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Research Article

BACTERIOLOGICAL PROFILE AND ANTIBIOTIC SENSITIVITY PATTERN OF HOSPITAL-ACQUIRED SEPTICEMIA IN A TERTIARY CARE HOSPITAL IN NORTH EAST INDIA

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ABSTRACT

Objective: The objective of this study was to determine the bacterial agents responsible for hospital acquired septicemia and to determine the antibiotic sensitivity profile of the bacterial isolates.

Methods: A total of 350 hospitalized cases clinically suspected to have hospital acquired septicemia were included in this cross-sectional observational study over a period of 1 year. Blood samples were collected for culture with aseptic precautions following universal precautions. Antimicrobial susceptibility testing of the bacterial isolates was performed according to Clinical and Laboratory Standards Institute Guidelines.

Results: Out of 350 blood culture samples collected, 41.4% (145) were culture positive. Gram-positive bacteria were isolated in 61.4% of these blood culture positive samples and the most frequently identified were coagulase negative staphylococci (35.2%) and *Staphylococcus aureus* (22.8%). Among the Gram-negative bacteria *Escherichia coli* (19.3%), *Typhi* (9.7%), and *Klebsiella* spp. (6.9%) were the main isolates. In our study, staphylococci showed maximum resistance to penicillin and erythromycin. Enterobacteriaceae had maximum resistance to gentamicin, amoxyclav, and ciprofloxacin.

Conclusion: Gram-positive pathogens predominated in the blood stream infections. Résistance to aminoglycosides, cephalosporins, especially in Gram-negative bacteria was significantly high. Therefore, rapid microbiological diagnosis and the determinants of antimicrobial susceptibility become relevant for early initiation of antimicrobial therapy.

Keywords: Coagulase negative staphylococci, Hospital acquired septicemia, Antimicrobial resistance.

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INTRODUCTION

Continuous or transient presence of microorganisms within the blood stream is bacteremia, while its dissemination throughout the body with evidence of systemic responses toward microorganisms with variable severity is septicemia [1]. In developing countries, the steep increase in septicemia cases is a major health problem that creates the biggest challenge for clinicians in the selection of appropriate antimicrobial agents, as it is further complicated by the development of resistance in organisms to antimicrobial agents, which is the mainstay of treatment. Increasing antimicrobial resistance among septicemia cases has been reported in many studies conducted in India and other countries worldwide [2-6]. Bacteriological cultures to isolate the offending pathogens and knowledge about sensitivity pattern of the isolates remains the mainstay of definite diagnosis and management of septicemia [7]. These results have a minimum turnaround time of 2-3 days. Thus, it is a common practice to start early empirical therapy with broad-spectrum antibiotics in suspected patients of septicemia.

Knowledge of resistance patterns in common pathogens associated with these cases is a must before starting the empirical therapy. Since the causative organisms of septicemia vary region wise, knowledge of their resistance patterns is critical in a local geographic area.

Despite extensive research on septicemia is available worldwide and in India, no studies have been published from Sikkim. Hence, we undertook a cross-sectional study to investigate the causative organisms of hospital acquired septicemia and to assess their antibiotic susceptibility pattern to help clinicians to choose the appropriate antibiotics for empirical therapy until the specific results of culture/sensitivity are known.

METHODS

This observational cross-sectional study was conducted in a 500 bedded tertiary care hospital at Gangtok, Sikkim on 350 hospitalized patients who acquired signs and symptoms suggestive of septicemia, which were not present either at the time of admission or within 48 hrs of hospital stay. The study was conducted after obtaining Institutional Ethics Committee and Institutional Review Board approval. Written informed consent was obtained from patients or their relatives before the study. Patient details and clinical findings were obtained, and routine lab investigations were carried out. For blood culture, about 5-10 ml of blood was collected from adult patients with aseptic technique and immediately inoculated into BACTEC culture vials containing enriched broth (Soybean-Casein Digest broth with resins) and incubated in BACTEC 9050 blood culture instrument (Beckton-Dickenson, USA). Growth when detected by flag and an audible beep of the instrument was subcultured on 5% sheep blood agar and MacConkey agar plates and incubated aerobically at 37°C overnight for bacterial isolation. Identification of culture isolates was done according to standard bacteriological techniques and Kirby-Bauer disc diffusion method was used for antibiotic susceptibility testing of the isolates on Muller-Hinton agar according to the Clinical Laboratory Standard Institute 2010 guidelines (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4793966/>) [8].

RESULTS

Out of 350 patients investigated with blood culture, 145 (41.4%) were found to be culture positive (Table 1). Out of these 145 cases, the maximum numbers of the isolates were obtained from the age group 21-30 years (29%) (Fig. 1) and males (66%) (Fig. 2). The mean age of the culture positive cases was 48.09 (standard deviation ±19). Of 145 positive blood cultures, Gram-positive bacteria and Gram-negative bacteria accounted for 61.4% and 38.6%, respectively (Fig. 3). Among Gram-positive organisms, the most common was coagulase negative staphylococci (CoNS) (35.2%). Among Gram-negative organisms, Enterobacteriaceae group of organisms were the most commonly isolated bacteria (96%) (Table 1). The resistance to penicillin, erythromycin and cotrimoxazole was 71%, 51% and 32%, respectively, among Gram-positive organisms and all these isolates were found to be sensitive to tigecycline and vancomycin (Table 2).

