First, the retrospective design inherently limits the ability to establish causality and is susceptible to selection bias. The study's reliance on blood cultures, while standard, may not capture all causative pathogens, especially in patients who received empirical antibiotic therapy before sample collection, potentially leading to false-negative results. The study also lacks molecular diagnostic methods, such as PCR, which can detect fastidious or non-culturable organisms and provide rapid identification of antimicrobial resistance genes. Finally, the study does not address potential environmental or procedural factors within the ICU that could influence infection rates and resistance patterns. More data will be needed to quantify the exact impact of the presence of sepsis in these high-risk patients requiring stay in the ICU in hospitals, and what factors influence these patients' mortality and treatment outcomes.

CONCLUSION

This study underscores the predominance of GN bacilli, notably *K. pneumoniae*, *A. baumannii*, and *E. coli*, in ICU-acquired bloodstream infections, with a significant prevalence of MDR strains. Their increasing resistance patterns to commonly used antibiotics, including β-lactams and aminoglycosides, highlight the pressing need for vigorous antimicrobial stewardship programs and the improvement of targeted therapeutic strategies. The universal susceptibility of GP cocci to LZ and VA offers some therapeutic respite, though the emergence of resistance cannot be discounted.

To enhance the management of sepsis in ICU settings, future studies should incorporate prospective designs, employ advanced molecular diagnostics for rapid pathogen and resistance gene identification, and include comprehensive patient outcome data. To prevent antibiotic resistance, it is vital to discover it early, implement effective infection control measures, monitor resistance patterns regularly, and use antibiotics wisely. Such approaches will facilitate timely and precise antimicrobial interventions, ultimately improve patient prognoses, and curb the spread of resistant pathogens.

ACKNOWLEDGMENTS

The authors have to acknowledge all co-authors for this work.

REFERENCES

1. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, *et al*. Assessment of clinical criteria for sepsis: For the third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016;315:762-74.
2. Reinhart K, Daniels R, Machado FR, World Sepsis Day Steering Committee and the Global Sepsis Alliance Executive Board. The burden of sepsis: A call to action in support of World sepsis day 2013. Rev Bras Ter Intensiva 2013;25:3-5.
3. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, *et al*. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016;315:801-10.
4. Schultz MJ, Dunser MW, Dondorp AM, Adhikari NK, Iyer S, Kwizera A, *et al*. Current challenges in the management of sepsis in ICUs in resource-poor settings and suggestions for the future. Intensive Care Med 2017;43:612-24.
5. GBD 2021 Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance 1990-2021: A systematic analysis with forecasts to 2050. Lancet 2024;404:1199-226.
6. Chatterjee S, Bhattacharya M, Todi SK. Epidemiology of adult-population sepsis in India: A single center 5 year experience. Indian J Crit Care Med 2017;21:573-7.
7. Gandra S, Mojica N, Klein EY, Ashok A, Nerurkar V, Kumari M, *et al*. Trends in antibiotic resistance among major bacterial pathogens isolated from blood cultures tested at a large private laboratory network in India, 2008-2014. Int J Infect Dis 2016;50:75-82.
8. Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, *et al*. International study of the prevalence and outcomes of infection in intensive care units. JAMA 2009;302:2323-9.
9. Datta P, Rani H, Chauhan R, Gombar S, Chander J. Health-care-associated infections: Risk factors and epidemiology from an intensive care unit in Northern India. Indian J Anaesth 2014;58:30-5.
10. Phua J, Koh Y, Du B, Tang YQ, Divatia JV, Tan CC, *et al*. Management of severe sepsis in patients admitted to Asian intensive care units: Prospective cohort study.

