A Study of Clinico-Bacteriological Profile of Septicaemia in Neonates and Young Infants Admitted In Rims Hospital, Imphal

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Abstract:

Objectives: To describe the clinical features of septicaemia in neonates and young infants. To find out the various bacteriological profile of the septicaemia and their antibiotic susceptibility.

Materials and methods: A cross sectional study was conducted in the Department of Paediatrics in Regional Institute of Medical Sciences, Imphal in collaboration with Department of Microbiology, Regional Institute of Medical Sciences, Imphal amongst 100 clinically suspected sepsis in neonates and young infants admitted in RIMS hospital based on inclusion criteria. Detailed history and clinical examination was taken and then blood culture and other necessary investigation was done. Chi-square test was employed to test the association and p-value of <0.05 was taken as significant.

Results: Septicaemia in neonates and young infants was more common amongst male (58%), normal vaginal delivery (65%) and low birth weight (59%) patients. The most common clinical presentation was poor feeding (78%) followed by lethargy (75%) and respiratory distress (61%). Culture positivity was seen in 30% of suspected sepsis patients. Gram negative to positive ratio was 1.14:1. Klebsiella was the most common organism detected followed by E.coli (4), CONS and S. aureus. Among gram negative organisms Klebsiellasps (9) was the most common followed by E.coli (4), Pseudomonassps (1), Acinetobactersps (1) and Proteus ssp (1). Among the gram positive organisms, Coagulase negative Staphylococcus (CONS) and S.aureus were the most common (4 each) followed by MRSA and Enterococcus (3 each). All the gram negative isolates were sensitive to piperacillin/tazobactam, imipenem and meropenem. All the gram positive isolates were sensitive to linezolid and vancomycin.

Conclusion: From our study we observed that the most common clinical presentation of sepsis was poor feeding, lethargy and respiratory distress, and the most common causative organisms were Klebsiellasps, E.coli, CONS and Staphylococcus aureus. Some of the organisms were resistant to routinely used antibiotics; hence their resistance pattern should be considered essential before deciding the empirical treatment. Depending on the antibiotics sensitivity pattern of the isolates, an antibiotic policy should be formulated in the hospital which should be changed from time to time if necessary.

Key Words: Septicaemia, antibiotic susceptibility, antibiotic policy.

I. Introduction

Neonatal sepsis is a clinical syndrome characterised by a constellation of nonspecific signs and symptoms in association with bacteraemia during first month of life.1

Neonatal sepsis is a result of bacterial infection invading bloodstream causing some nonspecific systemic signs and symptoms, including temperature instability, respiratory distress, cyanosis, apnoea, bradycardia or tachycardia, feeding difficulties, hypotonia, lethargy, irritability, seizures, bulging fontanel, long capillary refill time, paleness, mottled skin, abdominal distension, and unexplained jaundice.2,3 Early diagnosis and prompt treatment are quite challenging. It needs initial empirical antibiotic treatment before the result of microbial culture showing sensitive antibiotic choice come out.5 Despite overall improvement in the health of children worldwide, mortality among young infants less than 2 months old remains high.4 Young infant mortality comprises 40% of the estimated 10.8 million child deaths worldwide annually.7 It is an important cause of morbidity and mortality among neonates in India with an estimated incidence of approximately 4% in intramural live births.6 India accounts for 27% of the global burden of neonatal deaths each year. Nearly two-thirds of the infant mortality and 46% of the under five mortality occurs in the neonatal period in India.5,8 It is recognized that to reduce infant and under-five mortality, health problems that occur during the first two months of life must be addressed as a high priority. Three-fourths of neonatal deaths occur in the first week of life.9,10

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Neonatal sepsis is classified into early onset sepsis if the patient presents within 72 hours of birth and late onset sepsis if the presentation is after 72 hours of birth. Early onset sepsis is conventionally regarded as maternally-acquired, with causative organisms, such as Escherichia coli and Group B Streptococcus (GBS) usually found in the maternal genital tract, whereas late onset sepsis is considered environmental in origin-either hospital or community acquired. Commonly implicated organisms in hospital acquired infections are Coagulase-negative Staphylococci, Staphylococcus aureus, and Gram-negative organisms such as Klebsiella and Pseudomonas species.

