International Journal of Infection Control
www.ijic.info ISSN 1996-9783

ORIGINAL ARTICLE

Central venous catheter-related bloodstream infections in an intensive care unit from a tertiary care teaching hospital in India

Gajanand Mittal[1], Rajni Gaind[1], P K Verma[2], Monorama Deb[1]

1. Department of Microbiology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India
2. Department of Anaesthesiology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India

doi: 10.3396/IJIC.v12i1.002.16

Abstract

Central venous catheters (CVC) have become essential in the management of critically ill patients and patients who require long-term medical care. Central line-associated bloodstream infections (CLABSI) are among the most frequent and lethal complications of catheter use. The objective of this study was to determine the incidence of CLABSIs and antibiotic susceptibility patterns of isolated bacteria from adults in an Indian intensive care unit between January 2012 and December 2014. A total of 434 samples were received in the laboratory from patients with a clinical diagnosis of sepsis after central venous catheterization. The semi quantitative method (roll-plate) was used for catheter tip culture. Two hundred and fifty six catheter tips (59%) were colonized. *Staphylococcus aureus* (42%) was the most common colonizer followed by the *Enterobacteriaceae* family, gram negative non-fermenters and *Candida albicans*. Thirty-three CLABSIs were identified, giving a CLABSI rate of 9.5 per 1000 catheter days. *S. aureus* was the major cause (63%) of CLABSI followed by *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Escherichia coli*. Meticillin-resistant *S. aureus* accounted for 76% of *S. aureus* CLABSIs. All *A. baumannii* and 33% of *P. aeruginosa* isolates were multi-drug resistant (MDR). All *E. coli* and *K. pneumoniae* were extended-spectrum β-lactamase (ESBL) producers, with 33% of *K. pneumoniae* being MDR. Central venous catheters are increasingly being used in critical care and have a direct bearing on patient mortality and morbidity. Microbiological surveillance may guide management of infectious complications.

Key words: Central venous catheter; Bacteraemia; Critical care

Corresponding Author
Dr. Monorama Deb,
Department of Microbiology, VMMC and Safdarjung Hospital, New Delhi – 110029, India
Email: dr.manoramadeb@yahoo.com

Introduction

Central venous catheters (CVCs) have become essential in the management of critically ill patients, as well as other patient populations who require long-term medical care.[1] Central venous catheters are used to access the vascular system for the delivery of medication, parenteral nutrition, the collection of blood samples and haemodynamic monitoring.[2] However, infections and non-infectious complications are frequently reported with central venous catheterization.[2] Central line-associated bloodstream infections (CLABSI) are one of the most frequent, lethal and costly complications of central venous catheterization; they are associated with significant morbidity and mortality.[3] They are also the most common cause of nosocomial bacteraemia.[3]

Bacterial colonization of the device and the contamination of infusate are primary causes of CLABSI. Colonization of the device may be either extra luminal (from surrounding skin or hematogenous seeding of the catheter tip) or intraluminal (due to biofilm formation by an organism leading to persistence of infection and hematogenous spread). Although rarer, it is contaminated infusate that leads to the majority of epidemic intravascular device-related BSIs.[4-6] The objective of this study was to determine incidence of CLABSIs and the antibiotic susceptibility pattern of isolated bacteria in an Indian intensive care unit (ICU).

Methods

The prospective, observational study was conducted in a 1535 bed tertiary care teaching hospital in New Delhi, India. It is a government hospital. The hospital admits on an average 12500 patients per month, with 60 ICU admissions per month. The hospital caters mainly to the poor and middle income groups and provides free treatment to all patients. The patients were admitted to the eight bed adult medical-surgical ICU between January 2012 and December 2014. This ICU admits patients of the hospital who require intensive care or ventilator support; patients were also admitted directly from the community and from other hospitals through the accident and emergency department.

