

A RETROSPECTIVE STUDY ON BLOOD STREAM INFECTIONS AND ANTIBIOTIC SUSCEPTIBILITY PATTERNS IN A TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Blood stream infections range from self-limiting infections to life-threatening sepsis causing significant mortality and morbidity worldwide and require rapid and aggressive anti-microbial treatment. Rational and correct use of antibiotics requires understanding of common pathogens and drug resistance patterns in a community. A retrospective study was conducted to identify the microbial profile in the blood culture isolates and their antibiotic susceptibility patterns in a tertiary care teaching hospital. The reports of specimens submitted for blood culture during the period of January to December 2009 to the microbiology laboratory were obtained, the positive cultures were identified, and data on the microbial species and their antibiotic sensitivity patterns were collected. There were 3442 blood culture samples, of which 289 (8.39%) were identified to be culture positive (174 (60.2%) males and 115 (39.7%) females; mean age 43.9 ± 24.08 years). Of 289 positive cultures, 277 (96.19%) showed bacterial growth, 106 (37.7%) were gram-positive and 168 (59.1%) gram-negative. *Candida* species were isolated from 12 (4.15%) specimens. *Staphylococcus aureus* and *E. coli* were the most common bacterial organisms identified to cause blood stream infections. *Staphylococcus aureus* was found to be highly sensitive to vancomycin (86.61%) linezolid and ciprofloxacin (60.16%); resistant to ampicillin, erythromycin and cephalosporins. *E. coli* was highly sensitive to amikacin (86.8%) and piperacillin + tazobactam (77%); resistant to ampicillin and cephalosporins. Specific antibiotic utilization strategies like antibiotic restriction, combination therapy and usage according to the standard antimicrobial susceptibility testing may help to decrease or prevent the emergence of resistance and incidence of blood stream infections.

Keywords: Bacteria, Blood stream infections, Antibiotics, Susceptibility

INTRODUCTION

Blood stream infections cause significant morbidity and mortality worldwide and are among the most common healthcare associated infections. Microorganisms present in circulating blood whether continuously or intermittently are a threat to every organ in the body. Approximately 200,000 cases of bacteraemia and fungemia occur annually with mortality rates ranging from 20-50%¹.

Since early 1950s, there is striking increase in incidence of bacteraemia caused by members of enterobacteriaceae and other gram negative bacteria *Escherichia coli* which was reported to be common in the past is being replaced by other multidrug resistant bacteria like *Klebsiella*, *Enterobacter*, *Salmonella*, *Citrobacter*, *Pseudomonas*, *Acinetobacter* etc.

Illness associated with blood stream infections range from self-limiting infections to life-threatening sepsis that requires rapid and aggressive anti-microbial treatment. The incidence of blood stream infections in patients has been reported to correlate with the increasing use of central venous catheters patient illness (e.g., oncology and burn and trauma and high risk nursery), and other pre disposing factors including intensive care unit (ICU) stay, lapses in hand washing and non adherence to infections control practices of medical staff. Respiratory, genitourinary, and intra abdominal foci are often identifiable sources of blood stream infections².

A wide spectrum of organisms has been described and this spectrum is subjected to geographical alteration. The diversity of bacteria recovered from blood cultures in the present day medical practice appears endless and published works from leading medical laboratories worldwide appear not to have really come up with final list of this group of organisms³.

The important factors contributing to this scenario probably being due to: the sources of clinical infections in a locality; the extent and precision of the laboratory procedures carried out; and also very importantly experience of the laboratory personally involved⁴. This factors listed above have also contributed in no small way to the pattern and the types of bacteria recovered from blood culture specimens in various health centers across the country ranging from

the specialist and teaching hospitals to the clinics at the district levels⁵.

Nowadays, bacterial drug resistance is an important problem and due to wide variations in bacterial drug resistance, results of studies and reports in one region or in one period of time are not necessarily true for other regions or periods of time. They are related with a series of social, environmental and technological changes^{6,7}.

The isolated bacteria are numerous and their associated diseases need urgent and invasive management with antimicrobial agents. Rational and correct use of these agents requires understanding of common pathogens and drug resistance patterns in the region⁸.

