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Bloodstream Infection among Patients in Intensive Care Unit of tertiary care hospital in Nepal: Incidence, Microbiological Profile and Outcome

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Bloodstream Infection among Patients in Intensive Care Unit of tertiary care hospital in Nepal: Incidence, Microbiological Profile and Outcome.

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Abstract

Background

Bloodstream infection (BSI) is an important cause of morbidity and mortality mostly among critically ill patients. Patients admitted in intensive care units (ICUs) are particularly vulnerable because of severe underlying illness, ongoing invasive procedures, prolonged hospitalization and exposure to broad-spectrum antimicrobial agents. This study aimed to determine incidence, microbiological profile, antimicrobial susceptibility pattern and outcome of BSI among adult patients admitted to ICU of tertiary care hospital, Nepal.

Methods

A prospective observational study was conducted in the adult medical and surgical ICU from September 2023 to August 2024. A total of 257 patients admitted to ICU were taken from the day of admission until discharge. Patients with clinical suspicion of BSI underwent blood culture. Blood cultures were processed using BacT/ALERT system, followed by conventional identification and antimicrobial susceptibility testing according to Clinical and Laboratory Standards Institute (CLSI) guideline 2024. Extended-spectrum beta-lactamase (ESBL), carbapenemase, metallo-beta-lactamase (MBL) and AmpC production were assessed among Gram negative

isolates. Severity of illness was assessed using Pitts Bacteremia Score (PBS) and a p value ≤0.05 was considered statistically significant. Data were analyzed using SPSS version 22.

Results

Among 257 patients admitted in ICU, 159 were clinically suspected of having BSI. 54 had positive blood cultures, with a positivity rate of 33.9%. The incidence of BSI was 21.0 per 1000 patient-days, while incidence of central line-associated bloodstream infection (CLABSI) was 17.0 per 1000 central-line days. Out of 54 BSIs, 8 (14.8%) categorized as community-acquired and while 46 (85.2%) as hospital-acquired BSI. Among hospital-acquired BSIs, 21 (38.9%) classified as CLABSI.

Gram-negative bacilli was most commonly isolated (81%), followed by Gram-positive cocci (15%) and fungi (4%). Among Gram negatives, *Acinetobacter baumannii* (37%) was the frequent isolate then *Klebsiella pneumoniae* (15%) and *Pseudomonas aeruginosa* (15%) respectively. Multidrug-resistant (MDR) was detected in 68% while extensively drug-resistant (XDR) in 45%. Carbapenemase production in 61.3%, MBL production in 45% whereas none produced AmpC. All six isolates of *Staphylococcus aureus* were methicillin-resistant.

Among patients with BSI, 16 (29.6%) improved and were discharged from the ICU, 20 (37.0%) left against medical advice and 18 (33.3%) developed complications and died. Mortality was significantly associated with MDR infection and high Pitts Bacteremia Scores. The mean ICU stay was longer among patients with BSI compared to others (19.7 versus 10.12 days).

Conclusion

BSI was common among critically ill patients in the ICU, with a high proportion of hospital-acquired infections and a burden of CLABSI was remarkable. Gram-negative bacilli, particularly *A. baumannii*, were the predominant pathogens and antimicrobial resistance was considerable. MDR infection and higher bacteremia scores were associated with poor outcome.

Keywords: bloodstream infection; intensive care unit; CLABSI; antimicrobial resistance; multidrug resistance; *Acinetobacter baumannii*; Nepal

Introduction

Bloodstream infection (BSI) is defined as presence of viable microorganisms in the bloodstream accompanied by clinical manifestations of infection.[1] Microorganisms may get introduced into the bloodstream via various routes such as introduction of intravenous catheter or it may occur secondary to foci of infection present at another body sites. [2] Critically ill patients are particularly susceptible to BSI due to severe underlying illness, multiple comorbidities, prolonged ICU stay, invasive procedures, mechanical ventilation and use of intravascular devices.[3] Central line-associated bloodstream infection (CLABSI) represents an important subset of healthcare-associated BSI. The presence of a central venous catheter provides a potential route for microorganisms to enter into the bloodstream, particularly while insertion and maintenance practice.[3]

