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Assessment of occurrence of the meningitis in neonates with late onset sepsis admitted to Patna Medical College and Hospital, Patna

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Abstract
Meningitis is an infection of the meninges, the membranes that protect the spinal cord and the brain. When the meninges become infected, they start to swell, putting pressure on the spinal cord or brain and causing potentially life-threatening complications. Meningitis is called an acute condition because symptoms strike quickly and suddenly. Hence the present study was planned to assess the Incidence of Meningitis in neonates with late onset sepsis.
The present study was planned in the Upgraded Department of Paediatrics (Neonatology) in Patna Medical College and Hospital, Patna from Jan 2018 to Sept 2018. Total 50 cases of new borns with signs and symptoms suggestive of sepsis with positive C-reactive protein (CRP) at or more than 72 h of postnatal age, were enrolled in the study.
Neonatal meningitis is a devastating disease that requires a high index of suspicion, prompt diagnosis, and rapid treatment. While the incidence and mortality have declined with improved neonatal intensive care practices and universal adoption of preventative screening and prophylaxis programs, the associated morbidity remains unchanged. Thus, continuous monitoring of causative agents of neonatal infection, control of emergence of drug resistance among them through specific and appropriate duration of treatment, preventive intervention for transmission to the neonate can be an appropriate approach for controlling neonatal deaths.

Keywords: meningitis, neonates, late onset sepsis, bacterial sepsis

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 30 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.
The signs of sepsis are non-specific and include: Body temperature changes, breathing problems Diarrhoea, Low blood sugar (hypoglycemia), Reduced movements, Reduced sucking, Seizures Bradycardia, Swollen belly area, Vomiting, Yellow skin and whites of the eyes (jaundice), hemorrhagic rash. A heart rate above 160 can also be an indicator of sepsis, this tachycardia can present up to 24 hours before the onset of other signs.
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 [2].
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 [3].

Meningitis is an infection of the meninges, the membranes that protect the spinal cord and the brain. When the meninges become infected, they start to swell, putting pressure on the spinal cord or brain and causing potentially life-threatening complications. Meningitis is called an acute condition because symptoms strike quickly and suddenly. Although meningitis is most often caused by viruses, bacterial meningitis is more serious. The bacteria that cause bacterial meningitis are just about everywhere—they even live inside your respiratory tract. But they don't always make you sick. Experts don't always know why bacterial meningitis occurs. Some people get it when their immune system is down or they've recently been sick. Suffering a head injury may also increase your bacterial meningitis risk [4].

Bacterial meningitis during the neonatal period is still one of the most devastating conditions, with a morbidity rate of 20% to 60% [5]. The nationwide mortality can be as high as 40% in treated cases in the first month of life, and up to 10% beyond the neonatal period. Multiple factors contribute to the susceptibility of infants to this illness. The immune immaturity of infants is the biggest contributor, especially pre-term infants. Because infants do not receive their first set of immunizations until 2 months of age, the risk is high for bacteremia, possibly resulting in bacterial meningitis.

Those populations at highest risk are preterm infants, males, the indigent population, and infants in daycare. Also, children of mothers with a history of a sexually transmitted disease, including genital herpes, and mothers who test positive for group B streptococcus are at high risk. Mothers who have eaten certain types of foods may be at risk for passing Listeria infection to their newborns, another pathogen found in the neonatal population. Gram-negative rods, most commonly Escherichia coli, contribute to significant mortality. Group B streptococcus continues to be the most common pathogen causing meningitis in the neonatal period. Hence the present study was planned to assess the Incidence of Meningitis in neonates with late onset sepsis.

Methodology

The present study was planned in the Upgraded Department of Paediatrics (Neonatology) in Patna Medical College and Hospital, Patna from Jan 2018 to Sept 2018. Total 50 cases of new borns with signs and symptoms suggestive of sepsis with positive C-reactive protein (CRP) at or more than 72 h of postnatal age, were enrolled in the study.

Sign and symptoms of sepsis were defined as the following: lethargy, reduced feeding ability, no spontaneous movement, temperature >38°C, hypothermia, cyanosis, abdominal distension, increased prefeed aspirates in preterm/low birth weight (LBW), pustular lesions, umbilical sepsis, presence of excessive crying, high-pitched cry, bulging fontanelle and/or occurrence of/or history of convulsions, grunting, flaring, retractions, tachypnea (respiratory rate >60/min), apnea lasting more than 20 s, tachycardia (heart rate [HR] >160/min) or bradycardia (HR <100/min), or capillary refill time >3 s. CRP >10 mg/L was considered positive as per our unit protocol. Quantitative CRP estimation was performed by using turbidimetric immunoassay method. Neonates with neural tube defects, such as spina bifida (meningocele, meningomyelocele, and lipomeningocele), anencephaly, and very sick neonates even after initial stabilization, were excluded from the study.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Results & Discussion

Neonatal sepsis remains one of the leading causes of morbidity and mortality both among term and preterm infants [6]. Although advances in neonatal care have improved survival and reduced complications in preterm infants, sepsis still contributes significantly to mortality and morbidity among very-low-birth-weight (VLBW, <1500 g) infants in Neonatal Intensive Care Units (NICUs) [6-11].

