Prevalence of Septicaemia and Antibiogram of Different Etiological Agents in Patients of Intensive Care Units of a Tertiary Care Centre in Northern India

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Abstract

Background

Septicaemia is a leading cause of mortality in ICU patients. Any delay in diagnosis and/or antibiotic treatment have been shown to increase in mortality. We planned to study the prevalence, bacteriological profile of septicaemia along with their antibiogram in patients of different ICUs in a tertiary care Hospital, Northern region.

Materials and Methods

Blood culture was performed on total of 223 blood samples from 218 patients suspected for septicaemic episodes using Brain Heart Infusion (BHI) broth. The isolates were identified by standard microbiological techniques and their antibiotic susceptibility testing was performed by Kirby Bauer method.

Results

Bacterial growth was seen in 54 samples (54 episodes of septicaemia) from 49 (22.47%) patients (40, 4, 5 from Neonatal ICU, Medicine ICU, Surgical ICU respectively). The commonest isolate was Staphylococcus aureus (45.45%) [80% in NICU, 12% in MICU & 8% in SICU], followed by Klebsiella (30.9%) [100% from NICU], and Pseudomonas aeruginosa (9.1%) [40% in NICU, 20% in MICU & 40% in SICU]. The Gram positive isolates showed high sensitivity against teicoplanin (96%), vancomycin (93%), netilin (76%), erythromycin (72%), & gentamicin (72%), The Gram negative isolates showed high sensitivity against imipenem & amikacin.
Conclusion

As prevalence of septicaemia and its etiology varies among hospitals, a rational protocol is warranted to manage sepsis of critically ill patients based on adequate knowledge of sensitivity pattern of prevalent causative agents.

Keywords: Sepsis, ICU, Klebsiella, Staphylococcus aureus, sensitivity

Introduction

Bloodstream infection (BSI) is one of the prevalent infections among patients admitted to Intensive Care Units (ICUs) and the incidence is increasing with advances in medical technologies. Sepsis causes significant morbidity and the mortality rate is estimated to vary from 25% to 80%.

Septicaemia is a term to denote those clinical states in which bacteria are present in the bloodstream and cause systemic symptoms such as fever, tachypnea, delirium, thrombocytopenia, leukocytosis or leucopenia, lactic acidosis, disseminated intravascular coagulation (DIC), elevations in C-reactive protein, haptoglobin and hypotension. Septicaemia is an acute condition. It has a connotation of urgency; unless the right things are done quickly, the patient is likely to die.

Organisms of group Enterobacteriaceae continues to be a major cause of Gram negative aerobic bacillary bacteraemia. This increase in invasion by Gram negative bacilli is perhaps because the organisms translocate more efficiently from the gastro-intestinal tract than do other bacteria. ICU associated infections are mostly due to Staphylococcus aureus & Coagulase negative Staphylococcus epidermidis arising from contaminated intra-vascular devices like artificial heart valves, intravenous and intra-arterial catheters.

Now it has become a common practice to institute early empirical therapy with broad-spectrum antibiotics in patients presenting with clinical features suggestive of septicaemia. Selection of appropriate antibiotics that can cover both positive and Gram negative micro organisms, at this phase is usually critical. This selection is depending on factors like epidemiological evidences, antibiotic resistance patterns and probable infective organisms. Prevalence of micro organisms causing septicaemia in ICUs depends on environmental and geographical locations. In developing countries like India, many hospitals are not equipped with isolation facilities and it is of high probability that prevalent microorganisms in hospitals of these countries may be different from those in developed countries. Apart from different prevalence, these micro-organisms show variable degree of resistance to antibiotics due to irrational use of antibiotics. This study aims to determine the prevalence of the bacterial agents causing septicaemia in three ICUs and to determine the antibiotic susceptibility pattern so as to help clinicians to adopt the appropriate antibacterial therapy. The epidemiological data on septicaemia would be helpful for the intensive care unit (ICU) physicians and

Prevalence of septicaemia and antibiogram in patients of ICUs scientific researchers, to understand the epidemiology of sepsis, and to evaluate the efficiency of therapeutic trials.

