ORIGINAL ARTICLE

Central Venous Catheter-related Blood Stream Infections: Incidence, Risk Factors and Associated Pathogens in a University Hospital ICU

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Abstract

Central Venous Catheters (CVCs) are indispensable in current intensive care treatment; also pose a greater risk of device related infections in comparison to any other type of medical device and are major cause of morbidity, mortality and increased expense. A cross sectional prospective study of one year duration was conducted in the tertiary care University Hospital ICU located in the rural region of Haryana, India, to determine the incidence of the central venous catheter related bloodstream infection (CRBSI), rate of catheter colonization and to identify the associated risk factors and the microbial spectrum of CRBSI along with the antimicrobial sensitivity pattern of microbial isolates. Sixty patients with central venous catheter inserted and admitted under ICU having signs and symptoms of septicaemia post 48 hours of central venous catheter insertion were included. The rate of CRBSI was assessed by paired quantitative blood culture method in the CVC and peripheral vein. The CRBSI incidence was 16.67% and catheter colonization was found to be 53.3%. Methicillin-resistant staphylococcus aureus and Acinetobacter baumanni were the predominant isolates. A statistically significant association of duration of catheterization with CRBSI was found. It is concluded that CRBSI incidence is high, with significant association of prolonged duration of catheterization with CRBSI. By knowing the changing trends of microbial flora, empirical therapy can be formulated for early and effective management of CRBSI.

Key Words

Catheter-related Bloodstream Infection, Central Venous Catheter Colonization, Intensive Care Unit, Septicaemia

Introduction

Central Venous Catheter (CVC) related bloodstream infection (CRBSI) and central line-associated bloodstream infection (CLABSI) are a major cause of morbidity, mortality and increased cost with prolongation of hospital stay (1).

According to Infectious Diseases Society of America, CRBSI is defined when simultaneous blood culture is done from both central venous catheter and peripheral venous catheter (PVC) and CVC blood culture shows a five-fold greater colony than for the blood culture from PVC (2). CDC defined CRBSI as presence of a recognized pathogen cultured from one or more blood cultures and organism cultured from blood is not related to infection at another site along with isolation of same organism from the catheter tip culture with the same antibiogram (1).

The pathogens mainly involved are Staphylococcus aureus, Coagulase negative Staphylococcus, Enterococcus sp., Candida sp., Acinetobacter sp., Pseudomonas sp. and Klebsiella sp. (3). For a positive quantitative catheter culture growth of > 1000 CFU/ml is considered as Central Venous Catheter colonization and for semi quantitative culture growth of more than 15 CFU is considered as significant (4). Intra-luminal colonisation becomes a significant risk in the pathogenesis of CRBSI with increasing dwell time. This risk is one of the reasons for the genesis of CRBSI maintenance bundles (5). This is also the reason why the CVCs must be removed as early as possible. This study was undertaken to determine the incidence of CRBSI in the ICU and to identify the

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factors influencing it and the organisms involved in its causation, which would help to institute better prophylactic measures.

Material and Methods

A prospective case-control study was carried out in Department of Microbiology, MM Institute of Medical Sciences & Research, Maharishi Markandeshwar (Deemed to be University), Mullana, Ambala, Haryana, India. The study was duly approved by IEC. The study was conducted on patients with central venous catheter inserted and admitted under ICU having signs and symptoms of septicemia after 48 hours of Central Venous Catheter insertion by systematic random sampling during 1 year. Two groups of CVCs namely internal jugular catheters and subclavian catheters were taken. Cases were defined as the patients who were diagnosed to have CRBSI while the Control population did not suffer from CRBSI. Number of hours of central venous catheter insertion was considered as a major co-morbid factor.

Paired Quantitative Blood Culture from Central Venous Catheter & Peripheral Vein were done from suspected cases of CRBSI. The catheter tip segment was also processed after the catheter was removed and received in microbiology laboratory and reported *(Figure 1).*