The microbiological profile of ICU-associated BSI varies, common isolates among gram-negative include *Acinetobacter*, *Klebsiella*, *Pseudomonas* and *Escherichia coli* whereas *Staphylococcus aureus* among gram-positive. *Candida* spp also accounts for 8-15% cases of BSIs and plays a major role in causing BSI.[2]

As there is limited availability of evidence regarding BSI and its antimicrobial resistance pattern among patients admitted in ICU, this study helps to determine incidence and microbiological profile of BSI as well as assess antimicrobial susceptibility and know the outcome.

Materials and Methods

Study design and setting

A prospective observational study was conducted in the Department of Microbiology in collaboration with the Department of Anaesthesiology and Critical Care. The study was conducted from September 2023 to August 2024 in the 24-bedded adult medical and surgical ICU.

Ethical approval was obtained from the Institutional Review Committee. (Ref. No. 149/080/081). Written informed consent was obtained from participants or from their close relatives on necessary.

Study population

All adult patients admitted to the medical and surgical ICU during the study period were included. A total of 257 patients were followed from the day of admission until their discharge. Patients clinically suggestive of BSI were monitored and blood culture was performed among them.

Blood culture and microbiological processing

At least two blood culture samples were collected from peripheral veins, preferably before antimicrobial administration. On suspicion of catheter-related infection paired samples were obtained from the peripheral vein and central venous catheter as well. Approximately 10 mL of blood was inoculated into BacT/ALERT culture bottles.

Blood culture bottles were incubated in the BacT/ALERT system. Positive bottles were subcultured on 5% sheep blood agar and MacConkey agar. Organisms were identified using gram staining, colony morphology and appropriate biochemical tests.

Antimicrobial susceptibility testing

Antimicrobial susceptibility testing was performed using Kirby-Bauer disk diffusion method on Mueller-Hinton agar following CLSI guideline 2024. *S. aureus* ATCC 25923 and *E. coli* ATCC 25922 were used as quality-control strains.

ESBL production was confirmed using combined-disc method. Carbapenemase production was assessed using modified carbapenem inactivation method (mCIM), while MBL production was assessed by EDTA-modified carbapenem inactivation method (eCIM). AmpC production was assessed using cefoxitin screening test followed by confirmation with AmpC sterile disc test.

Severity assessment and outcome

Severity of illness was assessed using Pitts Bacteremia Score and a score ≥4 was considered as critical illness. Outcome was categorized as improvement and discharge from ICU, leaving against medical advice (LAMA) or development of complications and death.

Statistical analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 22. Descriptive statistics were expressed as frequencies, percentages and means. Chi-square testing was used to assess associations between MDR/non-MDR status and outcome and between Pitts Bacteremia Score and outcome. Statistical significance was defined as $p \leq 0.05$.

Results

A total of 257 patients were enrolled in this study. Of these, 140 (54%) were male and 117 (46%) were female. Central venous catheters were inserted in 114 (44%) patients. Among 257 patients, 159 were clinically suspected of having BSI and underwent blood culture. 54 had positive blood cultures, thus culture positivity rate was 33.9%.

- **Classification of BSI**

Out of 54 culture-confirmed BSIs, 8 (14.8%) were classified as CA-BSI and 46 (85.2%) as HA-BSI, 21 had CLABSI and 25 had non-CLABSI.

Incidence of BSI: 21.0 per 1000 patient days.

Incidence of CLABSI: 17 per 1000 CL days.

- # Microbiological profile

Out of all the episodes of BSI, 44 (81%) were due to Gram negative organism, 8 (15%) Gram-positive cocci and fungal isolates 2 (4%). Among gram negatives, *Acinetobacter baumannii*, was the predominant isolate 20 (37%), followed by *Klebsiella pneumoniae* -8 (15%), *Pseudomonas aeruginosa* - 8 (15%), *E. coli*- 3 (6%), *Enterobacter cloacae*-3 (6%), *Acinetobacter lwoffii-1(2%)* and *Proteus mirabilis*-1 (2%) respectively. Six isolates (11%) were *Staphylococcus aureus*, 2 (4%) *Enterococcus faecalis* and 2 (4%) were *Candida albicans*.

