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Annals of Biological Research, 2012, 3 (4):1923-1928  
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## Blood stream infection in a teaching hospital

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### ABSTRACT

Blood stream infection is an important cause of morbidity and mortality. Etiology of this infection also varies with the geographical location, antibiotic practices. Aim of the present study is to identify the type of organisms isolated from blood culture as well as to determine their antimicrobial susceptibility pattern. During January 2011 to December 2011, a total of 479 blood samples were cultured in the Department of Microbiology, IMS & Sum Hospital. Positive blood cultures were subjected to appropriate identification methods. Antimicrobial susceptibility testing was then undertaken according to CLSI guidelines. Positive growth was seen in 126 (26.3 %) samples. Most common organism isolated was *Staphylococcus aureus* (92 cases, 73 %) followed by *Acinetobacter* (14 cases, 11%). Of the staphylococcus isolates 26% were resistant to Oxacilin. Thus it is concluded that there is a rising incidence of Staphylococcal as well as *Acinetobacter septicemia* replacing the common pathogens like *E.coli*, *Klebsiella* and *Pseudomonas*. The cause and risk factor for this alarming trend has to be looked into.

**Keywords-Blood** stream infections, *Staphylococcus aureus*, *Acinetobacter*, Oxacillin.

### INTRODUCTION

Sepsis is defined as 'Sudden inflammatory response syndrome (fever/ hypothermia, tachycardia/ tachypnoea, leukocytosis/ leukopenia)' occurring due to proven or suspected microbial etiology. Septicemia is the presence of either a causative microbe or its toxins in blood while bacteremia is the presence of bacteria in blood which is evidenced by a positive blood culture.

Blood stream infection is the most common cause of significant morbidity that leads to mortality especially in the developing countries [1]. Illness associated with bacteraemia ranges from self limiting infection to life threatening sepsis i.e. mortality ranging from 20 to 50 per cent [2]. Isolated bacteria from blood are numerous and their associated diseases require urgent and invasive management [3]. An association has been noted between the types of organism isolated and the prognosis of the patient i.e. organisms like *Enterococci*, gram-negative bacilli and fungus are associated with highest mortality [4]. Surveillance of blood stream pathogens in a hospital is important for monitoring the spectrum of micro-organisms that invade the blood stream and types of organisms associated with a particular clinical discipline. Septicemic or bacteremic illness is also being complicated by increasing antibiotic resistance worldwide. Information on trends and antibiotic resistance in bacteraemia in a given locality is needed to decide for prescribing infection control policy as well as to guide development of new antibiotics and vaccine. Early initiation of antibiotic treatment is essential for decrease of mortality and morbidity in patients with blood stream infections [5].

Bacteraemia in children is a potentially life-threatening condition which requires immediate and effective antimicrobial treatment. It contributes to 19 per cent of neonatal deaths [6] and even up to 30-50 per cent of the total neonatal deaths in developing countries [7,8]. It is estimated that up to 20 per cent of neonates develop sepsis and approximately 1 per cent of them die of related causes [8]. Sepsis related mortality is largely preventable with

rational antimicrobial therapy and aggressive supportive care. *Klebsiella pneumoniae* is the most frequently isolated pathogen (32.5 per cent), followed by *Staphylococcus aureus* (13.6 per cent) of neonatal sepsis [6]. Three of the most important influences on incidence of bacteraemia particularly in children are age, vaccination coverage and exposure to invasive procedures [9].

Taking into consideration the significance of blood stream infections as well as their ever changing etiology, this study is undertaken to reinstate the common pathogens associated with sepsis in our hospital as well as to note their resistance pattern.

## MATERIALS AND METHODS

Present study is based on retrospective analysis of data about blood culture results of specimens submitted for microbial analysis at the IMS & SUM Hospital, Bhubaneswar, India from January 2011 to December 2011. This is a tertiary care hospital attached to a medical college in Odisha and provides health services to the economically weaker sections of Eastern part of India. Blood samples were collected in standard blood culture bottles containing appropriate amount of blood in Brain Heart Infusion Broth with SPS (50 ml broth in adult bottles and 20 ml in pediatrics bottles) observing standard aseptic precautions. These were incubated at 35°C for 7 days and sub cultured intermittently at least thrice on blood agar & Mac-Conkey agar plates [10]. The broths were inspected daily for visible turbidity. Identification of growth on these plates was based on colony morphology, Gram staining and appropriate standard biochemical tests. Susceptibility to different antibiotics based on the type of growth was performed on Mueller Hinton agar by standard Kirby Bauer method. According to Clinical Laboratory Standard Institutes (CLSI) guidelines, sensitivity plates were incubated at 35°C overnight [11]. Susceptibility patterns to the commonly used antibiotics were noted for any organism.

