Microbiological Profile and Antimicrobial Resistance Pattern of Blood Culture Isolates in a Tertiary Care Teaching Institute in Central India

[1]Sonal P. Chavan, Assistant Professor, Microbiology Dept, Indira Gandhi Govt. Med College, Nagpur, Maharashtra, India

[2]Sharmila S. Raut, Professor & Head, Microbiology Dept, Indira Gandhi Govt. Med College, Nagpur, Maharashtra, India

[3]Shweta Sharma, JR2, Microbiology Dept, Indira Gandhi Govt. Med College, Nagpur, Maharashtra, India

[4]Ravindra K. Khadse, Assoc. Professor, Microbiology Dept, Indira Gandhi Govt. Med College, Nagpur, Maharashtra, India

[5]Rajni P. Tore, Associate Professor, Microbiology Dept, Indira Gandhi Govt. Med College, Nagpur, Maharashtra, India

Corresponding Author: Dr. Shweta , JR2 , Microbiology Dept, Indira Gandhi Govt Medical College, CA Road, Nagpur -18, Maharashtra, India

Abstract

Introduction: Bloodstream infections cause significant morbidity and mortality worldwide and are among the most common healthcare-associated infections. Early initiation of appropriate antimicrobial treatment is critical in decreasing morbidity and mortality among patients with bloodstream infections. Regular surveillance of blood stream etiology is important in monitoring the spectrum of bacterial pathogens and their sensitivity pattern in a particular area.

Therefore a retrospective analytical study was undertaken in a tertiary care hospital to identify the bacteriological etiology of blood stream infections and the antibiotic resistance pattern of the isolates as it would be a useful guide for clinicians initiating the empiric antibiotic therapy.

Methods: A total of 928 Blood samples from clinically suspected cases of bacteremia were studied for 6 months. Blood cultures, isolation of organisms and Antibiotic susceptibility testing was done by standard methods. Automated method like VITEK 2 Compact by Biomerieux was also used.

Results: Out of total 912 blood specimen, 212(22%) yielded growth. Out of 212 positive patients, males (140- 66%) predominated twice the number of females (72-34%). Maximum culture positivity was seen in 0-9 yrs age grp followed by 60-69 yrs. The frequency of isolation of Gram-negative bacteria (n=134, 63.2%) was found to be more than that of Gram-positive bacteria (n=50, 23.5%). *Candida* species were also isolated from a significant number of patients (n=30, 14.2%). The commonest organisms isolated were *Staphylococcus aureus* (17%) followed by *Escherichia coli* (16%) and *Klebsiella pneumoniae*(15%).

Staphylococcus aureus were highly sensitive to vancomycin (100% and 75%) and linezolid (100%

each). Methicillin resistance was higher (75%) in CoNS in contrast with *S. aureus* (61%). Amongst enterococcus, 50% strains were found to be vancomycin resistant (VRE). *Streptococcus sp* were found to be sensitive to all the drugs.

Amongst Gram negative bacterial isolates showed maximum sensitivity for colistin followed by tigecycline and amikacin. Ampicillin,amoxyclav, cephalosporins and doxycline showed very high resistance.

Conclusion: The increase in the prevalence of multidrug resistant bacteria emphasize the urgent need for rational use of antibiotics, formulation of antibiotic policy and implementation of infection control practices for the effective management and prevention of drug resistance. Routine surveillance of Microbial flora from septicaemic cases and their antimicrobial resistance pattern with existing guidelines will go long way in reducing multi drug resistance in pathogens.

Keywords: Septicemia, Blood culture, Antimicrobial resistance

Introduction

Bloodstream infections cause significant morbidity and mortality worldwide and are among the most common healthcare-associated infections. [1] The mortality rate ranges from 20% to 50% in cases of bacteremia. [2] The prevalence of resistance of blood borne isolates is increasing and it also varies in accordance with geographical and regional location. The infection caused by Multidrug Resistant (MDR) organisms is more likely to prolong the hospital stay, increase the risk of death, and require treatment with more expensive antibiotics. [3]

This increasing antimicrobial resistance is a worldwide concern and is subjected to regional variation. [2] The potential for antimicrobial resistance is one

consideration for physicians when selecting a regimen with which to treat patients. Determination of antibiotic sensitivity patterns in periodic intervals is mandatory in each region for the clinicians to be aware of the emerging pathogens that pose a threat to the community, to provide safe and effective empirical therapies. [4] Early initiation of appropriate antimicrobial treatment is critical in decreasing morbidity and mortality among patients with bloodstream infections . [1]

There appears to be a paucity of surveys from developing countries in general, and from the Indian subcontinent in particular. Thus, regular surveillance of blood stream etiology is important in monitoring the spectrum of bacterial pathogens and their sensitivity pattern in a particular area. Such data are not only necessary for the clinicians to be aware of the emerging resistant strains of pathogens that are a threat to the community but also provide platform to initiate effective empirical therapy.[2] Therefore a retrospective analytical study was undertaken in a tertiary care hospital to identify the bacteriological etiology of blood stream infections and the antibiotic resistance pattern of the isolates as it would be a useful guide for clinicians initiating the empiric antibiotic therapy.