Material and Methods

Data collection: The A total of 223 blood samples from patients having signs & symptoms of sepsis like fever or hypothermia, leukocytosis (W.B.C >12000/mm³) or leucopenia (<4000/mm³), tachypnea (HR>90 beat/min), admitted in different ICUs. The data were collected and sent to the Department of Microbiology for culture and sensitivity. Dates such as age, sex, I.C.U type, presenting symptoms, patient history were included.

Study Design and participants: This is a cross-sectional study of one year (from 1st January 2011 to 27th February 2012). A total of 218 patients, aged newborn to 90 years. Most of the patients were from the “0 to 28 days” group. Out of 218 patients, 56.9% were males and 43.1% were females.

Sample size calculation: The sample size was calculated using the formula:

\[ n = \frac{Z^2 \cdot P \cdot (1-P)}{d^2} \]

Where n=sample size, Z = Z statistic for a level of confidence, P = expected prevalence and d=the precision.

From the existing data, the prevalence of septicaemia in ICU patients varied from 12-38.5%. However most of the studies available were done on a western population setting. Keeping this limitation in mind and assuming the prevalence to be 364, if the maximum quoted prevalence rate of 38.5% and a precision of 0.05 are to be used. However, in the 1-year period we performed an interim analysis and terminated the study with 218 patients.

Inclusion criteria: 
During the study period, all the patients presenting to the different ICUs with signs and symptoms of sepsis were enrolled. To be eligible patients must have all of the following:
- Must be admitted or transferred to an Intensive Care Unit.
- Have a high clinical suspicion of an infection
- Have sepsis as defined by an infection together with two or more SIRS criteria

Exclusion Criteria: 
Patients with the following criteria will be excluded:
- Patients in whom the sepsis has been present before the beginning of the study period.

Statistical Analysis and Data Analysis: Descriptive statistics were calculated using Microsoft Office Excel 2010. Percentages were used in this study to analyze the data.
Prevalence of septicaemia and antibiogram in patients of ICUs

Table 1: The age group and sex of the patients admitted in ICUs.

<table>
<thead>
<tr>
<th>Age group</th>
<th>Number of patients</th>
<th>Number of positive cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>0-28 d</td>
<td>101</td>
<td>74</td>
</tr>
<tr>
<td>28d-20y</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>21y-40y</td>
<td>11</td>
<td>9</td>
</tr>
<tr>
<td>41y-60y</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>&gt;60y</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>124</td>
<td>94</td>
</tr>
</tbody>
</table>

Out of 218 cases, 49 patients were culture positive (63.27% male and 36.73% female). The patient distribution from different ICUs was 80.3%, 15.1% and 4.6% from NICU, MICU and SICU respectively. The total positive culture patients were 22.9%, 12.1% and 50% from the NICU, MICU and SICU respectively (Table 2).

Table 2: Number of patients from different ICUs and the number of patients showing positive blood cultures.

<table>
<thead>
<tr>
<th>ICUs</th>
<th>Culture and sensitivity</th>
<th>Blood culture positive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>NICU</td>
<td>101</td>
<td>74</td>
</tr>
<tr>
<td>MICU</td>
<td>18</td>
<td>15</td>
</tr>
<tr>
<td>SICU</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>218</td>
<td>31</td>
</tr>
</tbody>
</table>

NICU, Neonatal ICU; MICU, Medicinal ICU; SICU, Surgical ICU; C/S, Culture and sensitivity.

A total of 223 blood sampewere processed from a total of 218 patients and a total 54 episodes of septicaemia had been seen in ICU patients. 45 patients had single episode while 3 patients had double episode and only one patient had a triple episode of septicaemia (Table-3).

