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Prevalence and outcome of neonatal septicemia in north Indian region

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Abstract
Neonatal sepsis is a type of neonatal infection and specifically refers to the presence in a new born baby of a bacterial blood stream infection (BSI) (such as meningitis, pneumonia, pyelonephritis, or gastroenteritis) in the setting of fever.
The literature revealed that early identification is a significant to diminish morbidity and mortality of neonatal septicemia. Based on this findings the present study is planned to evaluate the etiological profile of neonatal septicemia cases and their antibiotic sensitivity pattern for planning strategy for the management of these cases.
From the above data it is concluded that *E. coli* is the most common cause of neonatal sepsis in patients admitted. Most of the empirical regimens/ commonly using antibiotics like Ampicillin, Amoxicillin, Cefotaxime and Gentamycin are highly resistant against both Gram positive and Gram-negative pathogens causing neonatal sepsis. Neonatal septicemia is a life threatening emergency. The study of etiological profile and their antibiotic sensitivity pattern plays a significant role.

Keywords: neonatal sepsis, gram positive, gram negative, antibiotic, resistance

Introduction
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. Neonatal sepsis is divided into two categories: early-onset sepsis (EOS) and late-onset sepsis (LOS). EOS refers to sepsis presenting in the first 7 days of life (although some refer to EOS as within the first 72 hours of life), with LOS referring to presentation of sepsis after 7 days (or 72 hours, depending on the system used). Neonatal sepsis is the single most common cause of neonatal death in hospital as well as community in developing country.
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 new born 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.
Culturing for microorganisms from a sample of CSF, blood or urine, is the gold standard test for definitive diagnosis of neonatal sepsis. This can give false negatives due to the low sensitivity of culture methods and because of concomitant antibiotic therapy. Lumbar punctures should be done when possible as 10-15% presenting with sepsis also have meningitis, which warrants an antibiotic with a high CSF penetration. CRP is not very accurate in picking up cases [1].
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 [2].

Trials of probiotics for prevention of neonatal sepsis have generally been too small and statistically underpowered to detect any benefit [3], but a randomized controlled trial that enrolled 4,556 neonates in India reported that probiotics significantly reduced the risk of developing sepsis [4]. The probiotic used in the trial was Lactobacillus plantarum.

A very large meta-analysis investigated the effect of probiotics on preventing late-onset sepsis (LOS) in neonates. Probiotics were found to reduce the risk of LOS, but only in babies who were fed human milk exclusively. It is difficult to distinguish if the prevention was a result of the probiotic supplementation or if it was a result of the properties of human milk. It is also still unclear if probiotic administration reduces LOS risk in extremely low birth weight infants due to the limited number of studies that investigated it. Out of the 37 studies included in this systematic review, none indicated any safety problems related to the probiotics. It would be beneficial to clarify the relationship between probiotic supplementation and human milk for future studies in order to prevent late onset sepsis in neonates [5].

The literature revealed that early identification is a significant to diminish morbidity and mortality of neonatal septicemia. Based on this findings the present study is planned to evaluate the etiological profile of neonatal septicemia cases and their antibiotic sensitivity pattern for planning strategy for the management of these cases.

Methodology

The study was planned by enrolling the 50 neonates admitted in Department of Paediatrics in Nmch Patna. The neonates diagnosed with the septicemia were enrolled in the present study. Neonatal septicemia was diagnosed as per the clinical criteria given by Vergnano *et al* [6]. Blood sample (0.5 to 2 ml) was collected with all aseptic precaution and was inoculated into blood culture bottle BactT/Alert® PF (BIOMERIEUX, INC. Durhams, NC 27704) containing 20 ml of broth.

The blood and broth were mixed gently and bottles were transported to laboratory for incubation in BacT/Alert 3D system and further processing was done as per manufacturer's guideline.

Those blood culture bottles which were indicated positive, query positive and query negative by Bact/ Alert 3D system were sub cultured on Sheep blood agar and MacConkey agar. The blood agar and MacConkey's medium were incubated at 35 ± 20 Celsius for 18 - 24 hours in aerobic atmosphere. Various organisms were identified on the basis of colony morphology and standard biochemical tests. Those blood culture bottles which were indicated as negative by 5 days (as per setting of Bact / Alert 3D system) were reported as "no growth". The isolates were subjected to antimicrobial susceptibility testing by Kirby Bauer disk diffusion method as per CLSI guidelines 2011 [7].

