ISSN 0975-6299 Vol 3/Issue 2/April – June 2012

International Journal of Pharma and Bio Sciences

RESEARCH ARTICLE MICROBIOLOGY

MICROBIAL ARRAY AND ANTIBIOTIC SENSITIVITY PATTERN OF CATHETER RELATED BLOOD-STREAM INFECTION AT A TERTIARY CARE HOSPITAL IN SOUTH INDIA.

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ABSTRACT

Epidemiological data regarding catheter related blood stream infections (CRBI) in developing countries are scarce and essential to fabricate infection control and antibiotic prescription policies. Intravenous (IV) catheter tips and two synchronous blood samples from 297 patients with intravenous catheters and ≥ 48 hours stay were subjected to culture and sensitivity. Concurrent isolation of the same organism from both blood samples and catheter tips as well as same sensitivity pattern was considered significant for CRBI. The microbial array of CRBI was clinically correlated with age, clinical signs and symptoms and mortality. Out of the 297 cases studied 21.2% were associated with CRBI. Out of the positive 183 isolates S. epidermidis accounted for most [62 i.e. (34.4%)] of the isolates from I.V. Catheter tips while P. aeruginosa [67 (36.6%)] was the commonest isolate from the blood. The incidence of CRBI's due to S. epidermidis P. aeruginosa, Klebsiella spp., S. aureus, E. coli was 12.8%, 3.4%, 1.7%, 1.7% and 1% respectively. The isolation rate of all organisms in cases of septicemia (261) due to CRBI was 18.8%. Fourteen asymptomatic cases had CRBI - all due to *S. epidermidis. S. epidermidis* was most prevalent in all age groups. Among the isolates associated with CRBI, *S. epidermidis* were sensitive to vancomycin (100%) and resistant to most other dugs. Eighty percent of the *S. aureus* associated with CRBI were MRSA while 62% of the gram negative organisms were ESBL producing. Microbial spectrum and the sensitivity pattern of CRBI observed may be used to formulate stricter infection control and antibiotic policy in view of resistance to second line antibiotics.

ISSN 0975-6299 Vol 3/Issue 2/April – June 2012

KEY WORDS

Catheter related blood stream infection, Microbial spectrum, antibiotic sensitivity.

INTRODUCTION

Intravenous catheters (IVC's) are an integral part of medical management especially in "in-patient care". Such catheters may have to be kept in situ for long periods under various circumstances like in the intensive care units for diagnostic, therapeutic and monitoring of cardiovascular function. The colonization of such catheters by organisms which may be skin commensals or even nosocomial may be associated with catheter related blood-stream infections (CRBI). The common organisms which colonise catheters are *Staphylococcoccus epidermidis, Staphylococcus aureus*, *Pseudomonas* and *Acinetobacter* species and fungi like *Candida albicans* and *Candida parapsilosis*. [1] These organisms are usually resistant to standard antibiotics and hence add to the cost of treatment tremendously and necessitate prolonged hospital stay which usually becomes a vicious cycle difficult to break ultimately contributing to increased morbidity and mortality. The cost of treating a single episode of catheter-related bloodstream infection (CRBI) has been estimated to be in excess of $28 000.[2] The most common clinical findings associated with CRBI's have poor specificity (for example, fever with or without chills), and inflammation or purulence around the intravascular device has high specificity but poor sensitivity.[3] Isolation of the organism concurrently from blood and IVC tips remains the gold standard for the diagnosis of CRBI. We carried out a study in our hospital which is a tertiary care centre and often caters to patients requiring long term indwelling catheters with the aim to report the incidence, microbial spectrum and sensitivity pattern associated with CRBI.

MATERIAL AND METHODS

The study was carried out in our hospital from October 2007 to September 2009. The following samples were randomly taken from patients with intra-venous catheters (central or peripheral) for ≥ 48 hours stay in the hospital from various wards and ICU's irrespective of the primary diagnosis except those with blood culture positivity prior to 48 hours of hospital stay.

1. Intravenous catheter (IVC) tips duly transported in a sterile container subjected to culture by the roll plate technique
2. Two blood samples, 5 mL each, collected with full aseptic precautions taken < 10 minutes apart from two separate venipuncture sites for culture by inoculation into BHI broth and subsequent plating on nutrient agar and blood agar/ appropriate selective media.

Culture of catheter segment was done by the semi-quantitative roll plate method[4] wherein the IVC tip was rolled across on agar plate and after 24 hours incubation, the colony forming units (CFU's) were counted. A yield of 15 CFUs or higher was considered significant. Isolates from IVC tips and blood were and further tested for identification and subjected antibiotic sensitivity testing by the Kirby-Bauer Disc Diffusion Method. Concurrent isolation of the same organism from both blood samples and catheter tips as well as same sensitivity pattern was considered significant for CRBI.

