

A study on Catheter related bloodstream infections (CRBSI) in Intensive care unit patients in a tertiary care hospital

Abirami E¹, Preethi Venkatesan², Priyadarshini Shanmugam^{3,*}, Shameem Banu Abdul Sattar⁴

¹PG Student, ²Assistant Professor, ³Professor, ⁴Professor & HOD, Dept. of Microbiology, Chettinad Hospital & Research Institute, Tamil Nadu

***Corresponding Author:**

Email: priyadarshini0018@gmail.com

Abstract

Introduction: Catheter related blood stream infections (CRBSI) independently increase hospital costs and length of stay. Knowledge about CRBSIs would help in improving infection control practices and managing nosocomial sepsis.

Objectives: To study the prevalence of central venous catheter related blood stream infections and to identify clinical risk factors & the microbiological profile of organisms causing CRBSI.

Materials & Methods: This was a prospective observational study carried out in the medical ICU of Chettinad Hospital and Research Institute, over a period of one year from March 2014 to February 2015. All adult non-immunocompromised patients admitted to the Intensive care unit(ICU), who had a non-tunnelled Central venous catheter(CVC) inserted were included. Blood cultures were taken at the time of CVC insertion. At the time of removal, catheters were cultured using semi-quantitative method(SQC) of Makialong with a paired peripheral blood culture. The incidence of BSI was measured per 1000 CVC days.

Results: A total of 82 patients with a cumulative 434 CVC days were included. Of this, 17 catheters (20.73 %) were positive for SQC. 3 patients (17.6%) had developed CRBSI, and the same organism with identical antibiogram pattern was isolated from both the blood and CVC tip. 10 patients (58.8%) had only catheter associated infection without bacteremia. 4 patients(23.5%) had positive blood cultures with different organism growing in CVC tip. CRBSI rate was 6.5/1000CVC days. The risk factors were diabetes mellitus, central line in situ for more than 7 days and emergency insertions. Out of the three definite CRBSIs, two patients grew *Klebsiella pneumoniae* and one patient grew *Staphylococcus epidermidis*. Of the 17 CVC tips which yielded positive growth, 53% were CoNS, followed by *Klebsiella pneumoniae*, *E.coli*, *Enterococcus* spp and *Candida*. CoNS was penicillin resistant and vancomycin sensitive. Majority of *Klebsiella pneumoniae* isolates were ESBL producers.

Conclusion: The knowledge of incidence of CRBSI and the microbiological spectra will be useful in formulating bundles of care and effective programs to control hospital acquired infections.

Introduction

In the era of modern medicine, nosocomial infection in critical care and high dependancy units is one of the greatest challenges. Nosocomial infection or "hospital- acquired infection" is defined as: "An infection acquired in hospital by a patient who was admitted for a reason other than that infection. An infection occurring in a patient in a hospital or other health care facility in whom the infection was not present or incubating at the time of admission".⁽¹⁾ Blood stream infections account for 14% of the hospital acquired infections and among them, Central venous catheters(CVCs) are the most common cause.⁽²⁾ CVCs are indicated for the administration of intravenous fluids, infusions of medications, and parenteral nutrition, as well as for hemodialysis access and

hemodynamic monitoring. The incidence of Catheter related blood stream infections (CRBSI) varies between ICUs due to differences in type of catheter used, insertion and utilization techniques, frequency of catheter manipulations and the patient cohort. Coagulase-negative Staphylococci (CoNS), and *Staphylococcus aureus* are the common causes of catheter related blood stream infections.^(3,4) Knowledge of the prevalence and the profile of the catheter related infections would help in improving infection control practices and managing nosocomial sepsis. The aim of this study was to study the prevalence & the risk factors associated with central venous catheter related blood stream infections and CVC colonizations for a period of one year in the intensive care unit of a tertiary care medical college hospital and to determine the microbiological profile and antibiotic resistance patterns of organisms causing CVC related blood stream infections

Materials and Methodology

This study was conducted in the 12-bedded Intensive care unit at the Chettinad Hospital & Research Institute (CHRI), a tertiary care hospital in Chennai. Institutional Ethical committee approval was obtained prior to commencing the study. It was a prospective observational study conducted over a period of 1 year from March 2014 to February 2015. All adult patients who were admitted to the ICU and with a central venous catheter(CVC) in place were enrolled for the study. Only those patients for whom the CVC had been inserted in our hospital were included. Written informed consent was obtained from all the patients/ Attendants.

