

Central venous catheter-related bloodstream infections (CVC-BSI) in patients of clinically suspected septicemia

Afroz Z¹, Jobayer M¹, Ahmed S², Anwar S², Miah MRA²

¹Department of Microbiology, Dhaka Medical College, Dhaka, Bangladesh, ²Department of Microbiology and Immunology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
Email: zeenatafroz35@gmail.com

Abstract

Central venous catheter-related bloodstream infections (CVC-BSI) are associated with morbidity and mortality especially in critically ill patients. This study was performed to find out the rate of CVC-BSI and CVC colonization, causative organism and their antibiogram in patients of Intensive Care Unit (ICU) and Department of Nephrology of tertiary care hospitals. A total of 100 patients from Bangabandhu Sheikh Mujib Medical University (BSMMU) and Dhaka Medical College Hospital (DMCH) who had CVC and clinically suspected of septicemia were included in the study. Paired CVC blood and peripheral venous blood (PVB) samples were collected from each patient and were cultured by automated blood culture method. CVC-BSI was diagnosed in 11% and CVC colonization in 43% patients by Differential time to positivity (DTP) method. Rate of CVC-BSI was 8/1000 CVC days and 11/1000 CVC days in BSMMU and DMCH respectively whereas CVC colonization rate was 32/1000 CVC days and 47.5/1000 CVC days in BSMMU and DMCH. The most common bacteria causing CVC-BSI was *Klebsiella spp.* (36.4%) followed by *Acinetobacter spp.* (27.3%), *Pseudomonas spp.* (18.2%) and *E. coli* (18.2%). Among bacteria isolated from CVC colonization majority were *Pseudomonas spp.* (30.23%) and *Staphylococcus epidermidis* (30.23%) followed by *Acinetobacter spp.* (27.91%), *Enterococcus spp.* (6.98%). Most of the isolated bacteria causing CVC-BSI were resistant to commonly used antibiotics, but showed good sensitivity to imipenem and colistin. Information about CVC-BSI, colonization and antibiogram of this study can help to guide the selection of suitable antibiotics for empirical therapy and to improve infection control measures of the hospital.

Introduction

Intravenous catheterization is one of the most common invasive procedures among patients admitted in hospitals. Vascular access poses significant potential risks of catheter related bloodstream infections.¹ Central intravenous catheter are infected with the greatest frequency² and central venous catheter-related bloodstream infection (CVC-BSI) is the third most frequent nosocomial infection and is a threat to patient's safety.³

There is a wide diversity between hospitals in the causative pathogens and their antimicrobial susceptibility pattern. Mansur et al.⁴ in Bangladesh in a study reported that rate of CVC-BSI is 14% and the most common causative

pathogens were *Pseudomonas*, *Acinetobacter* and *Staphylococcus aureus*. Organisms causing CVC-BSI commonly are *Pseudomonas spp.*, *Acinetobacter spp.*, *Klebsiella spp.*, *Proteus spp.*, *Enterobacter spp.*, *E. coli*, *Staphylococcus aureus*, coagulase negative *Staphylococcus*.^{5,6}

Differential time to positivity (DTP) method is highly sensitive and specific for diagnosing CVC-BSI without removal of CVC.^{7,8} DTP has been defined as the time difference between the culture of CVC blood and peripheral venous blood (PVB) to become positive and the cutoff value of DTP is ≥ 120 minutes.⁸ There are several denominators for detection of CVC-BSI rate, eg. CVC-BSI rate in 100 CVCs or in 1000 CVC days or in 100 patients. The most recommended denominator of detection of CVC-BSI rate is the 1000 CVC days.⁹

This study was designed to acquire information about the CVC-BSI rate, type of organism causing CVC-BSI and their antibiotic susceptibility pattern in tertiary care hospitals.

Materials and Methods

This cross sectional descriptive type of study was conducted during the period of July 2011 to June 2012.

Study population: Patients having clinical signs symptoms of septicemia who had CVC for more than 48 hours that was given after admission in Intensive Care Unit (ICU) and in Department of Nephrology.