OBSERVATIONS AND RESULTS

A total of 297 cases were included in the study of which 189 (63.6%) were males. The mean duration of IVC placement from all cases was 101.6 ± 12.4 hours with 88.2% of the IVC's being peripheral while rest were central lines. The mean duration of prior antibiotic therapy was 92.4 ± 9.8 hours. 24.1 % of the cases were neonates, while those in the age group 1 month to 14 years were 27.6%, the rest being > 14 years age.

Irrespective of the primary diagnosis for the purpose of "relevant clinical correlation" to our study, we grouped the clinical findings into three main groups:

1. Those with local thrombophlebitis with or without clinical signs and symptoms of septicemia – accounting for 105 (35.4%) cases.
2. Those with clinical signs of septicemia: consisting of two or more of the following present simultaneously: Increased (fever) or decreased (hypothermia) body temperature, Tachycardia or Bradycardia, Tachypnoea or Bradypnoea, Hypotension and/ or Leucocytosis – accounting for 261 (87.9%) cases.
3. Those cases with symptoms not fitting into septicemia, or totally asymptomatic (hereafter labeled as "Asymptomatic" group), which included samples from cases like: Cerebrovascular accidents (CVA), Post operative cases of Caesarian section, appendicectomy and others admitted in the orthopedics, ENT or Dermatology wards, Trauma patients etc accounting for 36 (12.1%) cases.

Out of these 297 cases studied 183 isolates were obtained - 36% were from I.V. Catheter tips (IVC), 46.8% were from blood, 21.2% from both blood and I.V. catheter tips (CRBI) and 14.8% were from I.V Catheter tip only. (Table 1) Out of the positive 183 isolates *S. epidermidis* accounted for most [62 i.e. (34.4%)] of the isolates from I.V. Catheter tips while *P. aeruginosa* [67 (36.6%)] was the commonest isolate from the blood. *S. epidermidis* accounted for 12.8% of CRBI [Table 1] The incidence of CRBI's due to *P. aeruginosa, Klebsiella spp., S. aureus, E. coli* was 3.4%, 1.7%, 1.7% and 1% respectively. *Candida albicans* isolated from blood in 3 neonates out of which one was proven to be associated with catheter tip positivity.

Table 1

Distribution of isolates from clinical samples (I.V. catheter tips and Blood)

Organisms	I.V Catheter tip Only	I.V Catheter + 2 Blood Cultures	Blood Culture Only	Total I.V. catheter tip isolates	Total isolates (%) [N = 297]
S. epidermidis	24 (8.1)	38 (12.8)	6 *	62 (20.9)	68 (22.9)
P. aeruginosa	8 (2.7)	10 (3.4)	57 (19.2)	18 (6.1)	75 (25.3)
S. aureus	8 (2.7)	5 (1.7)	5 (1.7)	13 (4.4)	18 (6.1)
E. coli	2 (0.7)	3 (1)	2	5 (1.7)	7 (2.4)
K. spp.	0	5 (1.7)	5 (1.7)	5 (1.7)	10 (3.4)
Acinetobacter spp.	0	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.7)
C. albicans	2 (0.7)	1 (0.3)	0	3 (1)	3 (1)
Total	44 (14.8)	63 (21.2)	76 (25.6)	107 (36)	183 (60.6)

(* = single blood culture sample isolates (probably non pathogenic/ not included in study)

The isolation rate of all organisms in cases of septicemia (261) due to CRBI was 18.8%. (Table 2) Out of the 105 cases with thrombophlebitis 45.7% were associated with CRBI while 38.9% of the 14 asymptomatic cases had CRBI - all due to *S. epidermidis*. (Table 2) Out of the 63 cases of CRBI's, *S. epidermidis* was most prevalent in all age groups (28.7% and 15.9% in the neonatal, pediatric and adults respectively). The second most common organisms in the neonatal period were *klebsiella spp.* and *S. aureus* (6.3% each) while that in the pediatric and adult patients was *Pseudomonas aeruginosa* accounting for 6.3%. Mortality attributable to CRBI's in the neonates was primarily associated with *K. pneumoniae* (6.3%) all of which were extended spectrum beta-lactamase (ESBL) producing while *Pseudomonas aeruginosa* accounted for most deaths associated with CRBI in the pediatric age group. *S. epidermidis* was associated with only 3 deaths 2 of which where neonates while the third was a 4 year old male child with primary diagnosis of tubercular meningitis.