Central venous catheters were inserted under aseptic conditions. A catheter tip culture was performed on all patients at the time of the removal of the catheter. The semi-quantitative method (roll-plate) was used for catheter tip culture as described by Maki *et al*.[7] Isolation of >15 colony forming units (CFU) was considered a positive culture. Peripheral blood cultures were collected from patients with clinical evidence of sepsis. Five mL of blood were collected under aseptic conditions and added to 45 ml of brain heart infusion broth. This was subcultured on 5% sheep blood agar and MacConkey agar after 48 hours of incubation at 37°C. Culture plates were examined after overnight incubation at 37°C and culture isolates were identified by conventional biochemical tests.[8] Sterile cultures were further incubated at 37°C until the seventh day. Antibiotic susceptibility was checked by the Kirby-Bauer disk diffusion method as per Clinical and Laboratory Standards Institute guidelines.[9] Prevalence data and antibiotic susceptibility profiles of bacteria were analyzed using WHONET 5.6.

This study was approved by the hospital ethical committee (s.no.-VMMC/SJH/Ethics/Sep-11/29).

Definitions

A definitive diagnosis of CLABSI requires that the same organism grows from at least one peripheral blood culture and a culture of the catheter tip.[10] Colonization was defined as growth of >15 CFU from a 5-cm segment of the catheter tip by the semi quantitative (roll-plate) culture.[10] Bloodstream infection was defined as a positive blood culture with negative catheter tip culture, or growth of a different organism isolated from the catheter tip.[3]

The CLABSI rates was expressed per 1000 CVC days and was calculated by the following formula:[11]

$$\text{CLABSI rate per 1000 catheter days} = \frac{\text{Number of CLABSI cases}}{\text{No. of CVC days}} \times 1000$$

Results

A total of 434 tip cultures were received by the laboratory from 434 ICU patients with a clinical diagnosis of sepsis following central venous catheterization. The patient sample included patients with acute poisoning, neurological cardiovascular

emergency, acute respiratory failure and patients undergoing emergency and elective surgery. Patients ranged in age from 17 to 82 years. The ICU had a bed occupancy rate of 100%. The patient to nurse ratio was 3.3:1 in the daytime and 5:1 in the nighttime.

The total duration catheters were in place was 3474 days. Of 434 catheters a total of 256 (59%) catheter tips were colonized with bacteria and *Candida* spp. Among the colonized catheters, gram positive cocci (42%) (*Staphylococcus aureus* (39%), *Enterococcus faecalis* (3%)) were most common, followed by organisms belonging to the *Enterobacteriaceae* family (28%): *Klebsiella pneumoniae* (16%), *Escherichia coli* (10%) and *Proteus mirabilis* (2%). Gram negative non-lactose fermenting bacteria were isolated from 27% of colonized catheters, including *Acinetobacter baumannii* (19%) and *Pseudomonas aeruginosa* (8%). *Candida albicans* was isolated from 3% of colonized catheters.

Fifty culture-proven bloodstream infections were observed, of which 33 were classified as CLABSI, giving a rate of 9.5 per 1000 catheter days. *Staphylococcus aureus* was the major cause (63%) of CLABSI, followed by *A. baumannii* (15%), *P. aeruginosa* (9%), *K. pneumoniae* (9%) and *E. coli* (3%). The positive predictive value of catheter tip culture for diagnosis of CLABSI was found to be 0.128.

Results of antibiotic susceptibility testing of colonized catheters and CLABSI isolates are shown in Table 1. Among colonized catheters 90% of MRSA isolates were resistant to gentamicin, ciprofloxacin and erythromycin, compared to 40-60% of meticillin-sensitive *S. aureus* (MSSA) isolates. Seventy two percent of MRSA isolates were resistant to clindamycin compared to 33% of MSSA isolates. Sixty to 80% of isolates of the family *Enterobacteriaceae* were resistant to ceftazidime, amikacin, gentamicin, netilmicin and ciprofloxacin. Forty to 50% of isolates were resistant to tazobactam/piperacillin and cefoperazone/sulbactam. Imipenem and meropenem resistance was found to be 9% and 29%, respectively. Among non-lactose fermenting gram negative bacteria, 80-90% of isolates were resistant to ceftazidime, amikacin, gentamicin and ciprofloxacin. 55% were resistant to netilmicin, tazobactam/piperacillin and meropenem, and 27% were resistant to cefoperazone/sulbactam and imipenem.

