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Original Research Article

A Study of Bacteriological Profile of Late Onset Sepsis at Neonatal Intensive Care Unit in Prathima Institute of Medical Sciences

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Abstract: Septicemia in new born remains a significant cause of mortality and morbidity in developing countries. Changing bacterial flora and emergence of resistant strains adds to the problem. Thus, neonatal septicemia requires accurate and timely clinical and laboratory diagnosis and proper management for better outcome. This study was aimed to find out the rate of neonatal sepsis in intramural newborns at our hospital, to correlate clinical profile with bacterial isolates in culture proven sepsis and determine the antimicrobial sensitivity pattern of microbial flora. The neonates were classified to have early or late onset septicaemia depending on their age at presentation. Risk factors were assessed, essential investigations sent by collecting samples under aseptic precautions. Empirical antimicrobial therapy was started according to antimicrobial guidelines in the NICU. The duration of treatment and hospital stay was noted in all neonates.
Keywords: late onset sepsis, bacterial profile, staphylococcus, pseudomonas

INTRODUCTION:

Neonatal Sepsis is defined as a clinical syndrome characterized by signs and symptoms of systemic infections accompanied with bacteraemia in the first month of life [1]. It is an important cause of morbidity and mortality among neonates and is one of the four leading causes of neonatal mortality in India [2-4]. Neonatal mortality rate is one of the indicators for measuring the health status of a nation [5]. There could be several of neonatal mortality but septicemia continues to be a major cause of neonatal mortality but septicemia continues to be a major cause of neonatal mortality and morbidity worldwide. Incidence varies from country to country, but it is much higher in developing countries than in developed nations.

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 most commonly caused by Coagulase-negative staphylococci (CONS), Staphylococcus aureus, Escherichia coli, Klebsiella and Pseudomonas and is usually acquired in the hospital or in the community. According to the National Neonatal Perinatal Database of India, Klebsiella pneumonia, Staphylococcus aureus, and E.coli are the three most common organisms causing neonatal sepsis both in hospital and community [6]. Hence, the study was conducted to determine the bacteriological profile of Late onset sepsis.

AIMS AND OBJECTIVES:

1. To identify the bacteriological profile of late onset sepsis.
2. To determine the antibiotic susceptibility patterns of isolates obtained.

RESULTS:

Of the total 120 clinically suspected late onset sepsis cases, 52 cases were blood culture positive sepsis cases, and 68 cases were culture negative cases. Culture positive rate is 43.3%.

Table-1: Distribution of cases according to Gender

Blood cultures	Male	Female	Total n(%)
Culture Positive	32(61.2%)	20(38.7%)	52(43.3%)
Culture negative	30(43.5%)	38(56.4%)	68(56.7%)
Total	62	58	120

- Of the 120 cases studied, 62 cases were male and 58 cases female.
- Among the culture positive cases, 32 cases were male and 20 cases were female.
- Of the culture negative cases, 30 cases were male and 38 were female.

Table-2: Distribution of cases according to Gestational Age

	Preterm	Term	Postterm
Clinically suspected	76(63%)	40(33%)	4(3%)
Culture positive	36(69%)	16(31%)	0(0%)
Culture negative	40(59%)	24(35%)	4(6%)

- Of the 120 clinically suspected cases, 63% were preterm; 33% were term and 3% were postterm cases.
- Of the culture positive cases, 69% were preterm, and 31% term neonates.
- A higher percentage of sepsis cases were seen in preterm neonates than term and postterm babies.

Table-3: Distribution of cases according to Place of Delivery

	Inborn	Referral / Out born
Clinically suspected	42(35%)	78(65%)
Culture positive	14(27%)	38(73%)
Culture negative	28(41%)	40(59%)

- Of the 120 neonates, only 35% were hospital inborn babies, of which 27% were culture positive.
- Of the 78 out born cases, 38 cases were culture positive cases.
- Maximum culture positive cases were from the out born neonates.

Table-4: Distribution of cases according Outcome

	Discharge	Death
Clinically suspected	108 (90%)	12 (10%)
Culture positive	46 (88%)	6 (12%)
Culture negative	62 (91%)	6 (9%)

- Of the 120 clinically suspected sepsis cases, 90% were discharged and 10% were dead.
- Among the culture positive cases, 12% were dead.
- Of the culture negative cases, only 9% were dead.
- Mortality rate is more in culture positive group.