BMJ 2011;342:d3245.
11. Hammond NE, Kumar A, Kaur P, Tirupakuzhi Vijayaraghavan BK, Ghosh A, Grattan S, *et al*. Estimates of sepsis prevalence and outcomes in adult patients in the ICU in India: A cross-sectional study. Chest 2022;161:1543-54.
12. La Via L, Sangiorgio G, Stefani S, Marino A, Nunnari G, Cocuzza S, *et al*. The global burden of sepsis and septic shock. Epidemiologia (Basel) 2024;5:456-78.
13. 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.
14. Zellweger R, Wichmann MW, Ayala A, Stein S, DeMaso CM, Chaudry IH. Females in proestrus state maintain splenic immune functions and tolerate sepsis better than males. Crit Care Med 1997;25:106-10.
15. Diodato MD, Knöferl MW, Schwacha MG, Bland KI, Chaudry IH. Gender differences in the inflammatory response and survival following haemorrhage and subsequent sepsis. Cytokine 2001;14:162-9.
16. Mahmood K, Eldeirawi K, Wahidi MM. Association of gender with outcomes in critically ill patients. Crit Care 2012;16:R92.
17. Schröder J. Gender differences in human sepsis. Arch Surg 1998;133:1200.
18. Gannon CJ, Napolitano LM, Pasquale M, Tracy KJ, McCarter RJ. A statewide population-based study of gender differences in trauma: Validation of a prior single-institution study1. J Am Coll Surg 2002;195:11-8.
19. Pietropaoli AP, Glance LG, Oakes D, Fisher SG. Gender differences in mortality in patients with severe sepsis or septic shock. Gend Med 2010;7:422-37.
20. Juliana A, Leela KV, Gopinathan A, Sujith R. Occurrence and resistance pattern of gram-negative bacteremia and sepsis in A tertiary care hospital - a four-year study. J Pure Appl Microbiol 2022;16:655-62.
21. Habyarimana T, Murenzi D, Musoni E, Yadufashije C, Niyonzima FN. Bacteriological profile and antimicrobial susceptibility patterns of bloodstream infection at Kigali university teaching hospital. Infect Drug Resist 2021;14:699-707.
22. Lei S, Li X, Zhao H, Xie Y, Li J. Prevalence of sepsis among adults in China: A systematic review and meta-analysis. Front Public Health 2022;10:977094.
23. Rowe TA, McKoy JM. Sepsis in older adults. Infect Dis Clin North Am 2017;31:731-42.
24. Michels EHA, Butler JM, Reijnders TD, Cremer OL, Scicluna BP, Uhel F, *et al*. Association between age and the host response in critically ill patients with sepsis. Crit Care 2022;26:385.
25. Nasa P, Juneja D, Singh O. Severe sepsis and septic shock in the elderly: An overview. World J Crit Care Med 2012;1:23-30.
26. GBD 2019 LRI Collaborators. Age-sex differences in the global burden of lower respiratory infections and risk factors, 1990-2019: Results from the global burden of disease study 2019. Lancet Infect Dis 2022;22:1626-47.
27. Madkour AM, ELMaraghy AA, Elsayed MM. Prevalence and outcome of sepsis in respiratory intensive care unit. Egypt J Bronchol 2022;16:29
28. Sivasubramanian V, Sasikumar S, Vadivelu G. Retrospective analysis of microbial profiles in bronchoalveolar lavage samples from patients with lower respiratory tract infections. Front Health Inform 2024;13:918-9.
29. Kessler U, Ebneter M, Zachariou Z, Berger S. Postoperative sepsis in infants below 6 months of age. World J Pediatr 2009;5:113-7.
30. Todi S, Mehta Y, Zirpe K, Dixit S, Kulkarni AP, Gurav S, *et al.* A multicentre prospective registry of one thousand sepsis patients admitted in Indian ICUs: (SEPSIS INDIA) study. Crit Care 2024;28:375.
31. Zhou J, Qian C, Zhao M, Yu X, Yu X, Kang Y, *et al*. Epidemiology and outcome of severe sepsis and septic shock in intensive care units in mainland China. PLoS One 2014;9:e107181.
32. Abe T, Ogura H, Shiraishi A, Kushimoto S, Saitoh D, Fujishima S, *et al*. Characteristics, management, and in-hospital mortality among patients with severe sepsis in intensive care units in Japan: the FORECAST study. Crit Care 2018;22:322.
33. Machado FR, Cavalcanti AB, Bozza FA, Ferreira EM, Angotti Carrara FS, Sousa JL, *et al*. The epidemiology of sepsis in Brazilian intensive care units (the sepsis PREvalence assessment database, SPREAD): An observational study. Lancet Infect Dis 2017;17:1180-9.
34. Baykara N, Akalın H, Arslantaş MK, Hancı V, Çağlayan Ç, Kahveci F, *et al*. Epidemiology of sepsis in intensive care units in Turkey: A multicenter, point-prevalence study. Crit Care 2018;22:93.
35. Esper AM, Martin GS. The impact of comorbid [corrected] conditions on critical illness. Crit Care Med 2011;39:2728-35.
36. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: Analysis of incidence, outcome, and associated costs of care. Crit Care Med 2001;29:1303-10.
37. Toufen C Jr., Franca SA, Okamoto VN, Salge JM, Carvalho CR. Infection as an independent risk factor for mortality in the surgical intensive care unit. Clinics (Sao Paulo) 2013;68:1103-8.
38. Pieroni M, Olier I, Ortega-Martorell S, Johnston BW, Welters ID. In-hospital mortality of sepsis differs depending on the origin of infection: An investigation of predisposing factors. Front Med (Lausanne) 2022;9:915224.
39. Nagarjuna D, Mittal G, Dhanda RS, Gaind R, Yadav M. Alarming levels of antimicrobial resistance among sepsis patients admitted to ICU in a tertiary care hospital in India - a case control retrospective study. Antimicrob Resist Infect Control 2018;7:150.
40. Rosenthal VD, Duszynska W, Ider BE, Gurskis V, Al-Ruzzieh MA, Myatra SN, *et al*. International nosocomial infection control consortium (INICC) report, data summary of 45 countries for 2013-2018, adult and

