Neonatal Sepsis: Haematological Perspectives

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ABSTRACT

Neonatal sepsis (NS) is a leading cause of neonatal morbidity and mortality and is considered a global public health challenge. The organisms and pathogens most commonly associated with neonatal sepsis vary by country. Pathogens range from Gram-positive and Gram-negative bacteria to viruses and fungi, with bacteria being the most commonly identified. Bacteria most commonly involved include *Staphylococcus aureus*, coagulase-negative *staphylococci* (CONS), *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Escherichia coli*, *Klebsiella pneumoniae, Pseudomonas aeruginosa, Salmonella typhi,* and Group B *Streptococcus* increase, or urine culture is usually delayed for a day or two. A battery of tests, including C-reactive protein, total leukocyte count, absolute neutrophil count, platelet count, neutrophil cytoplasmic vacuolization, and polymorphic gastric aspiration cytology, was performed in neonates with a clinical diagnosis of NS. It's an excellent screening test.
Keywords: Sepsis, neonates, haematological parameters, laboratory diagnosis, clinical findings

INTRODUCTION

Neonatal sepsis is a leading cause of neonatal morbidity and mortality and is considered a global public health challenge [1-10]. Symptoms and signs may be subtle, varied, and nonspecific. In addition, delays in diagnosis and initiation of treatment result in high morbidity and mortality. 5 million newborns die each year, mainly in Africa and Asia, of which 1.6 million (20%) are due to neonatal sepsis. The incidence of neonatal sepsis in developed countries ranges from 1 to 10 per 1000 live births, whereas it is three times higher in Pakistan [12]. Definitive diagnosis based on blood, CSF, or urine culture is usually delayed by a day or two. In neonates with clinical manifestations or epidemiological factors associated with NS, initiation of antibiotic therapy is recommended before diagnostic results are available. However, some patients with bacterial infections may have negative blood cultures (clinical infections), requiring other approaches to identify infection [12]. Many studies have been conducted to develop screening tests or scoring systems that can identify infected infants at initial evaluation and avoid other invasive diagnostic procedures, intravenous antibiotic therapy, mother-infant separation, and increased parental anxiety. Attempts have been made [13].

Current microbiological gold-standard blood culture screens have low yields in addition to long turnover times, and collection of small amounts of blood can

lead to false-negative results [14]. Additional traditional blood, including measurement of white blood cell count (WBC), absolute neutrophil count (ANC), immature-to-total neutrophil ratio (I/T), and C-reactive protein (CRP) Biologic tests may also require serial surveillance with low sensitivity and specificity [15]. To better predict sepsis, recent findings suggest using age-specific nomograms instead of fixed normal ranges for WBC, ANC, and I/T ratio [16]. Therefore, a rapid and accurate diagnostic test is needed to guide the management of neonates with sepsis. Detection of bacteria and inflammatory cells on postnatal day 1 Gram-stain gastric aspirate cytology (GAC) may indicate maternal amnionitis, a risk factor for early-onset infection [12].

Neonatal sepsis

Neonatal sepsis is a blood infection that occurs in infants less than 90 days of age. Early sepsis occurs in the first week of life. Late sepsis occurs after 1 week to 3 months. The organisms and pathogens most commonly associated with neonatal sepsis vary by country. Pathogens range from Gram-positive and Gram-negative bacteria to viruses and fungi, with bacteria being the most commonly identified. The most commonly implicated bacteria include Staphylococcus aureus, coagulase negative staphylococci (CONS), *Streptococcus pneumoniae, Streptococcus pyogenes, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Salmonella typhi,* and Group B *streptococcus* (GBS) [17]. Viruses include echovirus, enterovirus, parechovirus, coxsackie virus, adenovirus, parainfluenza virus, rhinovirus, herpes simplex virus respiratory syncytial virus, and coronavirus Candida albicans and other Candida species are the most common fungi associated with neonatal sepsis [18].

In the 1990s, the American Academy of Pediatrics (AAP) began to recommend the use of intrapartum antibiotic prophylaxis (IAP) to prevent perinatal GBS, and in 2002, the AAP and the American College of Obstetricians and Gynecologists instituted guidelines on the universal screening by culture of all pregnant women from 35- to 37-week gestation. Due to the widespread use of prophylactic antibiotics for neonates, particularly intrapartum antibiotic use in mothers with positive cultures for GBS, the incidence of GBS-associated neonatal sepsis has declined significantly, a decrease of 70% in the US [19]. During the same period, other countries such as Canada and Taiwan have recommended the universal use of IAP and have seen a decline in the incidence of neonatal sepsis secondary to GBS infection as well [20]. In countries where IAP is used, the most common causative agents of neonatal sepsis are Escherichia coli and Gram-positive bacteria [21].

Risk Factors

In early-onset neonatal sepsis (EONS), which is usually associated with vertical transmission of pathogens from mother to child, the most common pathogens are group B Streptococcus, Escherichia coli, CONS, Haemophilus influenzae, and Listeria monocytogenes [21-22].]. In late-onset neonatal sepsis (LONS), which is most commonly associated with iatrogenic or nosocomial infections, the most common pathogens are CONS, followed by Staphylococcus aureus and Escherichia coli [23]. Risk factors include use of central venous catheters and other invasive medical devices, and prolonged hospitalization [24]. Other risk factors include premature rupture of membranes, amnionitis, meconium aspiration, LBW, VLBW, ELBW, premature birth, >3 vaginal examinations during labor, maternal fever during labor, or other maternal infections during labor [25]. Among term infants, males have a higher incidence of sepsis compared with female infants, an association not seen in preterm infants [26].