Table-5: Bacterial isolates in Blood Culture

Organisms	N	%
Klebsiella pneumonia	16	31%
Staphylococcus aureus	11	21%
Escherichia coli	8	15%
CONS	10	19%
Pseudomonas aeruginosa	4	8%
Enterobacter sp	1	2%
Enterococcus sp	1	2%
Burkholderia sp	1	2%

- Of the 53 culture positive cases, majority were gram negative cases.
- Klebsiella pneumonia is the most common pathogen, with 31% of total isolates.
- Staphylococcus aureus is the most common gram positive pathogen, followed by CONS with 19%.

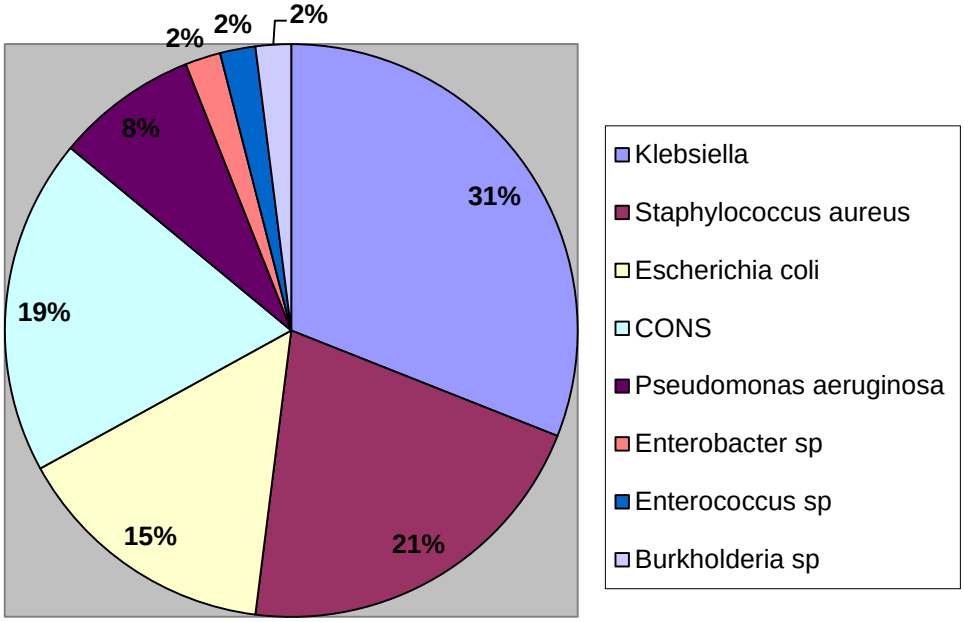

Fig-1: Bacterial isolates in Blood Culture

Table-6: Antibiotic sensitivity pattern of the Gram Positive bacterial isolates

Antibiotics	**Staphylococcus Aureus (11) N(%)**	**Coagulase negative staphylococcus (10) N (%)**	**Total (21) N(%)**
Ampicillin	1(13%)	1(14%)	3(14%)
Amikacin	7(66%)	7(71%)	14(68%)
Ceftriaxone	8(73%)	6(57%)	14(68%)
Gentamicin	5(46%)	4(43%)	9(45%)
Ciprofloxacin	7(60%)	7(71%)	13(63%)
Cefotaxime	8(73%)	7(71%)	15(73%)
Erythromycin	4(33%)	4(43%)	8(36%)
Cefoxitin	9(80%)	8(85%)	17(82%)
Amoxicillin	6(53%)	4(43%)	11(50%)
Vancomycin	10(93%)	10(100%)	20(95%)
Cefoperazone	7(60%)	7(71%)	13(63%)
Linezolid	11(100%)	10(100%)	21(100%)

- The isolated Gram positive bacteria showed high resistances to Ampicillin (13.6%) and considerable resistance towards Gentamicin (45%).
- They showed moderate susceptibility to third generation Cephalosporin (Cefotaxime-73%, Ceftriaxone-68%, Cefoperazone-63%), Amikacin-68%, and Ciprofloxacin-63%.
- They were highly susceptible to Linezolid (100%) and Vancomycin (95%).

