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Original Article

Epidemiology of Blood Stream Infections at a Level-1 Trauma Care Center of India

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ABSTRACT

Purpose: Bloodstream infections (BSIs) are one of the major life-threatening infections in hospitals. They are responsible for prolonged hospital stays, high healthcare costs, and significant mortality. The epidemiology of BSIs varies between hospitals necessitating analysis of local trends. Few studies are available on trauma patients, who are predisposed due to the presence of multiple invasive devices.

Materials and Methods: A prospective surveillance of all BSIs was done at a level 1 trauma center from April, 2011 to March, 2012. All patients admitted to the different trauma intensive care units (ICUs) were monitored daily by attending physicians for subsequent development of nosocomial BSI. An episode of BSI was identified when patients presented with one or more of the following signs/symptoms, that is, fever, hypothermia, chills, or hypotension and at least one or more blood culture samples demonstrated growth of pathogenic bacteria. BSIs were further divided into primary and secondary BSIs as per the definitions of Center for Disease Control and Prevention. All patients developing nosocomial BSIs were followed till their final outcome.

Results: A total of 296 episodes of nosocomial BSIs were observed in 240 patients. A source of BSI was identified in 155 (52%) episodes. Ventilator-associated pneumonia was the most common source of secondary BSI. The most common organism was *Acinetobacter* sp. (21.5%). *Candida* sp. accounted for 12% of all blood stream organisms. A high prevalence of antimicrobial resistance was observed in Gram-negative and-positive pathogens.

Conclusions: Trauma patients had a high prevalence of BSIs. Since secondary bacteremia was more common, a targeted approach to prevention of individual infections would help in reducing the burden of BSIs.

Keywords: Central line associated-BSI, ICUs, nosocomial blood stream infections, secondary bacteremia, trauma

INTRODUCTION

Nosocomial blood stream infections (BSIs) are a common and potentially life-threatening problem in intensive care units (ICUs) of hospitals worldwide.[1] They increase the length of stay and mortality in the ICUs. An estimated 2,00,000 to 3,00,000 cases occur each year, with mortality rates varying from 17.5%-50%.[2] The prolonged use of intravascular catheters and its improper management is a major risk factor for development of nosocomial BSIs.[3,4] Furthermore, respiratory, urinary tract, wounds, and gastrointestinal infections can contribute to BSIs.[2,5] The worldwide increase in the incidence of nosocomial BSIs is mainly attributed to the increased use of invasive devices and aggressive drug therapy along with increased frequency of invasive procedures.[6]

It is important to identify and track the source of all BSIs in order to understand the epidemiology of nosocomial BSIs and prioritize preventive efforts. Early detection of pathogens and determination of their susceptibility are essential for the optimization of treatment. Variability between hospitals in different countries is substantial and requires continuous

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analysis of local trends. Therefore, intensive surveillance is essential to decrease morbidity and mortality of nosocomial BSIs.[6,7] India has a high prevalence of antimicrobial resistance in hospitals.[8] Therefore, it is essential to intensify preventive efforts for nosocomial BSIs.

Trauma patients are usually middle aged males, with few, if any underlying illnesses, making them a unique cohort of patients predisposed to hospital acquired infections. The epidemiology, risk factors, preventive, and management efforts of central line associated BSIs (CLA-BSIs) are very different from secondary BSIs, wherein the source of BSI needs to be treated. With this aim, we studied the epidemiology of BSIs at a level-I Trauma Care Centre of All India Institute of Medical Sciences (AIIMS, New Delhi) hospital. The study evaluates the prevalence of primary versus secondary BSIs, causative microorganisms, antimicrobial resistance, and outcome in trauma patients.

MATERIALS AND METHODS

Hospital setting

The Jai Prakash Narayan Apex Trauma Centre (JPNATC) is the first level-1 Trauma Centre of India, where patients from all over India are referred. The Trauma Centre is a part of the AIIMS hospital, which itself is a 2,200-bedded, tertiary, referral, and teaching hospital of India. Of the total 152 beds in the Trauma Centre, 32 are ICU beds. A total of seven nurses function as full time Hospital Infection Control Nurses (HICNs) for the 152-bedded center and one data entry operator is specifically designated for surveillance work. A targeted surveillance of device-associated infections (DAIs) like ventilator-associated pneumonia (VAP), CLA-BSI, and catheter-associated urinary tract infections is being done based on the definitions proposed by Center for Disease Control and Prevention's National health care safety network (CDC's NHSN).[9,10] The HICNs visit every patient in the ICUs and record all the relevant details to diagnose a particular DAI. Recently, the surveillance for all DAIs has been switched over to an automated electronic format, with the help of an indigenously developed software.[11] All the the details are thus entered onto the software. All the basic demographic, clinical, radiological, and laboratory findings are extracted from the existing hospital/laboratory information system (HIS/LIS). The calculations and analysis of rates are done by the software.