Inclusion criteria: Patients above 18 years of age, willing to give consent and in whom the CVC had been inserted in the Intensive care unit of CHRI were included in this study.

Exclusion criteria: Patients with tunneled central venous catheters, immunocompromised patients and those suspected to have infective endocarditis were excluded from the study.

Detailed clinical history of the patients including age, sex, indication for ICU admission, comorbidities and use of systemic antibiotics were recorded. Details with regard to catheter insertion such as site of insertion, number of attempts, emergency/elective placement were also noted. A peripheral blood sample was collected from all patients in our study at the time of central venous catheter insertion to rule out existing bacteremia. All patients remained under daily follow up for any new onset of sepsis. In any case of new sepsis, detailed physical examination and investigations to rule out infection from other sources were done. The details

of the CVCs used in patients who died during the period of study were excluded. The skin surrounding the insertion site was carefully disinfected with chlorhexidine and the CVCs were removed under aseptic conditions. A 5-cm distal segment (tip) was collected in a sterile container from all catheters. All catheter tips were sent to the microbiology laboratory for semi quantitative culture (SQC) as described by Maki et al.⁽⁵⁾ In semi quantitative culture, the tip of the catheter was rolled minimum four times in a blood agar and then incubated at 37°C for 18 to 24 hours (Fig. 1). Positive catheter tip culture was identified as a growth with 15 colony forming units. For all the cases a paired peripheral blood culture was also sent. The duration of central venous catheter insertion and the reason for removal were noted. The organism was identified using the protocol in the Chart 1 & 2.



Fig. 1: Semi quantitative technique of Maki

Antibiotic Susceptibility Testing was performed by “Kirby-Bauer’s” disk diffusion method on Mueller Hinton agar plate. The test inoculum standardised with 0.5 McFarland standard was used to inoculate a Lawn culture on a Muller Hinton agar plate by making an even streaking of the swab over the entire surface of the plate in three directions, rotating the plate through an angle of 60° after each application. The inoculated plated was allowed to dry for few minutes in room temperature with lid closed and then the appropriate antibiotic discs were placed on the agar surface with the sterile forceps and pressed gently to make sure that the disc was in even contact with the medium. The discs were placed in such a way that they were 15mm away from the edge of the plate and the distance between each disc was not less than 25mm. Only 6 discs were placed per petri plate. The plates were incubated at 37°C aerobically overnight. The diameter of the zones were measured and interpreted as “Susceptible(S), Intermediate(I), Resistant(R)” as per CLSI guidelines 2015. The antibiotic discs used for Gram positive cocci were Azithromycin 15 µg, Erythromycin 15 µg, Clindamycin 2 µg, Cefoxitin 30 µg, Penicillin 10 µg, Cotrimoxazole 12.5/23.75 µg, Linezolid 30 µg,

Vancomycin (E strip), Tetracycline 30 µg, Chloramphenicol 130 µg, Ciprofloxacin 5 µg, Ofloxacin 5 µg, Gentamicin 10 µg, Teicoplanin 30 µg. For Gram negative organisms, the discs used for Enterobacteriaceae and Acinetobacter sp were: Ampicillin 10 µg, Cefazolin [1st generation cephalosporin], Gentamicin 10 µg, Tobramycin 10 µg, Amikacin 30 µg, Ciprofloxacin 5 µg, Norflox 10 µg, Nitrofurantoin 300 µg, Piperacillin/ Tazobactam 100/10µg, Cefuroxime [2nd generation cephalosporin] 30 µg, Cefotaxime [3rd generation cephalosporin] 30 µg, Cefipime [4th generation cephalosporin] 30 µg, Cotrimoxazole 12.5/23.75 µg, Imipenem 10 µg, Meropenem 10 µg., Tetracycline 30 µg, Chloramphenicol 130 µg, Aztreonam 30 µg, Ceftazidime 30 µg, Polymyxin B, Colistin (Estrip).