Due to constantly evolving antimicrobial resistant patterns there is need for constant antimicrobial sensitivity surveillance. There appears to be a paucity of surveys from developing countries in general, and from the Indian subcontinent in particular. Determination of antibiotic sensitivity patterns in periodic intervals is mandatory in each region for the clinicians to be aware of the emerging pathogens that pose a threat to the community, to provide safe and effective empirical therapies, develop rational prescribing practices and make policy decisions in a hospital and finally assess the effectiveness of all⁹.

A study was conducted to identify the bacteriological profile and their antibiotic susceptibility patterns by analyzing the data on the blood culture isolates of a tertiary care teaching hospital.

MATERIALS AND METHODS

A retrospective analysis of data was conducted in a 1700 bedded tertiary care teaching hospital of South India, after obtaining approval of the institutional ethical committee. Reports of specimens submitted for blood cultures during the period of January to December 2009 to the microbiology laboratory of the hospital were analyzed and the positive cultures were identified. Data including patient demographics (age, sex), microbial species (as recorded in the blood culture reports) and the antibiotic sensitivity patterns of identified pathogens were collected from all positive

blood culture reports. The antibiotic susceptibility patterns of the organisms were performed by Kirby- Bauer's disk diffusion method¹⁰ on Mueller Hinton agar plates. The antibiotic discs that were used to identify the susceptibility pattern of the bacterial pathogens and their concentrations included: Ampicillin (10 mcg), amikacin (30 mcg), cephalexin (30 mcg), ceftazidime (70 mcg), cefixime (5 mcg), cefipime (30 mcg), ceftazidime + sulbactam (70 mcg), ciprofloxacin (5 mcg), cotrimoxazole (trimethoprim /sulphamethoxazole 1.25/23.75 mcg), erythromycin (10 mcg), gentamicin (10 mcg), imipenem (10 mcg), linezolid (30 mcg), ofloxacin (5 mcg), piperacillin + tazobactam (100/10 mcg), tetracycline (30 mcg), and vancomycin (30 mcg). The data obtained were tabulated and analyzed to identify the common causative pathogens of blood stream infections and the antibiotics to which the identified organisms were sensitive and resistant. The results obtained were expressed by descriptive statistics.

RESULTS AND DISCUSSION

A total of 56,711 biological specimens were sent for culture to the microbiology lab during the period of January to December 2009. There were 3442 blood culture samples, of which 289 (8.39%) were identified as culture positive samples. The gender distribution of positive samples was found to be 174 (60.2%) males and 115 (39.7%) females with a mean age of 43.9 ± 24.08 years.

The positive samples belonged to 242 (83.7%) adults (age range >18years) comprising of 146 (50.5%) male and 96 (33.2%) female patients, with mean age of 51.2 ± 18.74 years; 12 (4.15%) adolescents (age range 13-18years) which included 8 (2.7%) male and 4 (1.38%) female patients with a mean age of 15.9 ± 1.67 years; 23 (7.95%) children (age range 1-12years) which included 16 (5.53%) male and 7 (2.42%) female patients with mean age of 3.9 ±

3.36 years; 12 (4.15%) infants (age range <1year) which included 4 (1.38%) male and 8 (2.76%) female patients with mean age of 0.23 ± 0.22 years [Table 1].

Out of 289 positive cultures, 277 (96.19%) showed bacterial growth, of which 106 (37.7%) were gram-positive and 168 (59.1%) were gram-negative. Among 277 cultures with bacterial growth, 274 (98.9%) were monomicrobial and 3(1.08%) were polymicrobial (both gram positive and gram negative). *Candida* species were isolated from 12 (4.15%) specimens. Majority of the cultures with bacterial isolates were obtained from adults above the age range of 18 years (227 monobacterial and 3 polybacterial growth). 23 children (age range 1-12 years), 12 adults (age range 13-18 years) and 12 infants (< 1 year of age) showed culture positive for mono bacteria [Table 2].

The most commonly isolated gram-positive bacteria were *Staphylococcus aureus* in 78 (72%), *Enterococcus faecalis* 24 (22.1%), *Streptococcus* 6 (5.5%) and *Micrococcus* in 1 (0.91%) blood cultures [Table 3].

