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PREVALENCE AND ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF BLOOD ISOLATES IN PATIENTS OF SEPTICAEMIA IN INTENSIVE CARE UNIT: RETROSPECTIVE STUDY

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ABSTRACT

Background: Septicaemia in critically ill patients is life threatening condition and requires rapid antimicrobial treatment. Infections caused by drug-resistant organisms are more likely to increase risk of death in these patients. The aim of the present study was to determine the bacteriological profile of bloodstream infections and their antibiotic susceptibility pattern in an intensive care unit (ICU) of a tertiary care centre in North India.

Materials and Methods: This cross-sectional study was done in a 30-beded adult and 10-beded paediatric Intensive care unit (ICU) from April 2017 to September 2017. Standard bacteriological methods were used for blood collection, bacterial isolation and antimicrobial susceptibility pattern.

Results: Total 241 patients were clinically diagnosed septicaemia during study period of six month and 482 blood samples were analysed, 60 sample yielded growth of 12 type of organism which include 11 type of bacteria and 1 Fungai isolates. Out of total 60 positive samples 46.66% isolates were gram positive bacteria and 46.66% were gram negative and 6.66% were fungi. 118 (48.96%) patients were from MICU followed by 23.65% from PICU. Most common age group was children less than 10 year 29.46% followed by more than 60 Year 16.59% with male preponderance 57.67% and mortality (36.66%) was higher in patients with positive blood culture compare to negative culture (19.66%).

Conclusion: This study provides information on antibiotic sensitivity and resistance of blood isolates found in ICU patients with septicaemia. It will guide the intensivists to formulate the initial empiric antibiotic therapy for the critically ill patients in ICU.

KEYWORDS : Septicaemia, intensive care unit, blood stream infection, bacteria, antimicrobial resistance

Introduction

Sepsis is a common cause of morbidity and death in critically ill patients, and blood culture samples are often drawn in an effort to identify a responsible pathogen. Blood culture results are usually negative, however, and even when positive are sometimes difficult to interpret [1] The practice of obtaining blood cultures from febrile patients had become well established in 1940[2]. Keefer had summarised his extensive personal experience about case fatality rate of bacteraemia and he noticed that mortality rate associated with gram positive bacteraemia was about 70-80% [3]. But later on the studies published between 1950 and 1970 describe mortality rate was 40% because of gram negative rod infections. [4] By 1941, correlation of blood culture results with clinical and post-mortem findings had provide a number of useful axioms. Keefer recognised the value of positive blood cultures, especially in patients without a clinical obvious localised infection. Various literatures have reported that septicaemia is one of the leading cause of death in Intensive Care Unit (ICU) patients. The overall case-fatality rate associated with bacteraemia is 15% to 20%, but reaches 35% to 50% in ICU patients [5]. Bacteraemia in ICU can either occur secondary to the dissemination of pathogens from a primary focus of infection at a clinical site into the blood stream, or can be primary where the source of infection is unclear. The common foci for secondary BSI in ICU are the respiratory, gastrointestinal and urinary tracts. [6] Now-a-days, widespread distribution of resistant gram positive and gram negative micro-organisms to currently available antibiotics has gained importance in all over the world. [7] Septicaemia caused by multi-drug resistant (MDR) organisms is more likely to prolong the hospital stay, increase the risk of death, and require treatment with more expensive antibiotics. Due to wide variations in bacterial drug resistance, results of studies and reports in one region or in a period of time are not necessarily true for other regions or periods of time. [8] It is therefore essential to document trends in the type of organisms isolated from blood cultures along with their resistance patterns in order to produce meaningful guidelines for the empirical treatment of patients with septicaemia. The objectives of the current study were to describe the frequency of micro-organisms isolated from blood cultures from patients with clinically suspected septicaemia, and the resistance of these bacteria to the commonly available antibiotic.

Methods and Materials

Study design, study area and sampling process

This retrospective cross-sectional study design was conducted in the adult paediatric and neonatal, ICU of tertiary care centre in Pacific Institute of Medical Sciences, Udaipur, Rajasthan, India. The study ICUs are closed ICU dealing with medical, surgical and gynaecological, paediatric and neonates patients. It 30 beds adults and 10 beds paediatric. Blood for culture was sent from all patients with clinically suspected septicaemia who were admitted in this ICU from April 2017 to September 2017 and who were on antibiotic within the last 2 weeks were excluded from this study.

Inclusion criteria of patients

Only ICU Patients with suspected and clinically diagnosed septicaemia. Clinical criteria include followings.

