



## CLINICAL PREVALENCE AND CAUSATIVE MICROBES RESPONSIBLE FOR NEONATAL SEPSIS IN NEONATES ADMITTED IN NMCH

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### ABSTRACT:

Neonatal sepsis is of two types; early onset sepsis and late onset sepsis. Early onset sepsis (EOS) present within first 72 hours of life. In severe cases, the neonates may be symptomatic at birth. Infants with EOS usually present with respiratory distress and pneumonia. Hence based on above findings the present study was planned to evaluate the immediate clinical outcomes of culture proven neonatal sepsis in the NICU.

The study was planned by enrolling the 320 neonates admitted in Neonatal unit of Department of Paediatrics in Nalanda Medical College and Hospital, Patna, from Dec 2017 to Jun 2018. The 40 neonates were diagnosed positive for septicemia was enrolled in the present study. The approval of the institutional committee was taken prior conduct of study. All the patients were informed consents. The data from the present study revealed that adequate care of the low birth weight babies is of utmost importance to prevent infection by *Klebsiella pneumoniae*. Amikacin should be used along with third-generation cephalosporins for empirical treatment of gram-negative neonatal sepsis. This empirical regimen should be modified later based on the antibiogram of the isolates.

**Keywords:** neonatal sepsis, epidemiology, microbiology, etc.

### INTRODUCTION:

Newborns are at significant risk from serious blood-stream infections, such as sepsis, as well as other serious bacterial infections such as pneumonia and meningitis. The situation is aggravated by AMR, as currently available

treatments become less effective. Of great concern are the 214,000 neonatal sepsis deaths estimated to result from drug-resistant infections across the world in 2015. At present, there is very little evidence to support the appropriate treatment of serious and drug-resistant

infections in neonates. The lack of alternative treatment options means the WHO recommended regimen has not been updated in more than 50 years, despite increasing rates of resistance. [1]

Neonatal sepsis is a type of neonatal infection and specifically refers to the presence in a newborn baby of a bacterial blood stream infection (BSI) (such as meningitis, pneumonia, pyelonephritis, or gastroenteritis) in the setting of fever. Older textbooks may refer to neonatal sepsis as "sepsis neonatorum". Criteria with regards to hemodynamic compromise or respiratory failure are not useful clinically because these symptoms often do not arise in neonates until death is imminent and unpreventable.

It is difficult to clinically exclude sepsis in newborns less than 90 days old that have fever (defined as a temperature > 38 °C (100.4 °F). Except in the case of obvious acute viral bronchiolitis, the current practice in newborns less than 30 days old is to perform a complete workup including complete blood count with differential, blood culture, urinalysis, urine culture, and cerebrospinal fluid (CSF) studies and CSF culture, admit the newborn to the hospital, and treat empirically for serious bacterial infection for at least 48 hours until cultures are demonstrated to show no growth. Attempts have been made to see whether it is possible to risk stratify newborns in order to decide if a newborn can be safely monitored at home without treatment despite having a fever. One such attempt is the Rochester criteria. [2]

Neonatal sepsis is of two types; early onset sepsis and late onset sepsis. Early onset sepsis (EOS) present within first 72 hours of life. In severe cases, the neonates 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. [3] Late onset sepsis usually presents after 72 hours of age. The source of infection is either nosocomial or community acquired, and neonates usually presented with septicemia,

pneumonia or meningitis. [4] Early diagnosis and proper management can reduce the neonatal mortality but aetiological agent do not remain the same and include a wide variety of both gram positive and gram negative bacteria. One should know the usual aetiological agent and its antibiotic susceptibility patterns in community, before commencing empirical therapy.