Prompt recognition and appropriate antimicrobial therapy are the key determinants of positive outcome in this serious paediatric emergency. Blood culture remains the gold standard for the diagnosis of neonatal sepsis. The spectrum of organisms causing neonatal sepsis is quite different in developed countries in comparison with developing countries like India. The pattern of organism differs from place to place and can change in the same place over period of time. Within developing countries, regional variation exists in the spectrum of organisms causing sepsis.

Although treatment of established cases is important, control of infections in young infants ultimately rests on prevention. Although efforts are under way in many developing countries to improve perinatal care, attention is also being given to maternal immunization as a means of protecting young infants from infection with passively acquired maternal antibody. This has been used with great success to control neonatal tetanus in developing countries and has recently been tried to prevent neonatal infections caused by encapsulated bacteria such as S. agalactiae, S. pneumoniae and H. influenzae. Developments in this area provide another valid reason for investigating the aetiology of infections in young infants in developing countries.

On the basis of available data WHO and other authorities have recommended that serious infections in very young infants in developing countries should be treated with penicillin and gentamicin initially. In practice many different combinations are used based on local interpretations of existing data; most regimens include a penicillin and an aminoglycoside. Some use chloramphenicol and when available, third generation cephalosporins, particularly cefotaxime, are used. In India, a lot of neonatal mortality is accountable by sepsis and its treatment failure due to emergence of drug resistance. The fact is that the isolated organisms have developed increased drug resistance over the last few years.

Antibiotics have been used extensively in the management of sepsis. On many occasions, antibiotics have been used empirically without identifying the causative organisms or knowing the antibiotic sensitivity, leading to development of resistance. It is therefore necessary to note which are the common organisms causing sepsis in our area and their sensitivity to antibiotics. This will help us to use appropriate antibiotics and reduce the development of antibiotic resistance. The antibiotic misuse has resulted in further confusion in diagnosis and emergence of drug resistant bacterial strains in the neonatal units with grave sequel. Thus the successful treatment with a favourable outcome of the neonate depends on an ongoing review of the causative organisms and their antibiotic susceptibility pattern.

With this background the study was conducted to describe the various clinical features and the spectrum of isolates in cases of sepsis in neonates (0-28days) and young infants (29-59days) admitted at RIMS Hospital, Imphal, and their antimicrobial susceptibility patterns.

AIMS AND OBJECTS: To describe the clinical features of septicaemia in neonates and young infants. To find out the various bacteriological profile of the septicaemia and their antibiotic susceptibility.

II. Materials And Methods

This was a hospital based cross sectional study conducted in the Department of Paediatrics, Regional Institute of Medical Sciences, Imphal in collaboration with Department of Microbiology. The study was conducted between September 2016 to August 2018 over a period of two years.

Study population:
All the infants with clinically suspected sepsicaemia in 0 to 59 days of age who were under treatment during the study period.

Inclusion criteria:
All newborns and young infants with anyone of the followings finding were included in the study
1. Body temperature ≤35.5°C
2. Body temperature ≥37.5°C
3. History of difficulty feeding
4. History of convulsions/seizures
5. Moving only when stimulated
6. Respiratory rate ≥60 per minute
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7. Severe chest indrawing during respiration
8. Skin manifestation like petechia, purpura etc.
9. Other features like abdominal distension, vomiting etc.

Exclusion criteria:
Newborns and young infants with the following were excluded
1. Patients more than 59 days old
2. Congenital central nervous system anomalies and intracranial haemorrhage
3. Respiratory distress syndrome caused by pneumothorax, hyaline membrane disease and atelectasis
4. Primary gastrointestinal disease such as an anatomical obstruction
5. Hematologic diseases eg. Iso-immune haemolytic disease, red cell enzyme defects and congenital leukaemia
6. Recognised major congenital anomalies
7. Central nervous system injury
8. Parents not willing to give consent

Sample size: The sample size of this study group was comprised of total 100 clinically suspected sepsis in neonates and young infants.

