Int.J.Curr.Microbiol.App.Sci (2017) *6*(7): 3940-3947

International Journal of Current Microbiology and Applied Sciences
ISSN: 2319-7706 **Volume 6 Number 7 (2017) pp. 3940-3947**
Journal homepage: http://www.ijcmas.com

Original Research Article https://doi.org/10.20546/ijcmas.2017.607.406

Multidrug Resistance Pattern in Confirmed Cases of Central Venous Catheter Blood Stream Infections in a Tertiary Care Hospital: A Prospective Study

Shilpa[1] and G.P. Aaftab[2]*

[1]Medanta Mediciti, Gurgaon, India
[2]Navodaya Medical College Hospital and Research Centre, Raichur, India
**Corresponding author*

Keywords

CVCBSI, Incidence rate, Antimicrobial resistance.

Article Info

Accepted:
29 June 2017
Available Online:
10 July 2017

A B S T R A C T

Central venous access which plays an important role in the management of critically ill patients, also puts patient at the risk of central venous catheter associated bloodstream infections (CVC-BSI). These infections are difficult to treat because they are being increasingly caused by multi-drug resistant organisms. This study was carried out to determine CVC-BSI rate in Intensive Care Units of a tertiary care hospital and to identify the antibiotic resistance profile of the infectious agents involved. Distal 5cm of the central venous catheter and blood samples were collected and processed using conventional culture methods as per standard protocol. During the study of one year, 720 patients were treated by indwelling catheter, of which 36 developed bloodstream infections, amounting to a CVC_BSI rate of 7.14 per 1000 catheter days. We observed that 73.07% of the Gram negative bacteria isolated from the cases were ESBL producers, 57.69% were AmpC producers and 34.61% were Co-producers of both ESBL and AmpC. Prevention of infusate contamination and aseptic handling by healthcare personnel will play a great role in bringing down the CVC-BSI rates and curb the nuisance of spread of multi drug resistant hospital acquired infections.

Introduction

Central line associated bloodstream infection (CLABSI) is a major contributing factor to in-hospital mortality and morbidity, extending the in-patient stay by 10 days and expenditure per patient by US$30,000 (Rello *et al*., 2000). In the intensive care unit setting the incidence of infection is often higher than in the less acute in-patient or ambulatory setting (Deepti *et al*., 2014). Nosocomial infections are frequently encountered in intensive care units (ICU) because of the severity of underlying diseases, the frequency of invasive interventions and the frequent use of wide-spectrum antibiotics (Dogru *et al*., 2010). Central Venous Catheter is often used as a portal for the delivery of medications, parenteral nutrition, collection of blood samples and monitoring hemodynamic variables in critically ill patients (Chopdekar *et al*., 2011). Central venous access not only plays an important role in the management of critically ill patients, but also puts patients at risk of various iatrogenic complications including central venous catheter associated bloodstream infections (CVC-BSI). Apart from the escalating rates, HAIs are now increasingly being caused by multi-drug-resistant organisms, which are difficult to

treat due to paucity of new antimicrobials (Mathur *et al*., 2015).

The most common microorganisms involved in Device associated nosocomial infections are those belonging to Enterobacteriaceae family, Acinetobacter species, Pseudomonas species, *Staphylococcus aureus*, and Coagulase Negative Staphylococci (Mehta *et al*., 2007; Kanj *et al*., 2012). Bio film formation in catheters has not only been implicated as an important factor involved in device related infection but also confers resistance to antimicrobial treatment. In a Centers for Disease Control and Prevention (CDC), National Nosocomial Infections Surveillance (NNIS) System report, the U.S. pooled mean rate of Central Venous Catheter (CVC)-related bloodstream infections, was 4.0 per 1000 CVC days (Rosenthal *et al*., 2006).

Over the past several decades, the frequency of antimicrobial resistance and its association with serious infectious diseases have increased at alarming rates (Pawar *et al*., 2008). Extensive antibiotic resistance has been observed in GNB. Antibiotic resistance develops through different mechanisms, such as the alteration of the drug target and drug inactivation by enzymes.

Production of Extended spectrum β-lactamases (ESBL),Amp C β lactamases (AmpC) and metallo β lactamases (MBL) are responsible for multidrug resistance of these pathogens (Joseph *et al*., 2010).