Gram-negative organisms showed high-level resistance to gentamycin (54%), amoxicillin/clavulanic acid combination (52%) (Table 3) and also to third and fourth generation cephalosporins.

Table 1: Pattern of the bacteria isolated (n=350)

Bacterial isloates	Number/percentage of the isolates
No bacteria isolated	205
Bacteria isolated	145
Gram-positive cocci	
CoNS	35.2
Staphylococcus aureus	22.8
Enterococcus spp.	3.4
Total	89 (61.4)
Gram-negative bacilli	
Escherichia coli	19.3
Klebsiella pneumoniae	6.9
Citrobacter spp.	0.7
Salmonella Typhi	9.7
Proteus mirabilis	0.7
Total	54 (37.2)
Gram-negative bacilli - nonfermenters	
Acinetobacter baumanii complex	0.7
Pseudomonas spp.	0.7
Total	02 (1.4)

CoNS: Coagulase negative staphylococci

Table 2: Antibiotic resistance pattern of the Gram-positive cocci (n=89)

Antibiotics	CoNS (51) (%)	*Staphylococcus aureus* (33) (%)	*Enterococcus* spp. (5) (%)
Amikacin	5	0	0
Gentamycin	16	3	80
Penicillin	75	63	80
Ampicillin	5	0	0
Ceftriaxone	3	3	0
Ciprofloxacin	27	15	60
Clindamycin	39	18	20
Cotrimoxazole	33.3	36	0
Erythromycin	55	36	100
Linezolid	4	0	0
Imipenem	0	0	0
Meropenem	0	0	0
Nitrofurantoin	10	6	20
Teicoplanin	0	0	20
Tigecycline	0	0	0
Tetracycline	10	3	80
Vancomycin	0	0	0
Piperacillin	3	0	0
Amoxyclav	6	5	1

CoNS: Coagulase negative staphylococci

DISCUSSION

In this study, an attempt was made to study the bacterial profile and their antibiotic susceptibility pattern of cases of hospital acquired septicemia. In our study, the blood culture yield was 145/350 (41.4%) which is quite similar to Khanal *et al.* [9] and Divyashanthi *et al.* [10] but quite higher in other studies of Arora *et al.* [11], China and Gupta [12], and Murthy and Gyaneshwari [13]. In India, variation in blood culture positivity rates might be due to the fact that most of the patients are given antibiotics before they come to the tertiary care hospital, and the other reason may be self-medication since antibiotics are readily available over the counter. Sincere efforts were made to collect the blood samples before the antibiotic administration, which could have led to high culture positivity rates.

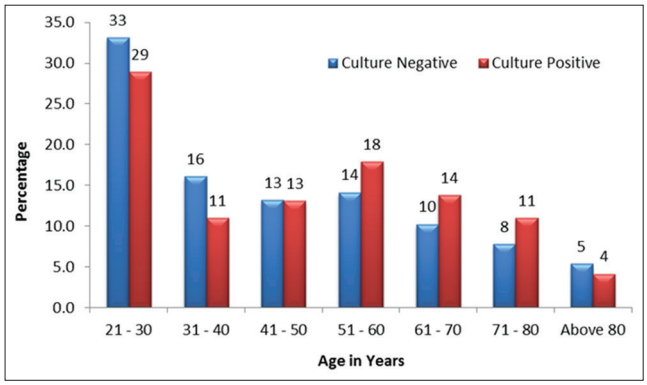

Fig. 1: Age-wise distribution of septicemia cases based on culture results (n=350)

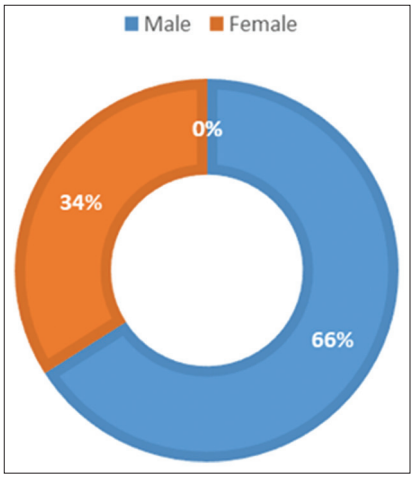

Fig. 2: Sex-wise distribution of the culture positive cases (n=145)

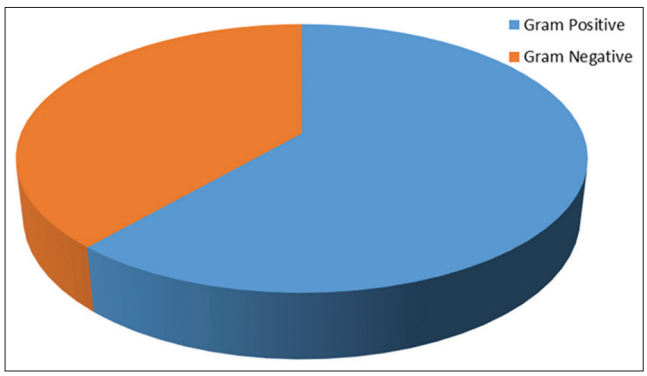

Fig. 3: Distribution of culture positive samples

Table 3: Antibiotic resistance pattern of the Gram-negative bacilli (n=56)

