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Role of the Hematological Profile in Early Diagnosis of Neonatal Sepsis in North India

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ABSTRACT
In our nation, neonatal septicaemia continues to be a leading cause of morbidity and mortality. About 30-50% of all newborn deaths in underdeveloped nations are due to neonatal sepsis. Even though it poses a threat to life, if caught early enough, the illness is treatable. Even though it poses a threat to life, if caught early enough, the illness is treatable. Unfortunately, the initial symptoms and warning signals are sometimes vague and readily confused with those from noninfectious sources. The investigation was carried out in the pathology department of a tertiary care facility in Lucknow. All newborns who were suspected of having sepsis or who had a history of infection in their mothers were enrolled in the trial. Complete blood counts, CRP measures and a blood culture with antibiotic sensitivity were all part of the sepsis work-up. A total leukocyte count (TLC), total neutrophil count (TNC) and platelet count were all included in the complete blood count. From the measured values, absolute neutrophil counts (ANC) were computed. The standard values were taken from Manroe values for the neonatal haematological markers. Prior to starting antibiotic therapy, blood samples were taken. The pathologist analysing the peripheral smear results was unaware of the newborn's infection status. Out of 150 newborns with possible sepsis were examined in total. Out of 150 clinically suspected cases, blood culture results showed that 60 neonates were septic and 90 neonates had probable sepsis. The gender distribution gap between the two groups was a significant finding. Males made up 50% of the group with suspected sepsis (n = 45), while females made up 50% of the group with proven sepsis (n = 60), with male newborns making up 60% (36/60) and female babies making up 40% (24/60). Preterm newborns made up 60% (54/90) of the group with suspected sepsis, compared to 70% (42/60) of the group with confirmed sepsis. The oldest was 41 weeks gestation and the youngest was 25 weeks. About 730-4250 g were the range for birth weight. Although, the Hematologic profile that we looked at is a straightforward, efficient and affordable diagnostic for the early diagnosis of newborn sepsis, its sensitivity in that regard is subpar. Aseptic practises in delivery rooms and wards are essential for preventing conditions that lead to newborn septicemia, such as prematurity and low birth weight neonates. Antibiotic use should be justified and using antimicrobials according to the right protocols will lessen the threat of worldwide resistance development. As a result, it is unable to serve as a reference point for decisions on antibiotic therapy.

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Key Words
Hematologic, neonatal sepsis, anti-microbials, antibiotic therapy

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INTRODUCTION

In our nation, neonatal septicaemia continues to be a leading cause of morbidity and mortality. It accounts for 15% of all newborn deaths and is one of the main causes of neonatal mortality in underdeveloped nations. Neonatal sepsis is characterised as a clinical condition of bacteremia with systemic infection signs and symptoms in the first four weeks of life[1]. When pathogenic bacteria enter the bloodstream, they may either create a severe infection with little localisation or they may become mostly localised to the meninges or the lung[2]. About 30-50% of all newborn deaths in underdeveloped nations are due to neonatal sepsis. Even though it poses a threat to life, if caught early enough, the illness is treatable. Even though it poses a threat to life, if caught early enough, the illness is treatable. Unfortunately, the early warning symptoms and signs are sometimes vague and easily mistaken for those from noninfectious sources. It is challenging to make an early clinical diagnosis because of these vague indications and symptoms[3]. According to the WHO, the majority of childhood deaths in underdeveloped nations like India occur before the age of five due to perinatal deaths[4] and one of the most frequent causes of such prenatal mortality are newborn infections[5,6]. The incidence of neonatal sepsis in India is 30 per 1000 live births, according to the National Neonatal Perinatal Database (NNPD 2002-03)[7]. Due to its vague clinical image, it is a difficult problem[8]. Making it challenging to make an early clinical diagnosis. Premature infants, in particular, are more vulnerable to serious infections since their symptoms may be nonexistent or subtle and difficult to identify. As a result, deadly septicaemia could happen suddenly[9]. Since sepsis in newborns can progress quickly and in some cases prove fatal, prompt detection is essential[10].

Analysing sepsis as soon as possible is crucial since prompting the onset of antibiotic treatment improves the outcome. In both neonates and adults, the standard for diagnosing septicemia is blood culture positive. It does, however, come with certain limitations because it necessitates a microbiological laboratory that is well-equipped and because the minimum turnaround time for results is between 24 and 72 hrs. Only 3-8% of newborns who were statistically tested for sepsis (7-13%) had sepsis that was confirmed by culture[11-14]. Antibiotic administration before to culture frequently exacerbates the issue of needless antibiotic exposure and bacterial resistance. Thus, the importance of numerous screening tests is seen, either separately or in combination. The Haematological Scoring System (HSS) developed by Rodwell *et al*.[15] looks viable, easy to use, less time demanding and cost-effective, according to numerous studies[15-17]. As a result, the current study is being conducted to assess the significance of the haematological profile in the early diagnosis of newborn sepsis because it is a quick and easy test that can be completed before starting the neonate on antibiotic medication.