Table-7: Antibiotic sensitivity pattern of the Gram Negative bacterial isolates

Antibiotics	Klebsiella pneumonia (16) N (%)	Escherichia coli (8) N (%)	Pseudom. Aeruginosa (4) N (%)	Total (28) N (%)
Ampicillin	1(9%)	1(7.1%)	01	2(7.5%)
Amikacin	11(68.1%)	6(71.4%)	2(50%)	19(68%)
Ceftriaxone	8(50%)	5(57%)	1(25%)	14(50%)
Gentamicin	7(45.4%)	4(50%)	1(25%)	13(45%)
Ciprofloxacin	12(72.7%)	6(71.4%)	2(50%)	20(70%)
Cefpodoxime	7(41%)	4(50%)	1(25%)	5(42.5%)
Ceftazidime	9(54.5%)	5(57%)	2(50%)	15(55%)
Piperacillin	7(45.4%)	4(50%)	1(25%)	13(45%)
Meropenem	16(100%)	8(100%)	4(100%)	28(100%)
Cefoperazone	8(50%)	4(50%)	1(25%)	13(47.5%)
Colistin	16(100%)	8(100%)	4(100%)	28(100%)
Ceftriaxone	7(45.4%)	4(50%)	1(25%)	13(45%)

- Among the Gram negative bacteria, many of them were resistant to ampicillin (7.5%), gentamicin (45%), third generation cephalosporins (ceftazi-dime-55%), cefotaxime-50%, ceftriaxone-45%) and piperacillin (45%).
- They were moderately susceptible to Amikacin (68%) and ciprofloxacin (70%), but highly susceptible to Colistin (100%) and Meropenem (100%).

DISCUSSION:

Sepsis is the commonest cause of neonatal mortality; it is responsible for about 30-50% of the total neonatal deaths in developing countries [7, 8]. It is estimated that up to 20% of neonates develop sepsis and approximately 1% die of sepsis related causes [7, 8]. Sepsis related mortality is largely preventable with prevention of sepsis itself, timely recognition, rational antimicrobial therapy and aggressive supportive care. Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life. It encompasses various systemic infections of the newborn such as septicemia, meningitis, pneumonia, arthritis, osteomyelitis, and urinary tract infections. Neonatal sepsis can be classified into two major categories depending upon the onset of symptoms; early onset sepsis (EOS): it presents within the first 72 hours of life. In severe cases, the neonate may be symptomatic at birth. Infants with EOS usually present with respiratory distress and pneumonia. The source of infection is generally the maternal genital tract.

Late onset sepsis (LOS) presents after 72 hours of age. The source of infection in LOS is either nosocomial (hospital-acquired) or community-acquired and neonates usually present with septicemia, pneumonia or meningitis [9, 10]. Various factors that predispose to an increased risk of nosocomial sepsis include low birth weight, prematurity, admission in intensive care unit, mechanical ventilation, invasive procedures, administration of parenteral fluids, and use of stock solutions. Factors that might increase the risk of community – acquired LOS include poor hygiene, poor cord care, bottle-feeding, and prelacteal feeds. In contrast, breastfeeding helps in prevention of infections.

Culture positivity:

In our study, 52 of 120 cases studied were culture positive, giving a culture positivity rate of 43.3%. This study is comparable with studies conducted by Zakariya *et al.;* [11] in JIPMER (41.6%), Maimonna Mustafa *et al.;* in Deccan College [12] (44%), Kuhu Pal *et al.;* [13] in west Bengal (40%), by Roy *et al.;* [14] (47.50%) and R.S. Jaswal *et al.;* [15] (42%).

Blood culture although considered to be gold standard in the confirmation of diagnosis of septicemia, has been found to be negative in 20 percent cases where infection was proven by immediate postmortem culture and autopsy [16]. In the mildly symptomatic neonate and at the earliest onset of septicemia, the false negative blood culture rate would be very high. In addition, upto 50 percent of the cases with congenital bacterial pneumonia proved by tracheal aspirate culture, blood culture is negative. Therefore blood culture should not be considered as the final arbiter for the clinical diagnosis of neonatal infection [16].