Consecutive sampling: The present study was intended to select all children in the age group of 0 to 59 days who present with features of septicaemia and admitted in Paediatric ward of RIMS Hospital, Imphal

Study variables:
1. Demographics profiles - Age, gender, birth weight, gestational age, immunization status
2. Clinical features of septicaemia:
3. Body temperature ≤35.5°C
4. Body temperature ≥37.5°C
5. History of difficulty feeding
6. History of convulsions/seizures
7. Moving only when stimulated
8. Respiratory rate ≥60 per minute
9. Severe chest indrawing during respiration
10. Skin manifestation like petechia, purpura etc.
11. Other features like abdominal distension, vomiting etc.

Outcome variables:
1. Bacteriological profile: different types of bacteria isolated after growth in culture media
2. Antibiotic susceptibility: Sensitivity of the particular bacteria to different antibiotics

III. Results And Observations

Figure 1: Bar diagram showing age distribution of the respondents
Majority of the patients were belong to 0-3 days old group. Mean age was 7 days with a standard deviation of 3.2 days.

**Figure 2:** Pie chart showing distribution of the respondents by gender

Male predominance was seen in this study in 58% of cases as shown in figure 2.

**Figure 3:** Bar diagram showing age distribution of the respondents stratified by gender

Among ages 0-3 days and 4-28 days male predominance was found and higher in 0-3 days group. For age 29-59 days there was equal distribution. The findings were statistically insignificant (p>0.05).

**Figure 4:** Pie chart showing distribution of the respondents by address
Majority of the patients were from rural areas in 72% of cases as shown in figure 4.

![Figure 5: Pie chart showing distribution of the respondents by religion](image)

Most of the patients were Hindu as shown in figure 5.

![Figure 6: Pie chart showing distribution of the respondents by gestational age](image)

Most of the patients were term and few (19%) were preterm as shown in figure 6.

![Figure 7: Pie chart showing distribution of the respondents by type of delivery](image)

Most common was NVD in 65% of cases as shown in figure 7.

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Low birth weight was found in 59% of the patients as shown in figure 8.

The most common clinical presentation was poor feeding in 78% of cases followed by lethargy (75%), respiratory distress (61%), etc.

Culture positivity was seen in 30% of suspected sepsis patients as shown in table 1.

**Figure 8:** Pie chart showing distribution of the respondents by birth weight

**Figure 9:** Bar diagram showing distribution of the respondents by clinical signs and symptoms

**Table 1:** Distribution of the respondents by clinical signs and symptoms

<table>
<thead>
<tr>
<th>Culture positivity</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>30</td>
<td>30.0</td>
</tr>
<tr>
<td>Negative</td>
<td>70</td>
<td>70.0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Culture positivity was seen in 30% of suspected sepsis patients. Gram negative to positive ratio was 1.14:1. Klebsiella was the most common organism detected followed by E.colispp, CONS and S. aureus. Among gram negative organisms Klebsiellaspp (9) was the most common followed by E.colispp (4), Pseudomonas spp (1), Acinetotbacterspp (1) and Proteus spp (1). Among the gram positive organisms, Coagulase negative Staphylococcus (CONS) and S. aureus were the most common (4 each) followed by MRSA and Enterococcus (3 each).

Table 2: Distribution of the respondents by bacteriological profile stratified by age