The study was conducted over a period of 1 year (April 2011 to March, 2012). All patients admitted to the trauma ICUs were monitored daily by attending physicians for subsequent development of nosocomial BSI. For the purpose of this study, CDC criteria were used to diagnose bacteremia.

Definitions

Blood stream infection was diagnosed by positive microbiology culture results of blood samples and associated clinical manifestations (enumerated below).

Laboratory-confirmed bloodstream infection (LCBI)

LCBI was identified when at least one of the following criteria were met which are as follows:[9,10]

1. Patient had a recognized pathogen cultured from one or more blood cultures and organism cultured from blood was not related to an infection at another site.
2. Patient had at least one of the following signs or symptoms: Fever (>38°C), chills, or hypotension and signs and symptoms and positive laboratory results were not related to an infection at another site and common skin contaminants (i.e. diphtheroids [*Corynebacterium* spp.], *Bacillus* spp. [not *B. anthracis*], *Propionibacterium* spp., Coagulase-negative staphylococci [including *S. epidermidis*], viridans group streptococci, *Aerococcus* spp, *Micrococcus* spp) were cultured from two or more blood cultures drawn on separate occasions.
3. Patient ≤1 year of age had at least 1 of the following signs or symptoms: Fever (>38°C, rectal), hypothermia (<37°C, rectal), apnea, or bradycardia and signs and symptoms and positive laboratory results were not related to an infection at another site and common skin contaminants (i.e. diphtheroids [*Corynebacterium* spp.], *Bacillus* spp. [not *B. anthracis*], *Propionibacterium* spp., Coagulase-negative staphylococci [including *S. epidermidis*], viridans group streptococci, *Aerococcus* spp, *Micrococcus* spp) was cultured from two or more blood cultures drawn on separate occasions.

CLA-BSI

A CLA-BSI was defined as a primary BSI in a patient that had a central line within the 48-h period before the development of the BSI and that was not related to an infection at another site. [9,10]

Secondary blood stream infection

Was defined as a culture-confirmed BSI associated with a documented healthcare-associated infection (HAI) at another site (i.e. met CDC criteria of infection at

another site). If the primary infection was cultured, the secondary BSI must have yielded culture of same organism and exhibited same antibiogram as the primary HAI site.[9,10]

Specimens were collected according to the protocol of the microbiology laboratory. A pair of blood samples for culture and sensitivity were collected aseptically from fresh peripheral venous pricks and inoculated into BacT Alert blood culture bottles (BioMerieux Ltd., France). In ICUs, phlebotomy is performed by either a designated phlebotomist or the clinical residents. The bottles were incubated for 7 days.

All patients at our Center are monitored from the time of admission to their final outcome for development of hospital acquired infections, based on standard definitions. For the purpose of this study, one microbiology resident and one HICN was specifically given the task of following up all patients who had a positive blood culture. Patients were monitored from time of the first blood culture yielding growth until their final outcome. Whenever any patient's blood culture bottle gave a positive signal, a gram stain was made,[12] the result of which was immediately informed to the clinicians and a repeat sample was taken by the HICN. In cases where a second set of blood sample was already sent by the clinicians due to febrile spikes, the sampling was not repeated. Simultaneously, the resident and HICN visited the patient and entered all the details about the use of intravascular catheter (dates of insertion, removal/replacement), antibiotic use, clinical features, other infections, culture reports, and final clinical response. The HICN visited the patient daily till discharge/death/transfer to other wards. The Microbiology resident compiled the reports of cultures from samples of blood and all other samples received from the patient within 72 h previous to the primary blood culture positivity and 72 h after the culture positivity. This was done to trace the source of bacteremia, which would define secondary bacteremia.