Gender:

In our study of the 120 cases studied, 62 cases were male and 58 cases were female. Among the culture positive cases, 32 (61.2%) cases were male and 20(38.7%) cases were female. Of the culture negative cases, 30(43.5%) cases were male and 38(56.4%) were female. These results are comparable with the observations made by Tallur et al (63.60%), Uddin Ahmed et al (63.00%), A.H. Movahedin *et al.;* (71.2%), Shrestha P *et al.;* (75%), Shansanam Gheibi *et al.;* (55.03%), and Ramesh Bhat *et al.;* (53.7%). Our results differed from that of Betty Chacko *et al.;* [17] who observed an equal proportion of cases among both males and females.

Gestational Age:

In this study, of the 120 clinically suspected cases, 63% were preterm; 33% were term and 3% were postterm cases. Of the culture positive cases, 69% were preterm, and 31% term neonates. A higher percentage of culture positive sepsis cases were seen in preterm neonates than term and postterm babies. According to Nelson Textbook of Pediatrics, the most important neonatal factor predisposing to infection is prematurity of LBW. Preterm LBW infants have a 3 to 10 fold higher incidence of infection than full-term normal birth weight infants. Possible explanations are as follows: premature infants have documented immune dysfunction; and premature infants often required prolonged intravenous access, endotracheal intubation, or other invasive procedures that provide a portal of entry or impair barrier and clearance mechanisms [18].

Place of Delivery:

In our study, of the 120 neonates, only 35% were hospital inborn babies, of which 27% were culture positive. Of the 78 out born cases, 38 cases were culture positive cases. The present study showed a higher proportion of culture positive cases among out born / referred neonates compared to neonates who are inborn. Our results were comparable with the observations made by G.P. Mondal *et al* [17] in their study. This could be mostly because our hospital is a referral unit, majority of all our admissions are out born and referred to us in critically ill conditions.

The results of the present study differ from the study by G.G. Christo *et al* [18] who observed an equal number of culture positive cases among both the hospital inborn and out born neonates. In the developed countries, Gram-positive organisms account for about 70% of all LOS. The common pathogens causing LOS in very low birth weight (VLBW) infants include CoNS followed by Staphylococcus aureus, Enterococcus spp., and GBS. About 18-20% of late-onset sepsis is caused by Gram-negative organisms especially Enterobacteriaceae spp. and E. coli. About 12% of LOS sepsis is caused by fungi especially Candida species.

The bacteriological patterns of neonatal septicemia have changed from time to time and place to place over the years in India. In developing countries like India 65-85% of septicemia is caused by Gram negative organisms and 15% by Gram positive organisms. The major isolates in our country include Klebsiella pneumonia. Escherichia coli, Staphylococcus aureus, Coagulase negative staphylococcus, Enterobacter Spp., Citrobacter Spp., Proteus mirabilis and Serratia. Interestingly Group B β streptococci which have been found to be of great concern in the west, have not established a major foothold in India. In this study, Pseudomonas aeruginosa isolates were found to be highly resistant to routinely used antibiotics, followed by Klebsiella pneumoniae and Escherichia coli. This increasing resistance could be due to irrational use of antibiotics. All Gram negative isolates were having considerable sensitivity to Amikacin and Ciprofloxacin; but were highly susceptible to Meropenem (100%) and Colistin (100%). These study findings correlated well with the findings of others viz. Aletayeb SMH *et al* [19].; and Waseem R *et al.* [20];

The ESBL producers were detected in 27% of Klebsiella pneumoniae and 21% of Escherichia coli isolates. The Gram positive isolates were having better susceptibility to Amikacin, Cephalosporins and Ciprofloxacin; but were more resistant to Ampicillin and Gentamicin in the present study. They showed high susceptibility to Linezolid and Vancomycin. Our findings correlated with the studies by Aletayeb SMH *et al* .[22]; and Roy I *et al.* [21];

CONCLUSIONS:

This study noticed that Gram negative bacteria were more commonly the cause of Late Onset Sepsis in neonates, and Klebsiella pneumoniae was the predominant pathogen. The study also noticed that these Gram negative bacteria were resistant to routinely used antibiotics, hence their resistant pattern should be considered essential before deciding the empirical treatment. The higher antibiotics such as Colistin and Meropenem should be reserved for multi-drug resistant Gram negative bacteria, whereas Linezolid and Vancomycin should be reserved for drug resistant Gram positive isolates.

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