- Temperature > 38· (100.4· F) or < 36· (96.8· F)
- Heart rate >90
- Respiratory rate >20
- Systolic blood pressure(SBP) <90 or SBP drop >40mm of Hg of normal
- Severe sepsis with hypotension with adequate fluid resuscitation
- Evidence of two organ failure
- WBC >12,000/mm3,<4000/mm3
- Lactate >4 mmol/L

Exclusion criteria

- Patients other than ICU admitted in this hospital with clinically diagnosed septicaemia.
- Patients on antibiotics last 2 weeks

Laboratory procedures

Two blood samples were collected from different venous sites from each patient. About 10 ml of venous blood for adult and 5 ml for children less than 1 year and 2ml for neonates was collected aseptically using 70% alcohol and 2% tincture of iodine and transferred into a bottle containing 22 ml of complex media and 8 ml of a charcoal suspension with average density of 1.0155 g/ml (BacT/AlertR FA Plus).Two aerobic blood culture bottle were used for each patients and growth in both bottle were considered positive. Blood culture broths were then transported within 30 min to our hospital microbiology laboratory and incubated at 37°C. The BACTEC system (and other conventional systems such as BacT/Alert) is superior to the DuPont Isolator system for the isolation of Streptococcus pneumoniae,

Pseudomonas aeruginosa, anaerobic bacteria, and other Streptococcus species [9]

Bacterial identification

Blood culture broths were checked for sign of bacterial growth (turbidity, haemolysis, clot formation) daily up to 7 days. Bottles which showed signs of growth were further processed by gram stain and sub-culture was made onto blood agar, MacConkey agar, Manitol salt agar (all Oxoid Ltd, UK) and incubated at 37°C for 24 h [10] Blood culture broths with no bacterial growth after 7 days were sub-cultured before being reported as a negative result. Bacterial isolates were identified by colony morphology, gram staining reaction, biochemical tests using the standard procedure for bacterial identification [10]

Antimicrobial susceptibility test

Following identification of the bacterial isolates, disc diffusion method was used and susceptibility and resistant for antibiotics were interpreted according to National Committee for Clinical Laboratory Standards(NCCLS) [10].The antibiotics discs were: Amikacin, Ofloxacin, Levofloxacin, Moxifloxacin, Cefuroxime Axetil, Ceftazidime Clavulanic acid, Piperacillin-tazobactam, Cefoparazone sulbactam, Meropenem, Imipenem, Colistin, Co-trimoxazole, Tobramycin, Tigicyclin, Linezolid, Clindamycin ,Amoxicillin-clavunilic acid, Ceftriaxone, Vancomycin, Ciprofloxacin, Gentamicin, Norfloxacin, Doxycycline. We selected these antimicrobial agents as they are available and frequently prescribed for the management of clinically diagnosed septicaemia.

Data collection and Analysis

Collected data included basic demographic characteristics of patients (age and sex), associated co-morbidities, clinical diagnosis, isolated organisms and antibiotic susceptibility patterns of the isolated organisms. In all a total of 482 blood cultures were received by the laboratory for processing over the six Month of period.

Data analysis:

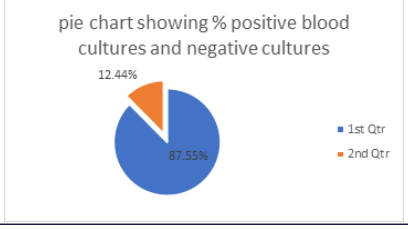
Data obtained on demographic characteristics of patients, clinical diagnosis, isolated organisms and antibiotic susceptibility patterns of the isolated organisms were analysed by simple descriptive statistics (i.e. proportions, ratios and percentages). Age of the patients were categorized into 0-10,11-20,21-30,31-40,41-50,51-60,>61 years. The isolated pathogens were categorized into Gram positive bacteria, Gram negative bacteria, and fungi. The microbial agents were tested for antibiotic susceptibility were tested by using the commonly available Antibiotics.