Among the CLABSI isolates, MRSA accounted for 76% of all isolates; 75-85% of MRSA isolates were resistant to gentamicin, erythromycin and clindamycin, and all were resistant to ciprofloxacin. Among MSSA isolates, 40-60% were resistant to gentamicin, ciprofloxacin and clindamycin. *Acinetobacter baumannii* were resistant to most of the antibiotics tested; all but one isolate were sensitive to cefoperazone/sulbactam. *Escherichia coli*, *K. pneumoniae* and *P. aeruginosa* were sensitive to most of the antibiotics tested except one *K. pneumoniae* and one *P. aeruginosa* isolate, which were resistant to most of the antibiotics tested. The antibiogram of these highly resistance isolates matched the corresponding isolates from the catheter tip.

Discussion

Since CVCs are increasingly being used in critical care and have a direct bearing on the mortality, morbidity and cost of treatment in catheterized patients, regular surveillance of CLABSIs can inform appropriate infection control practices and antibiotic policy.[2]

In the present study, the CVC colonization rate was 59%. This is similar to other studies in which the incidence rate of catheter colonization has ranged from 42-63%.[2,3,11,12] In our study, among colonized catheters, gram positive cocci (predominantly *S. aureus*) were the most common colonizers (42%) followed by the family *Enterobacteriaceae* and gram negative non-lactose fermenting bacteria. *Candida albicans* were isolated in 3% of colonized catheters. These findings are similar to previous studies.[3,11] Gahlot *et al.*[3] found that gram positive cocci (40%) were the most common microorganism colonizing CVCs followed by gram negative non-lactose fermenting bacteria (27%), fungi (*Candida* spp. 16%) and organisms belonging to the Enterobacteriaceae family (10%). In the study by Kaur *et al.*,[11] the microorganism most commonly colonizing the catheter was *S. aureus* followed by *A. baumannii, E. faecalis, P. aeruginosa,* non-albicans *Candida, E. coli, K. pneumoniae*, *P. mirabilis* and coagulase negative staphylococci (CoNS). Chopdekar *et al.*[2] found that

Table I. Frequency of antibiotic resistance (%) in gram-positive and gram-negative bacteria (n=434) isolated from central venous catheters

	Gram Positive Bacteria	% Resistance									
		PEN	GEN	CIP	CLI	ERY	GEH				
Colonization (n=107)	**MSSA** (n=21)	70	43	40	33	60					
	MRSA (n=78)	100	91	89	72	90					
	E. faecalis (n=8)	77		69			69				
CLABSI (n=21)	**MSSA** (n=5)	100	60	40	40	0					
	MRSA (n=16)		75	100	75	88					
	Gram Negative Bacteria	**CSL**	**TZP**	**CAZ**	**ETP**	**IPM**	**MEM**	**AMK**	**GEN**	**NET**	**CIP**
Colonization (n=141)	***K. pneumoniae*** (n=41)	58	37	81	39	13	32	79	65	70	70
	E. coli (n=26)	33	43	72	15	2.6	28.9	46.7	83	35	90
	P. mirabilis (n=5)	40	25	100		12	13	80	100	83	75
	Enterobacteriaceae (n=72)	47	38	78	27	9	29	66	72	59	77
	A. baumannii (n=49)	19	71	94		45	66	87	96	48	46
	P. aeruginosa (n=20)	43	26	62		13	41	76	80	70	74
	Non-fermenters (n=69)	27	55	85		34	59	83	92	55	83
CLABSI (n=12)	***A. baumannii*** (n=5)	20	100	100		100	100	100		40	100
	P. aeruginosa (n=3)	33	33	0	-	33	33	33	33	33	33
	K. pneumoniae (n=3)	66	33	100	33	33	33	66	-	66	100
	E. coli (n=1)		0	100	0	0	0	0	0	0	0