Sample Size: A total of 100 patients (23 from ICU of BSMMU and 41 from ICU of DMCH and 36 patients from Department of Nephrology of DMCH) were enrolled.

All laboratory works were performed in the Department of Microbiology and Immunology, BSMMU, Shahbagh, Dhaka.

Eight ml of blood was collected from both the CVC line and peripheral vein. After inoculation of blood into BACTAC culture vials they were transported to the Microbiology laboratory as soon as possible.

DTP was done by automated blood culture method as described by Raad et al.⁸ Paired vials (each vial containing 8 ml of blood) were introduced into BACTEC 9240 machine (Dickinson and Company, Maryland, USA). All samples were incubated at 37°C up to culture positivity and the vials were discarded if no growth was detected within seven days.

The time difference between the CVC blood culture and PVB culture to become positive (DTP) was calculated by following way:

DTP of the blood sample (expressed in minutes) = Time taken by peripheral venous blood culture to become positive – time taken by CVC blood culture to become positive

Positive sample of CVC blood and PVB were sub-cultured on blood agar and MacConkey agar and incubated aerobically at 37°C for 24 hours. If

growth was present then identification of the organism was done by colony morphology, Gram staining and biochemical tests.

Fig. 1: Show the graphical presentation of detection of CVC-BSI by DTP method.

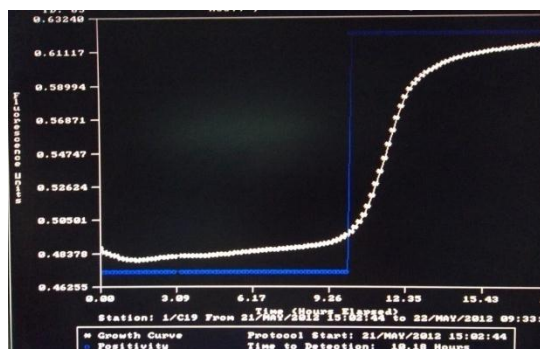


Figure - A

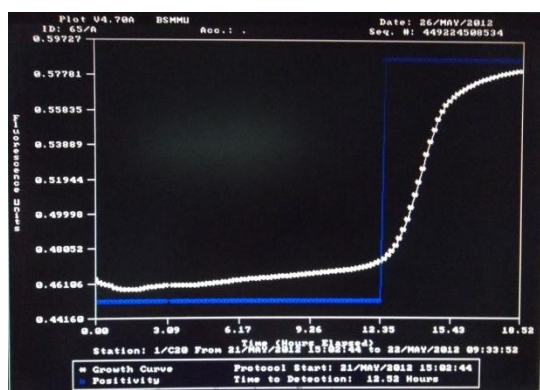


Figure - B

Fig. 1: Graphical presentation of detection of CVC-BSI by DTP method. Figure-A shows positive culture time (10.18 hrs.) of CVC blood and Figure-B shows positive culture time (12.52 hrs.) of PVB. The difference between CVC blood and PVB culture positivity is >120 minutes.

After organism identification antimicrobial sensitivity test was performed by disc diffusion method using Kirby-Bauer technique.¹⁰

- 1) Positive CVC-BSI: When difference in time between CVC blood culture positivity and PVB culture positivity is ≥ 120 minutes and isolated organism is identical in genus, species and antibiotic susceptibility pattern.
- 2) Non CVC-BSI/ BSI source other than CVC:
 - a) When difference in time between CVC blood culture positivity and PVB culture positivity is

<120 minutes or PVB culture become positive earlier than CVC blood culture and isolated organism is identical in genus, species and antibiotic susceptibility pattern.

b) If growth is present only in PVB culture but no growth in CVC blood culture.

3) CVC colonization: If growth is present only in CVC blood culture but no growth in PVB culture.

CVC-BSI rate was determined by the following method as mentioned by Salomao et al.¹¹

CVC-BSI rate = Total no. of CVC-BSI / Total no. of CVC days X 1000

CVC day determination: Total number of days of exposure to CVC by all of the patients in selected population during the selected time period.