<table>
<thead>
<tr>
<th>Bacteriological profile</th>
<th>0-3 days n(%)</th>
<th>4-28 n(%)</th>
<th>29-59 n(%)</th>
<th>Total n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture positive</td>
<td>15(34.0)</td>
<td>11(30.5)</td>
<td>4(20.0)</td>
<td>30(30.0)</td>
</tr>
<tr>
<td>Gram negative</td>
<td>8(18.2)</td>
<td>6(16.6)</td>
<td>2(10.0)</td>
<td>16(16.0)</td>
</tr>
<tr>
<td>Klebsiella spp</td>
<td>6(13.6)</td>
<td>3(8.3)</td>
<td>0(0.0)</td>
<td>9(9.0)</td>
</tr>
<tr>
<td>E. coli spp</td>
<td>2(4.5)</td>
<td>1(2.7)</td>
<td>1(5.0)</td>
<td>4(4.0)</td>
</tr>
<tr>
<td>Pseudomonas spp</td>
<td>0(0.0)</td>
<td>1(2.7)</td>
<td>0(0.0)</td>
<td>1(1.0)</td>
</tr>
<tr>
<td>Acinetobacters spp</td>
<td>0(0.0)</td>
<td>1(2.7)</td>
<td>0(0.0)</td>
<td>1(1.0)</td>
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<tr>
<td>Proteus spp</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>1(5.0)</td>
<td>1(1.0)</td>
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<tr>
<td>Gram positive</td>
<td>7(16.0)</td>
<td>5(13.8)</td>
<td>2(10.0)</td>
<td>14(14.0)</td>
</tr>
<tr>
<td>Coagulase negative</td>
<td>2(4.5)</td>
<td>1(2.7)</td>
<td>1(5.0)</td>
<td>4(4.0)</td>
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<tr>
<td>Staphylococcus (CONS)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>2(4.5)</td>
<td>1(2.7)</td>
<td>1(5.0)</td>
<td>4(4.0)</td>
</tr>
<tr>
<td>MRSA</td>
<td>2(4.5)</td>
<td>1(2.7)</td>
<td>0(0.0)</td>
<td>3(3.0)</td>
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<tr>
<td>Enterococcus spp</td>
<td>1(2.2)</td>
<td>2(5.5)</td>
<td>0(0.0)</td>
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<tr>
<td>Sterile</td>
<td>29(66.0)</td>
<td>15(41.5)</td>
<td>16(80.0)</td>
<td>70(70.0)</td>
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<tr>
<td>Total</td>
<td>44(100.0)</td>
<td>36(100.0)</td>
<td>20(100.0)</td>
<td>100(100.0)</td>
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</table>

Gram negative predominance was seen in age group 0-3days and age 4-28 days but in 29-59 days equal numbers was detected. Klebsiella (13.6%) was the most common organism in 0-3 days followed by CONS (4.5%), E. coli (4.5%) and staphylococcus aureus (4.5). For age group 4-28 days Klebsiella (8.3%) was the most common followed by Enterococccus (5.5) . Staphylococcus aureus was the most common in the age group 29-59 days.
Table 3: Distribution of the respondents by sensitivity profile of organism detected

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Klebsiella aspp (9)</th>
<th>Pseudomonas (1)</th>
<th>E. Coli aspp (4)</th>
<th>Acinetobacter aspp (1)</th>
<th>Proteus (1)</th>
<th>CONS (4)</th>
<th>Staphylococcus aureus (4)</th>
<th>MRSA (3)</th>
<th>Enterococcus (3)</th>
</tr>
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<tr>
<td>AMP SR</td>
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<td>1(25)</td>
<td>2(50)</td>
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<td>AMC SR</td>
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<td>1(100)</td>
<td>3(75)</td>
<td>2(50)</td>
<td>3(100)</td>
<td>3(100)</td>
<td>1(33.3)</td>
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<td>GEN SR</td>
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<td>2(50)</td>
<td>1(100)</td>
<td>1(100)</td>
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<tr>
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<td>2(50)</td>
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<td>1(100)</td>
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<td>1(25)</td>
<td>1(100)</td>
<td>1(100)</td>
<td>2(50)</td>
<td>1</td>
<td>2(66.7)</td>
<td>2(66.7)</td>
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<td>LE SR</td>
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<td>1(25)</td>
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</table>