Materials & Method

A total of 928 Blood samples from clinically suspected cases of bacteremia were studied for a period of 6 months from January 2018 to June 2018 admitted in our 600-bedded teaching hospital at Microbiology department, Indira Gandhi Govt Medical College, Nagpur. All the samples were collected from indoor patients processed in the Microbiology laboratory. Details like medical registration number, laboratory number, age and sex of the patients, and type and place of collection of specimens were recorded.

The vein puncture site was disinfected with 70% alcohol before collecting blood for culture. Approximately 5-10 ml of blood was collected from anticubital vein using strict aseptic precautions and inoculated immediately into blood culture bottles. In pediatric cases 1-2 mL of blood was collected. After collection, these bottles were immediately incubated overnight at 35ºC. After 24 hours incubation, these samples were sub cultured on Blood and MacConkey's agar plates and incubated at 37ºC overnight. Further subculture was followed on day 3 and day 5.The negative results were followed up to 7 days and final report was issued. Identification of growth was based on colony morphology, Gram staining and appropriate biochemical test.[5] Nonfermenters and the other organisms which were difficult to identify were subjected to VITEK 2 Compact by Biomerieux. Antibiotic susceptibility testing (AST) was performed on Mueller–Hinton agar plates with commercially available discs (Hi media, Mumbai) by Modified Kirby-Bauer [6] disc diffusion method and interpreted as per the CLSI 2017 guidelines.[7] The following antibiotics were tested for Gram positive bacteria includes Penicillin (10 units), Cefoxitin(10 µg), erythromycin (15 µg),clindamycin(2 µg) linezolid(30 µg) , Vancomycin (30 mcg- for enterococcus), gentamicin (5 µg), Amikacin ciprofloxacin (5 µg), levofloxacin (µg) and doxycycline(µg). Gram negative includes ampicillin (10µg), amoxyclav (30/10 µg), cefazolin(µg),cefuroxime(µg), ceftriaxone (30 µg),ceftazidime (70 µg), cefepime (30 µg) Piperacillin/Tazobactum((100/10 µg), Cefoperazone/Sulbactum(70 /10 µg), Imipenem (10µg), Meropenem(µg), Cotrimoxazole (25 µg) Gentamicin(5 µg), Amikacin (30 µg), Doxycycline(µg), Ciprofloxacin(µg), Levofloxacin(µg),Tigecycline(µg),

Colistin(µg). *Escherichia coli* (ATCC 25922), *Staphylococcus aureus* (ATCC 25923) and *Pseudomonas aeroginosa* (ATCC 27853) were used as reference strains for culture and susceptibility testing. Multidrug resistant organisms were subjected to Minimum Inhibitory concentration (MIC) by VITEK 2 Compact by Biomerieux.

Results & Discussion

Septicemia leads to a significant morbidity and mortality and it is amongst the most common health-care associated infections that requires rapid and aggressive antimicrobial treatment. In recent years, there has been an increase in the incidence of septicemia due to *Enterobacteriaceae and other Gram-negative* bacilli. Sensitive bacterial strains are now being replaced by multi-drug resistant (MDR) strains.[2] Likewise increase in incidence is also seen among Gram-positive isolates such as methicillin resistance in *Staphylococcus aureus (MRSA) and* vancomycin resistance in *Enterococci (VREs)*. [8]

In the present study, 928 blood samples were processed for culture and 212 yielded positive cultures (Table 1). The gender distribution of positive samples was found to be 140 (66%) males and 72(34%) females with a male: female ratio of 2:1(Table 1). These results are consistent with the study done by Kaur and Singh who made similar observation of male dominance in their studies. [9]

In our study, the highest rate of prevalence was found in 0-9 yrs age grp followed by age group 60-69 yrs as shown in Table 1. Sepsis and septic shock occur at all ages but most often in elderly patients. Advanced age is a risk factor for acquiring nosocomial blood stream infection in the development of severe forms of sepsis. Neonates are also vulnerable to infections because of their weak immunological barrier. This result is

consistent with other studies done among neonates in Ethiopia (28%), and Cameroon (34.9%). [10,11]