Ethical consideration: The protocol of this study was approved by Ethical Clearance Committee (ERC) of Bangabandhu Sheikh Mujib Medical University. Informed written consent was taken from the patient or from their attendant before collection of blood samples. The anonymity of the participants and confidentiality of information was maintained strictly.

Result

Out of 100 patients, CVC-BSI was diagnosed in 11%, CVC colonization in 43%, Non-CVC-BSI in 10% patients. Among 23 patients of ICU of BSMMU, CVC-BSI was detected in 8.70%, CVC colonization in 34.78% and Non-CVC-BSI in 17.40% patients, whereas in 41 patients of ICU of DMCH, CVC-BSI was detected in 14.63% and CVC colonization in 43.90% and Non-CVC-BSI in 7.32% patients. Out of 36 patients, CVC-BSI was detected in 8.33% and CVC colonization in 47.22%, and Non-CVC-BSI in 8.33% patients of department of Nephrology of DMCH (Table I).

Table II shows the rate of CVC-BSI and CVC colonization in 1000 CVC days in two institutes. Rate of CVC-BSI was 8/1000 CVC days in BSMMU and 11/1000 CVC days in DMCH whereas CVC colonization rate was 32/1000

CVC days in BSMMU and 47.5/1000 CVC days in DMCH.

Table I: Rate of CVC-BSI and CVC colonization detected among the patients of different institutes

Institutes	Patients	CVC-BSI n (%)	CVC colonization n (%)	Non CVC-BSI n (%)
BSMMU				
ICU	23	2 (8.7)	8 (34.8)	4 (17.4)
DMCH				
ICU	41	6 (14.6)	18 (43.9)	3 (7.3)
Dept. of Nephrology	36	3 (8.3)	17 (47.2)	3 (8.3)
Total	100	11	43	10

CVC-BSI: Central venous catheter related bloodstream infection
CVC colonization: Central venous catheter colonization

Table II: Rate of CVC-BSI and CVC colonization in 1000 CVC days among the episodes.

Type of infection	BSMMU		DMCH	
	Episodes Total	Episodes /1000 CVC days	Episodes Total	Episodes/1000 CVC days
CVC-BSI	2	8	9	11
CVC Colonization	8	32	35	47.5

CVC days: Central venous catheter days.

Bacteria causing CVC-BSI and CVC colonization were isolated from 54 patients. Among 11 cases of CVC-BSI, the isolated organisms were *Klebsiella spp.* 36.4%, *Acinetobacter spp.* 27.3%, *Pseudomonas spp.* 18.2% and *E. coli* 18.2%. Among 43 bacteria isolated from CVC colonization *Pseudomonas spp.* were 30.23%, *Staphylococcus epidermidis* 30.23%, *Acinetobacter spp.* 27.91%, *Enterococcus spp.* 6.98%, *Klebsiella spp.* and *Staphylococcus aureus* was 2.33% (Table III).

Among the isolated *Acinetobacter spp.* from CVC-BSI patients, 66.67% were sensitive to colistin and imipenem, 33.33% was sensitive to cotrimoxazole.

Table III: Bacteria isolated from CVC-BSI and CVC-colonization.

Isolated organism	CVC-BSI (n=11)	CVC Colonization (n=43)
<i>Acinetobacter spp.</i> (n=15)	3 (27.3%)	12 (27.91%)
<i>Pseudomonas spp.</i> (n=15)	2 (18.2%)	13 (30.23%)
<i>Klebsiella spp.</i> (n=5)	4 (36.4%)	1 (2.33%)
<i>E. coli</i> (n=2)	2 (18.2%)	0 (0%)
<i>Staph. epidermidis</i> (n=13)	Nil	13 (30.23%)
<i>Enterococcus spp.</i> (n=3)	Nil	3 (6.98%)
<i>Staph. aureus</i> (n=1)	Nil	1 (2.33%)

All *Pseudomonas spp.* were sensitive to imipenem, 50% was sensitive to ceftazidime and colistin; 100% *E. coli* were sensitive to gentamicin, 50% was sensitive to cotrimoxazole and imipenem. All *Klebsiella spp.* were sensitive to gentamicin and imipenem, 50% were sensitive to cotrimoxazole and 25% was sensitive to amikacin (Table IV).