MRSA: *Meticillin-resistant Staphylococcus aureus;* ***MSSA:*** *Meticillin-sensitive Staphylococcus aureus;* ***CSL:*** *cefoperazone/sulbactam;* ***TZP:*** *tazobactam/piperacillin;* ***CAZ:*** *ceftazidime;* ***ETP:*** *ertapenem;* ***IPM:*** *imipenem;* ***MEM:*** *meropenem;* ***AMK:*** *amikacin;* ***NET:*** *netilmicin;* ***CIP:*** *ciprofloxacin;* ***PEN:*** *penicillin;* ***GEN:*** *gentamicin;* ***CLI:*** *clindamycin;* ***ERY:*** *erythromycin;* ***GEH:*** *high gentamicin*

microbial patterns of catheter colonization revealed maximum colonization with *Candida* spp. followed by *P. aeruginosa, E. faecalis,* MRSA and CoNS.

In our study, the CLABSI rate was 9.5 per 1000 catheter days. In comparison, CLABSI rates from medical-surgical ICUs participating in the Centers for Disease Prevention and Control National Healthcare Safety Network (NHSN) in the United States in 2013 range between 0.8-1.1 per 1000 catheter days.[13] In various other studies in our region, CLABSI rates have been found to be 9.3-16.1 per 1000 catheter days.[2,3,11,12] As our patients receiving critical care were on antibiotic treatment, the rate of CLABSIs in the present study may have been influenced by this factor. The positive predictive value of catheter tip culture for the diagnosis of CLABSI was found to be very low (0.128). Therefore, pre-emptive antibiotic therapy based on positive catheter tip cultures would appear to be unjustified.

Staphylococcus aureus was the major cause (63%) of CLABSI followed by *A. baumannii*, *P. aeruginosa*, *K. pneumoniae* and *E. coli*. All these organism are known to produce biofilms, which are reported to be universally present on CVCs. Chopdekar *et al.*[2] found that *CoNS* were the major cause (50%) of CLABSI followed by *K. pneumoniae*, *P. aeruginosa* and non-albicans *Candida* spp. Gahlot *et al.*[3] found that 71% of CLABSIs were due to gram positive cocci, 22% to non-fermenting gram negative bacteria, and 7% due to *Candida* spp. Mansur *et al.*[12] found that the most common isolated pathogens associated with CLABSI were *Pseudomonas* spp., *Acinetobacter* spp., *S. aureus*, *Enterococcus* spp., *Staphylococcus epidermidis and Candida* spp. Kaur *et al.*[11] found that *S. aureus* was the most commonly isolated CLABSI pathogen, followed by *P. aeruginosa*, non-albicans *Candida* spp., *E. faecalis, A. baumannii* and *K. pneumoniae*. It is interesting that throughout the present study, CoNS were isolated in insignificant numbers. This is in concurrence with other studies from North India [3,11] which have similar settings.

In our study, the rate of multidrug resistant (MDR) bacteria was high among the CLABSI isolates. Among gram positive CLABSIs, MRSA accounted for 76% of cases. All *A. baumannii* and 33% of *P. aeruginosa* were MDR, including resistance to carbapenems. All *E. coli* and *K. pneumoniae* were ESBL-producers with 33% of *K. pneumoniae* being MDR, including resistance to carbapenems. A high prevalence of MDR isolates has been reported in other studies as well.[11,12] The high rates of MDR organisms in the ICU are representative of their prevalence throughout this hospital (data not shown).

Catheter colonization has an important role in the development of CLABSIs that may lead to septicemia and multi-organ failure. Central line-associated bloodstream infections are a common complication of central venous catheterization, resulting in substantial morbidity and mortality. A large percentage of CLABSIs can be prevented by use of appropriate hand hygiene, aseptic skin preparation, full barrier precautions, the avoidance of femoral catheters, the removal of unnecessary catheters as early as possible, comprehensive educational programs for staff, and in some instances use of antiseptic- or antibiotic-impregnated catheters. The diagnosis of CLABSI based on culture results and sensitivity patterns should guide the specific treatment of organisms.[14] The findings of this study may help with implementation of educational and training programs on CLABSIs for health care personnel and enable better management of these devices with regard to the prevention, diagnosis and treatment of CLABSIs.