The most prevalent gram-negative bacteria found in positive cultures were *Escherichia coli* in 61 (35.6%) cultures, followed by *Salmonella typhi* in 44 (25.7%), *Klebsiella pneumoniae* 24 (14.0%), *Pseudomonas aeruginosa* in 15(8.7%), *Acinetobacter baumannii* in 21 (12.2%), *Enterobacter sp.* in 4 (2.33%), *Aeromonas hydrophila* 1 (0.58%), *Moraxella catarrhalis* in 1(0.58%) culture specimens. *Staphylococcus aureus* and *E. coli* were the most common bacterial organisms identified to cause blood stream infections [Table 4]. 3 patients whose culture had polymicrobial growth had *Enterococcus faecalis* + *Klebsiella pneumoniae*, *Acinetobacter baumannii* + *Staphylococcus aureus*, and *Enterococcus faecalis* + *Escherichia coli* as organisms in one patient (33.33%) each.

Table 1: Age and sex distribution of positive blood culture

Age range (years)	No. of patients (n=289)			
	Males		Females	
	N	%	n	%
< 1 (Infants)	4	1.38	8	2.76
1 - 12 (Children)	16	5.53	7	2.42
13 -18 (Adolescents)	8	2.76	4	1.38
>18 (Adults)	146	50.5	96	33.2
Total	174	60.17	115	39.76

Table 2: Age and number of bacterial isolates per culture

AGE (years)	No. of Patients (N=277)	
	Monomicrobial	Polymicrobial
< 1 (Infants)	12 (4.33%)	0
1 - 12 (Children)	23 (8.30%)	0
13 -18 (Adolescents)	12 (4.33%)	0
>18 (Adults)	227 (81.9%)	3 (1.08%)
Total	274 (98.9%)	3 (1.08%)

Table 3: Distribution of gram positive organisms

Organisms	No of isolates (n=109)	
	N	%
<i>Staphylococcus aureus</i>	78	72
<i>Enterococcus faecalis</i>	24	22.01
<i>Streptococcus</i>	6	5.5
<i>Micrococci</i>	1	0.91
Total	109	100

Table 4: Distribution of gram negative organisms

Organisms	No of isolates (n=171)	
	N	%
<i>Escherichia coli</i>	61	35.6
<i>Salmonella typhi</i>	44	25.7
<i>Klebsiella pneumoniae</i>	24	14.0
<i>Pseudomonas aeruginosa</i>	15	8.7
<i>Acinetobacter baumannii</i>	21	12.2
<i>Enterobacter</i>	4	2.33
<i>Aeromonas hydrophila</i>	1	0.58
<i>Moraxella catarrhalis</i>	1	0.58

The antibiotic sensitivity and resistance patterns of gram positive and gram negative organisms were obtained from the laboratory reports. Of the gram positive organisms, *Staphylococcus aureus* was found to be highly sensitive to vancomycin (86.61%), followed by ciprofloxacin (60.16%), linezolid (47.36%), cephotaxime (34.56%), gentamicin (33.33%), cefixime and ampicillin (30.72% each), cefipime (23.04%), erythromycin (3.84%) and ceftazidime (1.28%); *Enterococcus faecalis* was found to be sensitive to vancomycin (100%), followed by linezolid (91.6%), ampicillin (25%), ciprofloxacin (20.8%), erythromycin and gentamicin (12.5% each); *Streptococcus* was sensitive to ampicillin (100%), followed by cephotaxime (100%), ciprofloxacin, linezolid and cefixime (16.66% each); *Micrococci* was found to be sensitive to vancomycin, linezolid and ciprofloxacin (100% each). Of all the antibiotics vancomycin and linezolid were highly sensitive against *Staphylococcus aureus* and *Enterococcus faecalis*. Erythromycin was found to be the least sensitive antibiotic [Table 5].