Table IV: Antibiotic susceptibility pattern of bacteria isolated from CVC-BSI.

Bacteria	Sensitivity (%)				
	Cip	Cot	G	Cro	Caz
<i>Klebsiella</i>	0	50	100	0	0
<i>Acinetobacter</i>	0	33.3	0	0	0
<i>E. coli</i>	0	50	100	0	0
<i>Pseudomonas</i>	0	-	0	-	50
	Ak	Imp	Net	TZP	CT
<i>Klebsiella</i>	25	100	0	-	-
<i>Acinetobacter</i>	0	66.7	0	0	66.7
<i>E. coli</i>	0	50	0	-	-
<i>Pseudomonas</i>	0	100	0	0	50

Cip-ciprofloxacin, Cot-Co-trimoxazole, G-gentamicin, Cro-ceftriaxone, Caz-ceftazidime, Ak-amikacin, Imp-imipenem, Net-netilmicin, TZP-piperacillin/tazobactam, CT-colistin.

Discussion

Central venous catheter-related bloodstream infections (CVC-BSI) are common type of nosocomial bloodstream infections.^{6,12} Although there are valid guidelines for good practice in central venous catheterization, CVC-BSI still is a serious problem especially in patients with long term catheterization.¹³

CVC-BSI and CVC colonization were detected by DTP method which is a newer and valid method for CVC-BSI diagnosis without removing the CVC. CVC-BSI rate was detected in 11% patients, CVC colonization 43% and non CVC-BSI was 10% in this study by DTP method. A cutoff value of DTP \geq 120 minutes was taken as standard value for diagnosing CVC-BSI which is supported by the findings of Blot et al.¹⁴ who found that DTP of \geq 120 minutes was sensitive and specific for diagnosing CVC-BSI.

The rate of CVC-BSI and CVC colonization were lower in patients of ICU of BSMMU than the patients of ICU of DMCH. The reason of low CVC-BSI in patients of ICU of BSMMU may be due to better infection control practice, such as CVC care, nurse patient ratio, visitor restriction, waste disposal etc. which is supervised by an infection control team. Holton et al.⁹ mentioned that effective infection control system, standardized CVC care and patient's immune status may contribute to the lower rate of CVC-BSI.

CVC colonization was found in 43% cases. Ideally intravenous catheters should remain sterile because bacteria from the colonization may cause silent infection and eventually clinical sepsis if the colonized catheters remain in situ for longer period.⁵ Such kind of colonized catheter should not be disregarded and as these organisms are potential pathogens that may sometimes cause diseases in the host these colonizing bacteria should be considered as a threat and patients with colonized catheters should be followed up for features of bloodstream infection.

The rate of CVC-BSI was found 8/1000 CVC days and 11/1000 CVC days in BSMMU and DMCH respectively whereas CVC colonization rate was 32/1000 CVC days and 47.5/1000 CVC

days in BSMMU and in DMCH. In a similar study at BIRDEM, Dhaka⁴ CVC-BSI rate was found 16/1000 CVC days and CVC colonization was 48.3/1000 CVC days. Such higher CVC-BSI rate was also reported in several studies in India,¹⁵ Taiwan¹⁶ and in Brazil¹⁷ ranging from 7.5 to 10.2 /1000 CVC days. The rate of CVC-BSI was 1.5 to 2.9/1000 CVC days in different ICUs of CDC National Healthcare Safety Network (NHSN) hospitals in the United States¹⁸ which is lower than this study. Developing countries have insufficient infection control measures, low nurse-to-patient ratio in hospital, limited financial or administrative support which may be responsible for higher CVC-BSI¹⁷. CVC colonization was also high in this study which might be due to prolong duration of CVC placement. Cronin et al¹⁹ reported 27% colonization in his study and mentioned that improper manipulation and prolonged placement of CVC is the reason for frequent CVC colonization.