The signs and symptoms of neonatal sepsis are nonspecific [9]. These include fever or hypothermia, respiratory distress including cyanosis and apnoea, feeding difficulties, lethargy or irritability, hypotonia, seizures, bulging fontanel, poor perfusion, bleeding problems, abdominal distension, hepatomegaly, gauiac-positive stools, unexplained jaundice, or more importantly, "just not looking right" [10-11]. Infants with hypoxia–acidosis may gasp in-utero and lead to pneumonia and meconium aspiration [12].

Table 1: Age group

Age of presentation	No. of Cases
3-7 days	23
8-12 days	8
13-17 days	7
18-22 days	8
23-27 days	4
Total	50

Table 2: Symptom/sign observed

Symptom/sign	No. of Cases
Lethargy	50
Seizures	46
Fever	25
Refusal/dec feeding	23
Respiratory signs	12
Abdomen distention	11
Shock/sclerema	5

Table 3: Occurrence of Meningitis

Gender	Meningitis	No meningitis
Males	6	21
Females	4	19
Total	10	40
Weight		
<1.5 kg	3	3
1.5-2.499 kg	6	14
>2.5 kg	1	23
Total	10	40
Gestation		
Preterm	6	14
Term	4	26
Total	10	40

Table 4: Distribution of Cases as Per Gram Positive and Negative

Gram positive organisms	No. of Cases
MRSA	2
CoNS	2
Total	4
Gram negative organisms	
Klebsiella	2
E. coli	1
Enterobacter	1
Acinetobacter	1
Pseudomonas	1
Total	6

Table 5: outcome of meningitis vs. non meningitis cases

	Meningitis	No Meningitis
Expired	2	4
Recovered	8	36
Total	10	40

Early diagnosis and therapy are essential for the prevention of morbidity and mortality of neonatal sepsis in the neonatal intensive care unit. Although males have been reported to be have two- to five-fold higher likeliness to develop septicemia than females, the nearly 2:1 ratio of male to female neonates in this study is similar to various studies that showed an increase in preponderance among male neonates [13-14]. Presentation of sepsis varies depending on severity of the disease process and immune status of the neonate. Awaisu *et al*. [15] and Jain *et al*. [16] reported respiratory distress as the most common presentation.

Kumar A, et.al.They revealed that the neonatal period is the first four weeks of life, any symptoms and signs clinically agree with sepsis during this neonatal period known as neonatal sepsis and if these pictures found after first 72 hours of life it is known as late onset of sepsis [17].

Bozaykut A, et.al. discussed the morbidity and mortality related to the maturity degree and time at which discovered and treated, there are very high risk of mortality and morbidity due to difficulties in rapid diagnosis as the conformation of NS if blood culture is positive but if the blood culture is negative, the physician cannot differentiate meningitis from sepsis clinically without lumbar puncture and CSF culture and sensitivity [18].

Most commonly isolated organisms in community-acquired infections were S. aureus, Klebsiella species, and Escherichia. These results are similar to a previous review, where the order of prevalence was S. aureus, E. coli, and Klebsiella species [19]. A recent study of hospital-acquired neonatal sepsis in developing countries showed a predominance of Gram-negative organisms with Klebsiella species being most commonly isolated, followed by S. aureus and then E. coli [20]. This is similar to our findings, which further suggest potential similarities in major pathogens between community- and hospital-acquired neonatal sepsis in developing countries.

As neonatal septicemia is a life-threatening emergency and delays in diagnosis and treatment with appropriate antibiotics may have devastating consequences, surveillance is needed to identify the common signs and pathogens of neonatal septicemia as well as the antibiotic sensitivity patterns for the agents of septicemia in a particular area.

The strength of the study includes adequate sample size and strict study protocol. Limitation of our study includes not evaluating the effect of exclusive breast milk feeding on the prognosis of neonates with LOS. Despite this, the present study provides important data on the incidence of neonatal meningitis in the Eastern Indian population. Moreover, there is an urgent need for studies looking at simple and sustainable interventions to reduce the burden of neonatal infection such as adequate implementation of simple infection control methods, exclusive breastfeeding, restriction of antibiotic use, increasing trend toward noninvasive ventilation, and rationalization of admissions to and discharges from neonatal units.

Conclusion

Neonatal meningitis is a devastating disease that requires a high index of suspicion, prompt diagnosis, and rapid treatment. While the incidence and mortality have declined with improved neonatal intensive care practices and universal adoption of preventative screening and prophylaxis programs, the associated morbidity remains unchanged. Thus, continuous monitoring of causative agents of neonatal infection, control of emergence of drug resistance among them through specific and appropriate duration of treatment, preventive intervention for transmission to the neonate can be an appropriate approach for controlling neonatal deaths.

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