The present study has been undertaken to determine CVCBSI rate, in Intensive Care Units of our hospital, a tertiary care government hospital, Karnataka Institute of Medical Sciences Hospital (KIMSH), Hubballi, to identify the infectious agents involved and their antibiotic resistance profiles during the period between December 2013and December 2014.

Materials and Methods

Source of data

Samples collected from patients admitted in different Intensive Care Units such as Medical, Surgical, Orthopedic, Paediatrics, Neoanatal and Obstetrics Intensive Care Units (ICU) of Karnataka Institute of Medical Sciences Hospital, Hubballi.

Inclusion criteria

Patients admitted to the ICUs having central line associated blood stream infection which is defined as an infection that is identified at least 48 to 72 hours following admission associated with Central venous catheter. Patients having infection at the time of or prior to hospitalization were excluded from the study.

The central line was removed aseptically and the distal 5cm of the catheter amputated. Simultaneously blood samples were drawn for blood culture and inoculated on to BHI broth.

Processing in laboratory

Samples were inoculated onto Thioglycollate broth, Chocolate agar, Blood agar and Mac Conkey agar. The plates were incubated aerobically overnight at 37°C and observed for growth on the next day. If growth was observed in Thioglycollate broth, subcultures were made on chocolate and Mac Conkey agar. Brain heart infusion broth for blood culture was incubated up to 7 days. If growth was observed, a subculture was made on to chocolate agar and Mac Conkey agar. The identification and antibiotic sensitivity was done by the disc diffusion test as recommended by CLSI guidelines (2012). Screening test for ESBL production was done using Ceftazidime disks. A zone diameter of ≤ 22 mm was considered as probable ESBL

producer, which was confirmed by Phenotypic confirmatory disc diffusion test using Ceftazidime and Ceftazidime + Clavulanic acid (CLSI, 2013).

Isolates were screened for AmpC production using Cefoxitin disk. Isolates with Cefoxitin zone of < 18 mm were considered as screen positives. Phenotypic confirmation of AmpC beta-lactamase was done by using AmpC disk test.

Screening test for MBL production was done using Imipenem disk. Isolates with zone of < 19 mm were considered as screen positive and were subjected to Imipenem-EDTA Combined disk test for Phenotypic confirmation (Behera *et al*., 2008).

Isolates were screened for KPC production using Ertapenem disk. Isolates with Ertapenem zones ≤21 mm were considered as screen positive.

Phenotypic confirmatory test for KPC production was done using Modified Hodge Test (MHT) (CLSI, 2013).

Isolates were screened for MRSA production by Cefoxitin disc diffusion method. Zone size was interpreted according to CLSI criteria: susceptible, ≥22 mm; resistant, ≤21 mm.

Calculation of CVCBSI rate

CVCBSI rates per 1000 device days were calculated by dividing the total number of central venous catheter associated infection by the total number of device days and multiplying the result with 1000 (Guanche *et al*.,).

Statistical analysis: Statistical analysis was done by Fischer's Exact test using SPSS software and test of proportions wherever applicable.

Results and Discussion

During the study period of one year, 720 patients were treated by indwelling catheter, of which 36 patients developed bloodstream infection. The total central venous catheter days amounted to 3600 in the study population. A total 36 episodes of CVCBSI occurred in these patients, amounting to a CVCBSI rate of 7.14 per 1000 catheter days. The different organisms isolated were *Staphylococcus* species 10 (27.7%), *Acinetobacter baumanii 9(25%), Pseudomonas aeruginosa 8(22%), Klebsiella pneumonia 6(16.66%) followed by Citrobacter koseri 2(5.55%) and Escherichia coli 1(2.77%)* as shown in table 1.

Based on the screening tests and confirmatory tests conducted to determine the drug resistance mechanisms, we observed that, out of the total 36 CVCBSI cases, 26(72.22%) were caused by Gram negative bacteria, of which 19 (73.07%) were ESBL producing infections, 15 (57.69%) were AmpC producers and 9 (34.61%) were Co-producers of both ESBL and AmpC. Among the total 14 *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* isolated, 3 (21.42%) were MBL producers (Tables 2 and 3).

