

Original Research Article

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Study of Central-Line Associated Blood Stream Infections (CLABSIs) and Central-Line Related Blood Stream Infections (CRBSIs) in a Tertiary Hospital, Bangalore, India

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ABSTRACT

Bloodstream infections caused by central venous catheter remains a serious and the most common cause of Hospital acquired infections (HAIs) worldwide. Central line-associated bloodstream infections remain a leading cause of serious healthcare-associated infections in ICUs in India, the rate being 7.9 per 1000 central line-days. Accurate measurement of the rates of BSIs arising from catheters is important because ICUs with high rates will need to institute further performance improvement initiatives in CVC insertion and management. The main aims of this study were to identify the various factors influencing the infections associated with CVC, the rate of infections associated with CVC, to identify the organisms involved in the causation of Central-line associated blood stream infections (CLABSIs) and Central-line related blood stream infections (CRBSIs) and to study the antibiotic susceptibility patterns of the isolated organisms. The present study revealed that rate of CLABSI was 8.26/1000 central-line days and CRBSI was 0.26/1000 central-line days mostly affecting the age group 51-60 years and males were more commonly than females. Staphylococci were the most common organism isolated. The study showed high incidence of resistance against conventional antibiotics such as Ampicillin, Amoxycillin-clavulanate, Gentamicin, Amikacin, Erythromycin and Azithromycin among the pathogens causing CLABSI/CRBSI. Since CVCs are increasingly being used in the critical care, regular surveillance for infections associated with them is essential. There is a change in the pattern on pathogens causing the bloodstream infections and their susceptibility pattern as compared to other studies. Hence, it is very important for strengthening of the infection control, instituting surveillance systems, and implementing evidence-based preventive strategies in order to prevent bloodstream infections caused by CVCs.

Keywords

Central line-associated bloodstream infections, Central line-related bloodstream infections, Surveillance

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Introduction

Bloodstream infections caused by central venous catheter remains a serious and the most common cause of Hospital acquired infections (HAIs) worldwide (Edwards *et al.*, 2007). Central line-associated bloodstream infections remain a leading cause of serious healthcare-associated infections in ICUs in

India, the rate being 7.9 per 1000 central line-days (Mehta *et al.*, 2007).

Central venous catheters (CVCs) are indispensable in modern-day medical practice, particularly in intensive care units (ICUs). They provide secure access to the central circulation for infusion therapy, nutritional support, hemodynamic monitoring, plasma

pheresis, apheresis and hemodialysis. CVCs have a higher infection risk than other indwelling vascular access lines. This causes significant morbidity and mortality to the critically ill patient (Raad *et al.*, 2007; Frasca *et al.*, 2010). Although such catheters provide necessary vascular access, their use puts patients at risk for local and systemic infections, including local site infection, catheter related blood stream infections, septic thrombophlebitis, endocarditis, and other metastatic infections (e.g., lung abscess, brain abscess, osteomyelitis and endophthalmitis) (Khanna *et al.*, 2013).

The CDC (Centers for Disease Control and prevention) defines a Central-line associated Blood Stream Infections (CLABSI) as a blood stream infection caused by an organism not related to another infection when a central line has been in place at some time during the 48 hr prior to the collection of the blood.

In contrast, a Central line-related Blood Stream Infections (CRBSI) is defined as a blood stream infection with either a positive catheter tip culture or a positive blood culture drawn from the central venous catheter consistent with a culture drawn simultaneously from a peripheral site (Horan *et al.*, 2008).

Incidence of bloodstream infections in patients with indwelling catheter is directly related to factors such as site of catheterization, type of procedure, number of attempts, length of catheter inside, duration of catheterization, systemic antibiotics, local site infection of catheter, reason for catheter removal, experience of venipuncturist (Patil *et al.*, 2011).

Patients with abrupt onset of signs and symptoms of sepsis without any identifiable source should prompt suspicion of infection of an intravascular device (Brachman, 2007).

The incidence of BSIs associated with peripheral venous catheters is usually low even though they are used most frequently for vascular access. The majority of serious catheter-related infections are associated with central venous catheters (CVCs), especially those that are placed in patients in ICUs (Naomi *et al.*, 2002).