## RESULTS

Number of blood samples analyzed in the Bacteriology Laboratory during the reference period was 479 of which 126 showed growths with a culture positivity rate of 26.3 per cent. *Coagulase-negative Staphylococcus*, *Micrococcus*, *Corynebacterium* and *Bacillus species* obtained during the analysis were classified as no growth as these organisms are considered as contaminants obtained from the skin during the process of collection. Highest numbers of samples tested (24.4%) were from the age group 15-40 years where as highest percentages (50 %) of positive cases were found in infants. The most common organism obtained in this study was *S. aureus* (73 %). It is predominant in all the age groups being highest in infants (92.8 %). Three cases of fungaemia causing septicemia were also detected (Table I).

**TABLE I: Distribution of blood culture isolates and the positive samples in various age groups**

Age Group	Total Sample	No Growth	Growth (% of total)	<i>S. aureus</i> (% of total growths)	<i>E. coli</i>	<i>Klebsiella spp</i>	<i>Acinetobacter</i>	<i>Pseudomonas</i>	<i>S.typhi</i>	<i>S. viridans</i>	Fungi
0-1	56	28	28(50.0)	26 (92.8)	0	2	0	0	0	0	0
2-5	52	45	7(13.5)	5 (71.4)	0	0	2	0	0	0	0
6-14	53	44	9 (16.9)	5 (55.6)	0	0	1	3	0	0	0
15-40	117	88	29(24.8)	21 (72.4)	3	0	2	0	3	0	0
41-60	100	78	22(22)	14 (63.6)	2	1	5	0	0	0	0
> 61	100	69	31 (31)	21 (67.7)	1	0	4	1	0	1	3
<b>Total</b>	<b>479</b>	<b>353</b>	<b>126 (26.3)</b>	<b>92 (73.0)</b>	<b>6</b>	<b>3</b>	<b>14</b>	<b>4</b>	<b>3</b>	<b>1</b>	<b>3</b>

As expected, the Neonatal Intensive care Unit (NICU) revealed highest percentage of positive samples (53.8 %) followed by Intensive Care Unit (33.3%). Most of the positive samples from NICU and pediatric wards were *Staphylococcus aureus*. In addition to it, 30 cases (23.8 %) of gram negative bacilli were also isolated of which *Acinetobacter* (14 cases, 11%) was the predominant pathogen. In contrast to *S.aureus* most of these (9/14) were isolated from adults (>40 years) and those attending outdoors (8/14). In addition to this, there were few percent of organisms belonging to Enterobacteriaceae, *Psuedomonas spp.* and *Streptococcus viridans*. (Table II)

TABLE II - Distribution of blood culture samples according to the place of collection

Place	Total cases	No growth	Growth(% of totalcases)	<i>S. aureus</i>	<i>E. coli</i>	<i>Klebsiella spp.</i>	<i>Acinetobacter</i>	<i>Pseudomonas</i>	<i>S. typhi</i>	<i>S.viridans</i>	Fungus
ICU	135	90	45(33.3)	35(77.8)	3	1	2	2	0	0	2
NICU	26	12	14(53.8)	12(85.7)	0	2	0	0	0	0	0
Ward	214	172	42(19.6)	30(71.4)	2	0	4	2	2	1	1
Paed	22	18	04(18.2)	04 (100)	0	0	0	0	0	0	0
OPD	82	61	21(25.6)	11(52.38)	1	0	8	0	1	0	0
<b>Total</b>	<b>479</b>	<b>353</b>	<b>126</b>	<b>92(73.0)</b>	<b>6</b>	<b>3</b>	<b>14</b>	<b>4</b>	<b>3</b>	<b>1</b>	<b>3</b>

