

Microbial profile and risk factors of central venous catheter associated blood stream infections in Tertiary Care Hospital, Amritsar

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Abstract

Introduction: Central venous catheter (CVC) related blood stream infections are associated with serious infectious complications resulting in significant morbidity, increased duration of hospitalization and added medical cost. **Aim:** The study was done to determine the incidence of central venous catheter related infections, their antimicrobial sensitivity pattern, biofilm production and associated risk factors in hospitalized patients. **Material and Method:** Catheter tip culture & blood cultures of 143 patients with indwelling central venous catheters were processed. **Result:** Out of 143 specimens, catheter tip colonization was observed in 45 samples, while 14 were both catheter tip as well as blood culture positive hence included as catheter related blood stream infections (CRBSI). CRBSI was found significantly associated with increased duration of catheterization, increased number of attempts and placement of CVC in internal jugular vein. Most common isolated organisms were *Klebsiella pneumoniae* followed by *Coagulase negative Staphylococcus*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* in CRBSI as well as in CVC colonization. Majority of them were resistant to Gentamicin, Ciprofloxacin, Ceftiazidime and Ceftriaxone. Biofilm production was determined by tissue culture plate method and was found to be maximum seen in *Klebsiella spp.* **Conclusion:** Incidence of CRBSI was 9.79% and of CVC colonization was 34.26%. Rate of CRBSI was 8.53 per 1000 CVC days. *Klebsiella pneumoniae* was most common isolate and predominant biofilm producer and was found to be multidrug resistant to Gentamicin, Ciprofloxacin, Ceftiazidime.

Keywords: Central venous Catheter, Catheter related blood stream infection (CRBSI), Biofilm production and antimicrobial therapy.

Introduction

Central venous catheters (CVC) are integral to modern practice and are increasingly used in hospitals as a portal for the delivery of medications, parenteral nutrition, collection of blood samples and monitoring hemodynamic variables in critically ill patients. CVC catheterization is often associated with serious infectious complications, mostly catheter related blood stream infections (CRBSI), resulting in significant morbidity, increased duration of hospitalization and additional medical costs. Patients with CVCs are at risk of developing local as well as systemic infectious complications like local insertion-site infection, catheter

related blood stream infections (CRBSI), septic thrombophlebitis, endocarditis and other metastatic infections [1]. Potential risk factors for CRBSI include underlying disease, method of catheter insertion, site of catheter insertion and duration, and purpose of catheterization. Biofilm formation in catheters has been implicated as an important factor involved in device related infection which also confers resistance to antimicrobial treatment [2].

CRBSIs are considered among the first and most “preventable” classes of nosocomial infections [3]. Surveillance of central venous catheter associated infections in a particular area helps in determining infection rates, risk factors and in further planning the

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preventive strategies to ensure a quality health care in any hospital. Hence the present study was conducted to know the incidence, microbiological profile, antimicrobial susceptibility, biofilm formation & associated risk factors in CVC associated infections in hospitalized patients.

Materials and Methods

Prospective study was conducted in the department of microbiology, Government Medical College, Amritsar over a period of 18 months (December 2013 to June 2015). A total of 143 hospitalized patients presenting with clinical signs and symptoms of septicemia after 48 hours of central venous catheterization were included in the study. Patients with obvious source of infection (pneumonia, urinary tract infection) at the time of admission and patients whose catheter was put outside our hospital were excluded from the study. Patient's demographic and clinical data and information related to CVC catheter was recorded.

The distal 5 cm of CVCs was collected aseptically in two universal sterile containers and transported to microbiology laboratory for processing. First catheter tip was rolled on across the surface of blood agar and Mac-conkey agar and put into a tube containing brain heart infusion (BHI) broth. Semi-quantitative method used by Maki et al was followed for catheter tip culture

Observations

The results of the catheter tip and blood cultures were interpreted according to following criteria: Catheter – related blood stream infection (CRBSI) was considered when the same organism (Identical species, antibiogram) was isolated from culture of the catheter tip and from the blood (drawn from a peripheral vein) of a patient with accompanying clinical symptoms of blood stream infection and no other apparent source of infection.