The resistance patterns of gram positive organisms were as follows: *Enterococcus faecalis* was found highly resistant to cephotaxime (5.19%), followed by ciprofloxacin and gentamicin (4.84% each), ampicillin (4.15%), cefixime and cefipime (3.1% each), erythromycin (1.7%), and linezolid (0.34%); *Staphylococcus aureus* was found highly resistant to ampicillin (16.60%) followed by cephotaxime (10.03%), cefixime (8.65%), gentamicin (7.95%), ciprofloxacin (7.26%), cefipime (6.9%), erythromycin (5.5%), vancomycin and linezolid (0.34% each); *Streptococcus* was resistant to gentamicin (0.69%) and ampicillin (0.34%); *Micrococci* was found to be resistant to erythromycin and ampicillin (100% each). Erythromycin and ampicillin were found to be the highly resistant antibiotics among gram positive organisms [Table 6].

Among gram negative organisms, the sensitivity patterns were as follows: *Acinetobacter* was highly sensitive to cefoperazone + sulbactam (90.4%), followed by amikacin (76.1%), ciprofloxacin and piperacillin + tazobactam (61.9% each), ceftazidime (28.5%), cephotaxime (14.2%); *E-coli* was highly sensitive to amikacin (86.8%), followed by piperacillin + tazobactam (77%), imipenem (54%), cefoperazone + sulbactam (52.4%), cephotaxime (26.2%),

ceftazidime (19.6%), ampicillin (11.4%) and cefipime (1.6%); *Klebsiella pneumoniae* was highly sensitive to piperacillin + tazobactam (70.8%), followed by amikacin and imipenem (66.6% each), cefoperazone + sulbactam (41.6%), ceftazidime (33.3%), ciprofloxacin (14.7%), cephotaxime (29.1%) and amikacin (4.1%); *Pseudomonas aeruginosa* was highly sensitive to amikacin (100%) followed by piperacillin + tazobactam (53.3%), cephotaxime (46.6%), imipenem, and cefoperazone + sulbactam 40% each, ciprofloxacin (33.3%), ampicillin (13.3%), ceftazidime and cefipime (6.66% each); *Salmonella typhi* was highly sensitive to cephotaxime (81.8%), ampicillin and ciprofloxacin (79.5% each), followed by cotrimoxazole (34.09%), imipenem (27.2%), cefipime (25%), ofloxacin and tetracycline (22.7% each), ceftazidime (20.4%), amikacin (18.18%), piperacillin + tazobactam (13.6%), cefoperazone + sulbactam (11.3%); *Enterobacter spp.* was found highly sensitive to piperacillin + tazobactam (100%). *Aeromonas hydrophila* was highly sensitive to amikacin, ceftazidime and imipenem (100% each). Majority of the gram negative organisms isolated were found to be sensitive to amikacin, imipenem, piperacillin + tazobactam and cefoperazone + sulbactam [Table 7].

Of the gram negative bacteria isolated, *Acinetobacter* was highly resistant to cephotaxime (90.4%) followed by ampicillin (76.19%) and cefipime (66.6%); *E. coli* was highly resistant to ampicillin (70.49%), followed by cephotaxime (50.8%), ciprofloxacin and cefipime (47.5% each), piperacillin + tazobactam (26.2%), imipenem (19.6%), ceftazidime (16.3%), cefoperazone+ sulbactam (14.75%); *Klebsiella pneumoniae* was highly resistant to cephotaxime (70.8%) followed by ciprofloxacin (62.5%), ceftazidime (45.8%), ampicillin (41.66%), cefipime (37.5%), cefoperazone + sulbactam (29.16%); *Pseudomonas aeruginosa* was highly resistant to ampicillin (60%), followed by ceftazidime and cefipime (40% each), cephotaxime (33.3%), amikacin (20%) and ciprofloxacin (13.3%); *Salmonella typhi* was highly resistant to ampicillin (31.8%); *Enterobacter spp.* was found highly resistant to erythromycin (100%); *Aeromonas hydrophila* was found to be highly resistant to ceftazidime, cotrimoxazole and piperacillin + tazobactam (100% each). Most of the gram negative organisms were resistant to ampicillin and cephalosporins [Table 8].