For Pseudomonas species the antibiotics used were Ceftazidime 30 µg, Gentamicin 10 µg, Tobramycin 10 µg, Carbenicillin 100µg, Piperacillin /Tazobactam 100/10µg, Amikacin 10 µg, Aztreonam 30 µg, Cefipime [4th generation cephalosporin] 30 µg, Ciprofloxacin 5 µg, Imipenem 10 µg, Meropenem 10 µg, Ofloxacin 5 µg, Polymyxin B, Colistin (Estrip).

Results

During the study period, a total of 94 patients had been inserted with a central venous cannula in the Intensive care unit of CHRI. 12 patients expired during the study period and were excluded from the study. 82 patients with a cumulative 434 CVC days were included in the study. During the study period a total of 17 catheters (20.73%) yielded positive growth by SQC. Microbiological profile of CVC tip culture is shown in Table 1. Of the 17 CVC tips showing positive growth, three (17.6%) patients had identical isolates from both the blood and the CVC tip. In these patients the antibiogram patterns were identical for both the isolates from the catheter tip and peripheral blood (CRBSI). CRBSI rate was 6.5/1000 CVC days. Four (23.5%) patients had positive peripheral blood cultures with different organism growing in SQC of CVC tip (Probable CRBSI). 10 patients (58.8%) had only CVC colonisation. Significant risk factors for CRBSI were presence of diabetes, CVC duration >7 days and emergency insertion. Factors such as indication for CVC insertion, site of insertion, total parenteral nutrition were not significantly associated with CRBSI incidence (Table 3). Of the three cases of CRBSI studied 2 isolates were *Klebsiella pneumoniae* and one was *Staphylococcus epidermidis*. Both the *Klebsiella* isolates were ESBL producers and the *Staphylococcus epidermidis* was resistant to penicillin (Fig. 2 & 3).

Table 1: Microbiological profile of CVC tip culture (n=17)

Organism	Total number of organisms in SQC positive CVP tip (n=17)	Percentage of SQC positive CVP tip (n=100%)
CoNS	9	53%
<i>Enterococcus</i> sp	1	6%
<i>Klebsiella pneumoniae</i>	3	18%
<i>E coli</i>	2	11%
<i>Pseudomonassp</i>	1	6%
<i>Candida</i>	1	6%

Table 2: Percentage of Positive and Negative Cultures

Result of SQC	Total number of cases (n =82)	Percentage
SQC Positive	17	20.73%
SQC Negative	65	79.26%

Table 3: Factors associated with CRBSI/probable CRBSI

Variables		Cumulative incidence of CRBSI and probable CRBSI	P value
Diabetes	Yes	4/21	0.04
	No	3/61	
TPN	Yes	1/8	0.675
	No	6/74	
Site of insertion	Internal Jugular Vein	5/51 (9.8%)	0.846
	Subclavian vein	1/23 (4.34%)	
	Femoral vein	1/8 (12.5%)	
Type of insertion	Elective	3/66	0.025
	Emergency	4/16	
Indication for insertion	Medications	5/52	0.647
	CVP monitoring	2/30	
Duration of CVC catheter	< 7 days	2/53	0.038
	≥ 7 days	5/29	

Chart 1: Algorithm for Identification of Gram-positive cocci - Catalase positive GPC