Results

A total of 241 patients were admitted in ICU with clinically diagnosed septicaemia during the study period of six month (April 2017 to September 2017). From these patients, 482 blood samples were collected and send for microbiological analysis. 60 (12.44%) samples yielded growth of 12 type of micro-organisms and 422 (87.55%) were negative [fig 1], out of them 46.66% was gram positive bacteria (GPB) and 46.66% was gram negative bacteria (GNB) and 6.66% was fungi.[Table 1]

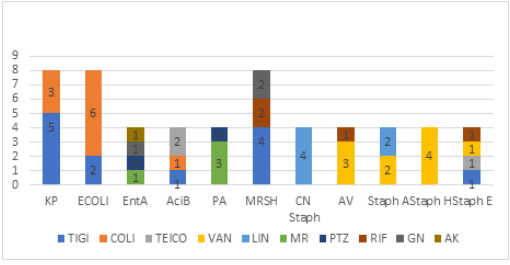
Frequency of isolated micro-organism [Table 1]

GPB=28 (46.66%)	GNB=28 (46.66%)	Fungi=4 (6.66%)
Staph. A=4 (14.28%)	Klebsiella P=8(28.57%)	Candida =4
Coagulase neg. staph = 4(14.28%)	E-coli=8(28.57%)	
Staph. H=4(14.28%)	Enterobacter A =4(14.28%)	
Staph. E=4(14.28%)	Acinetobacter. B =4(14.28%)	
Aero coccus viridian=4(14.28%)	Pseudomonas A=4(14.28%)	
MRSH=8(28.57%)		



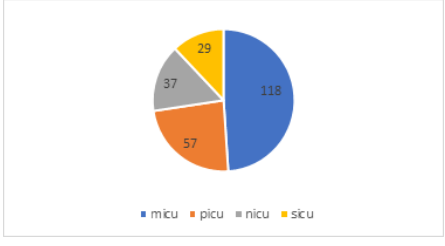
Positive blood culture in ICU Patients [fig 1]

Most common GPB was methicillin resistant staphylococcus hominis(MRSH) 28.57% followed by staphylococcus aureus (Staph. A) 14.28%, Coagulase negative staphylococcus (CN. Staph.)14.28%, Staphylococcus haemolytic (Staph. H)14.28%, Staphylococcus epidermis (Staph. E) 14.28%, and aero coccus viridian(AV) 14.28%, and most common GNB was Klebsiella pneumonia(KP) 28.57%and E-coli 28.57% followed by Enterobacter aerogene (Ent A) 14.28%, Acinetobactor brumanni (Aci B) 14.28%, and pseudomonas aeruginosa (PA) 14.28%.and in 6.66% cases candida species was detected. Most of the isolated organism was resistant to commonly used antibiotics. We found that gram positive bacteria was most sensitive to vancomycin, linezolid, teicoplanin, levofloxacin, and Rifampicin, and gram negative bacteria sensitive to Tigicyclin and Colistin only [fig 2]



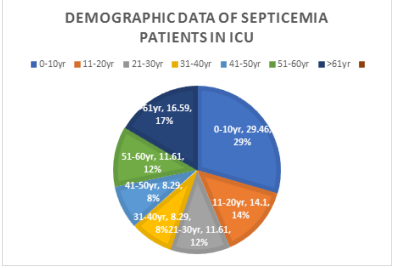
Antibiotic sensitivity patterns of growth organism [fig 2] VAN= Vancomycin, LIN=Linezolid, RIF=Rifampicin, GN=Gentamicin, AK=Amikacin, PTZ=Piperacillin-Tazobactum, MR=Meropenem, TICO=Ticoplanin , COLI=Colistin, TIGI=Tigicyclin

Most of the patients with septicaemia admitted in Medical ICU 118 (48.96%) followed by paediatric ICU (23.65%), (15.35%) in NICU, (12.03%) SICU.

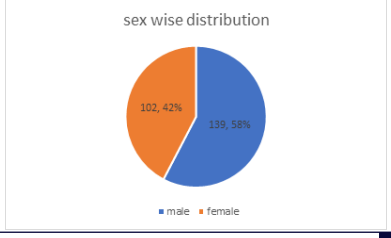


[Figure 3] showing frequency of septicaemia patients in differents ICU.