Higher number of Gram negative rods was isolated from CVC-BSI and CVC colonization in this study. Highest rate of isolated bacteria was *Klebsiella spp.* followed by *Acinetobacter spp.*, *Pseudomonas spp.*, and *E. coli*. This finding correlated with the study by Bicudo et al.¹⁷ in Brazil who showed prevalent organism of CVC-BSI was *Acinetobacter spp.* followed by *Klebsiella spp.* and *Pseudomonas spp.* Mansur et al.⁴ in Bangladesh found *Pseudomonas* and *Acinetobacter* were the major causative agents of CVC-BSI that is also in accordance with the present study. Higher rate of Gram negative rods was also reported in several other studies.²⁰⁻²²

In this study, *Staphylococcus* was not found as causative agent of CVC-BSI but coagulase negative *Staphylococcus* and *Staph aureus* caused CVC colonization in 30.23% and 2.33% cases respectively. Mansur et al.⁴ observed only CVC colonization by coagulase negative *Staphylococcus* and *Staph aureus* but no CVC-BSI caused by them.

Most of the organisms causing CVC-BSI were resistant to common antibiotics used in ICU of BSMMU and DMCH. All isolated Gram negative bacilli were resistant to ciprofloxacin,

ceftriaxone and netilmicin. *Klebsiella spp.* and *E. coli* were also 100% resistant to ceftazidime. *Pseudomonas spp.* showed 100% resistance to tazobactam-piperacillin, gentamicin and amikacin; *Acinetobacter spp.* were 100% resistant to gentamicin, amikacin, ceftazidime and tazobactam-piperacillin. This sensitivity pattern was consistent with the antibiogram of organism isolated from ICU patients of CVC-BSI in several studies done in Brazil¹¹ and India.¹⁵

Possible explanation of infection by these resistant strains in ICU is the selection pressure exerted by extensive use of antibiotics and may be due to transmission of resistant clones between the patients.²³ Infections with resistant strains are transmitted among the patients due to inadequate implementation of infection control measures in institutes.²⁴

Conclusion: The rate of CVC-BSI and CVC colonization were significant and the isolated organisms from CVC-BSI were resistant to most of the common antibiotics used. Knowledge of this antimicrobial susceptibility pattern may aid to make an empirical antibiotic protocol.

Acknowledgement:

We acknowledge the department of ICU of BSMMU & DMCH and Department of Nephrology for providing support for the study.

References

1. Rosenthal VD. Central line-associated bloodstream infections in limited-resource countries: a review of the literature. Clin Infect Dis 2009; 49(12):1899-907.
2. Raad I and Darouiche R. Prevention of infections associated with intravascular devices. Curr Opin Crit Care 1996; 2: 361-62.
3. Richards MJ, Edwards JR, Culver DH, Gaynes RP. Nosocomial infections in combined medical-surgical intensive units in the United States. Infect Control Hosp Epidemiol 2000; 21: 510-15.
4. Mansur FJ, Barai L, Karim MM, Haq JA, Fatema K, Faruq MO. Intravascular catheter related infection and antimicrobial susceptibility pattern of isolated bacteria in a tertiary care hospital of Bangladesh. Indian J Med Microbiol 2014; 32(1): 68-71.