() are percentages, S-sensitive, R-resistant


In the table above Klebsiellasp was sensitive in high percentage (88.9%) to imipenem and piperacillin/tazobactam, and also sensitive to meropenem (66.7%), levofloxacin (55.5%) and ciprofloxacin (55.5%). The only Pseudomonas spp detected in this study was sensitive to piperacillin/tazobactum, levofloxacin, imipenem, amikacin, clindamycin, linezolid vancomycin and ceftriaxone. And it was resistant to gentamycin, ciprofloxacin, azithromycin and doxycycline. E.coli spp was sensitive to imipenem in 75%, gentamicin, piperacillin/tazobactum, meropenem in 50% of the isolates. Acinetobacterspp was sensitive to gentamicin, piperacillin, piperacillin/tazobactum, levofloxacin, imipenem and amikacin. Proteus spp. was sensitive to ampicillin, amoxyclave, gentamycin, amikacin, ceftazidime/clavulanate, piperacillin, ceftriaxone, levofloxacin, imipenem, piperacillin/tazobactam and meropenem. In this study, CONS were all sensitive to vancomycin and linezolid (100%). It was also sensitive to gentamycin, amikacin, cotrimoxazole and tetracycline (75%). It was 100% resistant to penicillin, 75% to erythromycin, azithromycin, amoxyclave, cefoxitin, and 50% to ceftriaxone and clindamycin. Staphylococcus aureus was 100% sensitive to linezolid and vancomycin, 75% to erythromycin and cloramoxazole and half of the isolates were sensitive to ciprofloxacin, clindamycin, cefoxitin and azithromycin. MRSA was 100% sensitive to linezolid and vancomycin. It was also sensitive to tigecycline, cotrimoxazole and gentamicin in more than half of the isolates. It was resistant to amoxyclave in all the isolates and in more than half (66.7%) of the isolates to gentamicin, ciprofloxacin, cefoxitin and azithromycin. Enterococcus was sensitive to vancomycin and linezolid in high percentages. It was also sensitive to amoxyclave, piperacillin/tazobactum, linezolid, penicillin and cefoxitin in one isolate out of 3 isolates. So all the gram positive isolates were sensitive to linezolid and vancomycin.

IV. Discussion

Neonatal sepsis is one of the commonest cause of neonatal morbidity and mortality. A Cross-Sectional study was conducted in the Department of Paediatrics in Regional Institute of Medical Sciences, Imphal in collaboration with Department of Microbiology between September 2016 to August 2018 over a period of two years among 100 clinically suspected sepsicaemia in 0 to 59 days of age to describe the clinical features of sepsicaemia in neonates and young infants, and to find out the various bacteriological profile of the sepsicaemia and their antibiotic susceptibility. So, in this study sepsis of young infants were also included.

In this study out of 100 sepsis suspected cases, 30 cases were found to be blood culture positive. Same finding was noted in the study by Mokuolu AO et al[19] in which 30.8% had positive blood culture. Almost similar finding was found in the study by Muley VA et al[20] (26%).

Early neonatal sepsis (0-3days) was found in 53.3% of cases, late neonatal sepsis (4-28days) in 30% of cases and among 29-59 days in 16.7%. Mean age of sepsis for this study was 7 days.

Male predominance was seen in this study (58 males and 42 females) in the ratio 1.3:1. This was consistent with the finding by Begum M et al[21] where same finding (1.2:1) was noted. Other studies were also having the same finding like the study by Mokuolu AO et al[22] (1.2:1) and GalhotraS et al[23]. This could be gender biasness in presentation to the hospital for care. Population based studies would be needed to address this important question.

Patients with sepsis were preterm in 29% of cases. This is almost consistent with the study by Galhotraet al[23] where prematurity was found in 35% of cases. Two third of sepsis patients were delivered by vaginal delivery. Similar finding was observed in the study by Fareedul H et al[24] and Galhotra et al[23]. In this study low birth weight was found in 59% of cases with sepsis. This is similar with the study done by Galhotraet al[23] where LBW was found to be important risk factor for sepsis.
The most common clinical presentation was poor feeding in 78% of cases, lethargy (75%) and respiratory distress in 61% of cases. This finding was almost similar to the study by Fareedul H et al\textsuperscript{36} where poor feeding (56%) and respiratory distress (48%) were the most common clinical features and lethargy was found in 36% of cases. Other clinical features were neonatal jaundice (43%), fever (38%), hypothermia (27%) and vomiting (25%). Seizure, hypoglycaemia, loose motion, abdominal distension and skin manifestation were found in few numbers.

The most common organism detected was Klebsiellappp in 26% of culture positive patients. Gram negative to positive ratio was 1.14:1. This finding was consistent with the study by Bhurle A et al\textsuperscript{37} which concluded that gram negative organisms mainly Klebsiella pneumoniae was most common agent causing neonatal sepsis.

Similar finding was noted in the studies by HasibuanBS\textsuperscript{36}, Bhat RY et al\textsuperscript{37}, Muley VA et al\textsuperscript{31}, Desai KJ et al\textsuperscript{38} etc.

