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Original Article

Blood Stream Infections in Intensive Care Units: A Study from North India

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Abstract

Title : Blood stream Infections in Intensive Care Units. A Study from North India. *Study Design:* Prospective study. *Place and Duration of Study:* Sher-i-Kashmir Institute of Medical Sciences, Srinagar Kashmir. (July 2012 and Dec 2014). *Methodology:* A prospective analysis of blood specimens from various intensive care units (ICUs) was done over a period of four years. Antimicrobial susceptibility of culture positive isolates to various antibiotics was performed as per Clinical Laboratory Standards Institute (CLSI) guidelines.Gram-negative bacteria (GNB) were screened for extended spectrum β-lactamase (ESBL) and metallo-β-lactamase (MBL) production; whereas methicillin and vancomycin resistance was searched in *staphylococci* and *enterococci* isolates respectively. *Results:* The frequencies of Gram-positive and Gram-negative bacteria were 16.83% with yeast recovered in 5.78% of the specimens. *Acinetobacter spp* and *K. pneumoniae* were the most common Gram-negative bacteria and *S. aureus* the most common Gram-positive one. High level resistance to all the antimicrobials was seen; with *Acinetobacter spp* being the most multidrug resistant GNB isolated in the ICU setting. ESBL production was highest in *K. pneumoniae* isolates (77.1%). Also 49.6% of *Acinetobacter* isolates were found to be MBL producers. Methicillin resistance was seen in 95% of S. aureus and 91% of coagulase negative *staphylococci* (CoNS) isolates with vancomycin resistance seen in 46% of enterococcal isolates. *Conclusion:* An increasing trend over the years in the antibiotic resistance of blood stream pathogens in ICUs of this north Indian state was seen that calls for urgent measures to limit their continued rise.

Keywords: Gram-Negative Bacteria (GNB); Coagulase Negative *Staphylococci* (CoNS); Metallo-β-Lactamase (MBL).

Bloodstream infections (BSIs) occur more frequently in patients hospitalized in intensive care units (ICUs) than in other units. It has been shown that these patients stay in clinics longer than others. BSIs also cause an increase in hospital mortality rates and also increase hospitals charges. Early initiation of appropriate antimicrobial treatment is critical in decreasing morbidity and mortality among patients with BSI [1,2,3].

In the intensive care unit (ICU) setting, the incidence of infection is often higher than in the less acute in-patient or ambulatory setting. In the ICU, central venous access might be needed for extended periods of time; patients can be colonised with hospital-acquired organisms, and the catheter may be manipulated several times daily for administration

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of fluids, drugs, and blood products. Moreover, some catheters may be inserted in urgent situations, during which optimal attention to aseptic technique might not be feasible [4].

ICU-BSI can occur either secondary to the dissemination of pathogens from a primary focus of infection at a clinical site into the bloodstream, or can be primary where the source of infection is unclear. The common clinical site foci for secondary ICU-BSI are the respiratory, gastrointestinal and urinary tracts [5, 2, 6 and 7].

The frequency, epidemiology and microbiological profile of nosocomial BSIs vary among institutions and also among ICUs within hospitals. Drug resistance has rendered antimicrobial therapy difficult in India like everywhere else and highly resistant bacteria like the MBL producing Gram-negative bacteria are a common occurrence in the hospital settings especially the intensive care units [8, 9]. Recently the New Delhi metallo β-lactamase (NDM) producing multidrug resistant Gram-negative bacteria have been reported from Kashmir. (10) These have serious implications for the management of critically ill patients in ICUs, limiting the utilitiy of beta-lactam antibiotics, fluoroquinolones and aminoglycosides. The present study was designed to identify the microbiological profile and susceptibility pattern of the organisms isolated from Blood stream infections of patients admitted in the ICUs of our hospital which is the only tertiary care institute in the North Indian state of Jammu and Kashmir.

Design

This observational study was performed in the medical–surgical ICU of a teaching hospital with around 700 beds in SKIMS Srinagar J&K, during the years July 2012–Dec 2014. The intensive care units included the surgical ICU (13-bed ICU), neonatal ICU (8-bed ICU), medical ICU (8-bed ICU) and cardiac surgical ICU (6-bed ICU).