Blood culture positivity in our study was found to be 212 (22.8%) out of 928 cultures. These results are comparable to other studies from India and abroad. Studies from India by Nazir et al (25.3%)[12] and Arora et al (20.02%)[13] have shown comparable results. A study done by Ali et al in Gonder, Ethiopia, in 2008 showed comparable prevalence of 24.2% [14]. In contrast to above, the study done by Kitila et al[15] reported high frequency of positive blood cultures accounting for 32.5% whereas study by Gohel et al reported lower frequency of positive blood cultures accounting for 9.2%[3]. This variation may be due to many factors like geographical locations, patient type, timing and number of blood cultures or difference in blood culture system. [16,17] In India, the variation in isolation rate may also be due to the practice of prescribing antibiotics by the local health practitioners before the patients reach the tertiary care hospital. Also, as reported by Lee et al[18], the variation in blood culture positivity is also related to the number and amount of blood cultures taken for screening .

In our study, the frequency of isolation of Gram-negative bacteria (n=134, 63.2%) was found to be more than that of Gram-positive bacteria (n=50, 23.5%). Also, *Candida* species were isolated from a significant number of patients (n=30, 14.2%). Our findings are comparable to study from Jalandhar (GN-58.46 % and GP- 38.46 %)[19] and Uganda (GN-53.2 % and GP38.3 %)[20], which showed gram negative to be more common isolates than gram positives. However, Fayyaz et al[21] from Pakisthan also showed variable results having Gram positive (53%) to be more common than Gram negatives (45%) and 2% yeast out of total 245 isolates. Study done by Rajeevan et al[22]

in North Kerla also shows Gram positive (60-53.57%) to be more common isolates as compared to Gram negative bacilli (53- 46.4%) out of 113 isolates. This variation of etiologic agents from country to country might be due to geographical locations, epidemiological variation/difference in etiologic agents. The other factors might also be due to nature of patient population, variable sample size and span of study time .[22]

In the present study, the commonest organism isolated was S.aureus (17%) followed by E.coli (16%) and Klebsiella sp(15%). This is in accordance with Rajeevan et al[22] (S.aureus- 36%,E.coli-15.1% and Klebsiella pneumonia- 11.6%). Amongst gram positive organisms, Staphylococcus aureus was isolated in 17% of cases and CONS in 3.8% of cases in the present paper. The isolation of Staphylococcus aureus is consistent with the study of Roy et al[23] and Karlowsky et al[24] where the reported isolation of the organism was 14%, and 16.5%, respectively. However, reported isolation of CONS was 16.5%, and 42%, respectively, in these studies which are quite higher than isolation of CONS seen in our study but in accordance with Anbumani et al[16] where *Staphylococcus aureus* is reported as 36.4% and CONS as 1.12%. It is known that CONS isolated from blood are often skin contaminants which are clinically insignificant, we suspect that the observed low isolation of CONS in our paper could be due to strict aseptic practices of collection method followed for blood sampling of blood culture and also due to proper clinical correlation of cases and isolates.

Amongst gram negative, E.coli (16%) was the commonest isolate followed by *Klebsiella pnumoniae* (15%) and *Pseudomonas aeruginosa* (13.2%) which is in accordance with Gohel et al[3]. Also we isolated

Salmonella spp. in 5.7% cases which is in contrast with Gohel et al[3] but its comparable to Mehta et al[25]. The reason behind this may be that *Salmonella spp.* is community-acquired infection in general population which gains entry via feco-oral route. And Gohel et al[3] caters to specific renal population, that might possibly be the causative factor for this observed difference of Salmonella. In our study, we isolated *candida species* in 13.2% cases. In some studies candida isolates were (4.73%)[26] and (5.9%)[27] but not isolated from Quereshi et al[28]. Thus, predominance of either the gram positive, gram negative bacterial isolates or fungal isolates is influenced by geographical location, hospital microflora, immune status of patients and population involved in the study.