Table 5: Antibiotic sensitivity patterns of gram-positive organisms

Antibiotics	Organisms			
	<i>E. faecalis</i> (n=24)	<i>Staph. aureus</i> (n=78)	<i>Streptococcus</i> (n=6)	<i>Micrococci</i> (n=1)
Vancomycin (30 mcg)	24 (100%)	66 (84.61%)	1 (16.66%)	1 (100%)
Erythromycin (15 mcg)	3 (12.5%)	3 (3.84%)	-	-
Gentamicin (10 mcg)	3 (12.5%)	26 (33.33%)	-	-
Cephotaxime (30 mcg)	-	27 (34.56%)	6 (100%)	-
Ciprofloxacin (5 mcg)	5 (20.8%)	47 (60.16%)	1 (16.66%)	1 (100%)
Ceftazidime (30 mcg)	-	1 (1.28%)	-	-
Cefixime (5 mcg)	-	24 (30.72%)	1 (16.66%)	-
Cefipime (30 mcg)	-	18 (23.04%)	-	-
Ampicillin (10 mcg)	6 (25%)	24 (30.72%)	6 (100%)	-
Linezolid (30 mcg)	22 (91.6%)	37 (47.36%)	1 (16.66%)	1 (100%)

Table 6: Antibiotic resistance patterns of gram-positive organisms

Antibiotics	Organisms			
	<i>E. faecalis</i> (n=24)	<i>Staph. aureus</i> (n=78)	<i>Streptococcus</i> (n=6)	<i>Micrococci</i> (n=1)
Vancomycin (30 mcg)	-	1 (1.28%)	-	-
Erythromycin (15 mcg)	5 (20.8%)	16 (20.5%)	-	1 (100%)
Gentamicin (10 mcg)	14 (58.3%)	23 (29.4%)	2 (33.3%)	-
Cephotaxime (30 mcg)	15 (62.5%)	29 (37.1%)	-	-
Ciprofloxacin (5 mcg)	14 (58.3%)	21 (26.9%)	-	-
Ceftazidime (30 mcg)	2 (8.3%)	1 (1.28%)	-	-
Cefixime (5 mcg)	9 (37.5%)	25 (32.05%)	-	-
Cefipime (30 mcg)	9 (37.5%)	20 (25.6%)	-	-
Ampicillin (10 mcg)	12 (50%)	48 (61.5%)	1 (16.66%)	1 (100%)
Linezolid (30 mcg)	1 (8.3%)	1 (1.28%)	-	-

Table 7: Antibiotic sensitivity patterns of gram-negative organisms

Antibiotics	Acinetobacter (n=21)	E. coli (n=61)	Kleb. pneum (n=24)	P. aeruginosa (n=15)	S. typhi (n=44)
Ampicillin (10mcg)	-	7 (11.4%)	1 (4.1%)	2 (13.3%)	35 (79.5%)
Amikacin (30mcg)	16 (76.1%)	53 (86.8%)	16 (66.6%)	15 (100%)	8 (18.18%)
Ceftazidime (70mcg)	6 (28.5%)	12 (19.6%)	8 (33.3%)	1 (6.66%)	9 (20.4%)
Cephotaxim (30mcg)	3 (14.2%)	16 (26.2%)	7 (29.1%)	7 (46.6%)	36 (81.8%)
Ciprofloxacin (5mcg)	13 (61.9%)	17 (27.8%)	9 (14.7%)	5 (33.3%)	35 (79.5%)
Cefperz+sublact (70mcg)	19 (90.4%)	32 (52.4%)	10 (41.6%)	6 (40%)	5 (11.3%)
Co-trimoxazole (1.25/23.75mcg)	-	-	-	-	15 (34.09%)
Cefipime (30 cg)	-	1 (1.6%)	2 (8.35%)	1 (6.66%)	11 (25%)
Imipenem (10mcg)	12 (57.1%)	33 (54.0%)	16 (66.6%)	6 (40%)	12 (27.2%)
Ofloxacin (5mcg)	2 (9.5%)	-	-	-	10 (22.7%)
Tetracycline (30mcg)	-	-	-	-	10 (22.7%)
Piperacillin+tazobactam (100/10mcg)	13 (61.9%)	47 (77%)	17 (70.8%)	8 (53.3%)	6 (13.6%)