5. Brun-Buisson C, Abrouk F, Legrand P, Huet Y, Larabi S, Rapin M. Diagnosis of Central venous catheter-related sepsis-critical level of quantitative tip culture. *Arch Intern Med* 1987; 147(5): 873-77.
 6. Maki DG and Mermel LA. Infections due to infusion therapy. In: Bennett JV and Brachman PS. Eds. *Hospital infections*, 4th ed. Philadelphia: Lippincott-Raven, 1998: 689-724.
 7. Blot F, Schimidt E, Nitenberg G, Tancrede C, Leclercq B, Laplanche A, et al. Earlier positivity of central-venous- versus peripheral-blood cultures is highly predictive of catheter-related sepsis. *J Clin Microbiol* 1998; 36(1): 105-09.
 8. Raad I, Hanna HA, Alakech B, Chatzinikolaou I, Johnson MM, Tarrand J. Differential time to positivity: a useful method for diagnosing catheter-related bloodstream infections. *Ann Intern Med* 2004; 140(1): 18-25.
 9. Holton D, Panton S, Conly J, Embree J, Taylor G, Thompson W. Central venous catheter-associated bloodstream infections occurring in Canadian intensive care units: A six-month cohort study. *Can J Infect Dis Med Microbiol* 2006; 17(3): 169-76.
 10. Bauer AW, Kirby WMM, Sherris JC, Turck M. Antibiotic susceptibility testing by a standardized single disc method. *Am J Clin Pathol* 1966; 36: 493-96.
 11. Salomao R, Rosenthal VD, Grimberg G, Nouer S, Blecher S, Buchner-Ferreira S, et al. Device-associated infection rates in intensive care units of Brazilian hospitals: findings of the International Nosocomial Infection Control Consortium. *Pan Am J Public Health* 2008; 24(3): 195-202.
 12. Jarvis WR, Edwards JR, Culver DH, Hughes JM, Horan T, Emori TG, et al. Nosocomial infection rates in adult and pediatric intensive care units in the United States. National Nosocomial Infections Surveillance System. *Am J Med* 1991; 91: 185-91.
 13. Astagneau P, Maugat S, Tran-Minh T, Douard M, Longuet P, Maslo C, et al. Long-term central venous catheter infection in HIV-infected and cancer patients: a multicenter cohort study. *Infect Control Hosp Epidemiol* 1999; 20: 494-98.
 14. Blot F, Nitenberg G, Chachaty E, Raynard B, Germann N, Antoun S, et al. Diagnosis of catheter-related bacteraemia: a prospective comparison of the time to positivity of hub-blood versus peripheral-blood cultures. *Lancet* 1999; 354: 1071-77.
 15. Mehta A, Rosenthal VD, Mehta Y, Chakravarthy M, Todi SK, Sen N, et al. Device-associated nosocomial infection rates in intensive care units of seven Indian cities. Findings of the International Nosocomial Infection Control Consortium (INICC). *J Hosp Infect* 2007; 67: 168-74.
 16. Chen H, Wang F, Lin M, Lin Y, Huang L, Liu C. Risk factors for central venous catheter-related infections in general surgery. *J Microbiol Immunol Infect* 2006; 39: 231-36.
 17. Bicudo D, Batista R, Furtado GH, Sola A, de-Medeiros EAS. Risk factors for catheter-related bloodstream infection: a prospective multicenter study in Brazilian intensive care units. *Braz J Infect Dis* 2011; 15(4): 328-31.
 18. Edwards JR, Peterson KD, Andrus ML, Tolson JS, Goulding JS, Dudeck MA, et al. National Healthcare Safety Network (NHSN) Report, data summary for 2006, issued June 2007. *Am J Infect Control* 2007; 35: 290-301.
 19. Cronin WA, Germanson TP, Donowitz LG. Intravascular catheter colonization and related bloodstream infection in critically ill neonates. *Infect Control Hosp Epidemiol* 1990; 11: 301-08.
 20. Tan CC, Zanariah Y, Lim KI, Balan S. Central venous catheter related bloodstream infection: Incidence and an analysis of risk factors. *Med J Malaysia* 2007; 62(5): 370-74.
 21. Chatzinikolaou L and Raad I. Catheter related infections. *Iranian J Clin Infect Dis* 2006; 1(2): 79-87.
 22. Kurtz P, Rosa P, Penna G, Braga F, Kezen J, Drumond LE, et al. Antibiotic coated catheter to decrease infection. Pilot study. *Rev Bras Ter Intensiva* 2008; 20(2): 160-64.
 23. Meyer E, Jonas D, Schwab F, Reuden H, Gastmeier P, Daschner FD. Design of a surveillance system of antibiotic use and bacterial resistance in German intensive care units (SARI). *Infect* 2003; 31(4): 208-15.
 24. Rello J and Diaz E. *Acinetobacter baumannii*: a threat for the ICU? *Intensive Care Med* 2003; 29: 350-51.
-