Vascular catheters have become an increasingly important source of bacteremia, increasing from 3% in the mid-1970s to 19% in the early 1990s.

Primary bacteremia, including intravascular catheter sources, account for approximately one half of all ICU-related bacteremia (Beekmann and Henderson, 2015). A total of 250,000 cases of CVC-associated BSIs have been estimated to occur annually if entire hospitals are assessed rather than ICUs exclusively.

Attributable mortality is an estimated 12%-25% for each infection, and the marginal cost to the health-care system is \$25,000 per episode (Kluger and Maki, 1999).

Staphylococci continue to predominate as the most frequently encountered pathogens in device-related infections. Other commonly encountered isolates include *Enterococcus* spp., *Serratia marcescens*, *Candida albicans*, *Candida tropicalis*, *Pseudomonas aeruginosa*, *Klebsiella* spp., *Enterobacter* spp., *Citrobacter freundii*, *Burkholderia cepacia* complex, *Acinetobacter baumannii* (Beekmann and Henderson, 2015).

Accurate measurement of the rates of BSIs arising from catheters is important because ICUs with high rates of CRBSIs will need to institute further performance improvement initiatives in CVC insertion and management. By contrast, ICUs that have high rates of CLABSIs will find that changes in CVC-based

interventions are ineffective (Sihler *et al.*, 2010). This study was undertaken among patients admitted in PMSSY (Pradhan Mantri Swasthya Suraksha Yojana – Super speciality departments including Paediatric surgery, Surgical Gastroenterology, Neurosurgery, Neurology, Cardiology), Victoria hospital, Bowring and Lady Curzon Hospital, Vani Vilas Hospital attached to Bangalore Medical College and Research Institute to determine the rate of bloodstream infections caused by CVC and to identify the factors influencing it, which would help to institute better prophylactic measures.

Materials and Methods

The present prospective study was undertaken in the Department of Microbiology, Bangalore Medical College and Research Institute, Bangalore from November 2014 – October 2016.

The study included 150 patients admitted in Intensive care units in PMSSY, Victoria hospital, Bowring and Lady Curzon Hospital, Vani Vilas Hospital attached to Bangalore Medical College and Research Institute with central venous catheter in place for the past 48 hrs or more.

Aims and objectives

To study the various factors influencing the infections associated with CVC.

To study the rate of infections associated with CVC.

To identify the organisms involved in the causation of Central-line associated blood stream infections (CLABSIs) and Central-line related blood stream infections (CRBSIs).

To study the antibiotic susceptibility patterns of the isolated organisms.

Inclusion criteria

Patients presenting with clinical symptoms and signs of bacteraemia when the central venous catheter was in place for the past 48hrs and meet the criteria according to CDC definitions of CLABSI and CRBSI as follows:

Centres for Disease Control and Prevention Definitions of Catheter-Associated and Catheter-Related Blood Stream Infection (Horan *et al.*, 2008).

Catheter-Associated blood stream infections -

Criterion 1: Patient has a recognized pathogen cultured from 1 or more blood cultures and organism cultured from blood is not related to an infection at another site.

Criterion 2: Patient has at least one of the following signs or symptoms: fever ($>38^{\circ}$ C), chills, or hypotension and signs and symptoms and positive laboratory results are not related to an infection at another site and at least one of the following:

Common skin contaminant (e.g., diphtheroids, *Bacillus* spp., *Propioni bacterium* spp., coagulase-negative *Staphylococci* or *Micrococci*) is cultured from two or more blood samples drawn on separate occasions.

Common skin contaminant is cultured from at least one blood culture from a patient with an intravascular catheter, and the physician institutes appropriate antimicrobial therapy.

Catheter-Related blood stream infection is considered if positive blood culture with the same microorganism present in the tip of the catheter.

Quantitatively or semi-quantitatively evaluated and clinical and microbiological absence of another focus of infection.