MATERIALS AND METHODS

The investigation was carried out in the pathology department of a tertiary care facility in Lucknow. All newborns who were suspected of having sepsis or who had a history of infection in their mothers were enrolled in the trial. These newborns' records were preserved and later reviewed. Due to maternal intrapartum sepsis risk factors like prolonged membrane rupture, maternal urinary tract infection, maternal intrapartum temperature >38°C, chorioamnionitis and profuse vaginal discharge, some of these neonates were asymptomatic but were nevertheless examined for sepsis. Neonates were disqualified if they had any of the following conditions: significant congenital anomalies, inborn metabolic problems, hemolytic jaundice, or respiratory distress syndrome (caused by a surfactant deficiency). Each infant was assessed by a paediatric resident working in the NICU or a neonatology fellow who noted the neonate's signs and symptoms, risk factors during pregnancy and clinical evaluation. Complete blood counts, CRP measures and a blood culture with antibiotic sensitivity were all part of the sepsis work-up. a total leukocyte count (TLC), total neutrophil count (TNC) and platelet count were all included in the complete blood count. From the measured values, absolute neutrophil counts (ANC) were computed. The standard values were taken from Manroe *et al*.[18] values for the neonatal haematological markers. Prior to starting antibiotic therapy, blood samples were taken. The pathologist analysing the peripheral smear results was unaware of the newborn's infection status.

Each of the four haematological parameters was given a number. Table 1 displays the haematological scores that were employed. Infants were divided into

Table 1: Hematological scores used in the study

Hematological test	Abnormality	Score
Increase or decrease WBC	≤5,000 mm3 or ≥ 25,000 mm^3, 30,000 mm^3, 21,000 mm^3 at birth ,12-24 hrs and day 2 onwards, respectively	1
Increase or decrease total ANC 20	↓or↓	1
CRP	Positive	1
Platelet count	≤150,000 mm	3

Normal values as defined by reference ranges of Manroe *et al*.[18], CRP: C reactive protein and ANC: Absolute neutrophil count

two categories: Proven sepsis and Probable sepsis, based on clinical observations and laboratory evidence. When the results of the blood culture were favourable, sepsis was diagnosed. When the blood culture was negative but there was a significant clinical history of illness, the infant was diagnosed with likely sepsis.

RESULTS

Out of 150 newborns with possible sepsis were examined in total. Out of 150 clinically suspected cases, blood culture results showed that 60 neonates were septic and 90 neonates had probable sepsis. The gender distribution gap between the two groups was a significant finding. Males made up 50% of the group with suspected sepsis (n = 45), while females made up 50% of the group with proven sepsis (n = 60), with male newborns making up 60% (36/60) and female babies making up 40% (24/60). Preterm newborns made up 60% (54/90) of the group with suspected sepsis, compared to 70% (42/60) of the group with confirmed sepsis. The oldest was 41 weeks gestation and the youngest was 25 weeks. About 730-4250 g were the range for birth weight. Table 2 displays the demographic breakdown of the neonates that were diagnosed as being septic.

Hematologic profile analysis revealed that thrombocytopenia had superior sensitivity and specificity to other conditions. Individually, none of the tests showed sensitivities that were sufficient.

In Table 3, the specifics of each individual hematologic finding in 150 infants who had sepsis are highlighted. The table shows that while the specificity of the CRP and thrombocytopenia tests is in the acceptable range, the sensitivities of the individual tests are below that threshold. It goes without saying that the CRP was positive in 15/60 (25%) of kids with established septicemia and in 18/90 (20%) of babies with suspected sepsis. Similarly, thrombocytopenia by itself was not a reliable predictive screening method. It only had a sensitivity of 70% and was present in 42/60 cases of sepsis that had been verified. The investigation demonstrated that although these tests had low sensitivities, their specificities were higher. Combining the tests can provide a useful screening method for ruling out sepsis.

Of the 150 infants who had blood cultures taken, 60 (about 40%) were found to have sepsis. Acinetobacter (20%, n = 12), group B streptococcus (30%, n = 18), Staphylococcus aureus (25%, n = 15), *E. coli* (10%, n = 6), two isolates of Salmonella, one each of *Proteus vulgaris* and *Pseudomonas aeruginosa* and two isolates of *E. coli* were also found.

