Research Article

CATHETER RELATED BLOODSTREAM INFECTIONS (CRBSI) IN INTENSIVE CARE UNITS: A PROSPECTIVE STUDY OF ITS RATE, MICROBIOLOGICAL PROFILE AND ASSOCIATED FACTORS

RAO V. MALLIKARJUN*

Department of Microbiology, Shadan Institute of Medical Sciences and Research Centre, Hyderabad, 500008, Telangana, India
*Corresponding Author: Email - vishwanathrao56@gmail.com

Abstract- Background: Central venous catheters (CVC) are integral to the modern intensive care practices and its inevitable use also makes patients prone to Catheter-related bloodstream infection (CRBSI). The aim of the present study was to prospectively study the rate; microbiological profile with antibiotic susceptibility and associated factors of central venous catheter related bloodstream infections (CRBSI) in intensive care units of a tertiary hospital in South India. **Materials and Methods**: The present study was a case control study conducted on 109 patients with CVC in situ. Quantitative blood cultures (QBC) and catheter tip cultures were performed; microbiological profile and antimicrobial susceptibility were assessed. **Results**: CRBSI was diagnosed in (18/109) patients and the rate of CVC- Blood stream infection number of CVC days was calculated as 13.64 per 1000 catheter days. The mean age of cases was observed to be 51.25(+-6.98) yrs. Patients from surgical ICU; signs of inflammation around catheter site, length of ICU stay, having underlying co-morbid conditions were significantly associated with CRBSI. *Staphylococcus aureus* followed by Pseudomonas aeruginosa and non-albicans Candida were common CRBSI pathogens and the bacterial agents were found to be multidrug-resistant (MDR). **Conclusion**: The incidence of CRBSI was 16.52% and the rate was 13.64 per 1000 catheter day. CRBSI were significantly associated with higher mean age; longer duration of catheterisation and longer stay in ICU.

Keywords- catheter related bloodstream infections (CRBSI), antibiotic susceptibility microbiological profile, *Staphylococcus aureus*

Introduction

Intravascular catheters including central venous catheters are integral to the modern practices and are inserted in critically-ill patients for the administration of fluids, blood products, medication, nutritional solutions, and for hemodynamic monitoring [1]. Its inevitable use also makes patients prone to iatrogenic complications; which include Catheter-related bloodstream infection (CRBSI). Catheter-related bloodstream infection (CRBSI) refers to bloodstream infection attributed to an intravascular catheter by quantitative culture of the catheter tip or by differences in growth between catheter and peripheral venipuncture blood culture specimens [2]. It is one of the most frequent, costly complication of central venous catheterization (CVC) associated with morbidity, mortality and is the most common cause of nosocomial bacteremia [1]. Incidence of CRBSI reported varies from country to country and even hospital to hospitals. Incidence of CRBSI is lesser in western countries [1]. Studies across various hospitals in India and Taiwan have reported rates of CRBSI ranging from 0.48 /1000 catheter days to 14.26/1000 catheter days [3-9]. The organisms associated with CRBSI are usually the normal resident flora of the skin at the insertion site, which may lead to colonization of the catheter inserted. Gram-positive cocci are responsible for at least two-thirds of the infections and coagulase-negative staphylococci (60%) are the leading bacteria cultured from catheters, followed by gram negative cocci [9,10]. Additionally, microbial biofilms may pose a public health problem for persons requiring indwelling medical devices [11]. Prevention development of records and multidisciplinary guidelines of care for central venous catheter insertion and maintenance (bundle care), cutaneous antisepsis, maximum sterile barrier, correct use of central venous catheter insertion technique; use of

chlorhexidine-impregnated dressings; early catheter removal, use of antimicrobial catheters, and antimicrobial catheter lock solution [6,12]. Relatively few studies from south India have been conducted on central venous catheter associated bloodstream infections. Thus, the aim of the present study was to study the rate; microbiological profile with antibiotic susceptibility and associated factors of central venous catheter related bloodstream infections (CRBSI) in intensive care units of a tertiary hospital in South India.

Materials and Methods

The present study was a case control study conducted from October 2016 to September 2017. Approval from institutional ethics committee was obtained prior to commencement of the study. All patients above 18 years and having one or more central-line catheterization with sterile blood culture immediately after catheterisation were included in the study after obtaining informed consent. The study was finally conducted on 109 patients admitted in medical and surgical ICU of the teaching hospital. All patients who were diagnosed as having CRBSI were considered as cases and those patients who were not diagnosed with CRBSI served as controls. Each patient's age, gender, clinical diagnosis, CVC insertion site and duration of duration of CVC catheterization, treatment given, duration of ICU stay; hospitalization and clinical outcome were duly recorded. Cathetertip culture was done in all the patients at the time of removal of catheter. The catheter tip was collected under aseptic conditions. Maki's Roll over plate method and catheter flush culture, a semi-quantitative method used by Maki, *et al*., [13] was followed for catheter tip culture. Growth of organisms from a catheter segment by either semi-quantitative [≥15 colony forming unit (CFU)] or quantitative culture

[≥10^3 CFU] from a proximal or distal catheter segment in the absence of accompanying clinical symptoms was termed as catheter colonisation [14]. In all patients with clinical evidence of sepsis, central and peripheral blood cultures were done. Requisite blood sample collection was done under aseptic precautions in Hartley's blood culture broth and cultures were processed by standard microbiological methods [15].