- # Antimicrobial susceptibility

All *S. aureus* isolates were confirmed as MRSA. All were resistant to penicillin and cefotaxime, while all were susceptible to vancomycin and linezolid. Susceptibility to ciprofloxacin, cotrimoxazole and azithromycin was 83%. (Figure 1)

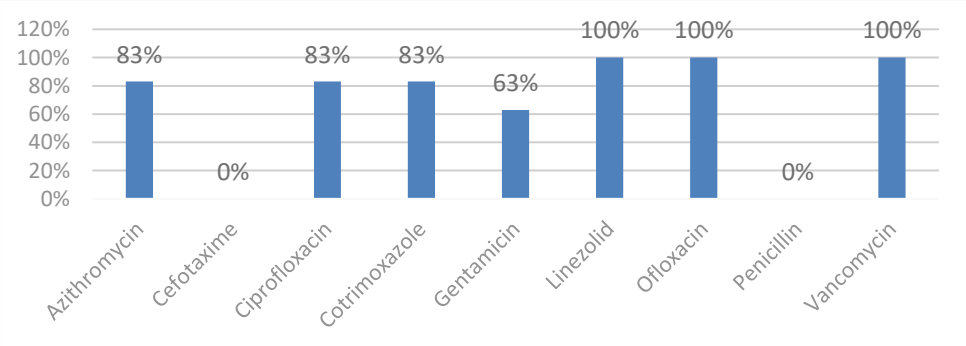


Figure 1: Antimicrobial susceptibility pattern of *S.aureus*

All *E. faecalis* isolates were susceptible to ciprofloxacin, ofloxacin and vancomycin, high-level gentamicin and linezolid. (Figure 2)

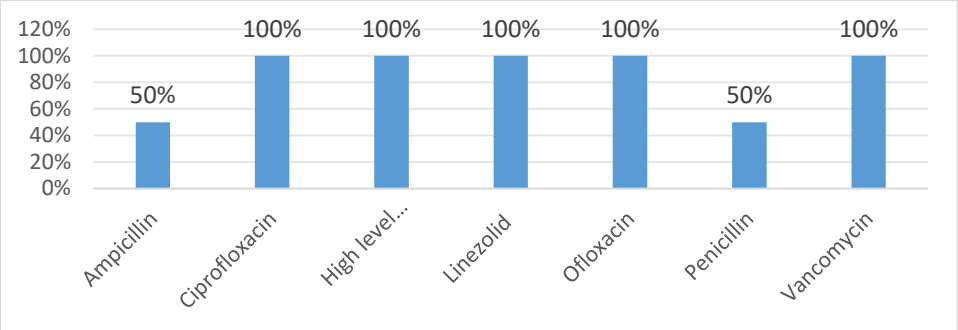


Figure 2: Antimicrobial susceptibility pattern of *E. faecalis*

Among Gram-negative isolates, 68% were MDR and 45% were XDR. ESBL production was detected among *A. baumannii*, *K. pneumoniae*, *P. aeruginosa*, *E. coli*, *E. cloacae*, *A. lwoffii* and *P. mirabilis*. Carbapenemase production was detected in 61.3% of Gram-negative isolates, MBL production in 45% and none of the Gram-negative isolates demonstrated AmpC production.

The antimicrobial susceptibility patterns of Enterobacterales and Acinetobacter species are presented in tables 1 and 2.