Note that, in neonates, sepsis is difficult to diagnose clinically. They may be relatively asymptomatic until hemodynamic and respiratory collapse is imminent, so, if there is even a remote suspicion of sepsis, they are frequently treated with antibiotics empirically until cultures are sufficiently proven to be negative. In addition to fluid resuscitation and supportive care, a common antibiotic regimen in infants with suspected sepsis is a beta-lactam antibiotic (usually ampicillin) in combination with an aminoglycoside (usually gentamicin) or a third-generation cephalosporin (usually cefotaxime—ceftriaxone is generally avoided in neonates due to the theoretical risk of kernicterus.) The organisms which are targeted are species that predominate in the female genitourinary tract and to which neonates are especially vulnerable to, specifically Group B Streptococcus, Escherichia coli, and Listeria monocytogenes (This is the main rationale for using ampicillin versus other beta-lactams.) Of course, neonates are also vulnerable to other common pathogens that can cause meningitis and bacteremia such as Streptococcus pneumoniae and Neisseria meningitidis. Although uncommon, if anaerobic species are suspected (such as in cases where necrotizing enterocolitis or intestinal perforation is a concern, clindamycin is often added.

Granulocyte-macrophage colony stimulating factor (GM-CSF) is sometimes used in neonatal sepsis. However, a 2009 study found that GM-CSF corrects neutropenia if present but it has no effect on reducing sepsis or improving survival. [5]

Hence based on above findings the present study was planned to evaluate the immediate clinical outcomes of culture proven neonatal sepsis in the NICU.

**Methodology:**

The study was planned by enrolling the 320 neonates admitted in Neonatal unit of Department of Paediatrics in Nalanda Medical College and Hospital, Patna, from Dec 2017 to Jun 2018. The 40 neonates were diagnosed positive for septicemia was enrolled in the present study. The approval of the institutional committee was taken prior conduct of study. All the patients were informed consents.

Blood for bacterial culture was collected aseptically and 2 ml of blood was added to each of two bottles containing 20 ml of Tryptone soya broth (Hi-Media Labs. Mumbai, India) the bottles were incubated aerobically at 37°C for 7 days and sub cultured on sheep blood agar and MacConkey agar overnight, for 48 h or for 7 days or for an in-between period when visible turbidity appeared. In positive cases, Gram – positive isolates were identified at the species level by conventional biochemical and serological tests.

All organisms were classified based on the time-point at which the blood was collected for culture as follows; those causing early onset sepsis (EOS-less than and up to 72 h of life) and those causing late onset sepsis (LOS-greater than 72 h of life). The organisms were further classified based on their Gram’s stain status.

**Results & Discussion:**

The data from the 40 positive cases were collected and presented as below. India is a developing nation with a distant dream to achieve to achieve MDG 4 but remains unfulfilled due to the lack of appropriate neonatal care. The maintenance of neonatal health should be the priority of every society.

Following was the observations from the data generated from the present study.

**Table 1: Clinical Details of Mother**

Parameters	No. of Cases
Mother Age:	
Less than 20 years	12
20 to 30 years	20
Above 30 years	8
Literacy:	
Literate	18
Illiterate	22
Economic Status:	
Lower	26
Middle	40
Higher	4
Parity of Mother:	
1	35
2	5
More than 2	0
Mode of Delivery:	
Normal	21
Caesarean	19

**Table 2: Type & Causative Microbes**

Parameters	No. of Cases
Type of Sepsis:	
Early Onset Sepsis	15
Late Onset Sepsis	25
Causative Bacteria:	
Gram Positive	12
Gram Negative	28

**Table 2: Positive Cases and Drug Sensitivity**

Organisms	Blood culture positive Cases
Gram-positive :	
Staphylococcus aureus	8
Methicillin-resistant Staphylococcus aureus	3
Staphylococcus epidermidis	1
Total Cases	12 cases
Gram-negative:	
Klebsiella pneumoniae	15
Acinetobacter	6
Citrobacter	4
Pseudomonas	3
Total Cases	28 cases

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life [17]. Although bacteria are the most common agents implicated in neonatal sepsis, neonatal sepsis syndrome can also be caused by organisms other than bacteria like adenovirus, enterovirus Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life [17]. Although bacteria are the most common agents implicated in neonatal sepsis, neonatal sepsis syndrome can also be caused by

organisms other than bacteria like adenovirus, enterovirus Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life. [6] Although bacteria are the most common agents implicated in neonatal sepsis, neonatal sepsis syndrome can also be caused by organisms other than bacteria like adenovirus, enterovirus, coxsackievirus, rubellavirus, Toxoplasma species and Candida species. [7] Therefore, only a proportion of the blood culture from cases with clinical sepsis will be positive for pathogenic organisms. In addition, collection of blood samples after administration of empirical antibiotics can also result in poor recovery of the bacterial pathogens in culture. In a study done in neonatal intensive care units of Georgia, 63% of the clinically suspected cases were blood culture positive. In the present study the blood culture positivity rate was 41.6%, which is lower than the above study. However, in other studies from India, the culture positivity rate was 13–22% [7, 8].