pediatric units, device-associated module. Am J Infect Control 2021;49:1267-74.
41. Garg R, Tellapragada C, Shaw T, Eshwara VK, Shanbhag V, Rao S, *et al*. Epidemiology of sepsis and risk factors for mortality in intensive care unit: A hospital based prospective study in South India. Infect Dis (Lond) 2022;54:325-34.
42. Pop-Vicas A, Opal SM. The clinical impact of multidrug-resistant gram-negative bacilli in the management of septic shock. Virulence 2014;5:206-12.
43. Rolain JM, Loucif L, Al-Maslamani M, Elmagboul E, Al-Ansari N, Taj-Aldeen S, *et al*. Emergence of multidrug-resistant *Acinetobacter baumannii* producing OXA-23 Carbapenemase in Qatar. New Microbes New Infect 2016;11:47-51.
44. Odih EE, Sunmonu GT, Okeke IN, Dalsgaard A. NDM-1- and OXA-23-producing *Acinetobacter baumannii* in wastewater of a Nigerian hospital. Microbiol Spectr 2023;11:e0238123.
45. Kumarasamy KK, Toleman MA, Walsh TR, Bagaria J, Butt F, Balakrishnan R, *et al*. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: A molecular, biological, and epidemiological study. Lancet Infect Dis 2010;10:597-602.
46. Joshi PR, Acharya M, Kakshapati T, Leungtongkam U, Thummeepak R, Sitthisak S. Co-existence of *bla*$_{(OXA-23)}$ and *bla*$_{(NDM-1)}$ genes of *Acinetobacter baumannii* isolated from Nepal: Antimicrobial resistance and clinical significance. Antimicrob Resist Infect Control 2017;6:21.
47. Zack KM, Sorenson T, Joshi SG. Types and mechanisms of efflux pump systems and the potential of efflux pump inhibitors in the restoration of antimicrobial susceptibility, with a special reference to *Acinetobacter baumannii*. Pathogens 2024;13:197.
48. Rahi AA, Al-Hasnawy HH. Expression of genes associated with efflux pump and porins in *Acinetobacter baumannii* isolates recovered from different clinical specimens. Biomed Biotechnol Res J 2024;8:464-73.
49. Shin J, Kim DH, Ko KS. Comparison of CTX-M-14- and CTX-M-15-producing *Escherichia coli* and *Klebsiella pneumoniae* isolates from patients with bacteremia. J Infect 2011;63:39-47.
50. Pazhani GP, Chakraborty S, Fujihara K, Yamasaki S, Ghosh A, Nair GB, *et al*. QRDR mutations, efflux system and antimicrobial resistance genes in enterotoxigenic *Escherichia coli* isolated from an outbreak of diarrhoea in Ahmedabad, India. Indian J Med Res 2011;134:214-23.
51. Logan LK, Coy LR, Pitstick CE, Marshall SH, Medernach RL, Domitrovic TN, *et al*. The role of the plasmid-mediated fluoroquinolone resistance genes as resistance mechanisms in pediatric infections due to Enterobacterales. Front Cell Infect Microbiol 2023;13:1249505.
