

ORIGINAL RESEARCH

INTENSIVE CARE

Bacterial bloodstream infections in medical and surgical intensive care units: a study of distribution and susceptibility patterns

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Abstract

Aim: Blood stream infections are common in critically sick patients and the clinicians have to use antibiotics to manage. The susceptibility of the microorganisms varies widely from institution to institution, and from country to country. This study was carried out to document the distribution and antimicrobial susceptibility patterns of bloodstream bacterial infections over a six-month period in the medical and surgical intensive care units (ICUs) at NRI Academy of Medical Sciences, in the Southern Region of India.

Methodology: This was a retrospective study conducted from June 2020 to December 2020. The study included all patients of either gender, aged above 18 years, admitted in the medical and surgical ICUs for whom blood specimens for culture were positive for BSI. The data for each of the ICUs was compared separately for the type and the number of isolates. The antibiotic susceptibility was assessed for both the ICUs together. The data was analysed using the Medcalc® software.

Results: Medical and surgical intensive care units had 103 and 30 culture positive cases respectively. Among the culture positive cases, fermentive and non-fermentive gram-negative were equally isolated at 51 (38.3%) samples each and 31(23.3%) were gram-positive organisms. Altogether, Acinetobacter (20.3%) was the major isolate followed by E. coli (14.2%) and Klebsiella (13.5%). Acinetobacter was most sensitive to colistin (70.4%) followed by levofloxacin (63.0%) and tigecycline (55.6%). E. coli were sensitive to colistin and tigecycline, (100%), followed by amikacin (78.9%), meropenem (68.4%), gentamicin (63.2%). Similar sensitivity was observed for Klebsiella.

Conclusion: This study highlights the predominance of gram-negative bacteria in the ICUs and the emergence of multidrug resistant organisms and higher rate of antimicrobial resistance among gram-negative and gram-positive organisms which is an alarming issue. The knowledge of the pathogens causing BSIs in the ICUs and their antibiotic sensitivity patterns can be of help to the clinicians in choosing appropriate empiric antimicrobial therapy. Appropriate empiric therapy is key for decreasing the length of hospital stay and mortality associated with severe sepsis and septic shock associated with blood stream infection in the ICUs.

Key words: Antimicrobial susceptibility; Blood Stream Infection; Intensive Care Unit

Abbreviations: BSI - Bloodstream infections; ICU - Intensive Care Unit; MICU - Medical Intensive Care Unit; SICU – Surgical Intensive Care Unit

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1. Introduction

Bloodstream infections (BSIs) are infectious diseases defined by the presence of viable bacterial or fungal microorganisms in the bloodstream (later 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.¹ It is estimated that around 30 million people are affected by BSI, causing 6 million deaths worldwide annually.² This high incidence of BSI is attributed to ageing of patients on admission, increasing number of patients with compromised immunity, and the acquisition of virulence factors by bloodstream pathogens.^{3,4} Additionally, other factors causing BSI are linked to invasive procedures and use of invasive devices such as endotracheal intubation, central venous cannulations, mechanical ventilation, and urinary catheterizations in the intensive care units.⁵ Apart from this, the risk of infectious diseases in India is highest in the world, due to the irrational use of antimicrobial agents leading to antimicrobial resistance.⁶

The microorganisms causing BSI may include Gram-negative bacteria such as *Escherichia coli* (*E. coli*), *Pseudomonas aeruginosa* (*P. aeruginosa*), *Klebsiella*, *Acinetobacter baumannii* (*A. baumannii*), *Neisseria meningitidis*, and *Haemophilus influenzae*, and Gram-positive bacteria such as coagulase-negative staphylococci (CoNS), *Staphylococcus aureus* (*S. aureus*), *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Streptococcus agalactiae* and *Enterococcus faecium* (*E. faecium*).⁷ However, the pattern of the causative agents constantly changes over time,⁸ which demands the need for periodic surveillance among the population. Moreover, it is also important to implement antimicrobial stewardship strategies personalized to the geographic location. Due to these reasons, this study was aimed to study the distribution and antimicrobial susceptibility patterns of BSIs over a six-month period in the medical and surgical intensive care units (ICUs) at NRI Academy of Medical Sciences, in the Southern Region of India.

2. Methodology

2.1. Study design and setting

This was a retrospective study conducted at NRI Academy of Medical Sciences from June 2020 to

December 2020. It is also an academic teaching hospital and is one of local tertiary referral units. There are 15-bedded medical and surgical ICUs apart from exclusive pediatric ICU. However, this study was restricted only to the medical and surgical ICUs. Institutional ethics committee approval was obtained for data collection, waiving requirement for patient consent.

