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Research Article

TRENDS IN THE MICROBIOLOGICAL SPECTRUM AND ANTIMICROBIAL RESISTANCE AMONG ICU PATIENTS DIAGNOSED WITH BACTEREMIA – A RETROSPECTIVE STUDY

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ABSTRACT

Objectives: The objectives of this study were to determine the trends of microorganisms and their antimicrobial resistance pattern among ICU patients diagnosed with bacteremia.

Methods: This retrospective study was conducted in the microbiology laboratory at a tertiary care teaching hospital from August 2021 to July 2022. A total of 2492 blood culture samples were collected from hospital ICUs from the patient with suspected septicemia. All samples were processed using the automated blood culture system BACT/ALERT 3D/60 for the recovery of pathogenic microorganisms, and antimicrobial susceptibility testing was performed using the automated VITEK 2 Compact system. A Chi-square test was done to assess the statistical significance of our results.

Results: Out of 2492 blood culture samples, 296 (11.87%) were identified as culture positive, in which 252 (85.13%) were Gram-negative isolates, 38 (12.83%) were Gram-positive isolates, and 06 (2.02%) were other organisms (contaminants). Gram-negative isolates showed maximum sensitivity to colistin 205 (81.40%), and Gram-positive isolates showed maximum sensitivity to vancomycin 35 (92.10%).

Conclusion: Early blood culture results could provide the basis for the appropriate use of antibiotics that can improve clinical prognosis and help in reducing mortality.

Keywords: Bloodstream infections, ICUs, Antimicrobial resistance.

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INTRODUCTION

Bloodstream infections remain one of the major causes of morbidity and mortality among hospitalized patients. BSI is defined by the presence of viable bacterial (bacteremia) or fungal microorganisms in the bloodstream, demonstrated by the positivity of one or more blood cultures that elicit or have elicited an inflammatory response characterized by the alteration of clinical, laboratory, and hemodynamic parameters. BSI and sepsis are two sides of the same phenomenon, since sepsis is an infectious syndrome triggered by an infectious disease, while BSI is sepsis triggered by viable microorganisms circulating in the bloodstream [1]. Studies show a worldwide increase in the rate of bacteremia every year affecting millions of people who succumb to death. Intensive care units (ICUs) are the main epicenter of sepsis as they harbor vulnerable and high-risk patients [2]. A steep rise in the number of septicemic patients has become a major health issue and it has been recognized as one of the biggest challenges for clinicians to select appropriate antimicrobial agents. This has been further complicated by the resistance of microorganisms to antimicrobial drugs [3].

Another threat that is becoming significant to public health is antimicrobial resistance (AMR), which hinders the empirical therapy of these infections. It is very challenging to describe the magnitude of the problem of these AMR pathogens as the level of AMR varies with respect to geographical areas and health-care setups. This can ultimately lead to a delay in antimicrobial therapy and may result in adverse outcomes [2].

Blood cultures are the mainstay in the diagnosis of the causative microorganism and its bacterial load. However, it takes 2 to 3 days to get the culture report and to start the appropriate empirical treatment [4]. Henceforth, mortality can be reduced by starting the appropriate use of antibiotics at the earliest [3]. Antibiograms can be designed based on our study, and empirical therapy can be started at the earliest without waiting for blood culture result report to reduce unnecessary mortality due to BSI.

In this study, we aim to look into the trends of microorganisms and their AMR patterns. As there are only a few studies that have been conducted regarding adult sepsis in ICU patients, hence we undertook a retrospective study to evaluate the spectrum of microorganisms causing septicemia in adult patients and their antimicrobial resistance pattern in the intensive care units (ICUs) of a tertiary care teaching hospital.

METHODS

This study was conducted retrospectively in the microbiology laboratory of a tertiary care teaching hospital after obtaining approval from the Institutional Research and Ethics Committee. The study was conducted for a period of 1 year (August 2021–July 2022). A total of 2492 blood culture samples were collected and processed using standard CLSI guidelines from hospital ICUs [5].

Inclusion criteria

All adult patients 18 years of age or older were admitted to the ICUs and diagnosed with bacterial septicemia after 48 h of admission to the hospital.