Table 8: Antibiotic resistance patterns of gram-negative organisms

Antibiotics	Acinetobact (n=21)	E.coli (n=61)	Kleb. pneum (n=24)	P. aeruginosa (n=15)	S.typhi (n=44)
Ampicillin (10mcg)	16 (76.2%)	43 (70.5%)	10 (41.7%)	9 (60%)	14 (31.8)
Amikacin (30mcg)	8 (38.09%)	1 (1.63%)	5 (20.83%)	3 (20%)	4 (9.09%)
Ceftazidime (70mcg)	11 (52.3%)	10 (16.3%)	11 (45.8%)	6 (40%)	8 (18.1%)
Cephotaxim (30mcg)	19 (90.4%)	31 (50.8%)	17 (70.8%)	5 (33.3%)	2 (4.54%)
Ciprofloxacin (5mcg)	4 (19.0%)	29 (47.5%)	15 (62.5%)	2 (13.33%)	-
Cefperzone+sublact (70mcg)	2 (9.52%)	9 (14.75%)	7 (29.16%)	-	-
Co-trimoxazole (1.25/23.75mcg)	-	1 (1.63%)	2 (4.16%)	-	2 (4.54%)
Cefipime (30 mcg)	14 (66.6%)	29 (47.5%)	9 (37.5%)	6 (40%)	2 (4.54%)
Imipenem (10mcg)	6 (28.5%)	12 (19.6%)	-	-	-
Ofloxacin (5mcg)	-	1 (1.63%)	-	-	-
Tetracycline (30mcg)	-	-	-	-	2 (4.54%)
Piperacillin+tazobactam (100/10mcg)	6 (28.5%)	16 (26.2%)	3 (12.5%)	-	-
Erythromycin (15 mcg)	-	-	1 (4.16%)	-	-

Bacteriological profile and the antimicrobial susceptibility are constantly evolving. Study of bacteriological profile with antibiotic susceptibility pattern plays an important role in effective management of bacteremia cases. Many studies have been undertaken to determine the organisms responsible for blood stream infections all over the world. Results have varied in different centers and different parts of the world. Many factors e.g. socioeconomic, geographic, use of ventilators, and administration of different antibiotics etc., play a very important role in explaining this difference. The results of the retrospective study conducted in our tertiary care hospital demonstrated the distribution of microbial isolates causing blood stream infections and their susceptibility pattern to most commonly used oral and parenteral anti-microbial agents. This study revealed that 289 (8%) out of 3442 total blood samples screened were positive for the presence of micro-organisms of which 277 (96%) were bacteria and 12 (4%) were fungi. A study done by Anbumani et al¹¹ in the same hospital setting where our study was conducted, had reported the frequency of positive blood cultures as 7.89%.

In contrast to the above reports, the studies done in India, by Khanal et al¹², Sharma¹³, Mehta et al¹⁴, Arora and Devi¹⁵, have reported high frequency of positive blood cultures accounting for 44%, 33.9%, 16.4%, 9.94%, and 20.2% respectively. On comparison, our report and the report given by Anbumani et al¹¹ represent an incidence lower than that reported above.

The variation in blood culture positivity is related to different factors such as the number and amount of blood cultures taken for screen as reported by Lee et al¹⁶. They believed that for achieving a detection rate of >99% as many as four blood cultures may be needed. Similar comment was made by other investigators that more than three blood cultures are needed for 99% test sensitivity. The system and type of blood culture medium formulation used for

bacterial detection are other factors affecting the final bacterial yields¹⁷.

In India, variation might be due to the fact that most of the patients are given antibiotics before they come to the tertiary care hospital and other reason is that in most of the cases self medication is very common as the medicines are available at the counter.

Most of the cultures in the present study yielded monomicrobial growth. The polymicrobial growth isolation rate was 1.08%. The reported polymicrobial isolation rate was between 1 to 15% in various studies. The polymicrobial growth could mean contamination or a severe infection with bad prognosis¹⁸⁻²⁰.

In most of the studies, gram-negative bacilli have taken over the gram-positive organisms, especially in hospital settings. Mehta et al¹⁴ have reported the incidence of 80.96% for gram-negative and 18% for gram-positives which was similar to present findings. Our study revealed that gram-negative bacteria were predominant (58%). This has been an observation among similar studies done in the patients in the developing countries²¹⁻²⁴. The most common gram-negative organism isolated in the present study was E. coli accounting for 21.1% of total isolated bacteria, followed by Salmonella typhi (15.22%).