Exclusion criteria

Patients with obvious source of infection (fever, pneumonia, urinary tract infection and cellulitis) other than central venous catheter by history, clinical examination, blood culture, chest X-ray, urine examination, etc. and relevant investigations pertaining to the suspected infection were excluded.

History taking

Detailed history of each case was taken regarding name, age, sex, ward, diagnosis, purpose of catheterization, site of catheter, duration of catheterization, length of catheter *in situ*, presenting symptoms leading to removal of catheter, type of procedure, number of attempts, experience of venipuncturist and any history of systemic antibiotics.

Sample collection and processing (Maki *et al.*, 1977; Isenberg, 2007)

Catheter tip collection

The skin was cleaned with 70% alcohol prior to catheter removal. The catheter was held at the proximal end and carefully removed from the patient with a sterile instrument, taking care to avoid contact with the skin. The distal 5 cm was cut with sterile blade and collected in a sterile tube and transported to the lab as soon as possible.

Catheter tip processing

Extraluminal Maki's roll over plate method and endoluminal catheter flush culture was used for processing. It was performed on MacConkey agar and Blood agar.

Extraluminal Maki's roll over method

Forceps was dipped in 95% alcohol, flame sterilized and allowed to cool. The catheter tip

was transferred from transport container to agar plate using sterile forceps. The catheter tip was rolled back and forth across agar surface using slight pressure at least four times. It was made sure that the catheter tip was having good contact with the surface of the plate. The plates were incubated for at least 72 hrs at 35⁰ C in a CO₂ incubator.

Endoluminal catheter flush culture

The catheter segment was aseptically transferred to a sterile test tube (12 by 75 mm). Using a sterile syringe 1 ml of sterile trypticase soya broth was drawn. A needle was placed into lumen of catheter and the broth was dispensed through catheter segment. The tube was capped and vortexed to dislodge adherent bacteria. The sample was serially diluted 100-folds. 100 µl of each dilution was inoculated onto agar plates. Cross-streaks were made for well isolated colonies. The plates were incubated for 72 hrs at 35⁰ C in a CO₂ incubator.

Collection of peripheral blood sample and processing

Blood sample collected under aseptic precautions from the peripheral vein in Brain Heart Infusion broth for qualitative culture were incubated at 37⁰ C. Subcultures were made on MacConkey's and blood agar plates after 24, 48 and 72 hr and incubated for 24 hrs at 37⁰ C.

Identification and interpretation

Catheter tip culture: Agar plates were examined at 24, 48 and 72 hrs. Significant growth is defined as ≥ 15 colony forming units (CFU) by Maki's roll over plate method or $\geq 10^3$ CFU/ml by the endoluminal catheter flush method.

Blood culture: Agar plates were examined at 24, 48 and 72 hrs.

The organisms were identified by colony morphology, gram staining, and biochemical tests performed by routine laboratory techniques (Koneman *et al.*, 1997).

Antibiotic sensitivity testing

Antibiotic sensitivity pattern was interpreted using Kirby-Bauers disc diffusion method as recommended by Clinical Laboratory Standard Institute (CLSI) (Clinical and Laboratory Standards Institute, 2014).

Results and Discussion

Out of 150 cases studied, 95 (63.33%) were male and 55 (36.67%) were female. Male to female ratio was 1.73:1. The mean age for males and females was 43.48 years and 42.87 years respectively. The most common age group studied was 51-60 years of which 70% and 30% were males and females respectively. This was followed by 1-20 years (16%; 54.16% males and 45.84% females), 31-40 years (14%; 66.67% males and 33.33% females) and 41-50 years (14%; 71.43% and 28.57%).

In our study most common indication for central line insertion was hemodialysis (58.67%), followed by infusion of intravenous fluids, medications and hemodynamic monitoring (40%). Majority of the study group was distributed in Nephrology department (58.67%), followed by Medicine (8.67%), Paediatric surgery (7.33%) and remaining 25.32% distributed among other departments.