Demographic data of septicaemia patients admitted in ICU were that maximum patients from 0-10 year age group 29% followed by more than 61 year 17%, minimum patients were between 31-40 and 41-50 year with male preponderance (58%) and male to female ratio was 1.36.[Fig 4,5]

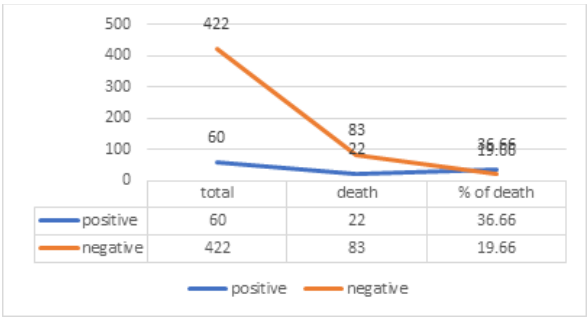


Age wise distribution of septicaemia patients [fig 4]



Sex wise distribution of septicaemia patients [fig 5]

Mortality rate was higher in positive blood culture 36.66% septicaemia patients compare to negative blood culture 19.66% [Fig. 5]



Outcome of septicaemia patients [Fig 5]

Discussion

Despite the availability of effective antimicrobial agents against nearly all blood isolates, mortality rate among patients with documented bacteraemia or fungemia remains high. Many studies results showed that mortality rate among bacteraemia cases is 12 fold higher than patients without bacteraemia [4]. The host factors like age and associated comorbidities also contributes to mortality. Extreme age and children are more susceptible to blood stream infection [11] In our study most commonly affected age group was children and elderly patients. Blood cultures are taken from all patients admitted in ICU with suspected infection, however, the reported incidence of positive blood culture is low varies from 3.2% to 4.3%. [12] Our study results showed that positive blood culture in 12.44%, is very similar to Prashant Nasa et al study in which 10.6% blood culture was found positive and also in agreement with study of Culshaw et al (12.2%)[13,6] with high incidence of gram negative bacteraemia, Escherichia coli was most common GNB isolated [13] The spectrum of organisms responsible for bacteraemia has changed. Gram negative bacilli have taken over the gram positive organisms causing septicaemia especially in hospital settings [14.15] Mehdinejad et al found 86.5% gram negative bacteria among all organisms isolated from blood cultures[8] Significant number of gram negative organisms were also detected in our study. The severity of the underlying condition of the critically ill patients admitted in ICU and the need for multiple intravascular and other devices make these patients vulnerable to bloodstream infection. But our results was slight different with above studies in which we found equal incidence of GNB and GPB with most common GPB was methicillin resistant staphylococcus hominis(MRSH) 28.57% and most common GNB isolated was Klebsiella pneumonia(KP) 28.57%and E-coli 28.57%.These isolated GNB was resistant to most of the antibiotics only colistin and tigicyclin were found to be effective in most of the cases. Other GNB was Acinetobacter expressed multi-drug resistance pattern. These gram negative cocco-bacilli showed >75% resistance to all antibiotics except colistin (25% sensitive) and tigecycline (25%) and more sensitive to teicoplanin (50%).Widespread use of carbapenems, especially in ICU settings, is responsible for this high level of resistance [7] Easy dissemination of this micro-organism and its ability to acquire multiple resistance mechanisms further complicate the scenario. Pseudomonas was more sensitive to combination of piperacillin-tazobactum and meropenem. Western literature reported higher incidence of GPB which is also supported by our study in which GPB was isolated in 46.66% of patients [13]. In the study done by Gohel et al, 70.6% of isolated Staphylococci were methicillin resistant. [16] In our study most common GPB was MRSH and linezolid, and teicoplanin, vancomycin, rifampicin should be considered as effective antibiotics. In 6.66% of ICU patient candida fugal species was isolated and it was associated with longer hospital stay, higher cost of care and increased morbidity and mortality. We have noticed that candida was isolated in immunocompromised patients like premature neonates and elderly patients with associated comorbidities. Unfortunately testing for antifungal drug sensitivity has not been started in our institute. Mortality rate was significantly higher in patients with positive blood culture (36.66% vs 19.66%), this was favoured by Prashant N et al study[13].

Knowledge of epidemiology, risk factors and outcomes of BSIs caused by resistant bacteria has a major influence on global management of ICU patients. So, further study may be done to evaluate all these factors in ICU patients with septicaemia. Even though bacteraemia may be present in minority of patients at time of ICU admission, surveillance of bacteraemia is important as it may help in identifying high risk factors associated with mortality and morbidity in septicaemia patients.

Conclusion

Findings of the present study showed that both gram negative bacteria and gram positive bacteria are equally dominated the blood isolates in patients with septicaemia. Most of the organisms are resistant to cephalosporins ,aminoglycosides, and fluoroquinolone's. The rise in antibiotic resistance in blood isolates emphasizes the importance of hospital infection control policies, rational antimicrobial prescribing practices, and invention of new antimicrobial drugs and vaccines. And we also noticed that blood culture is effective tool to established causative organism, nevertheless it is negative in most of the septicaemia cases.

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