2.2. Study population

The study included all patients of either gender, aged above 18 years, admitted in the medical and surgical ICUs for whom blood specimens for culture were positive for BSI. The study population contained 133 patients who were divided into two groups. The first group were patients from medical ICU (MICU) and the second group were patients from surgical ICU (SICU). The patients in whom blood culture was negative, the patients in whom more than one species of the same organism was isolated and patients with incomplete case records were excluded from this study.

2.3. Data Collection

Data was collected from the medical records section using a structured data collection tool. Results of blood culture, gram stain, isolates identity and antimicrobial susceptibility were recorded.

2.4. Statistical analysis

The data for each of the ICUs was compared separately for the type and the number of isolates. The antibiotic susceptibility was assessed for both the ICUs together. Descriptive statistics such as frequency and percentage for categorical variables was used. Chi-squared test was used to observe the difference between the two groups. The statistical significance was fixed at 5% level ($p < 0.05$) at 95 % confidence interval. The data were analysed using the Medcalc® software.

3. Results

The number of cases admitted during the study period were 210 and 107 in the medical and surgical ICUs respectively of which 165 samples in medical ICU and 78 samples in surgical ICU were sent for culture and sensitivity. After considering the inclusion and exclusion criteria, 103 and 30 cases in the medical and surgical ICUs respectively were considered for analysis. Among the culture positive cases, fermentive

Table 1: Distribution of isolates in MICU and SICU

Organism	MICU	SICU	95 % CI	p value
Fermentative gram-negative bacteria				
<i>E. coli</i>	15 (29.4)	4 (7.8)	6.51 - 35.98	< 0.01
<i>Klebsiella</i>	13 (25.5)	5 (9.8)	0.74 - 30.18	< 0.05
<i>Aeromonas salmanocide</i>	5 (9.8)	2 (3.9)	-4.91 - 17.42	NS
<i>Enterobacter</i>	3 (5.9)	0 (0.0)	NA	NA
<i>Serratia marcescens</i>	2 (3.9)	0 (0.0)	NA	NA
<i>Salmonella typhi</i>	2 (3.9)	0 (0.0)	NA	NA
Total	40 (78.4)	11 (21.6)	38.33 - 69.64	< 0.001
Non- Fermentative gram-negative bacteria				
<i>A. baumannii</i>	22 (43.1)	5 (9.8)	16.43 - 47.98	< 0.001
<i>B. cepacia</i>	6 (11.8)	2 (3.9)	-3.30 - 19.86	NS
<i>P. aeruginosa</i>	6 (11.8)	1 (2.0)	-0.65 - 21.53	NS
<i>Achromobacter denitrificans</i>	5 (9.8)	1 (2.0)	-2.23 - 19.09	NS
<i>Stenotrophomonas</i>	2 (3.9)	0 (0.0)	NA	NA
<i>Sphingomonas</i>	1 (2.0)	0 (0.0)	NA	NA
Total	42 (82.4)	9 (17.6)	46.98 - 76.20	< 0.001
Gram-positive bacteria				
CONS	10 (32.3)	4 (12.9)	-1.62 - 38.63	NS
<i>S. aureus</i>	9 (29.0)	4 (12.9)	-4.43 - 35.30	NS
<i>Enterococcus</i>	2 (6.5)	2 (6.5)	NA	NA
Total	21 (67.7)	10 (32.3)	10.50 - 54.77	< 0.01
NS- Not significant; NA-Not applicable; Data given as n (%)				

and non-fermentive gram-negative were equally isolated at 51(38.3%) samples each and 31(23.3%) were gram-positive organisms. Altogether, *Acinetobacter* (20.3%) was the major isolate followed by *E. coli* (14.2%) and *Klebsiella* (13.5%).

The fermentive gram-negative bacteria were predominantly isolated from the medical ICU (78.4%) as seen in Table 1. *E. coli* was predominant (29.4%) followed by *Klebsiella* (25.5%) and *Aeromonas salmanocide* (9.8%) in the medical ICU. Whereas, in the surgical ICU *Klebsiella* (9.8%) was the major isolate as seen in Table 1. However, there was statistically significant difference between only *E. coli* and *Klebsiella* isolates between the two ICUs ($p < 0.01$

and $p < 0.05$ respectively). Similarly, the non-fermentative gram-negative bacteria were mainly isolated from the medical ICU ($n = 42, 82.4\%$). *A. baumannii* was the major isolate in both medical ($n = 22, 43.1\%$) and surgical ICU's ($n = 5, 9.8\%$) as seen in Table 1. Moreover, there was statistically significant difference between only *A. baumannii* isolates between the two ICUs ($p < 0.001$). Likewise, the gram-positive bacteria were mainly isolated from the medical ICU. Coagulase-negative staphylococci (CoNS) was the predominantly isolated organism in medical ICU ($n = 10, 32.3\%$). In the surgical ICU, CONS and *S. aureus* were equally isolated ($n = 4, 12.9\%$) as seen in Table 1. However, there was no