All the samples were cultured on Blood Agar and MacConkey Agar and were incubated at 37°C for 18-24 hours. The strains were identified on the basis of colony morphology, Gram staining, motility and biochemical tests as per standard microbiological protocol. Antimicrobial susceptibility testing was done by Kirby-Bauer disc diffusion method in accordance with CLSI guidelines. The antimicrobial drugs tested for gram-positive bacteria included erythromycin (15µg), penicillin (10units), cefoxitin (30µg), cephalexin (30µg), trimethoprim-sulfamethoxazole (1.25/23.75µg), linezolid (30µg), doxycycline (30µg), clindamycin (2µg), vancomycin (30µg) and amoxicillin/clavulanic acid (20µg/10µg). For gram-negative bacteria they were gentamicin (10µg), amikacin (30µg), amoxicillin/clavulanic acid (20µg/10µg), piperacillin/tazobactam (100µg/10µg), cefepime (30µg), ciprofloxacin (5µg), imipenem (10µg), meropenem (10µg), ceftazidime (30µg), netilmicin (30µg), doxycycline (30µg) and colistin.

CRBSI rate was calculated as no. of CRBSI cases divided by number of catheter days and multiplied by 1000. CRBSI incidence was formulated as number of CRBSI cases divided by total no. of samples and multiplied by 100. Catheter colonization rate was determined by number of catheter colonization cases divided by total no. of cases multiplied by 100.

Results

During the study, a total of 60 patients with central venous line catheterization were enrolled. The rate of CRBSI in the ICU at our hospital was found to be 15.27 per 1,000 catheter days, with incidence of 16.67% (10 cases). Catheter colonization was found in 32 (53.33%) cases and 14 (23.33%) cases were sterile. The rate of BSI was 6% *(Figure 2).*

Methicillin-resistant *Staphylococcus aureus and*

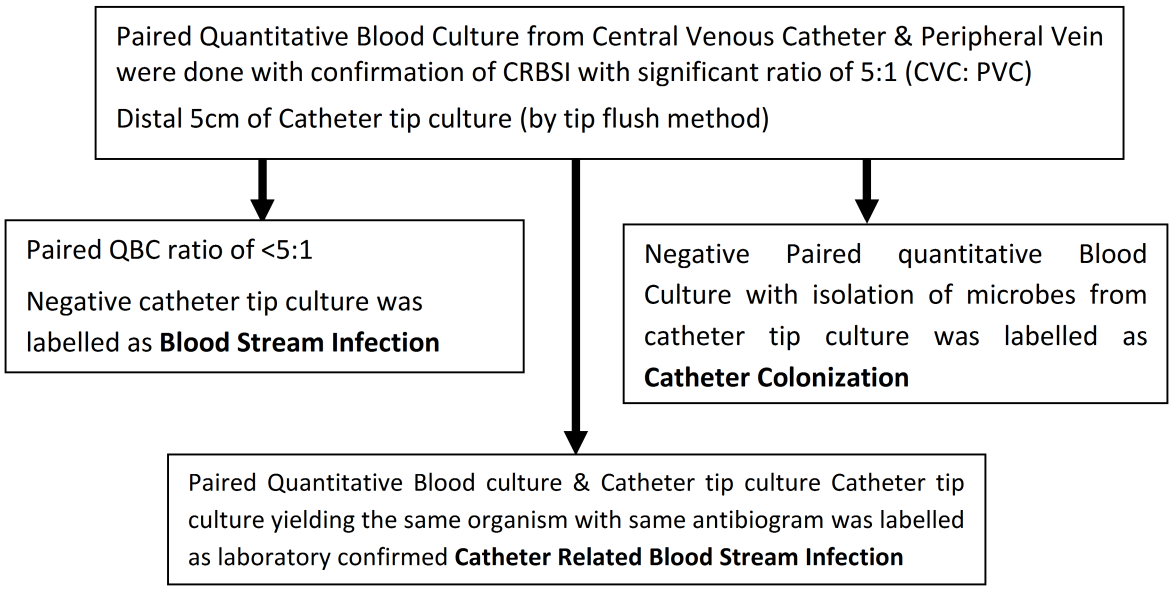

Figure 1: Protocol of the Study

Acinetobacter baumanni were the predominant isolates (40%). The gram-negative organisms collectively preceded gram-positive organisms in confirmed CRBSI cases. Candida colonization was seen in majority of tips *(Figure 3).* MRSA was the prime cause of BSI.

When logistic regression analysis of all the risk factors in CRBSI was done, the present study revealed that the duration of catheterization (*p* value 0.004) and clinical outcome (*p* value 0.017) in confirmed CRBSI cases showed statistically significant association with CRBSI *(Table 1).* When the antibiotic sensitivity *(Table 2 & 3)* in patients with confirmed CRBSI was done, all Methicillin resistant Staphylococcus aureus (MRSA) isolates were found to be sensitive to Linezolid (100%) and Vancomycin (100%). All gram-negative isolates were resistant to most of the antibiotics except for colistin.