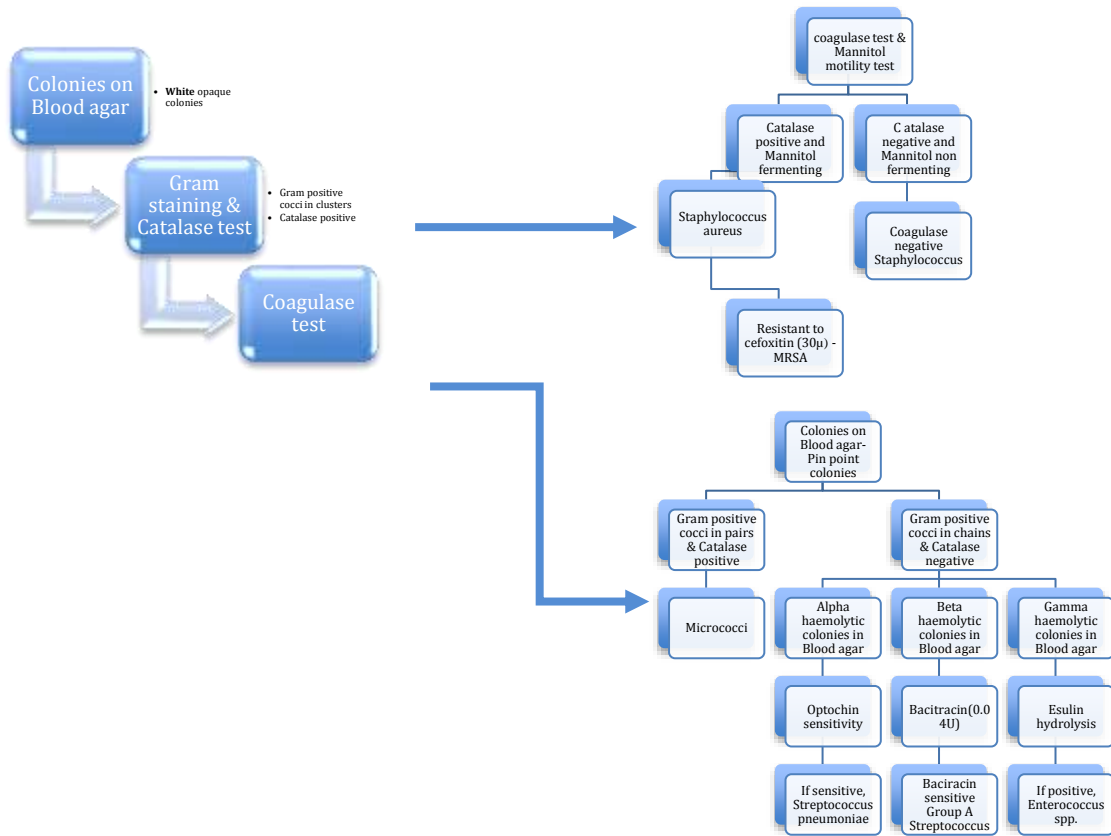


Chart 2: Algorithm for Identification of Gram-negative bacteria

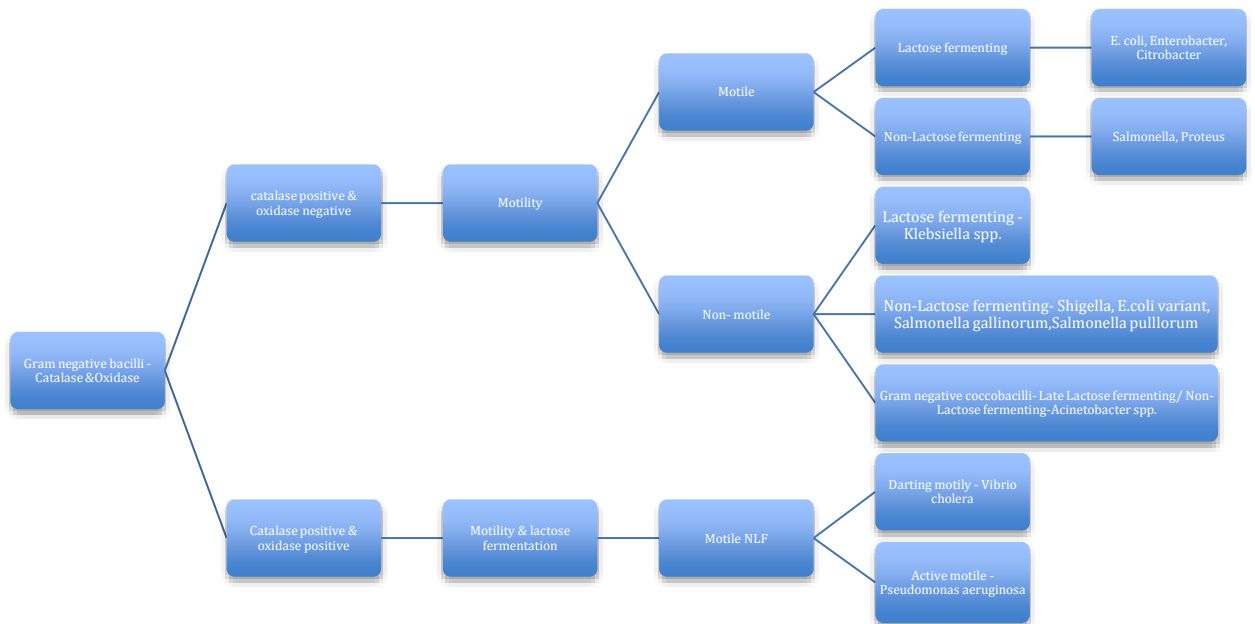
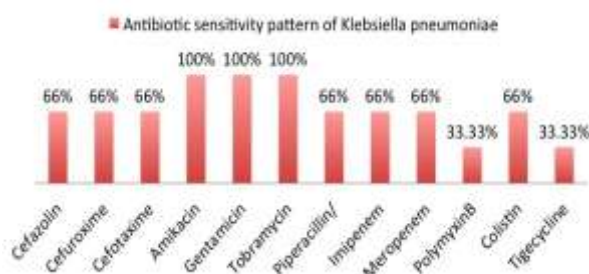
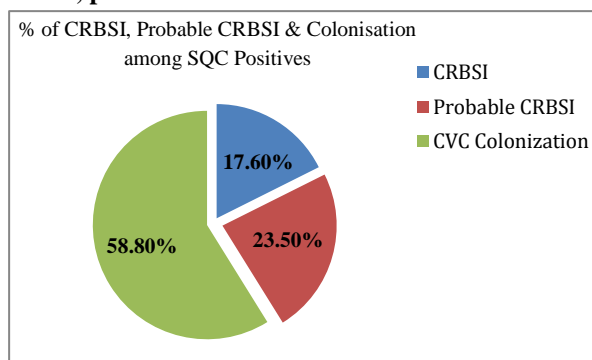
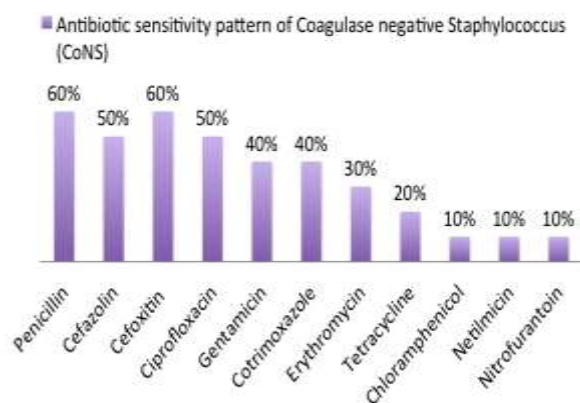


Chart 3: Percentage of CRBSI, probable CRBSI & Catheter colonization among SQC positive**Fig. 2: Antibiotic sensitivity pattern of *Klebsiella pneumoniae*****Fig. 3: Antibiotic sensitivity pattern of Coagulase negative Staphylococcus (CoNS)**

Discussion

Catheter related blood stream infections (CRBSI) can lead to both increased ICU stay and mortality.⁽⁶⁾ The rate of central venous catheter related bloodstream infections in patients admitted to our ICU was 6.5 per 1000 catheter-days. "The International Nosocomial Infection Control Consortium (INICC)" study conducted in 12 ICUs in seven Indian cities quoted similar result of 7.92 per 1000 catheter-days⁽⁷⁾ whereas a study from Netherlands reported a lower rate of CRBSI at 1.2 per 1000 catheter days for central venous catheters.⁽⁸⁾ The "semi quantitative technique" evaluated by Maki *et al.* was found to be sensitive and specific in detecting the central line associated bloodstream infections.⁽⁵⁾ In a study by Patil *et al.*, 15 (27.88%) catheters out of 54

were positive on SQC, out of which four (7.41%) were definitive central line associated bloodstream infections which was similar to our results.⁽⁹⁾ But Justeet *al.* reported 33.6% of the CVCs were positive on SQC.⁽¹⁰⁾ The variations in the incidence of CVC colonisation could be due to differences in the duration of CV catheters, site of insertion, mean age of the study group and the choice of skin disinfectant. If the CRBSI rates did not decrease even after implementation of comprehensive control measures, chlorhexidine/silver sulfadiazine or minocycline/rifampin -impregnated CVC can be used for patients in whom the catheter is expected to remain in place for more than 5 days.⁽¹¹⁾ As per the CDC guidelines, no recommendations are made with regard to the type of catheter material, which can be used to minimize CRBSI.