Out of 54 episodes of septicaemia, 53 were mono-microbial; while one was polymicrobial (2 isolates), so total 55 bacterial isolates. Most of the isolates were from the NICU, followed by SICU and MICU. Out of the 55 isolates, 26 (47.27%) were Gram-positive cocci and 29 (52.72%) were Gram-negative bacilli. Staphylococcus aureus was the most frequently isolated Gram-positive organism while Klebsiella spp(30.9%) heads the list among the Gram-negative isolates in ICU patients. The etiological agents in different ICUs are listed in Table-4.
Prevalence of septicaemia and antibiogram in patients of ICUs

Table 6: Sensitivity pattern in percentage (%) of Gram negative isolates.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Ak</th>
<th>A</th>
<th>Ac</th>
<th>Ca</th>
<th>Ce</th>
<th>Co</th>
<th>Cf</th>
<th>G</th>
<th>I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Klebsiella</td>
<td>58.8</td>
<td>0</td>
<td>0</td>
<td>11.75</td>
<td>11.75</td>
<td>35.3</td>
<td>23.5</td>
<td>0</td>
<td>88.2</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>80</td>
<td>NT</td>
<td>NT</td>
<td>100</td>
<td>60</td>
<td>5</td>
<td>60</td>
<td>80</td>
<td>60</td>
</tr>
<tr>
<td>Citrobacter</td>
<td>0</td>
<td>NT</td>
<td>NT</td>
<td>0</td>
<td>0</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Acinetobacter</td>
<td>100</td>
<td>50(IIS)</td>
<td>NT</td>
<td>50</td>
<td>100</td>
<td>100</td>
<td>50 NT</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Enterobacter</td>
<td>100</td>
<td>50 NT</td>
<td>50</td>
<td>50 NT</td>
<td>100</td>
<td>50(IIS)</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEC</td>
<td>100</td>
<td>NT</td>
<td>NT</td>
<td>0</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>E.coli</td>
<td>100</td>
<td>NT</td>
<td>NT</td>
<td>0</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

The antibiotic susceptibility testing (AST) of the Gram-positive and Gram-negative isolates were tabulated in Table-5 and Table-6 respectively.

Discussion:

Septicaemia prevalence:

The prevalence of septicaemia varies with considerable fluctuation over time and place which indicate that there is a need for continuous monitoring of causative organisms and their drug susceptibility pattern at a local level. In our study, the prevalence of septicaemia was 22.47% (Table-2), which is comparable to the results of previous studies16,17 whereas the Iranian ICUs study has reported a high prevalence rate (38.5%) of septicaemia18. The high variability in the prevalence rate could be due to differences in sticking to aseptic techniques from one hospital to another. The practices like hand washing, sterilization and disinfection of equipment and devices, aseptic precautions during invasive procedures and staff education play an important role in the prevalence of septicaemia especially in ICUs.

Blood culture positivity:

In the present study, 24.21% cases had positive blood culture (Table-3). Various authors have reported blood culture positivity in the range of 7.89-56%19, 20, 21. A low blood culture isolation rate in some studies might be due to several reasons, e.g. Administration of antibiotics before blood collection, so the timing of blood collection for culture should be judiciously done or the possibility of infection with anaerobes. A study has reported that 26% of all the septicaemia was caused by anaerobes22.

Table 3: Number of episodes of septicaemia.

<table>
<thead>
<tr>
<th>ICUs</th>
<th>Blood samples</th>
<th>Septicaemic isolates</th>
<th>Number of episodes in patients</th>
<th>Single Episode</th>
<th>Double Episode</th>
<th>Triple episode</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICU</td>
<td>180 (80.7%)</td>
<td>45</td>
<td>36</td>
<td>3</td>
<td>1</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>MICU</td>
<td>33 (14.8%)</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>SICU</td>
<td>10 (4.5%)</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>223</td>
<td>54</td>
<td>45</td>
<td>3</td>
<td>1</td>
<td>54</td>
<td></td>
</tr>
</tbody>
</table>

NICU, Neonatal ICU; MICU, Medicinal ICU; SICU, Surgical ICU.