Exclusion criteria

All the patients below 18 years of age admitted in ICUs and wards were diagnosed with a condition other than bacterial septicemia or patient diagnosed with septicemia at the time of admission to the hospital.

Study procedure

Before the start of antibiotics, 5–10 ml of blood was collected from a peripheral/central vein using aseptic precautions. Then, the sample was sent to the microbiology laboratory for further processing. Blood samples were processed using the automated blood culture system BACT/ALERT 3D/60 (Biomerieux) for the recovery of pathogenic

microorganisms. Once the blood culture bottle beeped positive, it was further subcultured on blood agar and MacConkey agar. After 24–48 h of aerobic incubation at 37° C, microbial growth obtained was identified using an automated VITEK 2 Compact system (Biomerieux).

For Gram-positive (GP) organisms, a GP card was used, and for Gram-negative (GN), a GN card was used. After the isolation of bacteria, it was further processed for antimicrobial sensitivity testing by an automatic VITEK 2 Compact system. For Gram-positive, a P628 card was used which included the following panel of antibiotics: gentamicin, levofloxacin, erythromycin, clindamycin, daptomycin, cefotaxime, tetracycline, co-trimoxazole, vancomycin, teicoplanin, and linezolid. For Gram-negative organisms, N405 card and N406 were used in the case of lactose fermenting and non-lactose fermenting organisms, respectively. Both cards included the following panel of antibiotics: amikacin, gentamicin, ceftriaxone, cefotaxime, amoxiclav, levofloxacin, imipenem, co-trimoxazole, tigecycline, colistin, cefoperazone–sulbactam, and piperacillin–tazobactam. *Staphylococcus hemolyticus* and *Staphylococcus epidermidis* were considered contaminants, and their antimicrobial susceptibility was not performed. The blood culture bottles were retained for 5 days before proclaiming them as negative.

Statistical analysis was done using a Chi-square chart. $p<0.001$ was considered statistically significant. Since it is a retrospective study, the whole of the data was collected from hospital records.

RESULTS

A total of 2492 blood culture samples were received in the microbiology laboratory, at a tertiary care teaching hospital, and 296 (11.87%) were identified as culture positive. These were included for further study of antibiotic susceptibility testing. Thus, the total sample size for this study was 296 (Fig. 1).

Out of the total 2492, blood culture samples, 296 (11.87%) were culture positive and 2196 (88.13%) were culture negative (Fig. 2).

The total sample size is 296. Out of them, 252 (85.13%) were Gram-negative isolates and 38 (12.83%) were Gram-positive isolates and 06 (2.02%) were contaminants (Fig. 3).

The total sample size was 296. Out of them, 252 (85.13%) were Gram-negative isolates and among them, the maximum isolates were *Klebsiella pneumoniae* 73 (29%), followed by *Escherichia coli* 71 (28%), *Acinetobacter baumannii* 39 (15%), and *Pseudomonas aeruginosa* 25 (10%). The remaining isolates were *Serratia marcescens, Elizabethkingia meningoseptica, Sphingomonas paucimobilis, Acinetobacter lwoffii, Enterobacter cloacae, Burkholderia cepacia, Salmonella typhi,* and *Pseudomonas putida* in decreasing order (Fig. 4).

The total sample size was 296. Out of the total number of samples, 38 (12.83%) were Gram-positive isolates and the most frequent isolate was *Staphylococcus aureus* which was isolated in 24 (63.15%) samples, followed by *Enterococcus faecalis*, isolated in 14 (36.84%) samples. The rest were contaminants (*Staphylococcus hemolyticus* and *Staphylococcus epidermidis*) which were isolated in 6 (2.02%) samples. The contaminants were not processed for antimicrobial susceptibility (Table 1).

Gram-negative isolates showed maximum sensitivity to colistin 205 (81.40%), followed by amikacin 127 (50.40%), tigecycline 85 (33.80%), and imipenem 79 (31.40%). Maximum resistance was shown to cefotaxime (98.40%), ceftriaxone (95.20%), and amoxiclav (92.80%). Results were significant as the *p<0.001* (Table 2).