Presence of diabetes was found to be a significant factor in our study which was same as the study by Jia *et al.*⁽¹²⁾ Lorente *et al.* reported that in order to minimize the CRBSI risk, central line should be inserted in the following order subclavian, jugular and femoral vein.⁽¹³⁾ Deshpandeet *al.* reported that there was no statistically significant difference in the incidence of infection and colonization at the subclavian, internal jugular and femoral sites⁽¹⁴⁾ as in our study. The differences in the results could be related to the differences in indications for which CVCs were inserted, use of TPN and the duration of CVCs.

The association between emergency insertion of CVC and increased incidence of BSI was statistically significant. The study by Patil *et al.* also showed that catheter related infections were higher when inserted during an emergency than as an elective procedure.⁽⁹⁾ The compromise in the aseptic measures during insertion and the increased number of attempts during suboptimal condition in emergencies could probably explain the increased incidences. The catheter associated blood stream infections increased in a statistically significant fashion with increased duration of catheterization. Similarly Charalambous *et al.* also showed that central venous catheterization longer than five to seven days was associated with a higher risk of catheter-related infection.⁽¹⁵⁾ No attempts were made to replace catheters in our study as the CDC guidelines recommend against routinely replacing CVCs to prevent catheter-related infections.⁽¹¹⁾

The CVC tip cultures showed similar results as with the study conducted by Ramanathan Parameswaran *et al.* showing 64% of the pathogens causing CRBSI were Gram-positive and 36% were Gram-negative.⁽¹⁶⁾ On the contrary, Krishnan *et al.* isolated 56% gram negatives and 27% gram positives.⁽¹⁷⁾ CoNS was a major isolate

from the patients in our study. Similarly Rodrigo et al observed that most common isolate as CoNS accounting for 54%(18). In our study, the 2 *Klebsiella* spp isolated constitutes 18% of the isolates from CVC culture. Similarly the study by Almuneef et al reported that 16% of the isolates were *Klebsiella pneumoniae*.⁽¹⁹⁾ But lower rates were reported by Patil et al, who observed that out of 20 isolates, two (10%) were *K. pneumoniae*.⁽⁹⁾ Of the CoNS isolated in our study 60% were MRCoNS but 100% were sensitive to vancomycin, teicoplanin and linezolid. Multiple drug resistance were found in Gram negative organisms with only 12.5% of *Klebsiella pneumoniae* isolates sensitive to amikacin and 50% to meropenem, similar to the results of Ramanathan et al.⁽¹⁶⁾ The antimicrobial sensitivity patterns of common isolates provide guidelines for the physician in critical care medicine to start appropriate empirical antibiotic therapy depending upon the clinical scenario. This can be cost-effective and can prevent indiscriminate use of antibiotics.

Since our study design required a paired blood culture at the time of sepsis or at the time of removal of CVCs, patients who did not have suspected primary blood stream infections and the expired patients were not included in the study. However, some of these patients might have had unrecognized blood stream infection and hence led to an under-estimation of the rate of BSI in our study. The population in the present study sample is relatively small. More prospective studies of sufficient size, which address all potential risk factors will enhance our understanding of the pathogenesis of CVC-related BSI and guide to develop more effective strategies for their prevention.

Conclusion

The overall incidence of definite CRBSI in the present study was 3.7 per 1000 catheter days and the probable CRBSI was 4.9 per 1000 catheter days. CRBSI was higher among catheters that were placed insitu for 7 days or more. CVC infections were higher in emergency procedures as compared with elective procedures and also in diabetic patients. "The importance of hand hygiene, strict asepsis and ideal catheter care has to be reinforced and the health care workers in the critical care areas should be proficient in the techniques of sterile central venous catheter care". The knowledge of incidence of CRBSI and the microbiological spectra will be useful in formulating bundles of care and effective prevention programs of hospital acquired infections.