Table 4: Bacterial isolates from different ICUs in order of frequency.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Ak</th>
<th>A</th>
<th>Ac</th>
<th>Ca</th>
<th>Ce</th>
<th>Co</th>
<th>Cf</th>
<th>G</th>
<th>I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sa, Staphylococcus aureus; Kleb, Klebsiella species; Pseu, Pseudomonas eruginosa; Entero, Enterobacter species; Ac, Acinetobacter species; Cit, Citrobacter species; E. coli, Escherichia coli; NEC, Non lactose fermenting Escherichia coli; CoNS, Coagulase negative Staphylococcus; NICU, Neonatal ICU; MICU, Medicinal ICU; SICU, Surgical ICU.</td>
<td>20</td>
<td>17</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>46 (83.6)</td>
</tr>
<tr>
<td>MICU</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4 (7.2)</td>
</tr>
<tr>
<td>SICU</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5 (9.1)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>25</td>
<td>17</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>55 (100)</td>
</tr>
</tbody>
</table>

Sa, Staphylococcus aureus; Kleb, Klebsiella species; Pseu, Pseudomonas eruginosa; Entero, Enterobacter species; Ac, Acinetobacter species; Cit, Citrobacter species; E. coli, Escherichia coli; NEC, Non lactose fermenting Escherichia coli; CoNS, Coagulase negative Staphylococcus; NICU, Neonatal ICU; MICU, Medicinal ICU; SICU, Surgical ICU.

• 53 cases were monomicrobial while 1 case was polymicrobial (2 isolates)

* Gram positive isolates

Table 5: Sensitivity pattern in percentage (%) of Gram positive isolates.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Ak</th>
<th>Cl</th>
<th>CD</th>
<th>E</th>
<th>Ne</th>
<th>Ox</th>
<th>P</th>
<th>T</th>
<th>Va</th>
<th>Tei</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus</td>
<td>64</td>
<td>32</td>
<td>28</td>
<td>72</td>
<td>72</td>
<td>76</td>
<td>40</td>
<td>16</td>
<td>50</td>
<td>93</td>
</tr>
<tr>
<td>CoNS</td>
<td>100</td>
<td>NT</td>
<td>NT</td>
<td>100</td>
<td>0</td>
<td>NT</td>
<td>100</td>
<td>0</td>
<td>100 (IS)</td>
<td>100</td>
</tr>
</tbody>
</table>

Ak, Amikacin; Cl, Ciprofloxacin; Co, Cotrimoxazole; E, Erythromycin; G, Gentamycin; Ne, Netilin; Ox, Oxalillin; P, Penicillin; T, Tetracyclin; Va, Vancomycin; IS, intermediate sensitive; NT, Not tested; S. aureus, Staphylococcus aureus; CoNS, Coagulase negative Staphylococcus.
Is gender and age a risk factors in sepsis?

In the present study, positive cultures were reported in 63.3% males and 36.7% females (Table-1); similar observations were reported in a previous study. Previous studies also suggested that male gender increases the risk for developing sepsis. They demonstrated the immunosuppressive effects of male sex hormones and immune enhancing effects of female sex hormones in the context of depression of immune function after trauma and haemorrhage in males.

The ages of patients ranged from newborn to 90 years. The numbers of positive blood cultures from NICU, SICU and MICU were 22.9%, 50% and 12.1% respectively (Table-2). Whereas the highest positive rate was in NICU (81.63%), it could be attributed to lower immunity in neonates. This is further supported by previous studies that pointed out a high rate of positive cultures (47.5% and 24.88%) in neonates. Exposure to life-saving invasive procedures, severity of sickness and the potential for patient-to-patient transmission common risk factors for all ICU’s patients.

