

Causative Organisms and associated antimicrobial resistance in Central Line-Associated Blood Stream Infections from patients admitted in ICU of Tertiary Health Care Hospital of Jammu region.

Bharti R¹, Multani H², Sharma P^{3*}, Sudhan Sharma S⁴

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¹ Rajni Bharti, Senior Resident, Department of Microbiology, GMC Jammu, Jammu and Kashmir, India.

² Harman Multani, Lecturer, Department of Microbiology, GMC Jammu, Jammu and Kashmir, India.

^{3*} Priyanka Sharma, Lecturer, Department of Microbiology, GMC Jammu, Jammu and Kashmir, India.

⁴ Shashi Sudhan Sharma, Professor and Head, Department of Microbiology, GMC Jammu, Jammu and Kashmir, India.


Introduction: CLABSI (Central Line-Associated Bloodstream Infection) is the presence of bacteremia originating from a central line catheter¹. CLABSI is a common cause of healthcare-associated infection and is a major cause of morbidity and mortality. We did this study to study the incidence, bacteriological profile and antimicrobial susceptibility pattern of the isolates in CLABSI in the Intensive Care Unit (ICU) patients.

Material and methods: This prospective study was conducted for one year in the Department of Microbiology on patients admitted to the ICU for more than 48 hours with a Central line catheter. The CLABSI rate was calculated. The formula for CLABSI Rate used was CLABSI incidence rate which was calculated as no. of CLABSI / no. of central line days × 1000.

Results: Out of 448 patients 306 have central line. Out of 306 patients, 140 develop symptoms related to device-associated infections. Among 140 patients 27 developed central line associated bloodstream infection. The CLABSI rate found was 17.76 per 1000 catheter days. Staphylococcus aureus was the most common pathogen isolated among gram-positive cocci. Among gram-negative bacilli was Acinetobacter sp. Multi-drug resistance was seen in the first line of antibiotics used.

Conclusion: CLABSI had a significant impact on the overall healthcare costs. Knowledge about risk factors and infection control measures for CLABSI prevention is crucial for best clinical practice.

Keywords: Anti-Microbial Resistance, Central Line-Associated Bloodstream Infection, Intensive Care Unit, Medical Devices

Corresponding Author	How to Cite this Article	To Browse
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Introduction

CLABSI is the presence of bacteremia originating from a central line catheter [1]. CLABSI is a common cause of healthcare-associated infection and is a major cause of morbidity and mortality. Central venous catheters (CVCs) are associated with a greater risk of device-related infections as compared to any other medical device [2]. The diagnosis of CLABSI is confirmed by isolation of the same microorganism from the catheter tip and at least one blood culture, with the presence of clinical manifestations of infection and no other detectable source of infection³. The patient must have at least one of the following features: fever (temperature ≥ 38 degrees Celsius), chills, or hypotension. Central venous catheters (CVC) are being used with increasing frequency in hospitals both in an ICU as well as outside ICUs. According to the Centre for Disease Control and Prevention-National Healthcare Safety Network- 2013 report, the mean incidence of CLABSI per 1000 central line days was found as 0-2.9% in critical care units and 0-1.2% in inpatient wards [4]. In India, several multicentre studies showed the CLABSI rate ranging from 2.40-5.1 per 1000 central line days [5]. CLABSI is caused by the following etiological agents: Coagulase-negative staphylococcus including *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Burkholderiacepacia*, *Acinetobacter baumannii*, *Klebsiella species*, *Enterobacter species*, *Citrobacter freundii*, *Serratia marcescens*, *Malassezia furfur*, *Enterococcus species*, *Corynebacterium* especially. *jeikeium*[6]. Among gram-positive organisms, the Methicillin-resistant *Staphylococcus aureus* emerged as a significant pathogen. The resistant gram-negative organisms, including extended-spectrum β -lactamase (ESBL)-producing, carbapenem-resistant, and fluoroquinolone-resistant Enterobacteriaceae are also known as major threats [7][8][9][10]. MDROs (Multi-drug resistant organisms) are responsible for 20% to 67% of all CLABSIs, making it critical to understand the best management strategy for these patients [11], [12]. There are two types of central lines: (1) Tunneled catheters which are implanted surgically (by creating a subcutaneous track before entering the vein) into the internal jugular, subclavian, or femoral vein for long-term (weeks to months) use such as chemotherapy or hemodialysis and (2) Non-tunneled catheters are more commonly used.