The tips of central vascular catheters, if received, were processed by the roll plate method of Maki *et al.*,[13] However, for the interpretation of CLA-BSI, the result of catheter tips was not taken into consideration. All samples were processed according to standard methods.[14] Identification of bacteria and yeasts was done by the Vitek-2 system (BioMerieux Ltd., France). Antimicrobial susceptibility testing was performed by the disc diffusion method, according to the Clinical and Laboratory Standards Institute guidelines[15] and by the Vitek 2 system (BioMerieux Ltd., France).

The study was approved by the institute's ethical committee.

RESULTS

During the study period, a total of 2,249 admissions occurred in the ICUs of the Trauma Centre, amounting to 12,336 patient days. After exclusion of blood cultures found to be contaminated, as per standard definitions, a total of 241 patients were found to suffer from blood stream infections during the study period. Of these, one patient was found to have *Salmonella typhi* and was therefore excluded from analysis, since it usually has a community origin. Thus, a total of 240 patients had nosocomial BSIs, making the incidence of bacteremia to be 10.6%. A total of 296 episodes of BSIs were recorded in these 240 patients. The age of the patients ranged from 1 to 71 years (median 30 years). The length of stay of the patients ranged from 2 to 208 days (median 26 days). The total length of stay of the 240 patients was 7,381 days. A total of 177 (74%) patients were males and 63 (26%) females. The total number of CVC days in these patients was 3,133 with a range of 0-34 days (median 8 days).

No source of BSI could be traced in 120 of the 296 (40.5%) episodes. In 21 episodes, the central venous catheter (CVC) tip grew the same pathogen as the blood isolate. However, the CVC tips were not available in all cases and our definition of CLA-BSI did not require CVC tip culture positivity. Therefore, all the above 141 episodes were considered as primary BSI. Thus, the rate of primary BSI was 47.6%, whereas the rate of secondary BSI was 52.3% (155 episodes).

In 109 episodes (37%), the source of BSI was traced to respiratory tract infections, with the bronchalveolar lavage (BAL)/tracheal aspirate growing the same organism in significant numbers and the clinical picture fitting into VAP. Surgical site infection/wound infection was the source of BSI in 20 (7%) episodes and urinary tract infection was the source of BSI in 17 (6%) episodes. In five episodes, the same organism was isolated from multiple sources. Of these five episodes, in three episodes, *Acinetobacter* Sp. was isolated from blood, BAL and the wound. In one episode, *Klebsiella pneumoniae* was isolated from blood, BAL and urine and in one episode, *Enterobacter* Sp. was isolated from blood, urine, and wound.

In two episodes of polymicrobial bacteremia, a different origin was traced to both organisms. Thus, in one of these two episodes, *Acinetobacter baumannii* originated from the respiratory tract and *Klebsiella pneumoniae* originated from

the wound. In the second episode, *Acinetobacter baumannii* originated from the respiratory tract and *Candida* Sp. originated from urine.

There were two episodes of BSIs caused by *Klebsiella pneumoniae* and *Enterococcus faecalis*, wherein the strain of *Klebsiella* originated from the respiratory tract, but the source of *Enterococcus* could not be found. We included these two episodes as secondary BSIs.

In eight cases, cerebrospinal fluid was also positive with the same organism as blood, which was considered as cases of disseminated septicaemia with meningitis.

A total of 316 organisms were isolated from the 296 episodes of BSIs. *Acinetobacter baumannii*; 68 (21.5%) was the most common, followed by *Klebsiella pneumoniae*; 56 (18%), *Staphylococcus aureus*; 46 (14.5%), *Candida* Sp; 38 (12%), *Enterococcus* Sp; 28 (9%), *Pseudomonas aeruginosa*; 26 (8%), *Escherichia coli*; 13 (4%), coagulase-negative staphylococci; 13 (4%), *Serratia marcescens*; 7 (2%), *Burkholderia* Sp.; 6 (2%), *Enterobacter* Sp.; 5 (1.5%), *Stenotrophomonas maltophilia*; 5 (1.5%), *Proteus mirabilis*; 2 (0.6%), and *Providenci*a Sp., *Pseudomonas stutzeri,* and *Chrysobacterium* Sp.; 1 each (0.3% each). The organism-wise source of BSIs is shown in Table 1.