Among the 6 *Staphylococcus aureus* isolated from central line catheter samples of CVCBSI, 4 were Methicllin resistant *Staphylococcus aureus* (MRSA). However, out of the 4 CoNS, 2 were detected to be MR CoNSby cefoxitin disc diffusion test (Table 4). All the 36 cases of CVCBSI recovered with no deaths recorded

The pathogens isolated from CVCBSI patients showed multi drug resistance. The ESBL and AmpC beta lactamase producing organisms were almost unanimously resistant to ampicillin, cefazolin, cefotaxime, ceftriaxone, cefepime and tetracycline. The most effective antibiotic was Imipenem

followed by amikacin for the Gram negative isolates. The *S. aureus* was resistant to ampicillin and ciprofloxacin. All the *Staphylococci* isolates were sensitive to azithromicin, clindamicin, linezolid and vancomycin. The overall resistance pattern of the pathogens isolated from the CVCBSI patients is given below in table 5.

Nosocomial infections are one of the most important causes of mortality and morbidity as well as of the increase in health expenditures. It has been reported that ICUs account for 25% of nosocomial infections. In the ICU, central venous access might be needed for extended periods of time; patients can be colonised with hospital-acquired organisms, and the catheter may be manipulated several times daily for administration of fluids, drugs, and blood products. By several analyses, the cost of central venous catheter (CVC) associated bloodstream infections (BSIs) is substantial, both in terms of morbidity and in terms of financial resources. Through this study, an attempt has been made to assess the Central venous catheter associated bloodstream infection (CVCBSI) rate, in different Intensive Care Units of our hospital, to identify the infectious agents involved and their antibiotic resistance profiles during the period between December 2013 and December 2014.

In this study the central venous catheter associated bloodstream infection (CVCBSI) rate in 1000 catheter days was found to be 7.14. Various authors have reported variable data on CLABSIs from India (Kaur *et al*., 2012). Notably, Mehta *et al*., (2007) reported an overall hospital associated infection (HAI) rate of 4.4% and 9.1% per 1000 ICU-days and a CLABSI rate of 7.9 per 1000 catheter-days from a prospective surveillance carried out between July 2004 and March 2007 in 12 ICUs of the seven hospital members of the INICC in seven Indian cities. Recently Kaur *et al*., (2012) and Patil *et al*., (2011) from hospitals in India reported CLABSI rate of 2.8 per 1000 catheter days and 18.5%, respectively. Staphylococcus 10(27.7%) was the most common pathogen of CVC-BSI in the present study. Kaur *et al*., (2015) at Chandigarh India also reported *Staphylococcus aureus* as the most common pathogen in their study. The isolation of *S. aureus* from CVC-BSI cases probably suggests the hub colonisation by skin flora of the patient or medical personnel as the origin of infection. The isolation of *S.aureus* in large number points towards the lapse in catheter care. The other CVC-BSI associated pathogens were *Acinetobacter baumanni* 9(25%), *P.aeruginosa* 8(22%), *Klebsiella pneumoniae* 6(16.66%) and the same scenario was cited by Latif *et al*., (2009) who found that non fermenters like *P.aeruginosa* and *Acinetobacter* spp are the second most common bacterial agents in ICU settings after Gram positive cocci to be responsible for causing septicaemia.

Femoral venous site is most commonly associated with infectious complications followed by jugular and subclavian veins. Multi lumen catheters have been found to be increasingly implicated in CVC-BSI than single lumen catheters.

Antimicrobial resistance represents a major problem in the management of hospital acquired infection. Organisms isolated from patients in intensive care units are more likely to be resistant to antibiotics than those isolated from general ward patients or outpatients. Among Gram negative bacilli 19(73.07%) were ESBL producers, 15(57.69%) Amp C producers, 09(34.61%) were ESBL and AmpC Co-producers. Among *Klebsiella pneumoniae* and Pseudomonas aeruginosa 03(21.42%) MBL producers. None of the *Klebsiella pneumoniae* isolates were KPC producers.