Amongst gram positive bacteria, both CoNS and *Staphylococcus aureus* showed no resistance to vancomycin (0%) linezolid (0%) and least to Amikacin(5.4%) and highly resistant to penicillin(77.7%) and erythromycin(62%) which is in accordance with Nazir et al[12] . Methicillin resistance was higher (75%) in CoNS in contrast with *S. aureus* (61%) . Shilpi et al[2] found 26.5% of total MRSA and 18.6% MRCoNS. Sumita et al[22] showed 32.5% MRSA and 88.2% MRCoNS. Gohel et al[3] and Garg et al[29] showed 70.6% and 75.6% MRSAs respectively which is comparable to our study but very high than that of Shilpi et al (26.5%)[2] and Sumita et al[22]. The occurrence of MRSA is more common because of indiscriminate use of higher antibiotics as an emergency empirical therapy. This prompts us for meticulous antibiotic policies and strict implementation of hospital infection control measures. Amongst enterococcus, 50% strains were found to be vancomycin resistant (VRE). This is in accordance with Gohel et al (40%)[3] and Karlowsky et al(35.8%)[24].

In gram negative isolates, Enterobcateriacea and nonfermenters showed no resistance to colistin and least resistance was observed with carbapenems, colistin, aminoglycosides, and tigecycline which is accordance with Gohel et al[3] and Shilpi et al[2]. Enterobacteriacae showed very high resistance to Ampicillin, ,Amoxyclav, Cephalosporins and Cotrimoxazole except Salmonella. The fact that cephalosporins are one of the most commonly used antibiotics for inpatients as well as for outpatients could be the reason for such high level of resistance being observed in the developing countries[2].

In the present study, total Gram-negative isolates to be carbapenem-resistant were 54.7% and 26.7% among nonfermenters and *Enterobacteriaceae*, respectively which is similar to Shilpi et al[2] The greatest threat with MDR and carbapenem-resistant Gram-negative bacteria is that the infections are usually untreatable due to the limited options of the antibiotics available, resulting into increased mortality. Worldwide, their incidence is rising with variations due to regional and geographical differences. With the shortage of newer drugs availability and increasing resistance, use of limited option drugs such as colistin by clinicians could soon lead to the condition of so-called pan-drug resistance.

The present study provides information on the prevalence of bacterial pathogens causing blood stream infections along with their antibiotic susceptibility profile. The study identified Gram-positive , Gram-negative bacteria and candida species to be responsible for blood stream infections. Vancomycin, Linezolid and Amikacin were found to be most effective for Gram-positive bacteria whereas Colistin, Tigecycline and amikacin were found to be most effective for Gram-negative isolates.

Figures & Tables

Table 1: Age and Sexwise Distribution of the patients having positive blood cultures

(n= 212)

Age (Yrs)	Males	Females	Total Positive cultures
0-9	16 (7.5)	14 (6.6)	30 (14.2)
10-19	8 (3.8)	4 (1.9)	12 (5.7)
20-29	14 (6.6)	8 (3.8)	22 (10.4)
30-39	18 (8.5)	6 (2.8)	24 (11.3)
40-49	16 (7.5)	8 (3.8)	24 (11.3)
50-59	16 (7.5)	10 (4.7)	26 (12.3)
60-69	44(20.8)	18 (8.5)	62 (29.2)
70-79	6 (2.8)	2 (0.9)	8 (3.8)
>80	2 (0.9)	2 (0.9)	4 (1.9)
	140 (66)	72 (34)	212

Note: Out of 212 positive patients, males (140- 66%) predominated twice the number of females (72-34%). Maximum culture positivity was seen in 60-69 yrs (29.2%) age grp followed by 0-9 yrs (14.2%). Males were predominantly more in number as compared to the females. Blood Culture positivity was seen in 212 (22.8%) cases.

Table 2: Distribution of Isolates in Blood cultures (n=212)

| Type	Number (%)
Staphylococcus aureus	36 (17)
Escherichia coli	34 (16)
Klebsiella sp.	32 (15.1)
Pseudomonas aeruginosa	28 (13.2)
Candida albicans	24 (11.3)
Acinetobacter baumannii	14 (6.6)
Salmonella Typhi & Paratyphi A	12 (5.7)
Coagulase Negative Staphylococci	8 (3.8)
Serratia marscesens	4 (1.9)
Enterococcus faecalis	4 (1.9)
Enterobacter cloacae	4 (1.9)
Streptococcus pneumoniae	2 (0.9)
Spingomonas paucimobilis	2 (0.9)
Burkholderia cepacia	2 (0.9)
Stenotrophomonas maltophilia	2 (0.9)
Candida parapsilosis	2 (0.9)
Candida glabrata	2 (0.9)
Total	212

Note: The commonest organisms isolated were Staphylococcus aureus (17%) followed by Escherichia coli (16%) and Klebsiella pneumoniae(15%). Amongst Fungal isolates, Candida albicans (11.3%) was the commonest isolate followed by C. parapsilosis (0.9%)