A diagnosis of CRBSI was defined by any of the following 3 criteria:

1. Sameorganism recovered from percutaneous blood culture and from quantitative (>15 colony-forming units) culture of the catheter tip;
2. Sameorganism recovered from a percutaneous and a catheter lumen blood culture, with growth detected 2 hours sooner (i.e., 2 hours less incubation) in the latter;
3. Sameorganism recovered from a quantitative percutaneous and a catheter lumen blood culture, with 3-fold greater colony count in the latter[16].

In unpaired central lines; ≥ 100 CFU colony count was considered significant; while a central-to-peripheral blood culture colony count ratio of 5:1 was considered indicative of CVC-Blood Stream Infection [16].

Antibiotic sensitivity pattern was done by Kirby-Bauer disk diffusion method on method and in case of vancomycin resistant enterococci (VRE), minimal inhibitory concentration (MIC) was calculated by agar dilution method [17]. Multidrug-resistant (MDR) isolates were phenotypically characterised into methicillin-resistant *S. aureus* (MRSA), VRE, metallo-β-lactamase (MBL) and extended-spectrum β-lactamase (ESBL) producers. The rate of CVC- Blood stream infection was expressed in number of CVC days [18].

Data Analysis

Data was analysed using Statistical Package for Social Sciences (SPSS 23.0). Fischers exact test was used to analysed significance of difference of proportion between the cases and controls. A P value of less than 0.05 was considered significant and <0.001 was considered highly significant.

Results

The present study was conducted in a total of 109 patients. CRBSI was diagnosed in 18 (16.52%) patients and the rate of CVC- Blood stream infection number of CVC days was calculated as 13.64 per 1000 catheter days. The mean age of cases was observed to be 51.25 (+-6.98) yrs which was significantly higher than controls (p<0.05) but if classified according to < 50 yrs and more than 50 yrs; there was no significant difference between the groups. There were 11 (61.11%) males and 7 (38.89%) females and among controls there were 52(57.14) males and 39 (42.86) females and gender showed no significant difference statistically. Patients from surgical ICU especially presenting with perforative peritonitis and with signs of inflammation around catheter site were significantly associated with CRBSI. Uncontrolled diabetes mellitus, renal failure, hypertension, COPD were the co-morbid conditions significantly associated with CRBSI. Length of ICU stay was significantly more in cases. Mortality was not significantly higher in cases 4 (22.2%) as compared to controls 34 (37.36%).

Demographic and clinical characteristics of cases and controls are presented [Table-1].

Colonisation

Colonisation was observed in 52 (52.52%) of 99 catheter tips sent for colonisation with both bacterial and fungal agents. The commonest pathogen colonising the catheters was *S. aureus* (n=14; 26.92%), followed by *Enterococcus faecalis* (n = 7; 13.46%), *Pseudomonas aeruginosa* (n = 6;11.53 %), non-*albicans Candida* (n = 6; 11.53 %), and Coagulase negative staphylococci (n = 6; 11.53 %), Acinetobacter c. Baumannii (n = 4; 7.69%), *Klebsiella pneumoniae* (n = 4; 7.69%), *Escherichia coli* (n=3;5.76%), *Proteus mirabilis* (n =1; 1.94 %), *Citrobacter koseri* (n = 1; 1.94 %). Microbiological profile of organisms causing colonisation is depicted in [Table- 2].

Blood culture

Bacteraemia was seen in 67 patients (63.30%) out of 109 patients. From blood cultures, 16 (88.88 %) cases had polymicrobial infection and four cases (11.11%)

showed mono-microbial infection. Among the isolated pathogens responsible for CVC-BSI; *S. aureus* was most common and was isolated in one fourth of cases (n = 4; 25 %) followed by *P. aeruginosa* (n = 3; 18.75 %), non-*albicans Candida* (n = 3; 18.75 %), coagulase negative staphylococci(n = 2; 12.5 %);*K. pneumoniae* (n = 2; 12.5 %); *E. faecalis* (n = 1; 6.25 %) and *Acinetobacter cbc* (n = 1; 6.25 %). The most commonly isolated polymicrobial infection was *S. aureus* with non-*albicans Candida* while *K. pneumoniae* with *E. faecalis* and *Acinetobatercbc* with non-*albicans Candida* were other combinations. The drug-susceptibility pattern based on CLSI guidelines for implicated both Gram-negative and Gram-positive bacteria in CRBSI. Five strains of MRSA (79.5.5% of *S. aureus* strains) and one strain of VRE (MIC ≥ 512 µg/ml) were implicated in CRBSI. All the CRBSI isolates of *K. pneumoniae* showed ESBL production when tested by disc potentiation.