Antibiotic	<i>E. coli</i> (n = 19)	<i>Klebsiella</i> (n = 18)	<i>Aeromonas</i> (n = 7)	<i>Enterobacter</i> (n = 3)
Amikacin	78.9 (15)	66.7 (12)	100.0 (7)	33.3 (1)
<u>Cefepime</u>	15.8 (3)	11.1 (2)	57.1 (4)	33.3 (1)
<u>Cefoperazone+Sulbactam</u>	52.6 (10)	5.6 (1)	57.1 (4)	33.3 (1)
Cefotaxime	NT	5.6 (1)	NT	33.3 (1)
Ceftazidime	5.3 (1)	11.1 (2)	NT	33.3 (1)
Ceftriaxone	5.3 (1)	5.6 (1)	57.1 (4)	33.3 (1)
Ciprofloxacin	21.1 (4)	22.2 (4)	14.3 (1)	66.7 (2)
<u>Colistin</u>	100.0 (19)	100.0 (18)	57.1 (4)	100.0 (3)
<u>Co-trimoxazole</u>	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
Gentamicin	63.2 (12)	50.0 (9)	57.1 (4)	100.0 (3)
Imipenem	52.6 (10)	16.7 (3)	100.0 (7)	33.3 (1)
Levofloxacin	15.8 (3)	5.6 (1)	28.6 (2)	0.0 (0)
Meropenem	68.4 (13)	16.7 (3)	57.1 (4)	66.7 (2)
<u>Piperacillin+Tazobactam</u>	42.1 (8)	16.7 (3)	NT	33.3 (1)
<u>Tigecycline</u>	100.0 (19)	72.2 (13)	57.1 (4)	66.7 (2)

NT - Not tested

Drugs	Acinetobacter (n = 27)	<i>B. cepacia</i> (n = 8)	<i>P. aeruginosa</i> (n = 7)
Amikacin	25.9 (7)	50.0 (4)	42.9 (3)
<u>Cefepime</u>	18.5 (5)	75.0 (6)	57.1 (4)
<u>Cefoperazone + Sulbactam</u>	48.1 (13)	50.0 (4)	42.9 (3)
Ceftazidime	NT	75.0 (6)	57.1 (4)
Ceftriaxone	0.0 (0)	0.0 (0)	0.0 (0)
Ciprofloxacin	29.6 (8)	37.5 (3)	57.1 (4)
<u>Colistin</u>	70.4 (19)	NT	42.9 (3)
<u>Co-trimoxazole</u>	29.6 (8)	75.0 (6)	NT
Gentamicin	0.0 (0)	0.0 (0)	0.0 (0)
Imipenem	18.5 (5)	37.5 (3)	57.1 (4)
Levofloxacin	63.0 (17)	75.0 (6)	28.6 (2)
Meropenem	25.9 (7)	75.0 (6)	42.9 (3)
<u>Piperacillin + Tazobactam</u>	25.9 (7)	NT	57.1 (4)
<u>Tigecycline</u>	55.6 (15)	50.0 (4)	42.9 (3)

NT- Not tested

Table 4: Susceptibility pattern of Gram-positive isolates

Drugs	CoNS (n = 14)	<i>S. aureus</i> (n = 13)	<i>Enterococcus</i> (n = 4)
Ampicillin	0.0 (0)	0.0 (0)	0 (0)
Cefoxitin	35.7 (5)	38.5 (5)	50 (2)
Ciprofloxacin	42.9 (6)	53.8 (7)	0 (0)
Clindamycin	64.3 (9)	0.0 (0)	NT
Cotrimoxazole	64.3 (9)	61.5 (8)	50 (2)
Erythromycin	78.6 (11)	61.5 (8)	NT
Gentamicin	57.1 (8)	84.6 (11)	25 (1)
Linezolid	100.0 (14)	100.0 (13)	75 (3)
Penicillin	0.0 (0)	0.0 (0)	25 (1)
Teicoplanin	50.0 (7)	53.8 (7)	25 (1)
Tigecycline	100.0 (14)	76.9 (10)	NT
Vancomycin	71.4 (10)	53.8 (7)	75 (3)

NT- Not tested

statistically significant difference observed between the two ICUs. Nonetheless, there was an overall statistically significant difference observed between the ICUs for fermentive gram-negative ($p < 0.001$), non-fermentive gram-negative ($p < 0.001$) and gram-positive ($p < 0.01$) isolates.