Figure 1: Antibiotic Resistance pattern of Gram Positive Organisms
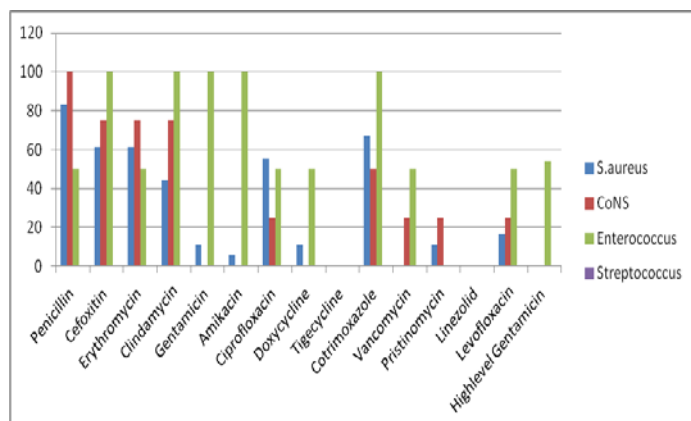
Note: CoNS and Staphylococcus aureus were highly sensitive to vancomycin (100% and 75%) and linezolid (100% each). Methicillin resistance was higher (75%) in CoNS in contrast with S. aureus (61%). This was tested using cefoxitin disc. Amongst enterococcus, 50% strains were found to be vancomycin resistant (VRE). Streptococcus sp were found to be sensitive to all the drugs.

Figure 2: Antibiotic Resistance pattern of Enterobacteriaceae
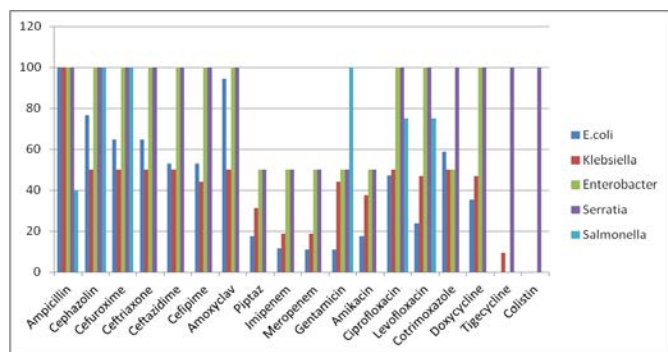
Note- Amongst Enterobacteriaceae, high resistance was shown by Enterobacter, Serratia, E,coli, Pseudomonas sp and Klebsiella sp. Maximum sensitivity was seen for Colistin, Tigecycline followed by Imipenem,Meropenem, Pipercillin Tazobactum and Amikacin. Ampicillin,amoxyclav, cephalosporins and doxycline showed very high resistance.

Figure 3: Antibiotic Resistance pattern of Nonfermenter
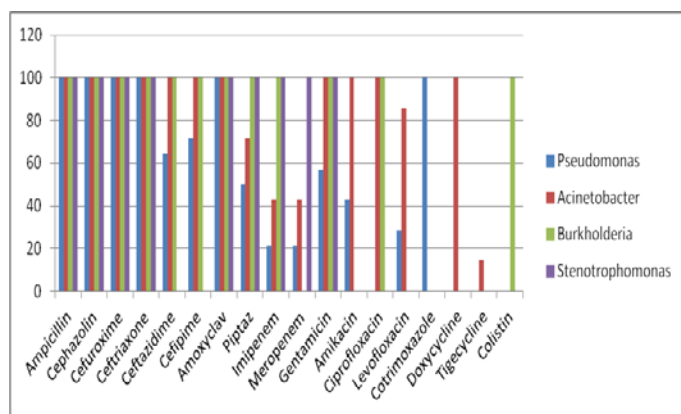
Note- Amongst Nonfermenters, Maximum sensitivity was shown to Cotrimoxazole, Colistin, Tigecycline Levofloxacin and Amikacin. High resistance was shown to Ampicillin, Cephalosporins except ceftazidime and cefipime.

Conclusion

The increase in the prevalence of MDR bacteria emphasize the urgent need for rational use of antibiotics, formulation of antibiotic policy and implementation of infection control practices for the effective management and prevention of drug resistance. Routine surveillance of Microbial flora from septicaemic cases and their antimicrobial resistance pattern with existing guidelines will go long way in reducing multi drug resistance in pathogens. Efforts need to be extended to prevent and control serious hospital-acquired infections.

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