Table 2: Basic characteristics of babies of proven sepsis (n = 60)

Sex	Male 60% (36/60)	Female 40% (24/60)
Premature	70% (42/60)	
Weight	730 g, 4250 g	Mean = 2170±746
Gestational age	25-41 weeks	Mean = 33±3.1

Table 3: Sensitivities and specificities of babies with suspected sepsis n = 150

Hematological test	Sensitivity (%)	Specificity (%)
Increase or decrease WBC∞	38	82
Increase or decrease ANCΔ	38	80
CRP	25	88
Platelet count $\leq$150,000 mm^3	70	86

Normal values as defined by reference ranges of Manroe *et al*.[18], ∞$\leq$5,000 mm^3 or $\geq$25,000 mm^3, 30,000 mm^3, 21,000 mm^3 at birth, 12-24 hrs and day 2 onwards, respectively $\leq$1800 0r $\geq$5400, 14000, 5400 at birth, 12- 48 hrs and 48 hrs onwards, respectively

DISCUSSIONS

The systemic response to infection in newborn newborns has been referred to as neonatal septicaemia, sepsis neonatorum and neonatal sepsis. Neonates are more vulnerable to bacterial invasion of the blood stream than older children or adults are because they are unable to fully summon the minimal inflammatory response and the dangers are significantly higher in preterm newborns. In India, there are 30 cases of neonatal sepsis for every 1000 live births (NNPD 2002-03). Because of the varied and ambiguous clinical presentation of newborn septicaemia, it is challenging to identify and diagnose this illness early[10].

Although, blood culture is the preferred method for septicemia diagnosis, the procedure is time-consuming and necessitates a well-equipped laboratory. The sensitivity and specificity of a diagnostic test for newborn sepsis should be as high as possible. Tests should be affordable, simple to conduct and yield results quickly. A number of very sensitive and inflammatory markers have been examined by numerous researchers. But these are advanced and useless in developing nations.

The typical reference ranges for total neutrophil counts and indicators of immature neutrophil count in newborns were developed by Manroe *et al*.[18]. These ranges start at 1800 mm^{-3}, increase to 7200 mm^{-3} at 12 hrs of age, then drop and stay at 1800 mm^{-3} for 72 hrs or longer. The maximum Immature: Total Neutrophil [I:T] ratio was also discovered; it is 0.16 for the first 24 hrs of life, 0.13 for 60-120 hrs and subsequently 0.12 for 5-28 days[19]. Mature neutrophils are deposited in the bone marrow of the foetus, just like in the adult but they are also present in the liver and spleen. Neutropenia and the depletion of the nuetrophil storage pool, as determined by bone marrow aspiration, are common findings in deadly bacterial sepsis[20]. Infants with culture-proven sepsis commonly had degenerative neutrophil alterations, such as vacuolization and toxic granulation, according to Liu CH and Lehan C. The early detection of newborn sepsis seemed to benefit greatly from this test[20].

The purpose of the current study is to assess the efficacy of the white blood cell count and C-reactive protein as a pre-cursor to neonatal septicemia. This study was conducted because it is a quick, low-cost test that can be performed even if the infant has taken antibiotics. Despite the fact that blood cultures are the gold standard for identifying neonatal sepsis, blood cultures are not widely available in our nation, although blood pictures are. The authors observed a wide range of sensitivity (17-90%) and specificity (31-100%) in a systematic assessment of the literature of studies evaluating the effectiveness of CRP and leukocyte indices[21].

Identification of the sick newborn is the main challenge in neonatal infections and it is also crucial to identify the uninfected infant due to its ambiguous clinical signs[22]. Ninety children classified as having probable sepsis in the current investigation had clinical evidence but no microbiologic evidence of infection. Because deadly infections have been documented in the context of negative blood cultures, these infants provide a diagnostic and therapeutic conundrum[23]. The complete blood count with differential is frequently employed, either alone or in conjunction with other tests or clinical observations, despite the fact that other assays are used as a diagnostic tool for newborn sepsis[24]. The published criteria by Manroe are the most trustworthy when it comes to identifying practically all infants who have sepsis or who have suspected sepsis. The convenience and applicability of the Haematological Scoring System to all newborns, including those who have received antibiotics, is its main advantage.

We discovered that none of the several parameters individually has the necessary sensitivity. This is in line with several studies that have found no conclusive link between sepsis and either the total leukocyte count or the total neutrophil count[25]. Our findings concur with those of Monroe who advised against relying just on neutrophil counts without also noting changes in the ratio of mature to immature neutrophils. In our investigation, it was discovered that there was a poor association between the CRP and newborn sepsis. With a specificity of 88%, the sensitivity was only 25%. The study contains contradictory findings regarding CRP levels. Ahmed *et al*.[26] also demonstrated a low predictive value in their research. In our study, 60% of the preterm births were in the group with probable sepsis, while 70% were in the group with confirmed sepsis. This may have been caused by weakened immune systems and low immunoglobulin G levels in premature newborns. This discovery of the preterm infant's sensitivity to sepsis is also supported by the literature.

CONCLUSION

Although, the Hematologic profile that we looked at is a straightforward, efficient and affordable diagnostic for the early diagnosis of newborn sepsis, its sensitivity in that regard is subpar. Sepsis prevention must be given the attention it deserves. Aseptic practises in delivery rooms and wards are essential for preventing conditions that lead to newborn septicemia, such as prematurity and low birth weight neonates. Antibiotic use should be justified and using antimicrobials according to the right protocols will lessen the threat of worldwide resistance development. As a result, it is unable to serve as a reference point for decisions on antibiotic therapy.

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