Table 2

Comparison of the distribution of CRBI isolates with clinical manifestations: A Clinico - microbiological correlate. *[N = 297]*

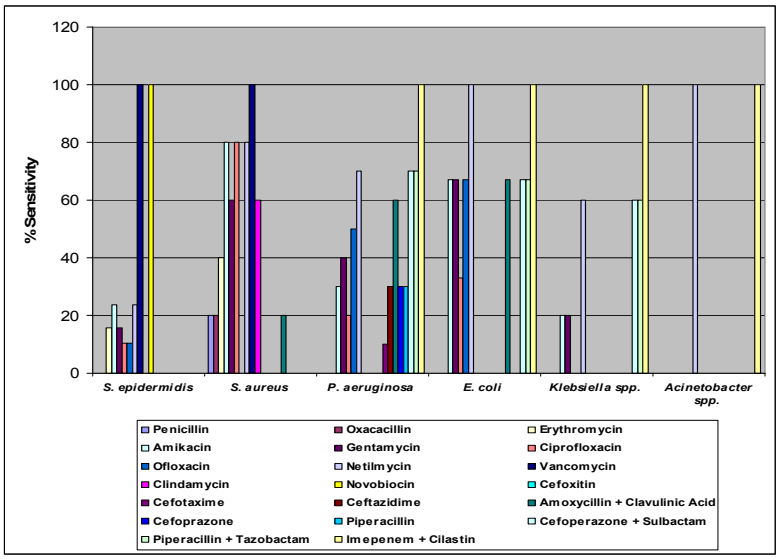
Clinical Manifestation	*S. epidermidis* (%)	*P. aeruginosa* (%)	*S. aureus* (%)	*E. coli* (%)	*Klebsiella spp.* (%)	*Acinetobacter spp.* (%)	*C. albicans* (%)	Total (%)
Local thrombophlebitis * (n = 105)	35 (33.3)	6 (5.7)	5 (4.8)	0	0	0	2 (1.9)	48 (45.7)
Septicemia † (n = 261)	24 (9.2)	10 (3.8)	5 (1.9)	3 (1.1)	5 (1.9)	1 (0.4)	1 (0.4)	49 (18.8)
Asymptomatic ‡ (n = 36)	14 (38.9)	0	0	0	0	0	0	14 (38.9)

* ***Cases with local thrombophlebitis with or without signs of clinical sepsis.***
† ***Cases with signs of clinical sepsis as defined in the text.***
‡ ***Cases with no signs of clinical sepsis.***

Among the isolates associated with CRBI, *S. epidermidis* were sensitive to vancomycin (100%), erythromycin(15.8%), amikacin (23.7%), netlimycin (23.7%), ciprofloxacin (10.5%). Eighty percent of the *S. aureus* associated with CRBI were MRSA. *P. aeruginosa* exhibited sensitivity to cefoperazone, ceftazidime (30%), piperacillin(30%), compared to cefoperazone + sulbactam(70%), piperacillin + tazobactam (70%), amoxicillin + clavulinate (60%), imepenem + cilastin (100%) indicating high degree ESBL producing strains prevalent in the hospital (61.8%). The sensitivity pattern of other gram negative organisms isolated from CRBI's is depicted in the Figure 1 and was suggestive of similar ESBL producers as *Pseudomonas aeruginosa.* Notably, 33 – 40 % resistance was noted to piperacillin + tazobactam combination amongst the gram negative isolates. The single *Acinetobacter spp.* isolated was resistant to all except imepenem + cilastin. Amongst the aminoglycosides, netlimycin showed 60 – 100 % sensitivity against most isolates except *S. epidermidis* (23.7%)

Figure I

Antibiotic sensitivity pattern of isolates from cases with catheter related bloodstream infections.



DISCUSSION

Catheter related blood-stream infections (CRBI) form a major portion of nosocomial infections accounting for 21.1% in our study. A total of 250,000 cases of CVC-associated BSIs have been estimated to occur annually if entire hospitals are assessed rather than ICUs exclusively.[5] The most common organisms associated with CRBI's are CNS, predominantly *S. epidermidis*.[6,7,8,9] A study during 1986–1989, reported CNS, followed by *Staphylococcus aureus*, were the most frequently reported causes of bloodstream infections (BSIs), accounting for 27% and 16% of BSIs, respectively.[10] (Table 3) Pooled data from 1992 through 1999 indicate that CNS (37%), followed by *S. aureus* and enterococci (13% each), are now the most frequently isolated causes of hospital-acquired BSIs.[11] (Table 3) The same study reported that gram-negative bacilli accounted for 19% of catheter-associated BSIs during 1986–1989 compared with 14% of catheter-associated BSIs during 1992–1999. [11] The incidence of CRBI due to Gram negative organisms in our study was 31.7%, with striking preponderance of ESBLs. In another study by Stéphane Hugonnet at al [12] out of 113 episodes of BSI, 33 (29.2%) were microbiologically confirmed, and 80 (70.8%) were clinical sepsis. The most frequently isolated microorganisms were coagulase-negative staphylococci (n = 21 / 18.6%). Other gram-positive cocci were *Staphylococcus aureus* (n = 1) and *Enterococcus faecalis* (n = 2). Gram-negative rods included *Enterobacter aerogenes* (n = 2), *Serratia marcescens* (n = 2), *Escherichia coli* (n = 1), *Proteus mirabilis* (n = 1), and *Pseudomonas* non-*aeruginosa* (n = 1). Other microorganisms found were *Candida albicans* (n = 1) and *Propionibacterium acnes* (n = 2). [Table 3] According to a study by Anisio Storti et al[7], their findings suggest that 23.8% catheters were related to bloodstream infections, a percentage much higher than that reported by Maki [13] , who noted that central venous catheters pose a greater risk of device-related infection than does any other indwelling medical device, with infections rates of 3 to 5%. A prospective surveillance programme in USA detected 108 episodes of nosocomial bacteremia caused by coagulase-negative