Tables 2, 3 and 4 display the rates of antibiotic sensitivity of most frequently isolated fermentive and non-fermentive gram-negative and gram-positive isolates respectively. Amongst the Fermentive Gram-negative isolates, all the isolates of *E. coli* were sensitive to colistin and tigecycline, (100%), followed by amikacin (78.9%), meropenem (68.4%), gentamicin (63.2%) and equally to cefoperazone + sulbactam and imipenem (52.6%). Similar sensitivity patterns were observed for *Klebsiella* too. Regarding *Aeromonas*, all the isolates were sensitive to amikacin and Imipenem (100%). With regard to *Enterobacter*, maximum sensitivity was observed with colistin and gentamicin (100%) as shown in Table 2. With regard to isolates of *Serratia* and *Salmonella*, they were mostly sensitive to colistin, imipenem and tigecycline. The sensitivity pattern of non-fermentive gram-negative isolates demonstrated that *Acinetobacter* was most sensitive to colistin (70.4%) followed by levofloxacin (63.0%) and tigecycline (55.6%). However, *Burkholderia cepacia* (*B. cepacia*) was

equally sensitive to cefipime, ceftazidime, cotrimoxazole, levofloxacin and meropenem (75.0%). Likewise, *P. aeruginosa* was equally sensitive to cefipime, ceftazidime, levofloxacin and piperacillin + tazobactam (57.1%) as shown in Table 3. Regarding the isolates of *Achromobacter denitrificans*, maximum sensitivity was observed with amikacin, colistin and tigecycline. However, the isolates of *Stenotrophomonas* and *Sphingomonas* were mostly sensitive to colistin alone. With respect to gram-positive isolates, all the isolates of CoNS were sensitive to linezolid (100%) followed by gentamicin (84.6%), tigecycline (76.9%), cotrimoxazole and erythromycin (61.5%) and ciprofloxacin and teicoplanin (53.8%). Regarding *S. aureus*, all the isolates were sensitive to linezolid and tigecycline (100%) followed by erythromycin (78.6%), vancomycin (71.4%) and equally sensitive to clindamycin and cotrimoxazole (64.3%). Whereas, *Enterococcus* was found to be most sensitive to linezolid and vancomycin (75%) followed by cefoxitin and cotrimoxazole (50%) as shown in Table 4.

All the fermentive gram-negative isolates, including *Serratia* and *Salmonella* were resistant to cotrimoxazole and more than 80 % of isolates were resistant to cefipime, ceftazidime, ceftriaxone and levofloxacin for *E. coli* and *Klebsiella* as shown in

Figure 1. Regarding, non-fermentive gram-negative bacteria, all the isolates of *Acinetobacter*, *B. cepacia* and *P. aeruginosa* were resistant to ceftriaxone and gentamicin. Whereas, more than 80 % of isolates of *A. baumannii* were resistant to cefipime and imipenem as seen in Figure 3. Regarding the isolates of *Achromobacter denitrificans*, most of the isolates were resistant to all the cephalosporins, fluoroquinolones and other beta-lactam antibiotics. With respect to gram-positive isolates, very high levels of resistance were observed with ampicillin. The other antibiotics to which the isolates showed high level of resistance were clindamycin and penicillin as seen in Figure 3. Few isolates were also resistant to linezolid, teicoplanin and vancomycin as well.

5. Discussion

BSIs are among the leading infections in ICUs. In an international study of the prevalence and outcomes of infections in ICUs, BSIs were accounted for 15% of infections and was the third-most common infection.⁹ Therefore, study of bacteriological profile of BSIs with their antibiotic susceptibility/resistance plays a significant role in the effective treatment of BSIs.

Results of this study demonstrate the distribution of bacterial isolates in medical and surgical ICUs and their susceptibility pattern to the commonly used antibiotics. In this study, it was observed that, there were significant differences between the proportions of bacterial isolates between the two ICUs. This may be due to the reason that patients in medical and surgical ICUs have different risk factors for BSI development, including greater severity of illness, use of different invasive procedures and impaired immunity. However, there was no significant difference observed between the susceptibility rates among bacteria isolated from medical and surgical ICUs.