They are temporary central venous catheters that are inserted percutaneously. They account for most CLABSI, within 7 to 10 days of catheterization; bacteria on the skin surface migrate along the external surface of the catheter from the skin exit site towards the intravascular space. The tunneled catheters have a cuff that causes a fibrotic reaction around the catheter, creating a barrier to bacterial migration. Because of the absence of a tunnel (a subcutaneous tract), the non-tunneled catheters are at higher risk for CLABSIs. CLABSIs that occur after ten days are usually caused by contamination of the hub (intraluminal) typically from a health care provider's contaminated hands but rarely from a host and often due to a breach of standard aseptic precautions to access the hub. Other less common mechanisms include hematogenous seeding of bacteria from a contaminated infusate or another source. The risk factors of CLABSI are chronic illnesses (hemodialysis, malignancy, gastrointestinal tract disorders, and pulmonary hypertension), immunosuppressed states (organ transplant, diabetes mellitus), malnutrition, total parenteral nutrition, extremes of age, loss of skin integrity (burns) and prolonged hospitalization before line insertion. The femoral venous catheters are associated with the highest risk of CLABSI followed by the internal jugular, and subclavian catheters. Further, the type of catheter, conditions of insertion (emergent versus elective, use of full barrier precautions versus limited), catheter care, and skill of the operator also influence the risk of CLABSI. *Pseudomonas* infection is commonly seen in association with neutropenia, severe illness, or known prior colonization. Certain bacteria such as staphylococci and *pseudomonas* produce an extracellular polysaccharide layer [slime (biofilm)], which favours increased virulence, adherence to catheter surface, and resistance to antimicrobial therapy [13]. We did this study to study the incidence, bacteriological profile and antimicrobial susceptibility pattern of the isolates in CLABSI in ICU patients.

Methodology

This prospective study was conducted in 2020 for one year in the Department of Microbiology of Government Medical College and Hospital, Jammu which is a tertiary care hospital with having referral of Jammu province.

Inclusion criteria were Informed consent of patients admitted to the ICU for more than 48 hours with a Central line catheter. Exclusion criteria were OPD patients and patients without Central line catheters. Patients showing clinical signs of infection on or before admission or transfer to the ICUs were not included in the study and Refusal of consent.

After taking informed consent, detailed history including the name, age, sex, underlying clinical condition, date of admission to the ICU, any history of previous antibiotic intake, the treatment being administered in the ICU, and clinical outcome of each patient. Laboratory samples for CLABSI were taken depending on the clinical suspicion from the patients admitted to the ICU for more than 48 hrs. All specimens were collected as per standard aseptic protocol and transported to the laboratory as early as possible. Gram staining was made from all specimens and examined to determine the presence, type of cells, relative number of microorganisms and their morphologies. All the samples were inoculated on Blood agar and MacConkey agar. Incubate Blood and MacConkey agar at 37°C overnight.

In case of significant growth, the isolated colonies were subjected to gram staining, antibiotic sensitivity test (Kirby-Bauer Disk Diffusion Method) and biochemical tests for identification as per established Departmental protocols. The identification of organisms was done with biochemical tests. The organism was reported as sensitive, intermediate or resistant based on the standard zone size. The following antibiotic discs with their respective concentrations were used: ampicillin(AMP) (10 µg), gentamicin(GEN) (10 µg), ciprofloxacin(CIP) (5 µg), tetracycline(TEC) (30 µg), erythromycin (15 µg), vancomycin (30 µg), chloramphenicol (30 µg), norfloxacin (10 µg), nitrofurantoin (300 µg), ceftazidime (30 µg), and ceftriaxone (30 µg) for Gram positive bacteria and ampicillin (10 µg), piperacillin (100 µg), ceftazidime (30 µg), cefepime (30 µg), ceftriaxone (5 µg), gentamicin (10 µg), ciprofloxacin (5 µg), tetracycline(TET) (30 µg), meropenem(MRP) (10 µg), amikacin(AMK) (30 µg), nitrofurantoin(NIT) (300 µg) and ceftazidime(CAZ) (30 µg) for Gram-negative bacteria.

Results

A total of 448 patients were included in the study out of which 329 were males and 119 were females.

Table 1: The age distribution of patients.

S.NO.	AGE(yrs)	Total no. of patients
1	≤50	301(67%)
2	51-64	71(16%)
3	65-79	58(13%)
4	≥80	18(4%)

Maximum patients (67%) were less than 50 years of age followed by 51-64 years(16%).

Table 2: Age distribution of patients with CLABSI.

Age(years)	CLABSI
≤50	22
51-64	4
65-79	1

Maximum patients (22) who developed CLABSI were under the age group of less than 50 years followed by 51-64 years of age.