Among the *Candida* Sp., *C. tropicalis* was the most common; 21 (55%), followed by *C. albicans*; 7 (18%), *C. parapsilosis*; 4 (10.5%), and *C. rugosa, C. glabrata* and *C. haemulonii*; 2 each (5% each).

Among the Coagulase Negative Staphylococci CONS, *S. haemolyticus* was the most common; 7 (54%), followed by *S. hominis*; 4 (31%), and *S. epidermidis*; and *S. cohnii*; 1 each (8% each).

Of the 28 *Enterococci*, 16 (57%) were *E. faecalis* and 12 (43%) were *E. faecium*.

The antimicrobial susceptibility of the bacterial isolates is shown in Table 2.

Of the 240 patients, a total of 83 expired, giving a crude mortality rate of 34.5%. A total of 112 episodes of BSI were recorded in these 83 patients. Of these, 40 (36%) episodes were primary BSIs and 72 (64%) were secondary BSIs. In 62 of the 83 patients (75%) patients, the cause of death was septicemia.

DISCUSSION

Among all types of nosocomial infections, BSIs are potentially the most fatal and costly. Patients admitted to ICUs have an even higher risk of nosocomial BSI than those admitted to other types of units. Reports on the incidence of BSI vary significantly, reflecting differences in individual risks, based on institutions, type of patients, comorbidities, and length of stay. On a national level, nosocomial BSI is the 10th leading cause of death in the U.S.[16] Intravascular catheter associated BSIs is one of the leading causes of morbidity and mortality in hospitals

Table 1: Sources of pathogens causing blood stream infections

	Source						
Organisms	None	Respiratory tract	Wound	Urine	CVP	Multiple	Total
Acinetobacterbaumannii	6	48	8	1	2	3	68
Klebsiellapneumoniae	18	29	4	3	1	1	56
S. aureus	23	14	3	2	4		46
Candida Sp	22			7	9		38
Enterococcus Sp	25			2	1		28
Pseudomonas aeruginosa	8	15	3				26
E. coli	6	1	2	4			13
Coagulase negative *Staphylococci*	13						13
Serratiamarsecens	1	3			3		7
Burkholderia Sp	2	3			1		6
Enterobacter Sp	1	1	1		1	1	5
Stenotrophomonasmaltophilia		5					5
Proteus mirabilis	1		1				2
Providencia Sp			1				1
Pseudomonas psutzeri	1						1
Chrysobacterium Sp	1						1
Total*	128	119	23	19	22¥	5	316

*Since some of the episodes were polymicrobial, the data in terms of number of episodes and number of microbes is not matching. ¥ CVP tips grew the same organism in 21 episodes. However, one episode was caused by *Klebsiella* pneumonia and *Acinetobacter baumannii*, both of which grew from the tip. Therefore, the source of both these organisms is separately counted under the CVP head. Thus, 22 organisms were isolated from CVP. There were two episodes of BSI caused by *Klebsiella pneumoniae* and *Enterococcus faecalis*, wherein the strain of *klebsiella* originated from the respiratory tract, but the source of Enterococcus could not be found. The organisms of these two episodes are included in their respective columns, CVP: ???, BSI: Bloodstream infections

Table 2: Antimicrobial resistance in bacterial isolates causing blood stream infections

Antibiotics Name	Organisms					
	Staphylococcusaureus (46)	CONS (13)	*Enterococcus* Sp. (28)	*Acinetobacter* Sp. (68)	Members of family *Enterobacteriacae* (84)	*Pseudomonas* Sp. (27)
Penicillin	46 (100)	13 (100)				
Oxacillin	19 (41)	10 (77)				
Vancomycin			11 (39)			
Clindamycin	14 (30)	8 (61.5)				
Gentamycin (HLAR)			11 (39)			
Netilmycin	4 (9)	2 (15)				
Piperacillin	-			66 (97)	79 (94)	20 (74)
Pipracillin/Tazobactam				62 (91)	53 (63)	21 (78)
Ceftazidime				66 (97)	76 (90)	20 (74)
Ceftriaxone				66 (97)	75 (89)	27 (100)
Cefepime				66 (97)	74 (88)	21 (78)
Imipenem				60 (88)	34 (40)	22 (81)
Meropenam				62 (91)	34 (40)	23 (85)
Amikacin	38 (83)	10 (77)		68 (100)	62 (74)	21 (78)
Ciprofloxacin	39 (85)	9 (69)	8 (28.5)	67 (98)	76 (90)	24 (89)
Levofloxacin	35 (76)	9 (69)		58 (85)	74 (88)	24 (89)
Tetracycline				49 (72)	63 (75)	27 (100)
Tigecycline				19 (28)	15 (18)	-
Co-trimoxazole				66 (97)	62 (74)	27 (100)
Colistin				2 (3)	0	0
Polymyxin				2 (3)	0	0
Ceftriaxone/sulbactam				65 (95.5)	61 (73)	25 (92.5)
Cefepime/Tazobactam				66 (97)	53 (63)	25 (92.5)
Cefoperazone/sulbactam				68 (100)	49 (58)	22 (81)
Netilmycin				57 (84)	53 (63)	20 (74)
Chloramphenicol				67 (98)	54 (64)	27 (100)