Site of catheterization, type of procedure, no. of attempts, duration of catheter *in situ* and experience of venipuncturist were found to be significant factors. CLABSI rate was found to be 8.26/1000 central-line days and CRBSI was 0.14/1000 central-line days, the total no. of central line days being 1452 during the study period. CRLI (Central line related local

infections)/colonization was seen in 12.67% of the cases, in which only central line tip was culture positive with no evidence of bloodstream infections (Table 1). Catheter colonization did not appear to have direct bearing on blood stream infection.

Out of 95 samples studied among male patients, the no. of CLABSIs were 9 i.e. 9.47% of the males were affected. And, out of 55 samples studied among female patients, the no. of CLABSIs were found to be 3 i.e. 5.45% of the females were affected. Whereas, both the cases of CRBSIs were found to be among male patients.

Overall, males constituted to (11/14) 78.57% and females (3/14) 21.43% of CLABSI and CRBSI cases.

The percentage of CLABSI was highest in the age groups 51-60 yrs (13.33%), 1-20 yrs (12.5%), 61-70 yrs (10.52%) followed by <1 yr (5.56%), 31-40 yrs and 41-50 yrs each being 4.76%. Both the cases of CRBSI were found among the age group 51-60 yrs. Overall, the age group 51-60 yrs had highest incidence (5/14) of CVC associated and related blood stream infections which was found to be 35.71%.

Blood stream infection was statistically significant among patients with IJV, emergency procedure, no. of attempts being 2, duration of catheter *in situ* more than or equal to 6 days and experience of the venipuncturist with p-value <0.05.

As the p-value for the factors- use of systemic antibiotics, presence of local site infection was >0.05, the development of CLABSI/CRBSI was not dependent on these 2 factors in the present study. The association with the length of catheter *in situ* could not be correlated as all the patients in the present study had length of the catheter *in situ* <20 cm.

We found out that in our study, there was increased odds of developing CLABSI/CRBSI in the patients in whom the site of CVC insertion was IJV, emergency procedure, no. of attempts being more than 2, duration of catheter *in situ* more than or equal to 6 days and catheter being inserted by inexperienced venipuncturist.

The frequency of developing blood stream infection was found to be highest for the route of insertion being IJV, followed by femoral vein and least for subclavian vein.

In the present study, majority of CLABSI cases were bacterial which was 10/12 (83.33%) remaining 2/12 (16.67%) being fungal. Whereas, among 2 cases of CRBSI, 1 was bacterial and 1 was fungal growth.

In the present study, out of 10 bacterial cases in CLABSI, 6 (60%) were caused by Gram positive isolates and remaining 4 (40%) by Gram negative isolates.

In CRBSI, 1 bacterial case isolated was caused by Gram positive organism.

In the present study, *Staphylococcus aureus* (42.86%) was the most common organism isolated, out of which MSSA accounted to (28.57%) and MRSA (14.29%), followed by *Candida tropicalis* (21.44%).

Acinetobacter baumannii, *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumonia* and *Enterococcus faecalis* were isolated in 7.14% cases each.

MSSA represented 4 (28.57%) among 14 isolates, out of which all were sensitive (100%) to Vancomycin, Cotrimoxazole, Linezolid, Tetracycline, Doxycycline and Ciprofloxacin. All the isolates were resistant to Penicillin G. Sensitivity to the rest of the drugs is as follows i.e., 3 (75%) sensitive to

Clindamycin and Chloramphenicol, 2 (50%) to Erythromycin, Azithromycin and Gentamicin.

Out of this, MSSA was isolated in a case of CRBSI, the sensitivity pattern being same in both tip culture and blood culture.

MRSA represented 2 (12.5%) among 14 isolates, out of which both were sensitive (100%) to Vancomycin, Linezolid, Tetracycline and Cotrimoxazole. Both the isolates were resistant to Penicillin G. 1 isolate (50%) was sensitive to Doxycycline.

Candida tropicalis accounted to 3 (21.44%) of the total 14 organisms isolated, in which 2 were isolated in CLABSI and 1 accounted for a case of CRBSI.

All the *Candida tropicalis* strains were susceptible to fluconazole (100%).