The etiological agents of neonatal sepsis vary between developed and developing countries [9-10]. Klebsiella pneumoniae and other Gram-negative organisms were the common causes of sepsis in the present study as well other studies from India and Nigeria [7, 8]. However, in the developed countries Group B Streptococcus and coagulase-negative staphylococci (CONS) are the predominant causes of sepsis [10]. The bacteriological profile of early-onset sepsis differs from that of late-onset sepsis as the mode of infection is different [11]. Early-onset neonatal sepsis is acquired transplacentally or as an ascending infection from cervix or during passage of the baby through a colonized birth canal [10].

In another study from North India, 30–80% of the Gram negative isolates were resistant to third-generation cephalosporins [12]. This suggests that the third-generation cephalosporins cannot be used alone for empirical treatment of neonatal sepsis and amikacin which shows good activity against the gram negative bacteria should always be included in the empirical regimen. This also emphasizes the need to routinely test for cephalosporin resistance and ESBL.

In our study all the isolates were resistant to penicillin. Ampicillin, gentamicin and ciprofloxacin shown lowest sensitivity with highest sensitivity to either cefotaxime or amikacin and hence a co-prescription of these two antibiotics appear prudent as the initial choice while awaiting for the blood culture reports. This combination has given us the best results in our neonatal intensive care unit. In developing countries, rates of blood stream infections (BSI) have been reported to be 1.7 to 33 per 1,000 live births, with rates in Asia clustering around 15 per 1,000 live births. [13] Blood culture has remained the gold standard for the confirmation of sepsis [14]. The rate of admission of early and late onset sepsis as well as the prevalence of organisms and their sensitivity patterns was much similar [15].

It can be concluded that though we are on the track of minimising morbidities and mortalities but still there is a long way to go, still we have a higher prevalence of neonatal sepsis even in inborn units and most common associated bacteria is *Klebsiella pneumoniae*, and most common indication for admission was respiratory distress which further led to neonatal sepsis. Among the patients with sepsis maximum patients were males and maximum patients belonged to urban areas and were successful in availing the government facilities for transportation upto the health facility. Neonates with sepsis were mainly preterm term and with low birth weight. Most of the neonates who had sepsis were admitted on the first day of their birth and maximum duration of stay of most of the neonates was 8 days and most of them were treated and discharged successfully.

Easy availability and widespread use of broad-spectrum antibiotics in the presumptive treatment of infections prevail in India. Blood culture facilities are not often available in most of the settings in rural areas. In such scenarios, clinicians have to depend on empirical antibiotic regimens. The high prevalence of resistance to Ampicillin makes it out of use in neonatal sepsis even in rural hospitals. The increasing resistance of Gram-negative organisms to extended-spectrum cephalosporins and carbapenems makes the choice of antibiotics difficult. Due consideration needs to be given to antistaphylococcal antibiotics in view of its high prevalence in both early-onset and late-onset neonatal sepsis.

Factor shown to be significantly associated with culture-positive sepsis was prematurity. None of the studied maternal factors had shown any significant association with culture-positive sepsis. Prematurity should be given more weightage in scoring systems assessing sepsis risk.

#### **Conclusion:**

The data from the present study revealed that adequate care of the low birth weight babies is

of utmost importance to prevent infection by *Klebsiella pneumoniae*. Amikacin should be used along with third-generation cephalosporins for empirical treatment of gram-negative neonatal sepsis. This empirical regimen should be modified later based on the antibiogram of the isolates.

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