Table 1: Antimicrobial susceptibility pattern of family Enterobacterales (n=15)

Antimicrobials	*K. pneumoniae(n=8)*	*E. cloacae (n=3)*	*E. coli (n=3)*	*P. mirabilis (n=1)*
Amikacin	3	2	2	0
Ampicillin-sulbactam	0	2	2	0
Cefixime	2	1	3	0
Cefotaxime	5	0	0	0
Ceftriaxone	4	0	2	0
Ciprofloxacin	2	2	3	0
Colistin	8	3	3	1
Cotrimoxazole	3	1	2	0
Gentamicin	2	2	1	1
Meropenem	2	1	3	0
Ofloxacin	3	3	0	0
Piperacillin	1	1	1	0

Piperacillin-Tazobactam	2	0	3	0
Tigecycline	4	0	2	0

Table 2: Antimicrobial Susceptibility pattern of *Acinetobacte*r species

Antimicrobials	*A.baumanii* (n=20)	*A.lwoffii* (n=1)
Amikacin	11	0
Ampicillin-sulbactam	13	0
Cefixime	10	0
Cefotaxime	0	0
Ceftriaxone	14	0
Ciprofloxacin	14	0
Colistin	20	1
Cotrimoxazole	16	0
Gentamicin	16	0
Meropenem	7	0
Ofloxacin	18	0
Piperacillin	6	0
Piperacillin-Tazobactam	12	0
Tigecycline	14	0

The antimicrobial susceptibility pattern of *P. aeruginosa* is shown in figure 3.

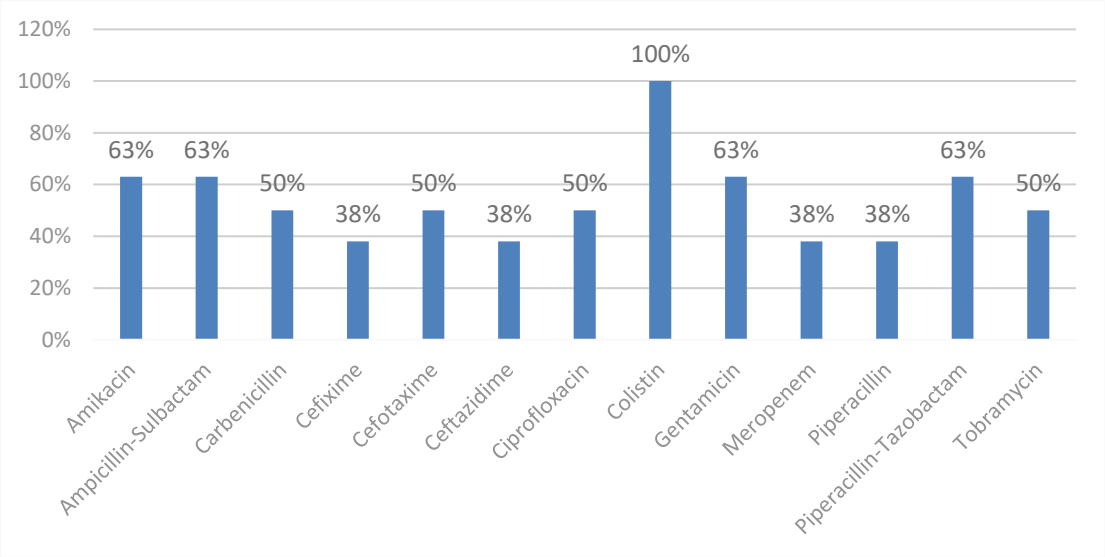


Figure 3: Antimicrobial susceptibility pattern o*f P. aeruginosa* (n=8)

The distribution of ESBL, AmpC, carbapenemase and MBl production among Gram-negatice isolates is shown in Table 3.

Table 3: β- lactamase production among gram negative isolates

Organism	**ESBL Producers**	**AmpC**	**Carbapenemase Producer**	**MBL Producer**
A.baumanni (n=20)	9	0	11	8
K.pneumonia (n=8)	6	0	7	7
P.aeruginosa (n=8)	5	0	5	3
E.coli (n=3)	2	0	0	0
E.cloacae (n=3)	1	0	2	1
A.Iwoffii (n=1)	1	0	1	1
P.mirabilis (n=1)	1	0	1	0

- **Outcome**

Among all 257 ICU patients, 135 (52.5%) were improved and discharged from ICU, 49 (19.1%) developed complications and died and 73 (28.4%) left against medical advice.