Antibiotics	*Escherichia coli* (28) (%)	*Klebsiella pneumoniae* (10) (%)	*Citrobacter* spp. (1) (%)	*Typhi* (14) (%)	*Proteus mirabilis* (1) (%)	*Acinetobacter baumanii* complex (1) (%)	*Pseudomonas* spp. (1) (%)
Amikacin	0	10	0	21	0	0	100
Gentamycin	60	80	0	21	0	100	100
Ampicillin	35	70	0	7	0	0	0
Piperacillin	0	30	0	7	0	100	0
Cefepime	32	50	0	0	0	100	100
Ceftriaxone	39	40	0	7	0	100	0
Cefuroxime	28	40	0	7	0	0	0
Ciprofloxacin	50	60	0	14	0	100	0
Cotrimoxazole	46	30	0	7	100	0	100
Imipenem	0	0	0	0	0	100	0
Meropenem	0	0	0	0	0	0	0
Nitrofurantoin	3	30	0	7	0	100	0
Tigecycline	0	0	0	0	0	0	0
Tetracycline	7	40	0	0	0	0	0
Amoxyclav	67	90	100	0	0	0	0

In this study, the highest prevalence rate was found in the age group 21-30 years and males were predominantly affected, which is in accordance with other studies [10,14]. The higher isolation of Gram-positive organisms are in accordance with the studies of China and Gupta [12], Kamga *et al*. [15], and Anbumani *et al*. [16] who reported similar incidences but some workers such as Mehta *et al*. [1], Mehdinejad *et al*. [17], and Barati *et al*. [18] have reported that Gram-negative organisms as the predominant pathogen in hospital settings.

The variations in the prevalence of organisms in different institutes worldwide may be due to epidemiological difference of etiological agents, the inclusion criteria for selection of subjects, prior use of antibiotics, clinical setting of the study, and presence or absence of risk factors.

CoNS was isolated in 35.2% and *Staphylococcus* in 22.8% of cases in this study. CoNS was mainly recognized as mere contaminants till 1970's; however, several studies have now reported an increasing incidence of infection by this group of bacteria [19,20]. The isolation of CoNS is consistent with the study of Arora *et al*. [11] and Karlowsky *et al*. [20] where the reported isolation of the organism was 42% and 21%, respectively. The presence of intravascular catheters, immunosuppression with severe neutropenia, and use of cytotoxic drugs may precipitate septicemia in these groups of patients, especially in the ICU setting and the majority of our study subjects were from ICU too [21]. Since ours is a tertiary care referral center catering to the entire state this profile would be representative of most other adjoining centers in the region. *Escherichia coli* (19.3%) and *Klebsiella* spp. (7.0) were the predominant Gram-negative bacteria isolated which is in accordance with other studies of Mehta *et al*. [1], Gupta [12], Kamga *et al*. [15], Karlowsky *et al*. [22], and Merin *et al*. [23].

CoNS exhibited high levels of resistance to penicillin and erythromycin which is similar to that of Arora *et al*. [10] and Mehdinejad *et al*. [17]. Such isolates are often resistant to multiple classes of antibiotics in addition to beta-lactams. Resistance to beta lactams is determined by the *mec*A gene harbored on a mobile genetic element, i.e., staphylococcal chromosomal cassette mec [24]. This not only limits treatment options but also enables transfer of these resistance elements to other staphylococci. All CoNS isolates were susceptible to vancomycin, teicoplanin and linezolid. These drugs may be included in therapy for patients with methicillin-resistant -CoNS infections; however, empirical use must be avoided before recording the results of susceptibility tests as overuse of these antibiotics can promote glycopeptide and oxazolidinone resistance. Among the Gram-negative isolates, the Enterobacteriaceae isolates in our study showed very poor sensitivity to gentamicin, amoxyclav, and ciprofloxacin. Least resistance was seen with carbapenems and tigecycline.

CONCLUSION

By this study, we want to highlight the fact that Gram-positive organisms, particularly CoNS and *Staphylococcus aureus* are the predominant group of organisms causing hospital acquired septicemia in our institution. There has been a shift from the predominance of Gram-negative organisms to Gram-positive organisms in the past decade worldwide, the reason for which is not clear. High resistance to cephalosporins is a cause of concern, as they are one of the most commonly prescribed antibiotics in this region. It is thus concluded that to curb the menace of rising drug resistance, rational and judicious use of antibiotics is essential according to the antibiotic resistance pattern of that particular institution. A regular epidemiological study of blood culture isolates and determination of susceptibility to antibiotics is necessary to guide the clinicians to:

i. Choose the appropriate empirical therapy.
ii. Switch over to the best regime based on the antibiotic susceptibility pattern to improve the overall outcome of the patient's health.

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