Table.1 Isolated organisms from CVCBSI patients

Sr no	Category	Number (%)	Organism	Number (%)
1	GNB	26 (72.22%)	*Acinetobacter baumanii*	9 (25%)
			Pseudomonas aeruginosa	8 (22%)
			Klebsiella pneumoniae	6 (16.66%)
			Citobacter koseri	2 (5.55%)
			Escherichia coli	1 (2.77%)
2	GPC	10 (27.77%)	*Staphylococcus aureus*	6 (16.66%)
			Coagulase negative Staphylococci	4 (11.11%)

Table.2 ESBL, AmpC and Co-producers

Specimen	**Total number of specimen**	**Total no of GNB (%)**	**ESBL positive no (%)**	**AmpC positive no (%)**	**ESBL + AmpC positive no (%)**
Central venous catheter	36	26 (72.22%)	19 (73.07%)	15 (57.69%)	9 (34.61%)

Table.3 MBL producing isolates obtained from CVCBSI urine samples

Specimen	**Total no of *Pseudomonas* and *Klebsiella***	**MBL positive (%)**
Central venous catheter	14	3 (21.42 %)

Table.4 Methicillin resistance detected in *Staphylococci* isolated from CVCBSI samples

Specimen	***S.aureus***	**CoNS**
CVC	6	4
MRSA	4 (66.66%)	-
MRCoNS (%)	-	2 (50%)

Table.5 Multidrug resistance pattern of the CVCBSI isolates

	Organism						
		Acineto bacter	*P.aeruginosa*	*Klebsiella*	*C.koseri*	*E.coli*	*Staphylococcus*
Resistance pattern (%)	Ak	100	63	67	50	00	60
	Amp	100	100	100	100	100	100
	Amc	100	100	84	100	00	60
	Cz	100	100	100	100	100	-
	Cpm	100	100	100	100	100	-
	Cx	100	100	84	100	00	60
	Ctx	100	100	84	100	00	-
	Caz	100	100	84	100	00	-
	Ctr	100	100	84	100	00	-
	Cip	100	100	100	50	100	100
	Cot	100	100	100	100	100	-
	Gen	100	63	67	50	00	60
	Imp	00	37	34	00	00	-
	Te	-	-	-	-	-	50
	Az	-	-	-	-	-	00
	Cd	-	-	-	-	-	60
	Cot	-	-	-	-	-	-
	E	-	-	-	-	-	00
	Lz	-	-	-	-	-	00
	Va	-	-	-	-	-	00

A study conducted by Mehta *et al*., (2007) in ICU of seven Indian cities found that 46.4% of all HCAI were caused by Enterobacteriaceae, of which 74.1% were ESBL producers. 27.3% of HCAI were caused by Pseudomonas spp, of which 42.0% were MBL producers. Among Staphylococci 66.66% were identified as MRSA and 50% were MR CONS by cefoxitin disc diffusion test. Some of the studies have reported very high rate of MRSA 84%. Mehta *et al*., (2006) found that overall 87.5% of all Staphylococcus aureus HCAIs were caused by methicillin-resistant strains in their study. Imipenem, followed by Amikacin were the most effective antibiotics for the multi drug resistant Gram negative isolates. Whereas the Gram positive isolates from the CVC blood stream infections were sensitive to Linezolid, vancomycin and azithromycin.

The present study showed much higher incidence of CVCBSI due to Gram negative bacilli than those due to Staphylococcal BSI. This proves the importance of prevention of infusate contaminate and aseptic handling by healthcare personnel, the absence of which is associated with Gram negative bacterial blood stream infections.

References

Behera, B., Mathur, P., Das, A., Kapil, A., Sharma, V. 2008. An evaluation of four different phenotypic techniques for detection of metallo-beta-lactamase producing Pseudomonas aeruginosa. *Indian J. Med. Microbiol*., 26(3): 233-237.

Chopdekar, K., Chande, C., Chavan, S., Veer, P., Wabale, V., Vishwakama, K., *et al*. 2011. Central venous catheter-related blood stream infection rate in critical care units in a tertiary care, teaching hospital in Mumbai. *Indian J. Med. Microbiol.*, 29(2): 169-71.

Clinical and laboratory Standards Institute. 2012. Performance standards for antimicrobials susceptibility testing. Twenty-second informational Supplement, 50.

Deepti, Sinha, S., Sharma, S.K., Aggarwal, P., Biswas, A., Sood, S., *et al*. 2014. central Venous Catheter Related Bloodstream Infections In Medical Intensive Care Unit Patients in a Tertiary Referral Centre. *Indian J. Chest Dis. Allied Sci.*, 56: 85-91.

Dogru, A., Sargin, F., Celik, M., Sagiroglu, A.E., Goksel, M.M., Sayhan, H. 2010. The Rate of Device-Associated Nosocomial Infections in a Medical Surgical Intensive Care Unit of a Training and Research Hospital in Turkey: One-Year Outcomes. *Jpn. J. Infect. Dis.*, 63: 95-98.