52. Gomaa Elsayed A, Fahmy EM, Abdellatif Alsayed M, Ahmed ME, El Sayed Zaki M, Mofreh Mohamed M. Study of plasmid mediated quinolone resistance genes among *Escherichia coli* and *Klebsiella pneumoniae* isolated from pediatric patients with sepsis. Sci Rep 2024;14:11849.
53. Muzaheed, Doi Y, Adams-Haduch JM, Endimiani A, Sidjabat HE, Gaddad SM, *et al*. High prevalence of CTX-M-15-producing *Klebsiella pneumoniae* among inpatients and outpatients with urinary tract infection in Southern India. J Antimicrob Chemother 2008;61:1393-4.
54. Veeraraghavan B, Shankar C, Karunasree S, Kumari S, Ravi R, Ralph R. Carbapenem resistant *Klebsiella pneumoniae* isolated from bloodstream infection: Indian experience. Pathog Glob Health 2017;111:240-6.
55. Pathak A, Tejan N, Dubey A, Chauhan R, Fatima N, Jyoti, *et al*. Outbreak of colistin resistant, carbapenemase (bla ($_{NDM}$), bla($_{OXA-232}$)) producing *Klebsiella pneumoniae* causing blood stream infection among neonates at a tertiary care hospital in India. Front Cell Infect Microbiol 2023;13:1051020.
56. Little ML, Qin X, Zerr DM, Weissman SJ. Molecular diversity in mechanisms of carbapenem resistance in paediatric *Enterobacteriaceae*. Int J Antimicrob Agents 2012;39:52-7.
57. Becker K, Heilmann C, Peters G. Coagulase-negative staphylococci. Clin Microbiol Rev 2014;27:870-926.
58. Szemraj M, Glajzner P, Olszowiec K, Sienkiewicz M. The prevalence of multidrug resistance in *Staphylococcus hominis* isolated from clinical materials. Sci Rep 2025;15:414.
59. Mehta Y, Hegde A, Pande R, Zirpe KG, Gupta V, Ahdal J, *et al*. Methicillin-resistant *Staphylococcus aureus* in intensive care unit setting of India: A review of clinical burden, patterns of prevalence, preventive measures, and future strategies. Indian J Crit Care Med 2020;24:55-62.
60. Mišić M, Čukić J, Vidanović D, Šekler M, Matić S, Vukašinović M, *et al*. Prevalence of genotypes that determine resistance of staphylococci to macrolides and lincosamides in serbia. Front Public Health 2017;5:200.
61. Singh S, Dhawan B, Kapil A, Kabra SK, Suri A, Sreenivas V, *et al*. Coagulase-negative staphylococci causing blood stream infection at an Indian tertiary care hospital: Prevalence, antimicrobial resistance and molecular characterisation. Indian J Med Microbiol 2016;34:500-5.
62. Sivaradjy M, Gunalan A, Priyadarshi K, Madigubba H, Rajshekar D, Sastry AS. Increasing trend of vancomycin-resistant enterococci bacteremia in a tertiary care hospital of South India: A three-year prospective study. Indian J Crit Care Med 2021;25:881-5.
63. Hota S, Patil SR, Mane PM. Antimicrobial resistance profile of enterococcal isolates from clinical specimens at a tertiary care hospital in Western Maharashtra, India. Cureus 2024;16:e73416.

Source of Support: Nil. **Conflicts of Interest:** None declared.