E. coli and *K. pneumonia* were isolated in 1 each (7.14%) of the 14 organisms. Both the isolates were sensitive (100%) to Piperacillin-tazobactam, Cefepime, Ciprofloxacin and Imipenem. Both the isolates were resistant to Amoxicillin-clavulanate. Further, *E. coli* was sensitive to Gentamicin, Amikacin, Cefoxitin and Cefotaxime. *K.pneumoniae* was sensitive to Cotrimoxazole.

P. aeruginosa and *A. baumannii* were isolated in 1 each (7.14%) of the 14 organisms. *P. aeruginosa* was sensitive to Ciprofloxacin, Polymyxin B and Colistin, whereas *A. baumannii* was resistant to all the routine and reserved drugs.

Enterococcus faecalis represented 1 (7.14%) among 14 isolates, which was sensitive (100%) to Ampicillin, Penicillin, Vancomycin and Linezolid. It was resistant to High level Gentamicin.

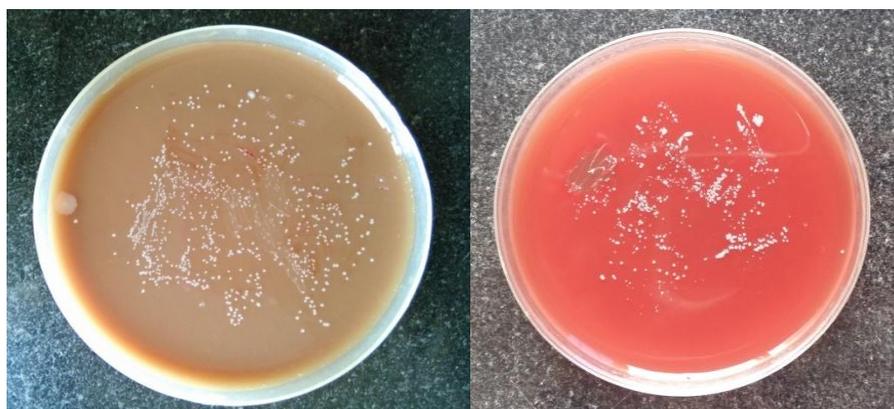
Table.1 Blood culture and CVC tip culture results

Blood culture	Tip culture	Impression	No. of cases	Rate per 1000 central line days
Positive	Negative	CLABSI	12 (8%)	8.26
Positive	Positive	CRBSI	2 (1.33%)	0.14
Negative	Positive	Catheter Tip Colonization	19 (12.67%)	
Negative	Negative	No CLABSI/CRBSI	117 (78%)	
		Total	150 (100%)	

Table.2 Comparison of organisms isolated

Study	GahlotR et al., (2013)	Datta et al., (2014)	Cheewinmethasiri et al., (2014)	Kaur et al., (2015)	Mittal G et al., (2016)	Present study
<i>S.aureus</i>	71%	12.36%	21.45%	27.6%	63%	42.86%
<i>Candida spp</i>	7%	4.5%	21.45%	17.2%	-	21.44%
<i>A.baumannii</i>	22%	26.97%	6%	10.3%	15%	7.14%
<i>P.aeruginosa</i>	-	14.61%	8.3%	20.6%	9%	7.14%
<i>E.coli</i>	-	2.25%	-	-	3%	7.14%
<i>K.pneumoniae</i>	-	29.2%	12.75%	10.3%	9%	7.14%
<i>E.faecalis</i>	-	10.11%	3.75%	14.8%	-	7.14%
CONS	-	-	15.05%	-	-	-
<i>Enterobacterspp.</i>	-	-	10.55%	-	-	-

Culture plates showing growth from Maki's Roll over method



Note: Significant growth defined as ≥ 15 colony forming units (CFU) is seen in the above pictures

Central venous catheters are the most frequently used indwelling medical devices and have become necessary tools for the successful treatment of patients with chronic or critical illness.