Discussion

According to *Fortun et al.* (6), the rate of incidence of tip colonization was 2.9 per 1000 catheter-days and of bacteremia was 1.2 per 1000 catheter-days. Similarly, Deshpande *et al*. (7) in 2005 reported that the incidence of catheter infection was 4.01/1000 catheter-days (2.29% catheter) and colonization was 5.07/1000 catheter-days (2.89% catheters), which was low. In a study by Tarpatzi *et al.* (8) in tertiary care hospital at Athens, Greece an incidence for CRBSI was 11.47/1000 catheter days was observed. The rate of colonization associated with CVCs placed in the present study was 15.27 per 1000 catheter-days, which is quite high compared with these studies. This variability of incidences in various studies could be due to various factors like techniques, site of catheterization, type of catheter used, catheter care and

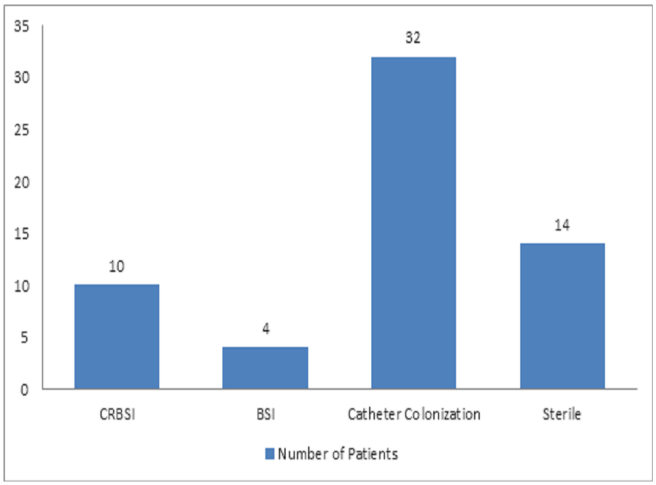

Figure 2: Bar Diagram Showing Distribution of Cases [CRBSI 10 (16.67%), BSI 4 (6%), Catheter Colonization 32 (53.33%) and 14 (23.33%) Sterile]

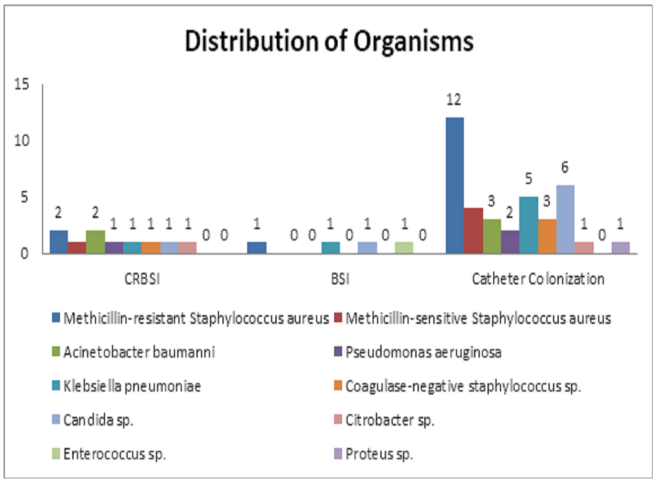

Figure 3: Bar Diagram Showing Distribution of Organisms in Central Venous Related Blood Stream Infection

Table 1: Showing Logistic Regression Analysis of the Risk Factors in CRBSI

Risk factors	Variables	Controls N=50 (83.3%)	Cases N=10 (16.7%)	Chi test	*p* value	Odd ratio	Result
Age (yrs.)	Below 40 years	17(34%)	5(50%)	0.918	0.338	2.687	Not Significant
	Above 40 years	33(66%)	5(50%)				
Gender	Female	23 (46%)	4 (40%)	0.121	0.728	-	Not Significant
	Male	27 (54%)	6 (60%)				
Site of CVC insertion	Internal jugular vein	4(8%)	2(20%)	1.335	0.248	.112	Not Significant
	Sub clavian vein	46(92%)	8(80%)				
Duration of catheterization	< 10 Days	30(60%)	1(10%)	8.284	0.004	1.289	Significant
	> 10 Days	20(40%)	9(90%)				
Clinical outcome	Death	8(16%)	5(50%)	5.696	0.017	-	Significant
	Survival	42(84%)	5(50%)				