Gram-positive isolates showed maximum sensitivity to vancomycin 35 (92.10%), followed by linezolid 33 (86.84%), teicoplanin 18 (47.36%), and tigecycline 16 (42.10%). They showed maximum resistance to cefotaxime (86.84%), levofloxacin (84.20%), gentamicin (81.60%), and co-trimoxazole (81.58%). Results were significant as the *p<0.001*.

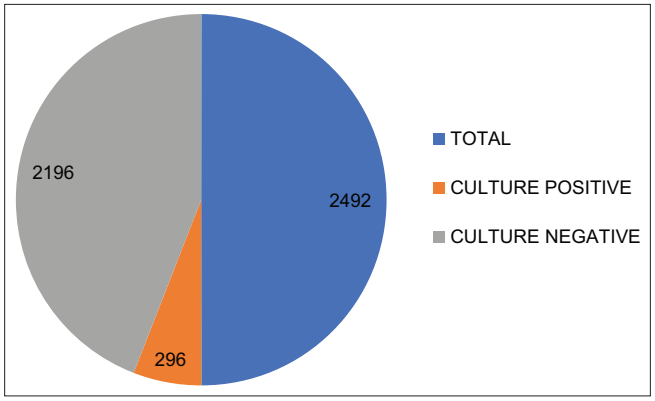

Fig. 1: Distribution of culture positive and culture negative samples

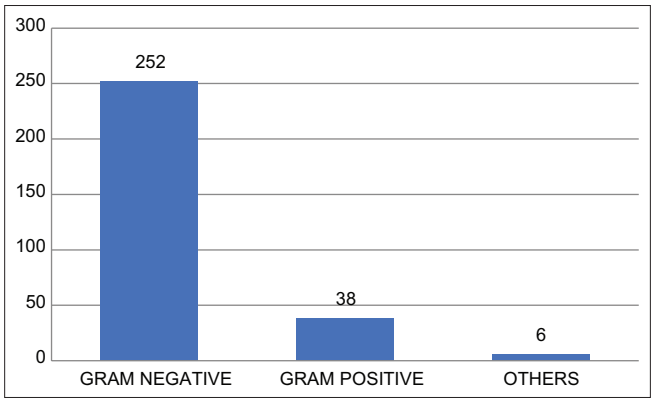

Fig. 2: Distribution of Gram-negative and gram positive bacteria

Table 1: Drug resistance in Gram-negative isolates

Drugs	Sensitivity, n (%)	Resistance, n (%)
Amikacin	127 (50.40)	125 (49.60)
Gentamicin	67 (26.60)	185 (73.40)
Amoxiclav	18 (7.20)	234 (92.80)
Cefotaxime	4 (1.60)	248 (98.40)
Ceftriaxone	12 (4.80)	240 (95.20)
Levofloxacin	51 (20.30)	201 (79.70)
Cefoperazone/sulbactam	75 (29.80)	177 (70.20)
Piperacillin/tazobactam	45 (17.90)	207 (82.10)
Co-trimoxazole	35 (13.90)	217 (86.10)
Imipenem	79 (31.40)	173 (68.60)
Tigecycline	85 (33.8)	167 (66.20)
Colistin	205 (81.40)	47 (18.60)

Table 2: Drug resistance in Gram-positive organisms

Drugs	Sensitivity, n (%)	Resistance, n (%)
Gentamicin	7 (18.40)	31 (81.60)
Levofloxacin	6 (15.80)	32 (84.20)
Clindamycin	11 (28.95)	27 (71.05)
Erythromycin	9 (23.68)	29 (76.32)
Daptomycin	8 (21.05)	30 (78.95)
Cefotaxime	5 (13.16)	33 (86.84)
Tetracycline	15 (39.48)	23 (60.52)
Co-trimoxazole	7 (18.42)	31 (81.58)
Teicoplanin	18 (47.36)	20 (52.64)
Tigecycline	16 (42.10)	22 (57.90)
Linezolid	33 (86.84)	5 (13.16)
Vancomycin	35 (92.10)	3 (7.90)