Results & Discussion

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

Table 1: Clinical Details:

Parameters	No. of Cases
Gender	
Male	29
Females	21
Type of Sepsis:	
Early Onset Sepsis	16
Late Onset Sepsis	34
Causative Bacteria:	
Gram Positive	13
Gram Negative	37

Table 2: Positive Cases and Drug Sensitivity

Organisms	Blood culture positive	Drug sensitivity
Gram-positive : 13 cases		
Staphylococcus aureus	5	Penicillin, Oxacillin, Vancomycin, Linezolid
Methicillin-resistant Staphylococcus aureus	4	Vancomycin, Linezolid
Staphylococcus epidermidis	4	Penicillin, Oxacillin, Vancomycin, Linezolid
Gram-negative: 37 cases		
Acinetobacter	23	Amikacin, Ciprofloxacin, Piperacillin, Tazobactam, Meropenem, Imipenem
Citrobacter	8	Amikacin, Ciprofloxacin, Ceftazidime, Piperacillin, Tazobactam, Meropenem & Imipenem
Pseudomonas	6	Piperacillin, Tazobactam, Meropenem And Imipenem

From the above data it is concluded that *E. coli* is the most common cause of neonatal sepsis in patients admitted. Most of the empirical regimens/ commonly using antibiotics like Ampicillin, Amoxicillin, Cefotaxime and Gentamycin are highly resistant against both Gram positive and Gram-negative pathogens causing neonatal sepsis.

The advancement in neonatal intensive care medicine is a double edge sword, with neonatal survival improvement on one side and increased rate of long term morbidity on another. The microorganism pattern of neonatal sepsis is different at different hospitals and its pattern changes with time hence periodic re-evaluation of the etiological agent is useful in the management of neonatal sepsis. Despite all efforts, a rapid sensitive diagnostic tool for neonatal septicaemia is yet to be found.

Number of studies have been done on the risk factors, etiology, haematological parameters and on the clinical profile of neonatal septicaemia. Blood culture is the gold standard for definitive diagnosis of neonatal septicemia, but it has its own limitations as it requires a well-equipped laboratory, has a

success rate of 40%, very time consuming, and may give spurious positive results. The results of blood culture may take about a week, necessitating initial empirical treatment of suspected septicemia. Overall incidence of culture proven sepsis varies between 1-8 cases per 1000 live births with almost equal distribution of early onset and late onset cases. This present study was undertaken to study the etiological profile in newborn with positive sepsis screen so that prompt therapy be instituted to reduce morbidity and mortality. The most common agents causing neonatal sepsis are bacteria and only a proportion of the blood culture from cases with clinical sepsis will show growth of organism.

The bacteriological profile of neonatal septicemia in our hospital is comparable to that of National Neonatal Perinatal Network Database Report [8]. According to this report Group B Streptococcus is not common in our country and we also did not isolate group B Streptococcus.

The etiological agents of neonatal sepsis vary between developed and developing countries [9]. Klebsiella pneumoniae and other Gram-negative organisms were the common causes of sepsis in the present study as well other studies from India [9] and Nigeria [11]. The bacteriological profile of early-onset sepsis is different from that of late-onset sepsis as the mode of infection is different [12]. An ascending infection from cervix, passage of the baby through a colonized birth canal and trans placental infections is main route of infection in case of early onset neonatal sepsis [13]. In the present study, Klebsiella pneumoniae was the common agent implicated in early-onset sepsis.

In another study from North India, 30–80% of the Gram negative isolates were resistant to third generation cephalosporins [10]. As Amikacin shows good activity against gram negative bacteria should preferably included in empirical regimen while third generation cephalosporins should not be used alone. In our study one Salmonella typhi was isolated and that was sensitive to ampicillin, amoxicillin clavulanic acid, ciprofloxacin and chloramphenicol. Sharma *et al*, [14] found 9 isolates of Salmonella spp. which were sensitive to ciprofloxacin and resistant to ampicillin and amoxicillin-clavulanic acid.

Conclusion

From the above data it is concluded that *E. coli* is the most common cause of neonatal sepsis in patients admitted. Most of the empirical regimens/ commonly using antibiotics like Ampicillin, Amoxicillin, Cefotaxime and Gentamycin are highly resistant against both Gram positive and Gram-negative pathogens causing neonatal sepsis. Neonatal septicemia is a life threatening emergency. The study of etiological profile and their antibiotic sensitivity pattern plays a significant role.

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