Table 2: Antibiotic Sensitivity Pattern of Gram-Positive Bacteria Among CRBSI Cases

ORGANISM	Gentamicin	Cefipime	Amikacin	Amoxycillin Clavulanic acid	Ciprofloxacin	Netilmicin	Imipenem	Meropenem	Doxycycline	Ceftazidime	Colistin	Piperacillin + tazobactam
Pseudomonas aeruginosa (N=1)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)	1 (100%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)
Acinetobacter baumanni (N=2)	0 (0%)	0 (0%)	0 (0%)	1 (50%)	0 (0%)	0 (0%)	1 (50%)	1 (50%)	0 (0%)	0 (0%)	2 (100%)	0 (0%)
Klebsiella pneumoniae (N=1)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	1 (100%)
Citrobacter species (N=1)	1 (100%)	0 (0%)	1 (100%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)

Table 3: Antibiotic Sensitivity Pattern of Gram-Negative Bacteria Among CRBSI Cases

ORGANISM	**Gentamicin**	**Cefipime**	**Amikacin**	**Amoxycillin Clavulanic acid**	**Ciprofloxacin**	**Netilmicin**	**Imipenem**	**Meropenem**	**Doxycycline**	**Ceftazidime**	**Colistin**	**Piperacillin + tazobactam**
Pseudomonas aeruginosa (N=1)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)	1 (100%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)
Acinetobacter baumanni (N=2)	0 (0%)	0 (0%)	0 (0%)	1 (50%)	0 (0%)	0 (0%)	1 (50%)	1 (50%)	0 (0%)	0 (0%)	2 (100%)	0 (0%)
Klebsiella pneumoniae (N=1)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	1 (100%)
Citrobacter species (N=1)	1 (100%)	0 (0%)	1 (100%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)

diagnostic criteria used for diagnosing CRIs.

The high infective complication rate in the present study may have been due to the fact that our hospital is catering to the lower socioeconomic group, the overall hygiene of the patients was poor, the patient population were mainly of above the age of 60 years, and it was usually done as an emergency procedure. However, Almuneef *et al*. (9) also observed a high CRBSI rate of 20.06 per 1,000 catheter days and according to another study by Yilmaz *et al*. (10) CRBSI rate of 18.8 per 1,000 centre-line days was reported.

The present study found catheter colonization rate of 53.3%, 27 samples were pure growth and polymicrobial growth was seen in 5 samples. Catheter colonization rate is comparable to study by Gahlot *et al*. (11) who observed rate of 62.5% and increase in CVC colonization rate with advancing duration of catheterization. Kaur *et al*. (12) observed colonization at 58.49%, out of a total 106 catheters processed, 62 CVCs were observed colonized. Results revealed by Chopdekar *et al*. (13) showed a total of 57.6% catheter tips were colonized with bacteria and fungi. *Candida spp*. was the most common associated microbe with colonization, is also in concordance with the results of catheter colonization in this study.

The present study observed Methicillin-resistant *Staphylococcus aureus* and *Acinetobacter baumanni* as the predominant isolates in CRBSI (40%). MRSA probably might have colonized catheter hub through

migration from skin or during handling of the catheter by health care providers in ICU, similarly *Acinetobacter baumanni* is also a common isolate of hospital acquired infection. This observation is comparable to a study by Parameswaran *et al.* (14) in which 64% of the pathogens causing CRBSI were Gram positive, out of which *Staphylococcus aureus* (40%) was the commonest pathogen causing CRBSI, followed by *Acinetobacter baumanni*. Kaur *et al.* (12) observed *Staphylococcus aureus* followed by *Pseudomonas aeruginosa* and *non-albicans Candida* were the common CVC-BSI pathogens. Many authors have reported CONS as a major isolate from the patients suspected of CRI by catheter culture. In contrast, Pawar *et al.* (15) in their study found *E. coli* (47%) *Acinetobacter* (11.7%) followed by *S. aureus* (11.7%) and CONS (5.8%). Similarly, Deepti *et al.* (16) in a study carried out at AIIMS, New Delhi, found no case of laboratory confirmed CLABSI, though in the only 1 case of BSI *Staphylococcus aureus* was observed.