Table-1 *Demographic and clinical characteristics*

	Cases (n=18)	Controls (n=91)	P value
Age (yrs)			
<50	7(38.89)	39(42.86)	0.75
>50	11(61.11)	52(57.14)	
Gender			
Males	11(61.11)	52(57.14)	0.755
Females	7(38.89)	39(42.86)	
ICU			
Medical	5(27.78)	63(69.23)	<0.001**
Surgical	13(72.22)	28(30.77)	
Underlying Co-morbidity			
Present	11(61.11)	25(27.47)	0.001**
Absent	7(38.89)	66(72.53)	
Catheter-insertion site			
Subclavian	11(61.11)	65(71.43)	<0.001**
Jugular	7(38.89)	26(28.57)	
Femoral	0(0.00)	0(0.00)	
Duration of catheterisation			
<10days	1(5.56)	63(69.23)	<0.001**
>10days	17(94.44)	28(30.77)	
Local signs of inflammation			
Present	4(22.22)	6(6.59)	<0.001**
Absent	14(77.78)	85(93.40)	
Length of ICU stay			
>15 days	12(66.67)	16(17.58)	<0.001**
<15days	6(33.33)	75(82.41)	

**: P<0.001 highly significant

Table-2 *Organisms causing catheter tip colonisation*

Organism	N	%
S. aureus	14	26.92
Enterococcus faecalis	7	13.46
Psuedomonas aeruginosa	6	11.53
Non-albicans Candida	6	11.53
Coagulase negative staphylococci	6	11.54
Acinetobacter c. baumannii	4	7.69
Klebsiella pneumoniae	4	7.69
Escherichia coli	3	5.76
Proteus mirabilis	1	1.94
Citrobacter koseri	1	1.94
	52	100

Discussion

In the present study, conducted in the medical and surgical ICU of a tertiary hospital, the rate of CRBSI was 13.64 per 1000 catheter days. CRBSI rate varies considerably in the different studies; both Asian and western. National nosocomial infection surveillance system of the Center for Disease Control and Prevention, Atlanta reports a 50 percent decrease in CLABSI between 2008 and 2014[13]. In the study by Chopdekar, *et al*., [4] the average CRBSI rate was 9.26 per 1000 catheter days but a maximum rate of 27.02 per 1000 catheter days was observed

in NICU. In another study reporting the findings of the International Nosocomial Infection Control Consortium intensive care units of seven Indian cities [3] the central venous catheter-related bloodstream infection (CVC-BSI) rate was 7.92 per 1000 catheter-days, both studies have reported rates lower than that of the present study. Deshpande, et al., [15] observed an incidence of catheter infection of 4.01/1,000 catheter days in their study which is lower than that of the present study but consistent with western hospitals' CRBSI statistics.

In a study by Kaur, et al., [5] the incidence of CRBSI was 14.59/1000 catheter days which is higher than that of the present study; also, much higher incidence rates (47.31/1000 catheter days) have been reported by another study from a tertiary care hospital in India reflecting the scenario of comparatively higher infection rates in various Indian hospitals and need for a national nosocomial surveillance system. Higher rates have been attributed to poor nurse-patient ratio, compromised infection control practices and the critically-ill patients with pre-existing sepsis [5]. In the present study, the mean age of patients with CRBSI was observed to be significantly higher than of controls whereas distribution of gender in both the groups was not significant. This is similar to the findings of other studies. Parameswaran, et al., [8], Kaur, et al., [5] in their studies did not find any significant age and gender difference amongst the two groups. Other factors found to be significantly associated with CRBSI in the present study (P<0.05) were duration of catheterisation, signs of inflammation at the catheterisation site, surgical patients more often of perforative peritonitis and length of ICU stay, all of which are consistent with findings of other studies [5,8,16].