Table 3: CLABSI incidence rate among patients admitted to ICU

Total no. of patients on the central line	306
Total no. of central line days	1520
No. of CLABSI	27
CLABSI incidence rate: No. of CLABSI/no. of central line days × 1000	17.76

306(68%) were on Central line catheter and CLABSI was diagnosed in 27(6.02%). The total Central line device days was 1520 and the CLABSI incidence rate was 17.76

Table 4: Type and the total number of organisms isolate in CLABSI

Organism	Number
Staphylococcus aureus	6
Methicillin-resistant Staphylococcus aureus (MRSA)	2
Acinetobacter sp.	7
Pseudomonas sp.	3
Klebsiella sp.	4
Enterococcus sp.	2
Citrobacter sp.	3
Total	27

Among gram-negative bacilli, *Acinetobacter sp.* (1.56%) was the common organism isolated followed by *Klebsiella sp.* (0.89%) followed by *Pseudomonas sp.* and *Citrobacter sp.* (0.67%). Among gram-positive cocci, *Staphylococcus aureus* (1.34%) was the common organism isolated followed by *Enterococcus sp.* (0.44%) and Methicillin-resistant *Staphylococcus aureus*(0.44%).

AST of *Staphylococcus aureus*- 17% were resistant to Erythromycin, Gentamicin, Clindamycin and Linezolid. 50% were resistant to Ciprofloxacin. 100% were sensitive to Cefoxitin, Teicoplanin, Cotrimoxazole, Doxycycline and Vancomycin.

AST of Methicillin-resistant *Staphylococcus aureus*- 50% were resistant to Ciprofloxacin. 100% were sensitive to Erythromycin, Gentamycin, Teicoplanin, Clindamycin Linezolid, Cotrimoxazole, Doxycycline, and Vancomycin. 100% were resistant to Cefoxitin (i.e. MRSA).

AST of *Acinetobacter species*- 100% were resistant to Cefotaxime, Ceftazidime, Ciprofloxacin, Gentamycin, Meropenem, Cotrimoxazole, Piperacillin-tazobactam and Imipenem. 86% were resistant to Amikacin. 100% were sensitive to Minocycline.

AST of *Pseudomonas species*- 33% of the species were resistant to Amikacin, Aztreonam and Ciprofloxacin. 100% were resistant to Meropenem, Piperacillin-tazobactam, Imipenem and Netilmicin. 100% were sensitive to Ceftazidime and Gentamycin.

AST of *Klebsiella species*- 100% were sensitive to Amoxycloxacillin, Ciprofloxacin, Meropenem, Gentamycin and Meropenem. 25% were resistant to Ampicillin, Amikacin and Cefotaxime. 50% were resistant to Cefotaxime and Ertapenem. 100% were resistant to Cotrimoxazole, Piperacillin-tazobactam, imipenem and Doxycycline.

AST of *Enterococcus species*- 100% resistant to Ampicillin, Ciprofloxacin, Erythromycin, Fosfomycin and high-level Gentamycin. 50% were resistant to Erythromycin. 100% were sensitive to Linezolid, Teicoplanin and Vancomycin.

AST of *Citrobacter species*- 100% were resistant to Ertapenem. 67% were resistant to Amikacin, Cefotaxime, Ceftazidime, Meropenem, Gentamycin, Meropenem, Cotrimoxazole, Minocycline and Levofloxacin

Discussion

During the period covered by our study, a total of 448 patients were included. They were within the age range of 1 – 80 years. The most common age group included in the study were <50 years, males were more in number than females.