E-coli were reported to be the most common gram-negative organisms isolated from blood stream infections in many studies. In the present study, we observed a gradual but definite rise in isolation frequency of Klebsiella pneumoniae (8.3%), Pseudomonas aeruginosa (5.1%) and Acinetobacter spp. (7.2%) among gram negative bacilli in blood stream infections. The high occurrence of non-lactose fermenters especially Pseudomonas spp. and Acinetobacter spp. is of concern. Both of these bacteria are associated with a high degree of resistance to antibiotics. Blood stream infections with Pseudomonas aeruginosa have been

associated with increased morbidity in some studies. Another significant finding of the study is the isolation of salmonella species in 15% of the cases. An increasing incidence of salmonella species has also been reported by Sharma et al¹³.

The incidence of gram-positive organisms had been 96% in our study, which is in coincidence with the findings of Roy, et al²⁵. The most common gram-positive organism isolated was *Staphylococcus aureus* (28%), followed by *Enterococcus faecalis* (8.7%) of the total bacterial isolates (n=277). *Staphylococcus* seems to be emerging as the dominant organisms in blood stream infections with 25% MRSA isolates. Similar trend has been reported in the data from the west over the last two decades. Nosocomial infection due to *Staphylococcus aureus* constitutes a major part of the total annual nosocomial infections²⁶.

The observation of the present study is in accordance with reports from two other developing countries. Similarly in a study conducted by Martin M Meremikwu et al²⁷ in Nigeria, they found that *Staphylococcus aureus* 25% and *E-coli* 12.1% as the most pathogenic bacteria recovered from the blood samples. This suggests that infections by these agents constitute a significant threat to survival in developing countries.^{28,29}

In the present study *Candida* isolates were seen in 12 (4%) of the cases. This is consistent with the study of Narain et al,³⁰ where as in other studies the incidence was much higher.³¹ Most of the gram negative bacilli in the study were multi drug resistant. The most common resistance was seen to ampicillin in all isolated gram negative bacteria. Other studies have also reported multidrug resistance for their isolated gram negatives. Amikacin, Imipenem and piperacillin + tazobactam were found to be most effective antibiotics for all gram negative bacterial isolates including non-fermenters. *Salmonella typhi* was found to be highly sensitive to ciprofloxacin and cephalexin. A combination of these two antibiotics may be effective in treating salmonella typhi infections.

Among the gram-positive organisms, high resistance was noted against Ampicillin. An increased ampicillin resistance of 64%, 87% was also reported by Guha et al³² and Karki et al³³ respectively in their studies. Resistance to third and fourth generation cephalosporins (cephalexin, cefixime and cefepime) was also observed with *Staphylococcus aureus* and *Enterococcus faecalis* in the present study. This could be due to the abundant use of these drugs especially third generation cephalosporin's in hospitals, as reported by Nathisuwan et al.³⁴ The study also showed that *Staphylococcus aureus* was found to be highly sensitive to vancomycin, linezolid and ciprofloxacin as reported by other investigators.¹⁴ *Staphylococcus aureus* also showed sensitivity to gentamicin.

Overall, present results indicate that amikacin and imipenem are highly active against gram negative and vancomycin and linezolid are highly active against gram positive organisms causing blood stream infections. These results are in concordance with other reports.³⁵ However, it should not be expected that this activity continues for a long time. Therefore it is advisable to continuously evaluate the sensitivity-resistance pattern of isolates in each region so as to make a rational use of antibiotics.

The present study provided much needed information on the prevalence of bacterial pathogens in blood stream infections and their antibiotic sensitivity patterns. The study identified both gram positive and gram negative bacteria were responsible for blood stream infections and most of them were multi drug resistant. The main forces driving the increase in antimicrobial resistant bacteria are poor infection control practices and inappropriate use of antibiotics. Specific antibiotic utilization strategies like antibiotic restriction, combination therapy and antibiotic recycling may help to decrease or prevent the emergence of resistance and antibiotic usage according to the standard antimicrobial susceptibility testing may reduce the incidence of blood stream infections.

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