Out of 54 patients with BSI, 16 (29.6%) were improved and discharged, 20 (37.0%) left against medical advice and 18 (33.3%) developed complications and died. Among 18 patients who developed complications and expired, 14 were infected with MDR bacteria. Similarly, 16 patients who improved and discharged from ICU, 9 were infected with MDR organism. Likewise 20 patients who went on LAMA, 9 were infected with MDR bacteria. The mean ICU stay was 10.12 days for the overall ICU patients and 19.7 days among patients with BSI. Patients with *K. pneumoniae* infection had a particularly prolonged mean ICU stay of 24.3 days.

The association between MDR and non-MDR status and outcome among patients with BSI is presented in Table 4.

Table 4: Outcome of patient of BSI with respect to MDR strains and Non - MDR strains

Outcome	MDR Strains	Non -MDR Strains	Total	P-value
Death	13	5	18	0.0021
Survival	5	11	16	
LAMA	9	9	18	

The association between Pitts Bacteremia score and patient outcome is presented in Table 5.

Table 5: Pitts Bacteremia Score and its association with outcome

Outcome	Mortality	Survival	LAMA	Total	P-value
≤ 4	0	13	5	18	
≥ 4	18	3	15	36	0.001

Discussion

This observational prospective study showed a burden of bloodstream infection (BSI) among adult patients admitted at ICU in tertiary care hospital of Nepal. Blood culture positivity among clinically suspected cases of BSI was around 34%, with a incidence of 21 per 1000 patient-days. This finding is comparable with the study by Vincent et al. [5] that reported incidence of BSI 15–30 per 1000 patient-days. The incidence of CLABSI in our study was 17 per 1000 central-line days which is also comparable with reports by Mishra et al. 17.04 [18], Chopdekar et al. 27.06 [19] and Johnson et al. 29.3 [20] per 1000 central –line days respectively. Differences in rate of CLABSI may be due to variations in infection-prevention practices and central-line care and maintenance.

Gram-negative bacilli were the predominant pathogens causing BSI in our study. *Acinetobacter baumannii* was the most frequent isolate, followed by *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. This finding is consistent with the study done by Pandey et al. [21], which also reported a predominance of Gram-negative organisms as a major cause of BSI. In contrast to this, some studies done at Western ICUs have reported Gram-positive organisms, particularly *Staphylococcus aureus*, as the predominant pathogen causing BSI. [7]

All *S. aureus* isolated in our study were methicillin-resistant (MRSA). S. *aureus* being common causative agents of bloodstream infections exerts a high burden in terms of morbidity and mortality. [4] MRSA among all hospitals in the NNIS system rose from 2.1% in 1975 to 29% in 1991 and to 35% in 1996.[9] In Asia, prevalence of MRSA infections reached a peak in the late 1900s and thereafter remained at a plateau mid 2000s with an estimation of about 70% of hospital-acquired (HA) *S. aureus* infections between 2004 and 2006. [10]

No coagulase-negative staphylococci (CoNS) were isolated in our study. CoNS remains an important cause of catheter-related bloodstream infections, ranging between 11% and 45%.[11] A greater prevalence of CoNS causing BSI between 25-57% [12] has been reported from the Western countries as these organisms normally inhabit skin and cause insertion related infection.

MDR bacilli accounted for 68% of all Gram-negative isolates in our study. The highest proportion of MDR was observed among *K. pneumoniae* (87.5%), *Acinetobacter* spp. (66.7%) and *P. aeruginosa* (62.5%). Higher mortality associated with MDROs may be related to the virulence of the pathogen, patient's co-morbidities, old age or severity of illness.[8] As per U.S. National Healthcare Safety Network increased occurrence of MDR-GNB has been reported especially among *Acinetobacter* spp. *E. coli*, *K. pneumoniae and Enterobacter* spp. [13] The high prevalence of MDR organisms is matter of concern because infections caused by these pathogens has limited therapeutic options and is associated with increased mortality.