Table III - Resistance pattern of the organisms to various antibiotics

		AMC	CTX	CTR	CFS		PIT		AK	GEN	AZM	CIP	OF	GAT	CAC	CAZ	LE	NX	CPM	CPT	NET	OX	V	LZ	TEI	IC	TOB
		S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R
<i>S. aureus</i>	S	37	42	45	58	46	84	79	28	35	52	89	16	ND	90	33	31	85	ND	68	87	83	74	NA	NA		
	R	55	50	47	34	46	8	13	64	57	40	3	76	ND	2	59	61	7	ND	24	5	9	18	NA	NA		
<i>S.viridans</i>	S						0	1			1	1		0													
	R	ND	ND	ND	ND	ND	1	0	ND	ND	0	0	ND	ND	1	ND	ND	ND	ND	NA	NA	NA	NA	NA	NA	NA	NA
<i>E.coli</i>	S	1	5		5	5	4	2	4	0	1	6	1		ND	3		5	2								
	R	5	1	ND	1	1	2	4	2	6	5	0	5	ND	ND	3	ND	1	4	NA	NA	NA	NA	NA	NA	NA	NA
<i>Klebsiella spp</i>	S	0	1	1	2	2	2	1		1	2	2	1	1	0	1		2	0						2	2	
	R	3	2	2	1	1	1	1	ND	2	ND	1	2	2	3	2	ND	1	3	NA	NA	NA	NA	NA	1	1	
<i>S.typhi</i>	S	0	2	0	3	3	3	3	1	1	3	1			0										3		
	R	3	1	0	0	0	0	0	2	2	0	2	ND	ND	3	ND	ND	ND	ND	NA	NA	NA	NA	NA	0	NA	
<i>Acinetobacter</i>	S	12	10	10	13	9	14	14		10	11	14	12	12	11												
	R	2	4	4	1	3	0	0	ND	4	3	0	2	2	ND	3	ND	13	ND	NA	NA	NA	NA	NA	NA	NA	NA
<i>Pseudomonas</i>	S	1	1	1	2	4	4	4		0	0	4	3	1							4				4		
	R	3	3	3	2	0	0	0	ND	4	4	0	1	3	ND	ND	ND	ND	ND	0	NA	NA	NA	NA	0	NA	

(AMC-Amoxycilin clavulanic acid, CTX-Cefotaxime, CTR-Ceftriaxone, CFS-Cefoperazone Sulbactam, PIT-Piperacilin Tazobactam, AK-Amikacin, GEN-Gentamycin, AZM-Azithromycin, CIP-ciprofloxacin, OF-Ofloxacin, GAT-Gatifloxacin, CAC-Ceftazidime clavulanic acid, CAZ-Ceftazidime, CFZ-Cefoperazone, LE-Levofloxacin, NX-Norfloxacin, CPM-Cefepime, CPT-Cefepime tazobactam, NET-Netilmycin, OX-Oxacilin, V-Vancomycin, LZ-Linezolid, TEI-Teicoplanin, IC-Imipenem cilastin, TOB- Tobramycin, ND-not done, NA-Not Applicable )

Among the *S.aureus* isolated 26% were resistant to Oxacillin (MRSA). These isolates had shown high degree of resistance to Beta lactam antibiotics. 60 % of *S.aureus* was resistant to Amoxycilin-clavulanic acid and 50% to Piperacilin-tazobactam. Resistance to third generation cephalosporins like Cephotaxime, Ceftriaxone and Cefepime was 55%, 50% and 66% respectively. Lowest resistance was noted with Cefoperazone-Sulbactam i.e. 37%. Experience with Flouroquinolones show that organisms were resistant to first generation quinolones, like Ciprofloxacin (61%) and Ofloxacin (43%), however second generation antibiotics like Gatifloxacin and Levofloxacin had retained their efficacy. Macrolides like Azithromycin was resistant in 69% of cases. More than 90% of isolates were sensitive to Aminoglycosides like Amikacin and Gentamycin. Linezolid and Vancomycin were sensitive in 75% of cases. Also notable in our study was finding of few Vancomycin resistant *Staphylococcus aureus* (VRSA) strains which were isolated from ICU patients.

The non-fermenters like *Acinetobacter* and *Pseudomonas* were susceptible to Gatifloxacin, Amikacin and Gentamycin. In addition, *Pseudomonas* was also sensitive to Piperacilin-Tazobactam and Imipenem-Cilastin. The members of Enterobacteriaceae obtained in the study were sensitive to most of the antibiotics but for Flouroquinolones. One isolate of *Klebsiella pneumoniae* obtained from the NICU was resistant to all the available antibiotics including Imipenem-Cilastin (**Table III**).

### DISCUSSION

Blood stream infections range from transient bacteremia to septic shock. Blood culture is a gold standard for accurate detection of etiological agents of infectious diseases and can assist in choice of appropriate antimicrobial therapy [12]. Furthermore, early detection of bloodstream infections could prevent implantation of microorganisms into vital organs such as the brain, heart or kidneys [13]. In the present study 27.6% of the samples revealed growth on culture. This is higher in contrast to studies by different workers [14-17] where the isolation rate was 4-10%. Our finding is consistent with similar studies [18-22] where the isolation rate was 20 - 59%. The variation in the blood culture positivity may be attributed to the factors like number and amount of blood culture taken for screen [23]. System and formulation of blood culture medium used for bacterial detection and the prior use of antibiotics by the clinicians are also other factors affecting bacterial isolation.

In this study culture positivity rates in case of infants is higher (50%) in comparison to other age groups. This finding is reiterated with previous studies by Nwadioha *et al* [24]. Higher incidence of culture positivity in infants is due to immaturity of their immune systems.