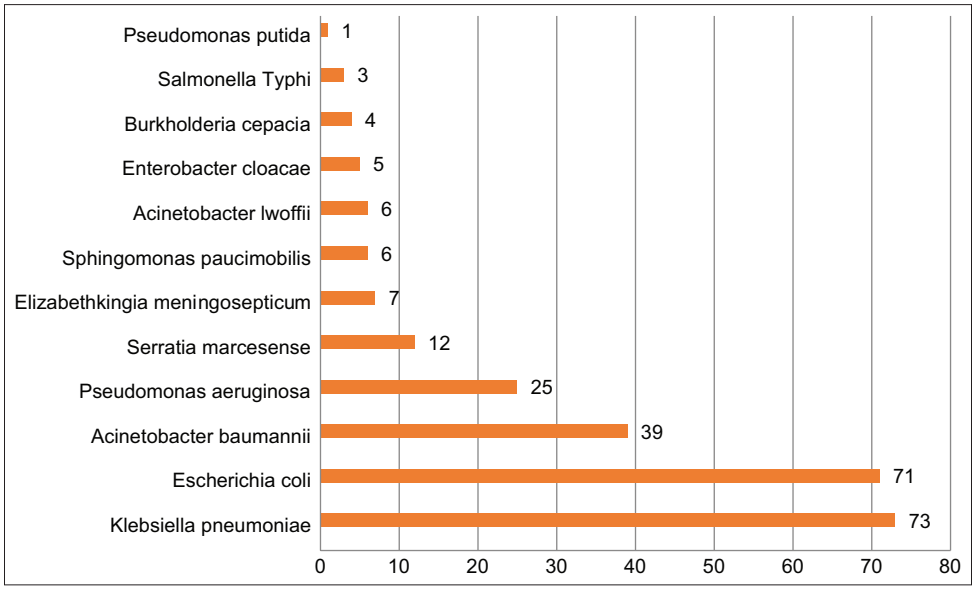

Fig. 3: Distribution of Gram-negative isolates

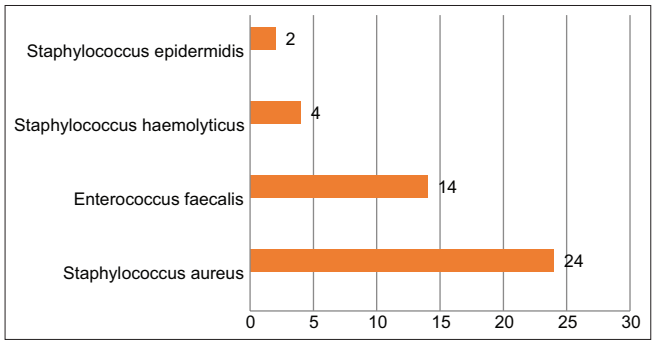

Fig. 4: Distribution of Gram-positive isolates

DISCUSSION

Due to dramatic changes in the spectrum of microbial pathogens causing BSI, there is a concomitant increase in drug resistance [2]. The emergence of AMR is often due to the excessive use of broad-spectrum antimicrobial agents in more than 60% of all ICU patients who receive antibiotics during their stay in ICUs [6]. However, a delay in prescribing empirical antibiotic therapy may cause an increase in mortality [7]. Several changes have been introduced in ICUs to improve mortality rates such as antimicrobial cycling and de-escalation therapy. The purpose of this study is to help in the control of BSI and prevent the irrational use of antibiotics.

Medical records of septic patients in the ICU were reviewed and those who fulfilled the inclusion criteria were included in our study. A total of 2492 blood culture samples were included, out of them, 296 (11.87%) were culture positive and 2196 (88.13%) were culture negative (Fig. 1). This finding was coherent with another study [8]. We found that culture-positive patients have higher comorbidity. All samples in our study were monomicrobial which was in coherence with other studies [9,10]. Knowing the positivity rate in ICUs helped us to improve our infection control practices and measures could be taken to lower the rate of hospital-acquired infections.