The numbers and percentages denote the resistant isolates, HLAR: High level aminoglycoside resistance, CONS: ???

across the world. Approximately, 5 million CVCs are inserted each year in the USA, of which, 3-8% lead to BSIs. This amounts to approximately 2, 50,000 CR-BSIs annually in the USA alone.[17]

We had a high prevalence of BSIs, as compared to some other studies. However, an incidence varying from 13.9% to 29.3% has been reported from Malaysian hospitals,[18-20] whereas an incidence of 17% was reported in an Italian surveillance[21] and 39% in a Mexican hospital,[22] showing tremendous geographic variation in the incidence. Trauma patients are on multiple invasive devices, which act as portals of colonization and invasion for pathogens. Moreover, most of the head injured patients are on ventilators, predisposing them to VAP and secondary bacteremia. Traumatic and surgical wounds further predispose such patients to secondary bacteremia. In trauma patients, since many central line insertions are carried out in emergency, strict aseptic precautions are often neglected. Moreover, hemodynamic instability and the need for repeated blood transfusions necessitate insertion of CVCs for long duration, apart from themselves acting as a risk factor for infections. Many a times, it is difficult to change the site of CVCs due to severe hemodynamic instabilities.

In our present study, secondary bacteremia was more predominant than primary bacteremia, which is in contrast to many other reports. In a 10-year microbiological surveillance of BSI in an Italian hospital, the rate of possible catheter-related BSI (CR-BSI) was 66.4% and the remaining 33.6% were non-CR-BSI. Gram-positive organisms predominated and fungi accounted for a very small percentage of BSIs in that study.[6] In a previous study conducted by us in 2001 at the AIIMS hospital, covering the entire 2,200 beds of the hospital, 77% of all the BSIs were found to be primary BSI. *S. aureus* was the most common isolate, followed by *Pseudomonas* Sp. and *Klebsiella* Sp. However, that study was a retrospective analysis of all culture data.[23] We feel that a proper surveillance and tracking of BSIs helps in identifying the actual source or origin of BSIs. Thus, prevention can be targeted to the primary site of infection, which in our case was VAP. The use of an automated surveillance system helped us in rapidly identifying the sources of infection. In the present study, *Acinetobacter* Sp. was the most common isolate, followed by *Klebsiella pneumoniae*. We found a preponderance of gram-negative bacteremia, in contrast to our previous study and other studies from developed and developing countries.[3,6,23,24] *Acinetobacter* Sp. have emerged as important nosocomial pathogens,

with high resistance to antimicrobials and a propensity to survive on environmental surfaces. BSI due to *Acinetobacter* Sp. is associated with a high mortality.[25] We found a high prevalence of candidemia in our study, most of which were primary BSIs. This could have been due to the prolonged use of intravascular catheters, other invasive devices, and the use of broad spectrum antimicrobials in trauma patients.

We feel that implementation of preventive bundles, education, intensive surveillance, and feedbacks have helped in reducing the rates of primary BSIs at our Centre. A similar reduction due to intensive team effort has been recorded in most US hospitals, the greatest reduction having been observed for *S. aureus* bacteremia.[4]

A high prevalence of antimicrobial resistance was observed in our study. In view of this, priority should be given to targeted prevention of all device associated infections and wound infections.

To conclude, in trauma patients, a high incidence of BSIs was observed, the majority of which were secondary to some other infections. Intensive surveillance and preventive efforts can enable us to further reduce the prevalence of blood stream infections.

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