Guanche-Garcell, H., Requejo-Pino, O., Rosenthal, V.D., Morales-Perez, C., Delgado-Gonzalez, O., Fernandez-Gonzalez, D. Device-associated infection rates in adult intensive care units of Cuban university hospitals: International Nosocomial Infection Control Consortium (INICC) finding.

Joseph, N.M., Sistla, S., Dutta, T.K., Badhe, A.S., Rasitha, D., Parija, S.C. 2010. Ventilator-associated pneumonia in a tertiary care hospital in India: role of multi-drug resistant pathogens. *J. Infect. Dev. Ctries.*, 4(4): 218-225.

Kanj, S.S., Kanafani, Z.A., Sidani, N., Alamuddin, L., Zahreddine, N., Rosenthal, V.D. 2012. International nosocomial infection control consortium findings of device-associated infections rate in an intensive care unit of a Lebanese university hospital, 4(1): 15-21.

Kaur, M., Gupta, V., Gombar, S., Chander, J., Sahoo, T. 2015. Incidence, risk factors, microbiology of venous catheter associated bloodstream infections – A prospective study from a tertiary care hospital. *Indian J. Med. Microbiol.*, 33(2): 248-254.

Kaur, R., Mathai, A.S., Abraham, J. 2012. Mechanical and infectiouscomplications of central venous catheterisations in a tertiary-level intensive care unit in northern India. *Indian J. Anaesthesia*, 56: 376-81.

Latif, S., Anwar, M.S., Ahmed, I. 2009. Bacterial pathogens responsible for bloodstream infection and pattern of drug resistance in a tertiary care hospital of Lahore. *Biomed.*, 25: 101-5.

Mathur, P., Tak, V., Gunjiyal, J., Nair, S.A., Lalwani, S., Kumar, S., *et al*. 2013. device-associated infections at a level-1 trauma centre of a developing nation: Impact of automated surveillance, training and feedbacks. *Indian J. Med. Microbiol.*, 33(1): 51-62.

Mehta, A., Rosenthal, V.D., Mehta, Y., Chakravarthy, M., Todi, S.K., Sen, N., *et al*. 2007. Device associated nosocomial infection rates in intensive care units of seven Indian cities. Findings of the International Nosomial infection Control Consortium (INICC). *J. Hosp. Infect.*, 67: 168-74.

Patil, H.V., Patil, V.C., Ramteerthkar, M.N., Kulkarni, R.D. 2011. Centralvenous catheter-related bloodstream infections in theintensive care unit. *Indian J. Crit. Care Med.*, 15: 213-23.

Pawar, M., Mehta, Y., Purohit, A., Trehan, N., Rosenthal, V.D. 2008. Resistance in Gram-negative bacilli in a cardiac intensive care unit in India: Risk factors

and outcome. *Annals of Cardiac Anaesthesia*, 11: 20-26.

Rello, J., Ochagavia, A., Sabanes, E., Roque, M., Mariscal, D., Reynaga, E., *et al*. 2000. Evaluation of outcome of intravenous catheter-related infections in critically ill patients. *Am. J. Respir. Crit. Care Med.*, 162(3 Pt 1):1027-30.

Rosenthal, V.D., Maki, D.G., Salomao, R., Moreno, C.A., Mehta, Y., Higuera, F. Device-Associated Nosocomial Infections in 55 Intensive Care Units of 8 Developing Countries. *Annals of Internal Med.*, 145(8): 582-591.

Singhal, S., Mathur, T., Khan, S., Upadhyay, D.J., Chugh, S., Gaind, R., *et al*. 2005. Evaluation of methods for AmpC beta-lactamase in Gram negative clinical isolates from tertiary care hospitals. *Indian J. Med. Microbiol.*, 23(2): 120-124.

How to cite this article:

Shilpa and G.P. Aaftab. 2017. Multidrug Resistance Pattern in Confirmed Cases of Central Venous Catheter Blood Stream Infections in a Tertiary Care Hospital: A Prospective Study. *Int.J.Curr.Microbiol.App.Sci.* 6(7): 3940-3947. doi: https://doi.org/10.20546/ijcmas.2017.607.406