Our study investigated the rate, microbiological profile, antibiotic profile and the risk factors for the development of central line-associated infections in a tertiary care hospital. In the present study, the rate of

CLABSI was 8.26/1000 central-line days in comparison with the study conducted by Mehta *et al.*, (2007) (7.9), Deepthi *et al.*, (2014) (8.2), Parameswaran *et al.*, (2011) (8.75), El-Kholy *et al.*, (2012) (9.1), Porto *et al.*, (2010) (9.5) and Mittal *et al.*, (2016) (9.5). Males (78.57%) were more commonly affected than females (21.43%). This correlates with the study of Khanna *et al.*, (2013) (72.7%), and other studies such as Apostolopoulou *et al.*, (2009), Bicudo *et al.*, (2011) and Datta *et al.*, (2014) where the incidence of bloodstream infections were more in males than females.

The male gender has been stated as risk factor for the development of CLABSI/CRBSI in most of the studies. However, the reason for this high incidence in males could not be attributable to any reasons. CLABSI/CRBSI were common in the age group 51-60 years, in comparison with the study conducted by Brito *et al.*, (2007), Apostolopoulou *et al.*, (2009) and Datta *et al.*, (2014). This could be attributable to the decreased immune status at that age group.

In the present study, 9.33% samples were culture positive in comparison with the study of Patil *et al.*, (2011) (7.41%), El-Kholy *et al.*, (2012) (8.2%), Porto *et al.*, (2010) (11.2%) and Apostolopoulou *et al.*, (2009) (11.8%). Lorente *et al.*, (2005) and Brito *et al.*, (2007) reported culture positivity as 2.04 % and 3.8% respectively which was lesser compared to the present study. The comparison of organisms isolated with other studies is shown in Table 2.

The most important predisposing factors for developing bloodstream infections were the site of CVC insertion being IJV, emergency procedure, no. of attempts being more than 2, duration of catheter *in situ* more than or equal to 6 days and catheter being inserted by inexperienced venipuncturist.

Overall, in the present study, there were basic similarities in the organisms isolated as compared with other studies that Gram positive organisms were predominant compared to Gram negative organisms which mainly consisted of *Staphylococcus* and predominant Gram negative organisms isolated were *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Escherichia coli* and *Acinetobacter baumannii* as in other studies, even though there was differences in the percentage of organisms isolated which could be attributable to differences in prevalence of organisms in different geographical areas.

In the present study, the most effective antibiotics against Gram positive isolates were Vancomycin, Linezolid (100% each), Cotrimoxazole, Tetracycline (85.7% each), Doxycycline (71.4%) and Ciprofloxacin (57.14%). They were least sensitive to Erythromycin, Azithromycin, Gentamicin (33.33%) and Penicillin (14.29%).

The most effective antibiotics against Gram negative isolates were Ciprofloxacin (100%), Piperacillin-tazobactam, Cefepime and Imipenem (66.67% each). They were least sensitive to Gentamicin and Amikacin (33.33% each). *A. baumannii* was resistant to all the drugs. Fluconazole was effective against all the fungal bloodstream infections in the present study.

From the study, it can be concluded that since central venous catheters are increasingly being used in the critical care, regular surveillance for infections associated with them is essential.

The data showed high incidence of resistance against conventional antibiotics such as Ampicillin, Amoxicillin-clavulanate, Gentamicin, Amikacin, Erythromycin and Azithromycin among the pathogens causing CLABSI/CRBSI.

Preventive measures against these infections include placement and maintenance of these catheters by skilled medical team, coating of catheters with antiseptic agents, topical disinfectants such as chlorhexidine, chlorhexidine-impregnated sponge dressing. The importance of strict asepsis has to be reinforced. All the intensivists are required to follow standard protocols that uniformly demand the use of sterile gowns, gloves, masks and large drapes during insertion to reduce CVC associated infection.

There is a change in the pattern on pathogens causing the bloodstream infections and their susceptibility pattern as compared to other studies which could be attributable to different geographical areas. Hence, it is very important for strengthening of the infection control, instituting surveillance systems, and implementing evidence-based preventive strategies in order to prevent bloodstream infections caused by central venous catheters.

Limitations of the study

The rate of blood stream infections in the present study could be affected by the small sample size of the study, less central-line days in our institution and the multitude of antibiotics received before the development of infection.

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