Central venous catheter (CVC) colonization was defined as the significant growth of a micro-organism (> 15 colony forming units) from the catheter tip by semi-quantitative culture.

The rate of CVC-BSI was expressed in number of CVC days and was calculated by the following formula:

$$\text{Catheter related} = \frac{\text{Number of catheter related Infections}}{\text{Total number of Catheter Days during the Time period}} \times 1000$$

Among 143 patients with total of 1641 catheter days, Rate of CRBSI was found to be 8.53 per 1000 CVC days. Catheter tip colonization was observed in 45 samples, while 14 were both catheter tip as well as blood culture positive. In present study incidence of CRBSI was reported to be 9.79% (14/143) and incidence of CVC colonization was 34.26 % (45/143).

Maximum number of cases of CRBSI were in the age group of 51- 60years (35.7%) and of CVC colonization were seen in 31-40 years of age (26.66%). Mean age was 36.78±20.20. Risk factors associated with CVC related infections were studied and are shown in [table-1]. The comorbid conditions studied in majority of CVC-BSI cases were diabetes

[4]. Inoculated medium was incubated under aerobic condition at 37°C for 24 hours. If BHI broth shows turbidity, subculture was made on blood agar and Mac-Conkey agar after 48 hours. Second tip part was cultured on SDA media, then incubated at 25°C and 37°C and observed for fungal growth.

10 ml blood of the same patient was collected aseptically from the peripheral vein at the time of withdraw of intravascular catheter in two BHI broths for blood culture. One bottle was incubated at 25°C and other at 37°C. Subculture was made on blood agar, Mac-Conkey agar, and SDA media.

The bacterial and fungal isolates recovered from blood culture and CVC catheter tip were identified and characterized by standard microbiological methods [5,6]. Antimicrobial susceptibility testing was performed on Mueller Hinton Agar (MHA) by Kirby Bauer disc diffusion method as per CLSI guidelines [7]. Multidrug-resistant (MDR) isolates were phenotypically characterized into *methicillin-resistant Staphylococcus aureus* (MRSA), VRE, metallo-β-lactamase (MBL) and extended-spectrum β-lactamase (ESBL) producers [7]. To detect biofilm production in isolated organisms Tissue culture plate (TCP) and tube method were used [8] Antifungal susceptibility for isolated yeasts was determined as per CLSI guidelines [9].

followed by Hypertension, prior antibiotics, chronic obstructive pulmonary disease and malignancy. No significant association was observed between co morbid conditions, CRBSI and CVC colonization. (p-.06).

Table-1: Various risk factors associated with CRBSI and CVC colonization.

Variable	Total	Percentage	p- value
Duration of Catheterization			
1-7	29	20.27	0.025
8-14	60	41.95	Significant
>14	54	37.76	
Number of attempts			
1	15	10.48	0.015
2	95	66.43	Significant
3	33	23.07	
Vein catheterized			0.023
Subclavian vein	68	47.55	Significant
Internal jugular vein	57	39.86	
Umbilical vein	18	12.58	

In this study out of 143 samples, a total of 45 catheter tip bacterial& fungal isolates were recovered while 14 isolates were recovered from blood cultures& confirmed by catheter tip culture. Most common isolated pathogens associated with catheter colonisation and CRBSI were *Klebsiellaspp*, *Coagulase negative Staphylococcus (CONS)*, *Staphy-lococcus aureus*, and *Pseudomonas aeruginosa etc.* [table 2]

Table -2: Distribution of bacterial and fungal isolates from catheter colonization and crbsi.

Organisms isolated	Number of isolates in catheter colonization	Number of isolates in CRBSI
Klebsiellaspp	10	4
Coagulase negative Staphylococcus (CONS)	9	3
Staphylococcus aureus	7	2
Pseudomonas aeruginosa	2	3
Escherichia coli	3	1
Acinetobacterbaumani	3	-
Enterococcus	3	-
Citrobacterspp	2	-
Enterbacterspp	1	-
Proteus spp	1	-
Candida Spp	4	1
Total	45	14

Antibiotic susceptibility pattern of gram positive and gram negative organisms isolated from catheter colonization & CRBSI is shown in Table 3 and 4. MBL production was observed in 6.66% and ESBL in 33.33% of isolates. Methicillin resistance was seen in 12.5% of isolates.