The present study demonstrated there were more gram-negative isolates (76.6%) than gram-positive isolates (23.3%). The most common gram-negative organisms isolated in our study were *E. coli*, *Klebsiella* and *Acinetobacter*. The results of this study are similar to findings in other studies conducted internationally as well as in India. In a systematic review of the gram-negative infections in adult intensive care units in the regions of Latin America and the Caribbean, it was found that gram-negative pathogens accounted for

50% of ICU infections, which were often complicated by the presence of multidrug-resistant strains.¹⁰ In another recently done study in four major universities of Japan, the authors observed that BSIs were most commonly caused by gram-negative bacteria.¹¹ In a study done in India by Sonawane et al. 71.86% of BSIs in the ICUs were caused by gram-negative pathogens.¹²

Recently, among the gram-negative bacteria, non-fermentive gram-negative pathogens have emerged as major hospital acquired pathogens as a result of irrational use of antimicrobials.¹³ These pathogens are commonly found in soil and water. In a hospital setting, they may be isolated from instruments such as ventilators, hospital linens as well as from the skin of health care workers,¹⁴ which may be the source of BSIs. In a study done in Eastern India, by Sarkar et al., non-fermentative gram-negative bacilli were the most common organisms causing BSIs, out of which *A. baumannii* followed by *P. aeruginosa* and *B. cepacia* were the major isolates at 51.34%, 42.09% and 4.38% respectively.¹⁵ However, in the present study, non-fermentive gram-negative bacteria were equally isolated as fermentive gram-negative bacteria from both the ICUs.

In the current study, gram-positive bacteria comprised the least proportion of all isolates. Among gram-positive bacteria, CoNS was the most common organism isolated, which is in congruence with the results of a study done in South India.¹⁶ However, in contrast, the results of a study by Kaur et al. in ICU patients reported *S. aureusto* be the most common pathogen (25.9%), followed by gram-negative organisms.¹⁷

E. coli, *Klebsiella* and *Enterobacter* showed highest susceptibility to colistin (100%) and lowest susceptibility to ceftriaxone and were totally resistant to cotrimoxazole. In addition, all the isolates of *E. coli* were susceptible to tigecycline. However, high rates of non-susceptibility were noted against quinolones, cephalosporins, beta lactam inhibitor group of drugs and carbapenems. The observations in this study are similar to the results of earlier study in Singapore by Hsu et al.¹⁸ Antimicrobial susceptibility pattern among non-fermentive gram-negative isolates demonstrated that most of them were multi-drug resistant organisms being resistant to three or more class of antibiotics. *A. baumannii* showed highest susceptibility to colistin

(70.4%) and lowest susceptibility to cefipime and imipenem (18.5%) and were totally resistant to ceftriaxone and gentamicin. High rates of resistance was noted to even carbapenems and aminoglycosides. The carbapenems are the antibiotics of choice for the treatment of serious infections due to multidrug-resistant *A. baumannii*. Unfortunately, the number of isolates of *A. baumannii* resistant to carbapenems has increased in the recent years, which is a big problem because the resistance to carbapenems limits the clinician's options for successful treatment and leads to increased mortality.¹⁹ This data is supported by various studies done in India, Indonesia and Iran.^{20,21,22} Apart from colistin, levofloxacin and tigecycline were found to be most effective against *A. baumannii* in this study.

Amongst the gram-positive isolates, CoNS and *S. aureus* showed highest susceptibility to linezolid (100%), were least susceptible to cefoxitin and were totally resistant to ampicillin and penicillin. This finding is also supported by a study of Ganguli NK et al.²³ This increasing incidence of resistance is alarming, as it limits the use of beta lactam drugs and advocates the use of higher antibiotics like vancomycin. This in turn risks the emergence of vancomycin resistance as observed in the current study.

6. Limitations

There are certain limitations to this study. It is a retrospective study and the research was conducted in only one institution with a small sample size, and covered only a limited period of six months of data collection.

7. Conclusion

This study highlights the predominance of gram-negative bacteria in the ICUs, the emergence of multi-drug resistant organisms and the higher rate of antimicrobial resistance among gram-negative and gram-positive organisms which is an alarming issue. The knowledge of the pathogens causing BSIs in the ICUs and their antibiotic sensitivity patterns can be of help to the clinicians in choosing appropriate empiric antimicrobial therapy. Appropriate empiric therapy is key for decreasing the length of hospital stay and mortality associated with severe sepsis and septic

shock associated with blood stream infection in the ICUs.

8. Conflict of interest

Nil

9. Authors' contribution

BC: Concept & conduction of study

VS: manuscript editing

NM: Literature search

10. References

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