Data Collection

The patients hospitalized longer than 48 h in the ICU were included in this study. The diagnosis of BSI was based on the criteria of the Center for Disease Control (CDC). (11) Blood cultures were taken from patients in BacT/Alert FA bottles. Bar coded, inoculated bottles were loaded into the BacT/Alert Microbial Detection System. Flag positive bottles were taken out from the system and streaked on Blood agar and MacConkey agar to be incubated at 37^0C overnight. Isolates were identified by VITEK 2 system Antimicrobial resistance patterns of isolated microorganisms were determined by VITEK 2 system according to the recommendations of the Clinical Laboratory Standards Institute (CLSI) (12) Descriptive statistics (frequency and percentage) was used for the presentation and comparison of data.

Definitions

BSI was defined as the isolation of a pathogenic microorganism from at least one blood culture specimen. Organisms of the skin flora commonly associated with contamination were required to be isolated from two separate blood culture specimens. A BSI was classified as primary in the absence of an identified source of infection or if it was catheter related. A BSI was classified as secondary in the presence of an identified source infected with the same microorganism at another body

Results

A total of 3112 were received from the medical–surgical ICU during the $2^{1/2}$ year study period out of which 524(16.83%) were culture positive (bacteria), 180(5.78%) were culture positive for yeasts; 2139(68.73%) were sterile and 269(8.64%) grew organisms generally regarded as contaminants. Most of the samples were received from the neonatal ICU 1725 (55.43%) followed by the surgical ICU 990 (31.81%), the medical ICU 182 (5.84%) (Table 1, Fig 1). Patients enrolled in the study included 1908(61.3%) males and 1204(38.7%) females. Majority of the patients had underlying respiratory or neurological disorders.

Among the BSI episodes caused by bacteria, 224 (42.74%) were caused by Gram-positive organisms and 300 (57.26%) by Gram-negative organisms. The most frequently isolated microorganisms of BSIs among gram positive organisms was *Staphylococcus aureus* (19.45%) followed by Coagulase negative *staphylococcus* (14.2%) and among gram negative batcteria it was *Acinetobacter spp* (14.55%) followed by *Klebsiella pneumonia* (12%) (Table 2). The proportion of *Enterococcal species* isolated from BSIs increased over the years from 6.6% in 2012 to 10.2% in 2014 ($p = 0.4522$). However, there was negligible change in the proportion of Gram-negative bacteria isolated from BSI, during this period ($p = 0.320$).

In the present study, 5% of *S. aureus* and 9% of Coagulase-negative *Staphylococci* (CoNS) were

sensitive to methicillin. All isolates were susceptible to vancomycin, teicoplanin and linezolid. All the isolates were resistant to Penicillin G. The rate of vancomycin resistance among *Enterococcus* spp. was 46% (n=22). Among these resistant isolates 20 were *Enterococcus faecium and 2 were Enterococcus fecalis.* Of 48 *Enterococcus* spp., only 10 (21%) isolates were susceptible to ampicillin. The effective antibiotics against the Gram-negative bacteria were amikacin, imipenem, gentamicin, levofloxacin and polymixin B. Among the Gram-negative bacteria, the rates of resistance to various antibiotics commonly used in the ICU were as follows: amikacin 52%, imipenem 51%, piperacillin-tazobactam 74%, ciprofloxacin 80%, ceftazidime 100%, levofloxacin 67%. None of the isolates of gram negative bacteria was resistant to polymyxin B. Piperacillin-tazobactam showed highest activity against *E.coli.*, whereas amikacin and gentamicin showed highest activity against *E.coli, Klebsiella and Enterobacter spp*. The rates of resistance to imipenem were 71% and 65% for *Acinetobacter* spp. and *P. aeruginosa*, respectively whereas imipenem showed good sensitivity for *E.coli* and *Enterobacter spp.*

Table 1:

	Total	Sterile	Contaminated	Yeast	Clinically Significant Bacteria
SICU	990	653	29	35	273
NICU	1725	1166	237	142	180
MICU	397	320	3	3	71
	3112	2139	269	180	524

Table 2:

Organism isolated	Cases(% isolated)
Enterobacteriaceae	133(25.45%)
Klebsiella pneumoniae	63(12%)
Enterobacter spp	29(5.45%)
Escherschia coli	26(5%)
Serratia spp	10(2%)
Salmonella Typhi	5(1%)
Acinetobacter spp	76(14.55%)
Coagulase negative Staphylococci	74(14.2%)
Staphylococcus aureus	102(19.45%)
Enterococcus spp	48(9.2%)
Stenotrophomonas maltophilia	28(5.4%)
Other (*Pseudomonas*, other non fermenters)	63(11.75%)