The patients were classified into Gram-positive bacteremia and Gram-negative bacteremia. However, the patients in the latter group were far more than the patients in the Gram-positive group. Out of the total 296 blood culture samples, 252 (85.13%) were Gram-negative isolates, 38 (12.83%) were Gram-positive isolates, and 06 (2.02%) were other isolates (contaminants). This is due to the fact that Gram-negative bacteria are more intrinsically resistant to antibiotics which makes them more dangerous in hospital settings, they remain the most dangerous superbugs today. The results of our study are in agreement with other studies [11,12]. However, some studies show findings that are in contrast to our study [13,14]. The ESKAPE (*Enterococcus, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species*) pathogens are the leading cause of hospital-acquired infections [15]. The majority of isolates in our study comprised them, so it is evident that the majority of BSIs in our ICUs were due to poor infection control practices. Hence, stress must be laid on health-care workers to improve their work practices and reduce nosocomial infections.

In our current study, out of 296 culture-positive samples, 252 (85.13%) were Gram-negative isolates, and the maximum was *Klebsiella pneumoniae* 73 (29%), followed by *Escherichia coli* 71 (28%), *Acinetobacter baumannii* 39 (15%), and *Pseudomonas aeruginosa* 25(10%). The minor isolates included *Serratia marcescens, Sphingomona spaucimobilis, Acinetobacter lwoffii, Enterobacter cloacae, Burkholderia, Salmonella typhi, and Pseudomonas putida*. Results were concordant with the study by Ratzinger and colleagues [8]. In his study, *Escherichia coli* was the most common Gram-negative bacterial isolate. In another study by Daniel *et al*., the most common Gram-negative pathogen was *Escherichia coli*. This finding is in contrast to many studies which identified Gram-positive as the common pathogen [13,14]. In the present study, 38 (12.83%) were found to be Gram-positive isolates and the maximum was *Staphylococcus aureus* 24 (63.15%), followed by *Enterococcus faecalis* 14 (36.84%). The remaining 6 (2.02%) were contaminants (*Staphylococcus hemolyticus and Staphylococcus epidermidis*) that were not further processed. The results are in agreement with the studies where the most commonly isolated organism was *S. aureus* [16].

The maximum sensitivity of Gram-negative isolates to antimicrobials was seen to colistin 205 (81.40%), followed by amikacin 127 (50.40%), tigecycline 85 (33.80%), and imipenem 79 (31.40%). The study included 61.08% isolates that were extended-spectrum beta-lactamase (ESBL) which is in accordance with some studies [2,7,16,17]. As a consequence, it becomes difficult for clinicians to treat bloodstream infections due to ESBL-producing Enterobacteriaceae [18].

Gram-positive isolates showed maximum sensitivity to vancomycin 35(92.10%), followed by linezolid 33 (86.84%), teicoplanin

18 (47.36%), and tigecycline 16 (42.10%) with 91.10% being methicillin-resistant Staphylococci (MRSA) and 57.14% were vancomycin-resistant Enterococci (VRE). Our result is in agreement with to study showing a higher incidence of MRSA and VRE, raising an alarm, and highlighting to undergo strict antibiotic protocols in intensive care units [19-21]. This finding contradicts one of the recent studies by Farah *et al.* and Rajeshwari KG possibly due to antibiotic selection pressure [22,23]. This raises a serious concern about the development of antibiotic resistance in critically ill patients in ICUs.

CONCLUSION

Early blood culture results could provide the basis for the appropriate use of antibiotics that can improve clinical prognosis and help in reducing mortality. The findings of our study suggest that there is a difference in host response and virulence factors of different bacterial isolates, and therefore, new countermeasures beyond conventional antimicrobial medications are needed in the community. Different methods must be adopted for early diagnosis to start early and appropriate treatment to reduce the upcoming increase in septicemia. With the help of the present study, we can frame an antibiogram and start early empirical therapy to reduce hospital-acquired infections. It can also be a guide to other tertiary care hospitals in the same region.

AUTHORS CONTRIBUTION

All the authors contributed equally to conceptualizing the theme as well as finalizing the draft.

CONFLICTS OF INTEREST

Nil.

AUTHORS FUNDING

Nil.

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