Most common organisms in all the age groups in the study are *Staphylococcus aureus*. This is in contrast to most of the studies in Indian subcontinent which reveal Gram-negative organism as the predominant pathogen. Latif *et al* [18] and Mehnijad *et al* [14] found *Klebsiella* as the most common organism in their study, Mehta *et al* [15] and Garg *et al* [19] revealed *Pseudomonas* as the most common cause and Sobhani *et al* [16] reveal *Salmonella* as the commonest isolated organisms. *Salmonella* bacteremia is common in areas where salmonellosis is considered endemic [16, 19]. Gram positive organisms (Coagulase negative Staphylococci) were isolated as the predominant organism in similar studies [17, 25]. In our study *S. aureus* is most common pathogen. Rising staphylococcal bacteremia may have originated from community-acquired infections [26]. Such changes in the etiology at various places are thought to be favored by geographical location changes and antibiotic policy advocated in the hospital. This also reflects the better isolation of patients in the hospital and hand washing practices in the ICU or high risk units in the hospital [27, 28]. Possibly for similar reasons cultures in USA and Europe is more likely to reveal Gram positive growth [29, 30]. National Nosocomial Infection Surveillance System of CDC [31] has suggested that 16% of acquired cases of bacteremia in USA are due to *S. aureus* alone.

Most common organism found in infants in this study was *S.aureus*. This is in contrast to most of the studies in Indian and African subcontinent, where *E.coli* or *Klebsiella* was described as the commonest cause of bacteremia in children [24, 32]. Few other authors [33, 34] have also revealed *S.aureus* as the common cause of bacteremia in infants.

The most common organism isolated in ICU was *S.aureus*. This is consistent with other studies [35] where *Staphylococcus* was of 46.9% of total population. The prevalence of MRSA bacteremia in our study (26 %) is comparable to few other studies in Indian subcontinent [18, 27]. Higher prevalence (75.6%) has been noted by Garg *et al* [19]. This could be a biased finding due to a very small number of *S.aureus* identified in the study. In USA, the rate of detection of such strains was 10% in 1995 which steadily increased to 29% in 2001 due to nosocomial infections [30]. The MRSA strains in our study were largely sensitive to Gatifloxacin, Levofloxacin, Vancomycin, Linezolid, Gentamicin and Amikacin. Previous authors working on MRSA cases have also revealed a sensitivity

pattern similar to our findings. MRSA bacteremia is associated with a higher mortality rate and a longer hospital stay and it is also regarded as an independent risk factor of death [36].

In our study one case of *S.viridans* isolated was sensitive to Flouroquinolones. This is in contrast to finding by Geetu M. et al [37] where the organisms were mostly resistant to these antibiotics. As the number of isolates in our case is very low, so to arrive at any conclusion further studies are required.

Fourteen cases of *Acinetobacter* found in this study. Tilley and Roberts reported 52 episodes of *Acinetobacter* blood stream infection during a six-year period, 41 of which were clinically significant [38]. *Acinetobacter* has been increasingly implicated as a cause of a wide spectrum of infections including community and hospital acquired infections associated with intravenous catheters and contaminated respiratory therapy equipment among patients with impaired host defenses in intensive care units [39, 40]. In contrast to this, in our study the organisms were associated commonly with outdoor patients. It has been found that prior colonization with *A. baumannii* as the most significant independent risk factor for *A.baumannii* bacteremia. The origin of *Acinetobacter* strains could not be traced by us. Although these organisms are normally considered to be of low virulence, they have the ability to develop resistance extremely rapidly due to genetic transfer. Thus the emergence of *Acinetobacter* strains as an important pathogen has to be thoroughly looked into.

### CONCLUSION

The predominant organisms isolated in our study were *Staphylococcus aureus* followed by *Acinetobacter*. Twenty six percent of *S.aureus* was resistant to Oxacillin and most of them were sensitive to Aminoglycosides, second generation Flouroquinolones, Linezolid and Vancomycin. Interestingly few *Staphylococcus aureus* strains isolated were also resistant to Vancomycin. In contrast, the *Acinetobacter* strains were sensitive to most of the antibiotics. Gatifloxacin, Cefoperazone Sulbactam, Piperacillin-Tazobactam, Amikacin, Gentamycin remains the most useful drug for Gram negative septicemia. For all age groups *Staphylococcus aureus* as the most common pathogen than the Gram negative bacteria is a surprising yet concerning aspect in this study. It also highlights the need to trace the origin of this pathogen and find effective means of control.

### Acknowledgement

We are thankful to the S'O'A University, Kalinga Nagar, Bhubaneswar Odisha for financial assistance to perform this research work.

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