The prevalence of ESBL and carbapenemase production was noted to be 57% and 61.3%. These findings are comparable to the reports from several South Asian healthcare settings which showed prevalence of ESBL-producing GNB between 19% and 60%, CRE between 5.3% and 59%. [13] Likewise ESBL positivity was confirmed in 42% of *K. pneumoniae* and 33% of *E. coli* isolates from several hospitals in India, 40% of Enterobacterales isolates from Pakistan and 16% in enteric and non-enteric gram-negative bacilli from Bangladesh. [14] In our study, carbapenem resistance was particularly high among *K. pneumoniae* (87.5%), *P. aeruginosa* (62.5%), and *Acinetobacter* spp. (55%).

MBL production was detected in 45% of Gram-negative isolates, majority of MBL production were detected among *K.pneumoniae*, *P.aeruginosa* and *Acinetobacter* spp respectively. Various studies conducted in different countries have reported variable rates of MBL production among Gram-negative organisms ranging from 13.4 to 61.5% for *E. coli* and 33–36% for *K. pneumonia.* [16] A study done at Nepal also demonstrated MBL production by *E.coli* as 38%, *Pseudomonas* spp. 31% and *K. pneumoniae* 19%. [17] The relatively high prevalence of MBL in our study may be due to exclusive inclusion of ICU patients. No AmpC-producing isolates were detected in the present study. However, a study by Yadav et al. reported AmpC production in 5% of isolates. [15]

BSI infected patients has been associated with various outcomes**.** Patients with BSI also had a longer ICU stay than the overall ICU population. Mortality rates in patients developing BSI vary

between 39–100%. [6] A study by Vincent et al. [5] highlighted that mortality rate in ICU patients with BSIs can range between 30-50%, particularly when severe infection occurs or if patient has multiple comorbidities. In our study mortality attributed to BSI was 33.33%, MDR strain was involved in 13 i.e 72%. The association of MDR and Non MDR strains in BSI with outcome of patients was found to be statistically significant i.e (p value <0.05). Overall mean length of ICU stay was 10.12 days and mean length of ICU stay in patients with BSI was longer i.e 19.7 days. And BSI attributable with *K. pneumoniae* was associated with even longer stay in ICU i.e 24.3 days.

The higher Pitts Bacteremia Score was significantly associated with mortality, patients with score ≥4 were considered to be critically ill. In 54 culture proven BSI, 67% of patients were considered critically ill and among them 18 (50%) of patients expired. PBS has the fewest parameters and is good predictor in assessing severity of illness and to correlate outcome

Strengths and Limitations

The prospective study and daily follow-up of patients from day of admission to discharge allowed identification of BSI and assessment of clinical outcomes. The study also included antimicrobial resistance characterization, including ESBL, carbapenemase and MBL detection, providing information regarding the burden of resistance.

However, the study was conducted at a single tertiary-care center and included a limited number of culture-confirmed BSI, the findings may not be generalizable to all ICUs in Nepal. And due to resource limitations antifungal susceptibility testing could not be performed.

Conclusion

Bloodstream infection represents an important healthcare-associated infection among critically ill adult patients in the ICU. The study illustrated an incidence of 21 BSI episodes per 1000 patient-days and a CLABSI rate of 17 per 1000 central-line days**.**

Gram-negative bacilli were the predominant pathogens, *Acinetobacter baumannii* being the most frequent isolate. Among Gram-negative a high proportion organisms were multidrug-resistant and extensively drug-resistant, with a significant production of carbapenemases and MBLs. All *S. aureus* isolates were MRSA.

One-third of patients with BSI died and mortality was significantly associated with MDR infection and high Pitts Bacteremia Score. Patients with BSI also experienced prolonged ICU stays.

Funding

No external funding was received for this study.

Ethical consideration

Ethical approval was obtained from the Instituitional Review Committee of B.P. Koirala Institute of Health Sciences, Dharan, Nepal (Ref. No. 149/080/081). The study was conducted in accordance with ethical principles of Declaration of Helsinki. Written informed consent was obtained from participants or their close relatives as appropriate.

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