Clinical findings

Given the relatively subtle findings seen during clinical examination, neonates are at significant risk of delayed detection of sepsis until more ominous clinical findings and vital sign abnormalities occur. Early-onset individuals may have a

history of fetal distress, including perinatal fetal tachycardia. Shortly after delivery, other clinical cues such as meconium-stained amniotic fluid and low Apgar scores may appear at the initial neonatal assessment. Caretakers may report a history of food intolerance, irritability, excessive sleepiness, or "looking weird." Vital sign abnormalities include both hypothermia and fever. Fever is more common in term infants, but premature infants are more likely to become hypothermia. Tachycardia or bradycardia, signs of poor circulation such as cold or pale extremities, and a rapid, lint-like pulse may occur. Respiratory symptoms and signs such as moaning, rhinitis, accessory muscle use, cyanosis, and apnea are common in neonatal sepsis. Neurological symptoms and signs include lethargy, seizures, irregular breathing, high-pitched crying, hypotension, hypoactive deep tendon reflexes, and abnormal primitive reflexes. Gastrointestinal signs include decreased food intake, vomiting, diarrhea, jaundice, abdominal distension, and hepatosplenomegaly. Cutaneous findings include petechiae, impetigo, cellulitis, and abscesses. Basal metabolic acidosis due to poor perfusion can manifest as tachypnea and shortness of breath in the absence of respiratory infection [27].

Diagnostic Testing

As the symptoms and signs of neonatal sepsis are often very subtle and vague, it is imperative to perform diagnostic testing in any neonate with significant risk factors and concerning signs and symptoms. There are various multivariate predictive scoring systems based on retrospective studies that may be used to predict the need for antibiotics and extensive laboratory evaluation of a neonate versus observation for concerning signs and symptoms. One such example is the EONS calculator based on a large retrospective population study performed in the US to support clinicians in the decision to start antibiotics in neonates suspected of having sepsis [28]. The newborn's prior probability of EONS obtained from maternal risk factors such as chorioamnionitis and premature rupture of membranes is combined with findings based on the clinical examination, creating a scoring system that can determine the need for antibiotics and level of monitoring required This scoring system has been shown to reduce the proportion of newborns undergoing extensive laboratory evaluation and administration of antibiotics without any adverse effects [29]. The number needed to treat (NNT) for the high-risk group requiring antibiotics determined by this scoring system was still 118, highlighting the challenges involved in coming up with better diagnostic tools in picking up EONS at an early stage [30]. A complete blood count (CBC) was performed to determine the total and fractional white blood cell (WBC) counts, the absolute and immature neutrophil counts, and the immature and total neutrophil count ratios. Must be evaluated. Absolute leukocytosis has a low susceptibility to neonatal sepsis, but is useful for clinical decision-making when there is mild to moderate clinical suspicion of sepsis. Interestingly, a low WBC count, a low absolute neutrophil count (ANC), and a neutrophil-to-prematurity ratio (I/T) greater than or equal to 0.2 were highly predictive of infection. has been shown [31]. Dividing the I/T by the total neutrophil count to obtain the I/T ratio has been shown to provide improved specificity and area under the curve over I/T and ANC alone in diagnosing EONS [32].The I/T2 ratio accounts for both elevated immature neutrophils and the neutropenia that is of concern in the setting of sepsis. ANC, I/T, and I/T2 sensitivity, specificity, odds ratio, and area under the curve were highest at 4 hours postpartum compared to previous [33]. Therefore, placental culture results should not be used as a reason for antibiotic therapy. Urinary tract infections are rare within the first 72 hours of life. Therefore, urine cultures are performed only when assessing LONS [28]. Neonates with evidence of EONS or LONS should undergo routine lumbar puncture (LP). Approximately 23% of neonates with culture-positive bacteremia also develop

meningitis [28]. Acute-phase reactants such as C-reactive protein (CRP), procalcitonin, interleukin (IL-6 and IL-8) levels, presepsin, haptoglobin, and neutrophil CD64 are potential biomarkers for neonatal sepsis. being investigated. CRP may not be elevated during the early stages of infection because it takes time to synthesize in the liver and eventually appears in the blood. Serial measurement of CRP in combination with other acute phase reactants such as procalcitonin, IL-6 and IL-8 can improve diagnostic accuracy [33]. Procalcitonin (PCT) is more specific than CRP against bacterial infection and increases faster than CRP in response to infection. In normal-weight infants, PCT levels above 0.5 ng/mL are associated with nosocomial infections, and in VLBW infants levels above 2.4 ng/mL should prompt antibiotic therapy [33].

CONCLUSION

Although the incidence of neonatal sepsis has declined in some parts of the world, it remains a significant problem worldwide. Tests for the identification and diagnosis of neonatal sepsis continue to be developed, and new test techniques are still being tested. Monitoring and management of risk factors and IAPs remain important in preventing and controlling infection in this vulnerable population. Treatment includes prompt administration of antibiotics and supportive care in an appropriate hospital setting. Continuous vigilance is essential in the diagnosis and management of neonatal sepsis. A battery of tests, including C-reactive protein, total leukocyte count, absolute neutrophil count, platelet count, neutrophil cytoplasmic vacuolization, and polymorphic gastric aspiration cytology, was performed in neonates with a clinical diagnosis of NS. It's an excellent screening test. These tests are readily available, inexpensive, reliable and sensitive in detecting neonatal sepsis. Combining the three tests increases the sensitivity and negative predictive value of these tests to nearly 100%.

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