Paired Quantitative Blood Cultures (QBC) was used for the diagnosis of CRBSI as it has been shown to be the best diagnostic method for implantable device-associated BSI. Quantitative catheter tip culture was done to look for colonisation of catheters with one or more organisms by culturing both external surface and the luminal surface of the catheters. In the present study, *Staphylococcus aureus* was the most common pathogen implicated in CRBSI, which suggests colonisation of the hub either by the patient's cutaneous flora or health care personnel and reflects a probable lapse in catheter care. *P. aeruginosa* and *Candida* especially non-*albicans Candida* were the next most common pathogen implicated in CVC-BSI in the present study, similar findings are reported by Kaur, et al., [5] who found *P. aeruginosa* as the next most common CRBSI pathogen and Latif, et al., who found *P. Aeruginosa* and *Acinetobacer* spp. to be the second most common bacterial agents causing septicaemia in ICU settings after Gram-positive cocci. [25] Non-albicans Candida are also being reported from nosocomial septicaemic cases [9]; in the present study they were isolated in(*n* = 3; 18.75 %) of the CVC-BSI cases. All these four organisms are known to produce biofilms, which are reported to be universally present on CVC [11].

On anti-microbial susceptibility testing; multidrug resistance was observed in almost all the isolates responsible for CRBSI and catheter colonisation in the present study. These findings are in concordance with other similar studies, where total resistance to amikacin and gentamicin was observed resistance among *P. aeruginosa* isolates in ICUs from other centres by Kaur, et al. [5,18]. In the study by Tang, et al. [6] *Candida* species compromised 4 CLABSI cases, and each one was caused by methicillin-resistant *Staphylococcus aureus* and coagulase-negative *Staphylococci*. Parameswaran, et al., in their study found MRSA to be responsible for 26.7% CRBSIs and single isolate of *A. Baumannii* resistant to all the routine drugs [8]. Limitations of the present study are cases are from a single centre and relatively less number of cases.

Conclusion
Catheter-related bloodstream infection (CRBSI) is an important cause of nosocomial bacteraemia and gram-positive bacteria were the most commonly detected pathogens. CRBSI were significantly associated with higher mean age; longer duration of catheterisation and longer stay in ICU.

Application of research: National level surveillance on nososcomial infections and implementation of proven and novel interventions are essential to minimize the risk and prevent CRBSI's in ICU settings.

Research Category: Antibiotic susceptibility microbiological profile

References
[1] Gahlot R., Nigam C., Kumar V., Yadav G. and Anupurba S. (2014) *International Journal of Critical Illness and Injury Science*, 2014; 4(2),162-167.
[2] Pawar M., Mehta Y., Kapoor P., Sharma J., Gupta A. and Trehan N. (2004) *J CardiothoracVascAnesth*, 18, 304-8.
[3] Mehta A., Rosenthal V.D., Mehta Y., Chakravarthy M., Todi S.K., Sen N., et al. (2007) *J Hosp Infect*., 67,168-74.
[4] Chopdekar K., Chande C., Chavan S., Veer P., Wabale V., Vishwakarma K., et al. (2011) *Indian J Med Microbiol*., 29,169-71.
[5] Kaur M., Gupta V., Gombar S., Chander J., Sahoo T. (2015)Indian J Med Microbiol 2015;33:248-54.
[6] Tang H.J., Lin H.L., Lin Y.H., Leung P.O., Chuang Y.C., Lai C.C. (2014) *BMC Infect Dis.*, 14(1), 356–356.
[7] Singh S., Pandya Y., Patel R., Paliwal M., Wilson A. and Trivedi S. (2010) *IJMM*, 28(4), 342–7.
[8] Parameswaran R., Sherchan J.B., Varma D.M., Mukhopadhyay C. and Vidyasagar S. (2011) *J Infect Dev Ctries*., 5, 452–8.
[9] Eggimann P. and Pittet D. (2002) *ClinMicrobiol Infect,* 2002,8,295-309
[10] Haddadin Y., Regunath H. Central Line Associated Blood Stream Infections (CLABSI) [Updated 2017 Mar 28]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018.
[11] Donlan R.M. (2001) *Emerg Infect Dis.,* 7, 277-81.
[12] Raad I., Hanna H. and Maki D. (2007) *Lancet Infect Dis*., 7, 645-57.
[13] CDC(2011) National and State Healthcare Associ ated Infections
[14] Patil H.V., Patil V.C., Ramteerthkar M.N. and Kulkarni R.D. (2011) *Indian J Crit Care Med.,* 15, 213-23.
[15] Deshpande K.S., Hatem C., Ulrich H.L., Currie B.P., Aldrich T.K., Bryan-Brown C.W., et al. (2005) *Crit Care Med*., 33, 13-20, discussion 234-5.
[16] Yilmaz G., Koksall., Aydin K., Caylan R., Sucu N., Aksoy F. (2007) *J. Parenter. Enter. Nutr*., 31, 284–287.
[17] Latif S., Anwar M.S., Ahmed I. (2009) *Biomed*., 25:101-5.
[18] Hocquet D., Berthelot P., Roussel-Delvallez M., Favre R., Jeannot K., Bajelot O., et al. (2007) *Antimicrob Agents Chemother*., 51, 3531-6.