References

1. AS B. Control of communicable diseases manual. 16 ed. Washington: American Public Health Association; 1995.
2. Maki DG, Kluger DM, Crnich CJ. The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies. *Mayo Clinic proceedings*. 2006;81(9):1159-71.
3. Raad I, Costerton W, Sabharwal U, Sacilowski M, Anaissie E, Bodey GP. Ultrastructural analysis of indwelling vascular catheters: a quantitative relationship between luminal colonization and duration of placement. *The Journal of infectious diseases*. 1993;168(2):400-7.
4. Cobb DK, High KP, Sawyer RG, Sable CA, Adams RB, Lindley DA, et al. A controlled trial of scheduled replacement of central venous and pulmonary-artery

5. catheters. *The New England journal of medicine*. 1992;327(15):1062-8.
5. Maki DG, Weise CE, Sarafin HW. A semiquantitative culture method for identifying intravenous-catheter-related infection. *The New England journal of medicine*. 1977;296(23):1305-9.
6. 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(5):290-301.
7. 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(2):168-74.
8. Wittekamp BH, Chalabi M, van Mook WN, Winkens B, Verbon A, Bergmans DC. Catheter-related bloodstream infections: a prospective observational study of central venous and arterial catheters. *Scandinavian journal of infectious diseases*. 2013;45(10):738-45.
9. Patil HV, Patil VC, Ramteerthkar MN, Kulkarni RD. Central venous catheter-related bloodstream infections in the intensive care unit. *Indian journal of critical care medicine : peer-reviewed, official publication of Indian Society of Critical Care Medicine*. 2011;15(4):213-23.
10. Juste RN, Hannan M, Glendenning A, Azadian B, Soni N. Central venous blood culture: a useful test for catheter colonisation? *Intensive Care Med*. 2000;26(9):1373-5.
11. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis*. 2011;52(9):e162-93.
12. Jia L, Yu H, Lu J, Zhang Y, Cai Y, Liu Y, et al. [Epidemiological characteristics and risk factors for patients with catheter-related bloodstream infections in intensive care unit]. *Zhonghua yi xue za zhi*. 2015;95(9):654-8.
13. Lorente L, Henry C, Martin MM, Jimenez A, Mora ML. Central venous catheter-related infection in a prospective and observational study of 2,595 catheters. *Critical care*. 2005;9(6):R631-5.
14. Deshpande KS, Hatem C, Ulrich HL, Currie BP, Aldrich TK, Bryan-Brown CW, et al. The incidence of infectious complications of central venous catheters at the subclavian, internal jugular, and femoral sites in an intensive care unit population. *Crit Care Med*. 2005;33(1):13-20; discussion 234-5.
15. Charalambous C, Swoboda SM, Dick J, Perl T, Lipsett PA. Risk factors and clinical impact of central line infections in the surgical intensive care unit. *Archives of surgery*. 1998;133(11):1241-6.
16. Parameswaran R, Sherchan JB, Varma DM, Mukhopadhyay C, Vidyasagar S. Intravascular catheter-related infections in an Indian tertiary care hospital. *J Infect Dev Ctries*. 2011;5(6):452-8.
17. Gopalakrishnan R, Sureshkumar D. Changing trends in antimicrobial susceptibility and hospital acquired infections over an 8 year period in a tertiary care hospital in relation to introduction of an infection control programme. *J Assoc Physicians India*. 2010;58 Suppl:25-31.
18. Deliberato RO, Marra AR, Correa TD, Martino MD, Correa L, Dos Santos OF, et al. Catheter related bloodstream infection (CR-BSI) in ICU patients: making the decision to remove or not to remove the central venous catheter. *PLoS One*. 2012;7(3):e32687.
19. Almuneef M, Memish Z, Balkhy H, Hijazi O, Cunningham G, Francis C. Rate, risk factors and outcomes of catheter-related bloodstream infection in a paediatric intensive care unit in Saudi Arabia. *Journal of hospital infection*. 2006;62(2):207-13.