References

1. Novikov A, Lam MY, Mermel LA, Casey LA, Elliott TS, Nightingale P. Impact of catheter antimicrobial coating on species-specific risk of catheter colonization: a meta-analysis. *Antimicrob Resist Infect Control* 2012; **1:** 40. http://dx.doi.org/10.1186/2047-2994-1-40
2. Chopdekar K, Chande C, Chavan S, *et al.* Central venous catheter-related blood stream infection rate in critical care units in a tertiary care, teaching hospital in Mumbai. *Indian J Med Microbiol* 2011; **29:** 169-171. http://dx.doi.org/10.4103/0255-0857.81796
3. Gahlot R, Nigam C, Kumar V, Gupta M. Catheter related bloodstream infections in ICU: a study from North India. *Int J Infect Control* 2013; doi: 10.3396/v9i2.013.13.
4. Safdar N, Maki DG. The pathogenesis of catheter-related-blood-stream infection with noncuffed short-term central venous catheters. *Intensive Care Med* 2004; **30:** 62-67. http://dx.doi.org/10.1007/s00134-003-2045-z
5. Linares J, Sitges-Serra A, Garau J, Perez JL, Martin R. Pathogenesis of catheter sepsis: A prospective study with quantitative and semiquatitative cultures of catheter hub and segments. *J Clin Microbiolol* 1985; **21:** 357-360.
6. O'Grady NP, Alexander M, Dellinger EP. Guidelines for the prevention of intravascular catheter-related infections. *Infect Control Hosp Epidemiol* 2002; **23:** 759-769. http://dx.doi.org/10.1086/502007

7. Maki DG, Weise CE, Sarafin HW. A semiquantitative culture method for identifying intravenous-catheter-related infection. *N Engl J Med* 1977; **296:** 1305-1309. http://dx.doi.org/10.1056/NEJM197706092962301
8. Winn WS, Allen SD, Janda WM, *et al.* In: Darcy P, Peterson N, Montalbano J, Eds. *Koneman's Color Atlas and Textbook of Diagnostic Microbiology*. 6th Ed. Philadelphia: Lippincott 1997; 1442-1535.
9. Clinical and Laboratory Standard Institute (CLSI): Performance standards for antimicrobial susceptibility testing. 24th International Supplement. CLSI document M100- S24.Wayne, Pennsylvania; 2014.
10. Mermel LA, Allon M, Bouza E. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2009; **49:** 1-45. http://dx.doi.org/10.1086/599376
11. Kaur M, Gupta V, Gombar S, Chander J, Sahoo T. Incidence risk factors, microbiology of venous catheter associated bloodstream infections – a prospective study from a tertiary care hospital. *Indian J Med Microbiol* 2015; **33:** 248-254. http://dx.doi.org/10.4103/0255-0857.153572
12. Mansur FJ, Barai L, Karim MM, Haq JA, Fatema K, Faruq MO. Intravascular catheter related infections and antimicrobial susceptibility pattern of isolated bacteria in a tertiary care hospital of Bangladesh. *Indian J Med Microbiol* 2014; **32:** 68-71. http://dx.doi.org/10.4103/0255-0857.124321
13. Dudeck MA, Edwards JR, Allen-Bridson K, *et al.* National Healthcare Safety Network report, data summary for 2013, Device-associated Module. *Am J Infect Control* 2015; **43:** 206-221. http://dx.doi.org/10.1016/j.ajic.2014.11.014
14. Goede MR, Coopersmith CM. Catheter - related bloodstream infection. *Surg Clin N Am* 2009; **89:** 463–474. http://dx.doi.org/10.1016/j.suc.2008.09.003