The gram-negative organisms collectively preceded gram-positive organisms in confirmed CRBSI cases which is in concordance with some other studies. Subba Rao *et al.* (17) reported Pseudomonas and Enterobacter as the major constituent in their study indicating towards a changing trend of organisms associated with CRBSI, Gram negative organisms are increasingly becoming more associated with catheter related infections.

The study while analysing the risk factors revealed statistically high significant association of prolonged duration of catheterization with CRBSI (*p*-value 0.004). The range of catheter in-situ was from 4 to 28 days, and total number of catheter days was 655. This finding is in accordance with certain other studies. Gahlot *et al.* (11) found increase in CVC colonization rate and in concordance increase in CRBSI with advancing duration of catheterization. Porto *et al.* (18) showed catheter duration of more than 5 days ($p < 0001$; OR=15.97) as the major risk factor for CRBSI. Peng *et al.* (19) showed CRBSI incidence is related directly to 3 things; (a) the number of venous lines insertion, (b) the use of antibiotics before CRBSI, and (c) the duration of catheterization; by the univariate analysis. In a study from a tertiary level hospital, in Chandigarh, Kaur *et al.* (12) concluded that catheter colonization usually started after the third day with maximum colonization being observed after 10 days of catheterization.

The current study observed no statistically significant association of co-morbidity with development of CRBSI. However, statistically significant association of CRBSI with the clinical outcome of the patients in the ICU was found (p-value < 0.05). Mortality in cases was 50% and in controls was as low as 16%, which is in contrast with the study by Kaur *et al.* (12).

The present study showed no statistically significant association (p-value 0.248) of site of insertion of CVC with development of CRBSI, 54 were placed in subclavian vein and 6 in the internal jugular vein respectively. There are a number of studies, that demonstrated similar results in support. In contrast a study carried out in a tertiary care hospital in India, Parmeswaran *et al.* (14) observed femoral venous catheter were responsible for 33.3% of infections followed by midline catheters (23.1%) and internal jugular catheters (22.2%). Subclavian venous catheters were observed to be associated with lowest risk (21.3%). Similarly, Lorente *et al.* (20) found CRBSI incidence rate was statistically significant and higher for femoral catheters than for jugular catheters ($p = 0.002$) and subclavian ($p < 0.001$) access, and higher for jugular site than for subclavian site ($p = 0.005$).

All methicillin-resistant *Staphylococcus aureus* (MRSA) isolates in confirmed CRBSI cases were found to be sensitive to Linezolid (100%) and Vancomycin (100%), 66% were sensitive to Amoxicillin clavulanic acid, erythromycin and cotrimoxazole. All gram-negative isolates were resistant to most of the antibiotics except for colistin. This observation is comparable to Khanna *et al.* (21) who also observed that all resistant *Staphylococcus* (MRSA) isolated from CRBSI were 100% sensitive to cotrimoxazole and chloramphenicol among routine antibiotic and 100% sensitive to vancomycin, teicoplanin, and linezolid among reserved antibiotics. All sensitive *Staphylococcus* (MSSA and MSCONS) were 100% resistant to ciprofloxacin.

The most sensitive routine antibiotics for *P. aeruginosa* isolated from CRBSI were piperacillin tazobactam and ciprofloxacin (100% sensitive each). There were no routine antibiotics sensitive for *E. coli* isolated from CRBSI and among reserved antibiotics meropenem was most sensitive (100%). For *K. pneumoniae*, the most sensitive routine antibiotics were gentamicin, netilmicin, amikacin (all 100% sensitive), and meropenem among reserved antibiotics (100% sensitive). Only one strain of *A. baumannii* isolated from CRBSI was resistant to all routine and reserved drugs (multidrug resistant).

The limitations of the present study were the number of the patients was less but CRBSI patients are difficult to assess and few in number. Also, all catheter sites were not taken into account as it was observed in literature search that only a few catheter sites are affected. However, further research is required with higher number of patients.

Conclusion

The CRBSI incidence was high with significant association of prolonged duration of catheterization with CRBSI. Maximal sterile techniques should be practiced while inserting CVC and in after care, regular monitoring of CVC and its need to continue should be measured promptly. By knowing the changing trends of microbial flora, empirical therapy can be formulated for early and effective management of CRBSI.

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