Table -3: Antimicrobial susceptibility pattern of different gram negative isolates.

<i>Antimicrobials</i>	<i>Klebsiellaspp</i> (n=14)	<i>Pseudomonas aeruginosa</i> (n=5)	<i>Escherichia coli</i> (n=4)	<i>AcinetobacterSpp</i> (n=3)	<i>Others</i> (n=4)
Amikacin	12 (85.71%)	3(60%)	2(50%)	1(33.33%)	2(50%)
Gentamicin	6(42.85%)	2(40%)	2(50%)	1(33.33%)	0
Ciprofloxacin	4(28.57%)	2(40%)	1(25%)	0	0
Ceftazidime	3((21.42%)	2(40%)	3(75%)	2(66.66%)	3(75%)
Ceftriaxone	3(21.42%)	3(40%)	2(50%)	1(33.33%)	3(75%)
Piperacillin – Tazobactam	12(85.71%)	3(60%)	3(75%)	2(66.66%)	4(100%)
CeftazidimeSulbactam	11(78.57%)	2(40%)	4(100%)	1(33.33%)	4(100%)
Ceftriaxone- Sulbactam	11(78.57%)	2(40%)	4(100%)	2(66.66%)	4(100%)
Imipenem	14(100%)	4(80%)	4(100%)	2(66.66%)	4(100%)
Polymyxinn B	14(100%)	5(100%)	4(100%)	3(100%)	3(100%)

Table -4: Antimicrobial susceptibility pattern of gram positive isolates.

<i>Antimicrobials</i>	<i>S. aureus</i> N=9	<i>CONS</i> N=12	<i>ENTEROCOCCUS</i> N=3
Amikacin	6(66.66%)	7(58.33%)	3(100%)
Gentamicin	3(33.33%)	2(16.66%)	1(33.33%)
Ciprofloxacin	3(33.33%)	2(16.66%)	2(66.66%)
Ampicillin	1(11.11%)	1(8.33%)	1(33.33%)
Cefoxitin	7(77.77%)	11(91.6%)	3(100%)
Erythromycin	3(33.33%)	5(41.66%)	1(33.33%)
Cephalexin	2(22.22%)	4(33.33%)	1(33.33%)
Linezolid	8(88.88%)	12(100%)	3(100%)
Vancomycin	9(100%)	12(100%)	3(100%)

Biofilm production of isolates was determined by tissue culture method and tube method. Organisms were graded as strong/high, moderate and weak biofilm producers. Most of the gram negative isolates especially *Klebsiella* spp and *Pseudomonas aeruginosa* were strong biofilm producers. Coagulase negative *Staphylococcus* (CONS) and *Staphylococcus aureus* were moderate biofilm producers.

Discussion

Central venous catheters (CVCs) are increasingly used in hospitals to manage critically ill patients. The problem of central line-associated blood stream infections has gained increasing attention in recent years because of increased morbidity and mortality in patients [13]. In present study, incidence of CRBSI was reported to be 9.79% and incidence of CVC colonization was 34.26%. Rate of CRBSI (Catheter related blood stream infection) was found to be 8.53 per 1000 catheter days which is in concordance by study done by K chopdekar et al (9.26 per 1000 catheter days) [10]. But a much higher incidence rate of 14.59 per 1000 catheter days was reported in a study done by M kaur et al [11]. This variability of incidences in various

studies could be due to various factors like insertion techniques, site of catheterization, type of catheter used, catheter care and diagnostic criteria used for diagnosing catheter related infection (CRIs). Incidence of catheter associated blood stream infections has been reported from 0.0 to 11.86 per 1000 catheter days in a study conducted by national nosocomial infection surveillance system in seven Indian hospitals [11].

In present study maximum numbers of cases of CRBSI were in the age group of 51- 60 years (35.7%) and maximum CVC colonization was seen in the age group of 31-40 years (26.66%). Both CVC colonization and CRBSI was found to be maximum in males as

compared to females. But in statistical analysis this association was found to be insignificant. In demographic analysis done by M Kaur et al significant mean age difference (P value < 0.05) was observed but the gender difference was found to be insignificant [11].