staphylococci (seven per 10,000 admissions) of which seventy-two (66.7%) patients had at least two culture bottles that showed growth of coagulase-negative staphylococci plus one or more cultures that showed growth at another site or on a vascular catheter. [14] Nasia Safdar et al (2005 USA)[15] noted that out of a total of 251 PICCs inserted in 115 patients were studied prospectively over a mean duration of catheterization of 11.3 days (total, 2,832 PICC-days) Fifty-two PICCs (20.7%) were colonized at removal. Six PICC-related BSIs (2.4%) were confirmed, all showing concordance between cultures obtained from an infected PICC and blood cultures. BSIs were caused by coagulase-negative staphylococci [4/(1.6%)] *Staphylococcus aureus*(1) and *Klebsiella pneumoniae*(1) at a rate of 2.1 per 1,000 catheter-days. A more rigorous adherence to asepsis protocols in the developed nations may explain the discrepancy in the observation between the latter and our study.

Table 3
***Most Common Pathogens Isolated From Bloodstream Infections*.**

Pathogen	Present study (%)	Schaberg DR et al[10] (%)	CDC (NNIS System report)[11] (%)	Stéphane Hugonnet et al[12] (%)	Anisio Stortiet al[7] (%)
Coagulase-negative staphylococci	21.1	27	37	18.6	29.6%
S aureus	6.1	16	13	0.9	8.3%
Enterococcus	-	8	13	1.8	-
Gram-negative rods	36.6	19	14		52.7
E coli	2.4	6	2	0.9	-
Enterobacter	-	5	5	1.8	8.3
P aeruginosa	25.3	4	4	-	16.7
K pneumoniae	3.4	4	3	-	-
Acinetobacter spp.	0.7	-	-	-	8.3

CDC: Centre for Disease Control
NNIS: National Nosocomial Infections Surveillance

A Columbian study[16] on device associated with infections among neonates reported that the most common micro-organisms isolated were Gram-positive bacteria (60 %), followed by Gram-negative bacteria (36.3 %) and fungi (3.03 %). Sixty nine percent of coagulase-negative staphylococci (CoNS) and 100 % of *Staphylococcus aureus* were resistant to methicillin and all staphylococci and enterococci were susceptible to vancomycin. [16] These findings are in concordance with our study except the fact that we had no isolates of enterococci. Enterobactereciae were susceptible to third-generation cephalosporins, carbapenems, ciprofloxacin and piperacillin-tazobactam. *Acinetobacter baumannii* was susceptible to all the antibiotics tested. Contrary to their findings most of the Enterobactereciae in our study were ESBL producers. An alarmingly high degree of resistance to amikacin, piperacillin + tazobactam compared to netlimycin observed in our study may be due to the prescription pattern of drugs in our institution, where netlimycin is reserved as a second line drug while amikacin is commonly used in combination with extended spectrum penicillins and third generation cephalosporins.

There were some drawbacks in our study. The study was based on a single tertiary care unit and the denominator for the rates was

small compared to the NNIS and the fact that we have used the roll plate technique for culturing catheter tips which does not detect intraluminal colonization.

CONCLUSION

negative CRBIs and its impact on outcome would provide the necessary impetus for us and other to change the current practice and adopt stricter infection control policies. The high incidence of resistance to second line antibiotics is alarming. Standard infection control (IC) programmes and device-associated infection (DAI) rates are limited in developing countries, although several studies have shown that surveillance programmes, infection rate feedback and education have resulted in a significant impact on CRBI.[17] With the health services in developing nations "coming of age", strict hospital asepsis protocols for not only insertion but care and maintenance of IVCs along with antibiotic policy is the need of the hour for most institutions.

The epidemiological data projec

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