These findings were also depicted in the studies of Sundaram GVG *et al.*, 2020[14] and Yoshida Tet *al.*, 2019[15]. The samples were collected during the whole study. Out of 448 patients, 306 have central lines. Out of 306 patients, 140 develop symptoms related to device-associated infections. The samples of all 140 patients were collected and processed. Among 140 patients 27 developed central line associated bloodstream infection. The CLABSI rate was calculated. The formula for CLABSI Rate used was CLABSI incidence rate which was calculated as no. of CLABSI / no. of central line days × 1000. The CLABSI rate found was 17.76 per 1000 catheter days. This formula was also used in the studies of Salama MF *et al.*, 2016[16] and Sun *et al.*, 2020[17]. In the present study, the most common organisms causing CLABSI were Gram-positive cocci than Gram-negative bacilli. In a similar study done by Yoshida T *et al.*, 2019[15] the most common organisms causing CLABSI were Gram-negative bacilli than Gram-positive cocci. Among gram-negative bacilli, *Acinetobacter sp.* (1.56%) was the common organism isolated followed by *Klebsiella sp.* (0.89%) followed by *Pseudomonas sp.* and *Citrobacter sp.* (0.67%). Among gram-positive cocci, *Staphylococcus aureus* (1.34%) was the common organism isolated followed by *Enterococcus sp.* (0.44%) and Methicillin-resistant *Staphylococcus aureus* (0.44%). In a similar study done by Yoshida Tet *al.*, 2019[15] most (61.8%) of the causative agents of CLABSI in the institution were Gram-negative, with a predominance of *Pseudomonas aeruginosa* (28.2 %). The Gram-positive ones accounted for 30.8% of the isolated microorganisms, highlighting *Staphylococcus aureus* being the main cause. In another similar study which was done by Salama MF *et al.*, 2016[16] among Gram-negative bacilli the most common organisms isolated were *Pseudomonas aeruginosa* followed by *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *E. coli*, *Stenotrophomonas maltophilia*, *Serratia marcescens* and *Enterobacter cloacae*. The least common Gram-negative bacilli found was *Proteus mirabilis*. Among gram-positive cocci, the most common organism was *S. epidermidis* followed by MRSA (Methicillin-resistant *Staphylococcus aureus*). In another study by Deron Cet *al.*, 2009 [18] out of 33 587 central line-associated BSIs from 1684 ICUs, 2498 reported central line-associated BSIs (7.4%) were MRSA and 1590 (4.7%) were methicillin-susceptible *Staphylococcus aureus* (MSSA).

In the present study, the *Acinetobacter species* were 100% resistant to Cefotaxime, Ceftazidime, Ciprofloxacin, Gentamycin, Meropenem, Cotrimoxazole, Piperacillin-tazobactam and Imipenem and 86% resistant to Amikacin. The *Klebsiellae species* were 25% resistant to Ampicillin, Amikacin and Cefotaxime, 50% resistant to Cefotaxime, Ertapenem and 100% resistant to Cotrimoxazole, Piperacillin-tazobactam, imipenem and Doxycycline. The *Enterococcus species* were 100% resistant to Ampicillin, Ciprofloxacin, Erythromycin, Fosfomycin and high-level Gentamycin and 50% resistant to Erythromycin. The *Citrobacter species* were

100% resistant to Ertapenem, 67% resistant to Amikacin, Cefotaxime, Ceftazidime, Feropenem, Gentamycin, Meropenem, Cotrimoxazole, Minocycline and Levofloxacin. In another study which was done by SeeIet *al.*, 2016[19] the highest overall prevalence of antimicrobial resistance was found in *Enterococcus faecium* (82.5% vancomycin-resistant), *Escherichia coli* (56.5% fluoroquinolone-resistant), and *Staphylococcus aureus* (45.6% methicillin-resistant). Carbapenem resistance was uncommon among *Escherichia Coli* and *Klebsiella species* (0.4% and 4.6%, respectively).

Only 28.9% of viridians group *Streptococci* had susceptibility information reported for penicillin. In this study, 33% of the *Pseudomonas species* were resistant to Amikacin, Aztreonam and Ciprofloxacin whereas 100% were resistant to Meropenem, piperacillin-tazobactam, Imipenem and Netilmycin. In another study done by Litwin A. et al., 2021[20]. *Pseudomonas aeruginosa* was the pathogen most frequently responsible for CLA-BSI 7/108 (6.48%) and in 2019 the *pseudomonas aeruginosa* were 22.2% resistant to Piperacillin/ tazobactam, Imipenem and Meropenem, 33.3% resistant to Ceftazidime, Cefepime, Amikacin, Gentamicin and Ciprofloxacin.

Conclusion

CLABSI is a highly prevalent problem in the intensive care unit. One of the significant reasons for central line removal is an infection or suspicion. This clinical practice leads to prolonged hospital stays and increased procedures and complication rates. One of the challenges with central lines is the variety of catheter types inserted by diverse staff which are sometimes undertrained.

But Infections continue to be a common problem in almost every study. Adopting best practices, providing hands-on training, introducing training sessions, maintaining checklists, strengthening Hospital Infection Control practices and establishing a culture of patient safety in healthcare institutions can reduce CLABSI to a greater extent.

What does this study add to existing knowledge?

Adherence to all elements of the care bundle leads to a significant decrease in CLABSI. Implementing a care bundle and auditing the adherence to each element should be included as a part of routine hospital infection control committee (HICC) practices.

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