In some studies like SrinivasaS et al\textsuperscript{39}, GalhotraS et al\textsuperscript{33} and Mokuolu AO et al\textsuperscript{30} gram positive like CONS and Staphylococcus aureus were the most common organissm detected.

In this study Klebsiellappp was sensitive in high percentage (88.9%) to imipenem and piperacillin/tazobactam, and also sensitive to meropenem (66.7%), levofloxacin (55.5%) and ciprofloxacin (55.5%). It was resistant to ampicillin, gentamycin, cefixime, ceftriaxone, amikacin and linezolid in more than half of the isolates. The only Pseudomonas spp detected in this study was sensitive to piperacillin/tazobactam, levofloxacin, imipenem, amikacin, ceftriaxone, linezolid vancomycin and ceftriaxone. And it was resistant to gentamycin, piperacillin/tazobactam, azithromycin and doxycycline. E.colisspp was sensitive to imipenem in 75%, gentamicin, piperacillin/tazobactam, meropenem in 50% of the isolates.

Acinetobacter spp was sensitive to gentamicin, piperacillin/tazobactam, levofloxacin, imipenem and amikacin. It was resistant to ampicillin, amoxicillin and ciprofloxacin. Proteus spp. was sensitive to ampicillin, amoxyclave, gentamycin, amikacin, cefazidime/clavulanate, ciprofloxacin, ceftriaxone, levofloxacin, imipenem, piperacillin/tazobactam and meropenem. So in this study all the gram negative isolates were sensitive to piperacillin/tazobactam, imipenem and meropenem.

In this study, CONS were all sensitive to vancomycin and linezolid (100%). It was also sensitive to gentamycin, amikacin, cotrimoxazole and tetracycline (75%). It was 100% resistant to penicillin, 75% to erythromycin, azithromycin, amoxyclave, cefoxitin, and 50% to ceftriaxone and clindamycin. Staphylococcus aureus was 100% sensitive to linezolid and vancomycin, 75% to erythromycin and cotrimoxazole and half of the isolates were sensitive to ciprofloxacin, clindamycin, cefoxitin and azithromycin.

MRSA was 100% sensitive to linezolid and vancomycin. It was also sensitive to tigecycline, cotrimoxazole and gentamicin in more than half of the isolates. It was resistant to amoxyclave in all the isolates and in more than half (66.7%) of the isolates to gentamicin, ciprofloxacin, cefoxitin and azithromycin.

Enterococcus was sensitive to vancomycin and linezolid in high percentages. It was also sensitive to amoxyclave, piperacillin/tazobactam, linezolid, pencycillin and cefoxitin in one isolate out of 3 isolates.

So all the gram positive isolates were sensitive to linezolid and vancomycin. In the study by GalhotraS et al\textsuperscript{33} all the gram positive isolates were sensitive to vancomycin and linezolid.

In a systemic review done by Hamer DH et al\textsuperscript{40}, Klebsiella species predominated in the first 3 days of life in 26% of all infections. S. aureus, GBS and E.coli were next mostly frequently isolated organisms causing 13% to 17% of infections. The ratio of gram negative to gram positive ratio was 1:4:1. A single pathogen, Klebsiella, accounted for 25% of all 3209 isolates. S. aureus and E. coli caused 15–18% of infections; 7% were caused by GBS, only half as common in this compared with the very early period. Acinetobacter and Pseudomonas (total 11.8%) increased slightly compared with the very early period. The overall Gram negative to Gram-positive ratio was 2:1. This was noted in the first week of life.

V. Conclusion

From our study we observed that the most common clinical presentation of sepsis were poor feeding, lethargy and respiratory distress, and the most common causative organisms were Klebsiellappp, E.colisspp, CONS and Staphylococcus aureus. Some of them were resistant to routinely used antibiotics; hence their resistance pattern should be considered essential before deciding the empirical treatment. Depending on the antibiotics sensitivity pattern of the isolates, an antibiotic policy should be formulated in the hospital which should be changed from time to time if necessary.
A Study of Clinico-Bacteriological Profile of Septicaemia in Neonates and Young Infants Admitting to a Tertiary Care Hospital: A Retrospective Analysis

References