Etiological agents:

The analysis of microbiological characteristics of septicaemia in this study showed that Gram-negative bacteria were the most common pathogens in septicaemia (52.72%) which was quite different from the report that Gram-positive bacteria were predominant in previous studies. However results in this study were consistent with some of previous studies. The reasons for the changes in the microbiological patterns of septicaemia in this study is probably a result of complex interactions involving patient’s underlying conditions, the demographic and geographic factors, the extensive use of extended-spectrum antibiotics, less attention to sanitary precautions, the invasive interventions, and the quality of care provided. The Staphylococcus aureus (45.45%) is the commonest pathogen among the Gram-positive isolates (80%, 12%, and 8% from NICU, MICU and SICU respectively) which may be due to increased use of invasive procedures.

A study among paediatric ICU patients reported that pharyngeal S. aureus carriage (92.6%) was more common than nasal carriage; it also exceeds the carriage rates in adults (58 to 84%). These pharyngeal / nasal S. aureus carriage is a well-known risk factor for infection.

The Gram-negative septicaemias in ICUs frequently originate from respiratory or gastrointestinal route, thus the common isolates being Klebsiella, Pseudomonas and Enterobacter species. This is confirmed by our study as amongst the Gram-negative isolates Klebsiella species (30.9%) [100% from NICU], Pseudomonas aeruginosa (9.1%) [40%, 20%, 40% from the NICU, MICU and SICU respectively], Enterobacter species (3.6%) [50% from NICU and 50% SICU], Acinetobacter species 3.6 [100 % from NICU] tops the list, while the other isolates were Escherichia coli, Non Lactose fermenter Escherichia coli and Citrobacter.

Prevalence of septicaemia and antibiogram in patients of ICUs species [1.8% each from NICU]. These findings further in line with some previous studies.

Antibiotic sensitivity profile:

The AST showed that Staphylococcus aureus were highly sensitive to Teicoplanin & vancomycin while they were highly resistant to penicillin 84%, cotrimoxazole (72%), and ciprofloxacin (68%) as those drugs are commonly used by the practitioners. A similar high rate of Penicillin resistance was seen in S. aureus(95.9%) in a study conducted in Lucknow. Forty percent of strains were methicillin resistant Staphylococcus aureus (MRSA). Klebsiella species showed good sensitivity against imipenem and amikacin while in case of Pseudomonas aeruginosa effective drugs were Ceftazidime, amikacin and gentamicin. None of the strains of Klebsiella were sensitive to ampicillin and amoxyclov, similar 100% resistance was reported in a previous study. Multiple drug resistance was also seen among Gram-negative isolates.

Conclusion:

Staphylococcus aureus and Klebsiella species are the common isolates causing septicaemia in ICU patients. Our study suggests that the use of broad spectrum antibiotic should cover these pathogens. The findings warrant that the life threatening complications of septicaemia can be prevented by isolation of the causative agent if possible and judicious use of preventive as well as therapeutic antibiotics.

Limitation of the study:

We have not done anaerobic blood culture. Use of automated blood culture techniques could have refined the results. The multiple episodes of septicaemia in a patient (n=4) have been included in the number of specimen which might affect the blood culture positivity rate.

Further scope of study:

The common risk factors like respiratory distress, prematurity, surgery, trauma and invasive procedures in different ICUs that predispose septicaemia could be considered in future studies. The inclusion of 2 viral and fungal agents would enhance the adoption of proper treatment policies.

Acknowledgments:

We would like to thank all the faculty and technical staff of department of Microbiology for their invaluable support.

Authors’ contributions:

All authors contributed equally in this study in various fields such as study design, acquisition of data, revision and preparation of the manuscript. All authors have gone through the manuscript and finalize the same for publication.
Conflict of interest:
There is no conflict of interest among authors arising from the study.

What this study adds:
The prevalence and etiological agents of septicaemia varies among hospitals thus such studies should be done at regular time interval to develop a rational protocol to manage morbidity of ICU patients.

Reference:
27. Martin GS. Sepsis, severe sepsis and septic shock: changes in incidence, pathogens and outcomes. Expert


**Article Information**

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<td>Accepted</td>
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