In present study catheter related infections were maximum when duration of central venous catheterization was more than 14 days and least in 1 to 7 days. In our study this association was found to be highly significant (p-.025). In a study done by R kaur et al and M kaur when CVCs that were used for greater than 7 days had a significantly greater association with infectious complications [10,11]. This can be attributed to skin organisms that colonized the distal intravascular tip of catheter ultimately cause bloodstream infection.

In our study, rate of CVC related infection was highest among internal jugular catheters insertion site (52.63%), followed by umbilical catheters insertion site (50%), least was observed in subclavian site (29.41%). This correlation was found to be statistically significant (p.023). This could be because of the close proximity of internal jugular vein to oropharyngeal secretions, presence of hair in the area, catheter motion and difficulty in maintaining sterile dressing as stated by Mermelet *al.*, [3]. Significant association was also obtained catheter associated infections and number of attempts for catheterization, as the multiple number of attempts increase chance of introduction of patients own flora by catheter in vein which can serve as source of blood stream infection. Patil HV et al reported the same correlation [13].

In our study *Klebsiella pneumoniae* (22.22%) was most common isolate in CVC colonization and CRBSI, followed by gram positive isolates i.e. *Coagulase negative staphylococcus* (20%) and *Staphylococcus aureus* (15.55%). Our findings are in concordance with study done by Mansur FJ et al who reported predominance of gram negative isolates as most common agents of CVC colonization and CRBSI [13]. The varying pattern of organism's isolated emphasize the importance of studying the pattern of infection in every setting and underscore the impact of environmental contaminant in the pathogenesis of device related infection. The relative high frequencies of gram negative organisms as predominant agents of catheter colonization and CRBSI was probably due to most of the studied catheter were collected from intensive care unit where chance of getting infection with gram negative organisms are very high. In our

study isolation of *Staphylococcus aureus* in large numbers from CRBSI cases probably suggests the hub colonization by the skin flora of the patient or medical personnel as the origin of infection.

Our study also observed predominance of non candida albicans species. Out of 5 fungal isolates, 3(60%) were *Candida tropicalis* and 2(40%) were *Candida albicans* similar finding were reported by FJ Mansur et al. in which candida non albicans were 6.7% of total isolated organism from CVC colonization [14].

In our study gram negative isolates showed maximum sensitivity to Polymixin B (100%) followed by Imipenem (93.33%). Metallo-beta lactamase (MBL) was reported in 20% of *Pseudomonas* isolates. Majority of *Klebsiella* spp were extended spectrum beta lactamases (ESBL) producers followed by *E.coli*. MBL production was observed in 6.66% of isolates especially in *Pseudomonas* spp and *Acinetobacter* spp. MRSA production was seen in 22.23% (n=2/9) of *Staphylococcus aureus* strains and 8.33% (n= 1/12) of *Coagulase negative staphylococcus* (MRSE). Similar findings were also reported in a study done by M Kaur et al [11]. The differences in organisms and their antibiotic susceptibility pattern as in various study reflects the difference in the resident flora of different hospital flora and their antimicrobial susceptibility pattern.

Most of the fungal isolates were resistant to Fluconazole (80%) and Ketoconazole (80%). Maximum sensitivity was observed to Amphotericin B (100%) and Nystatin (100%) and Itraconazole (80%).

Biofilm production was observed in 42.85% in CRBSI and 17.77% in CVC colonization. *Klebsiella* spp, was found to be maximum biofilm producer followed by *Pseudomonas aeruginosa*, CONS and *Staphylococcus aureus*. In present study among the fungal isolates biofilm production was observed in 60% especially in *Candida tropicalis*.

Conclusion

Bloodstream infections related to the use of central venous catheters are an important cause of patient morbidity, mortality, and increased health care costs. Our study highlights the predominance of multidrug resistant gram negative organisms which were also found to be biofilm producers. Continuous surveillance of catheter associated blood stream infections and

antimicrobial monitoring will provide information about changing pattern of organisms and guidelines for appropriate empirical antibiotic therapy. The importance of strict asepsis and ideal catheter care has to be reinforced. The management of CRBSI, including early and accurate diagnosis and therapeutic clinical decisions related to catheter removal, must be guided by current understanding of pathogenesis of infections.

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