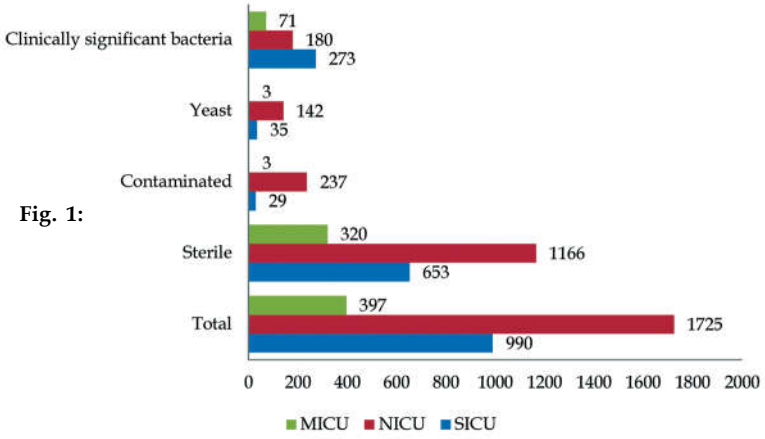

Fig. 1:

ESBL producing *K. pneuomoniae* accounted for 77.1% of the total number of *Klebsiella* strains isolated. Likewise, 37.4% of *E.coli*, were ESBL producers. Also 49.6% of *Acinetobacter* and 37.3% of *P. areuginosa* isolates were MBL producers. An increasing trend in the prevalence of these enzymes (ESBL, MBL) in the isolates was seen over the years.

Discussion

Nosocomial BSIs are associated with a high morbidity and mortality. Patients hospitalized in ICUs are at high risk of nosocomial BSIs because of their debilitated condition as a result of underlying

disease and frequent invasive diagnostic and therapeutic procedures [13,14]. Our data provides an understanding of the antibiotic resistance patterns of commonly isolated organisms in ICU patients in Kashmir. The scene is alarming and clearly demonstrates that drug resistance is on the rise and clinicians are left with very few options for treating patients with serious infections in the ICU.

Rise in the antimicrobial resistance among pathogens in ICU's due to inadvertent and non judicious administration of antibiotics generally before the availability of the culture results, is a matter of concern worldwide. Organisms causing nosocomial BSIs vary depending upon the location of patients within the institution [1].

In many studies, the dominance of Gram-positive pathogens has been documented. *CoNS, S. aureus* and *enterococci* were the three most common causes of nosocomial BSIs in many institutions [15, 16, 17 &18].

There has been a decrease in relative importance of infections as a result of Gram-negative bacteria over the past three decades [3,9]. In this study, the majority of ICU-acquired BSIs were as a result of *S. aureus* (19.45%). There was an increase in the proportion of *enterococci* among isolates from BSIs. This increase may be explained by extensive use of antibiotics and indwelling devices in this unit.

Increasing antimicrobial resistance rates among microorganisms isolated from BSIs are a significant problem worldwide. Methicillin-resistant *S.* aureus (MRSA), vancomycin-resistant enterococci(VRE), extended-spectrum beta-lactamase-producing *Klebsiellaspp.*, carbapenem-resistant enter obactericeae, *P.aeruginosa* and *Acinetobacter* spp. were seen more frequently in ICU patients than in non-ICU patients in many countries [1,20-27]. In the present study, 95% *Staphylococcus aureus* isolates were methicillin resistant. The rate of VRE was 46%. Vancomycin was used frequently in ICU. Amikacin, imipenem and polymyxin B were the most active compounds against Gram-negative bacteria.

In conclusion, this study demonstrates a high rate of antimicrobial resistance to several prescribed antibiotics among the microorganisms isolated from patients with BSIs. During this 3-year period, there was a tendency towards an increase in frequency of BSIs. The insufficient antibiotic-prescribing practices, especially the unnecessary use of broad-spectrum antibiotics together with the insufficient hospital infection prevention programme, are considered to be the cause of high antimicrobial resistance rate and an increased incidence of BSI.

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