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A study on Role of the Hematological Investigation in Early Diagnosis of Neonatal Sepsis at Hospital in West Bengal

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ABSTRACT
Neonatal sepsis remains a significant contributor to illness and death in our nation. newborn sepsis accounts for approximately 30-50% of all newborn mortality in underdeveloped nations. Although it is a serious disorder, it can be treated if detected early. Regrettably, the initial indications and symptoms are frequently vague and can be easily mistaken for those caused by non-infectious factors. The research was carried out in the Pathology Department of a tertiary care hospital in Haldia. All the newborns who were believed to have sepsis or had a maternal history of infection were included in the study. The sepsis investigation involved performing full blood counts, measuring C-reactive protein (CRP) and conducting blood culture tests to determine antibiotic sensitivity. A full blood count, including platelet count, total white blood cell count (WBC) and total neutrophil count (TNC). Absolute neutrophil counts (ANC) were determined based on the measured values. The standard values used were the reference values of the newborn hematological parameters from the study conducted by Manroe. Blood samples were taken prior to starting antibiotic treatment. The pathologist analyzed the peripheral smear data without knowing the infection status of the newborn. Analyzed were a total of 150 newborns with probable sepsis. Among 150 instances that were clinically suspected, 60 newborns were confirmed to have sepsis with blood culture, whereas 90 neonates were considered to likely have sepsis. An important discovery was the variation in the gender distribution of both groups. In the group of individuals suspected to have sepsis, 50% were male (n = 45) and 50% were female (n = 45). Among the babies in the confirmed septic group, 60% were male (36/60) and 40% were female (24/60). The percentage of premature infants in the group with probable sepsis was 60% (54 out of 90), while the group with confirmed sepsis included 70% (42 out of 60) of preterm neonates. The youngest was born after 25 weeks of pregnancy while the oldest was born after 41 weeks of pregnancy. The weight at birth varied from 730 grams to 4250 grams. Conclusion: The Hematologic profile that we examined is a straightforward, fast and cost-effective approach in the early detection of newborn sepsis. However, its ability to accurately detect neonatal sepsis is not sufficient. To prevent factors that increase the risk of neonatal septicemia, such as premature birth and low birth weight, it is important to use aseptic procedures in delivery rooms and wards. Implementing a logical approach to antibiotic usage and following appropriate guidelines for the use of antimicrobial drugs would help decrease the emergence of resistance, which is becoming a worldwide concern. Thus, it is unable to offer guidance for judgments on antibiotic treatment.

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Key Words
Neonatal sepsis, hematologic profile, WBC, CRP

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INTRODUCTION

Neonatal sepsis remains a significant contributor to illness and death in our nation. It is a significant factor in the death of newborns in impoverished nations, accounting for 15% of all neonatal deaths[1]. Neonatal sepsis is described as a clinical condition where bacteria are present in the bloodstream and the baby shows signs and symptoms of infection within the first 4 weeks of life[2]. When disease-causing bacteria enter the bloodstream, they can create a severe infection that is not limited to a specific area, or they may primarily affect the lungs or the meninges[3]. newborn sepsis accounts for approximately 30-50% of all newborn mortality in underdeveloped nations[4]. Although it is a serious disorder, it can be treated if detected early. Regrettably, the initial indicators and symptoms are sometimes vague and can readily be mistaken for those caused by noninfectious factors. The vague indications and manifestations complicate the process of determining an initial medical diagnosis[5].

The World Health Organization (WHO) states that perinatal fatalities are the primary cause of childhood mortality in poor countries such as India, particularly for children under the age of 5[6]. Neonatal infections are a frequent cause of perinatal mortality[7,8]. Based on the National Neonatal Perinatal Database (NNPD 2002-03), the occurrence of neonatal sepsis in India is 30 out of every 1000 live births[9]. The issue is somewhat frustrating due to its vague clinical presentation[10]. This makes it challenging to determine an initial clinical diagnosis. Infants, particularly those born prematurely, are susceptible to severe infections, as the symptoms of these infections may be lacking or mild and difficult to identify. Therefore, severe blood poisoning might happen suddenly[11]. Early detection of sepsis in newborns is crucial as the condition can worsen quickly and in certain cases, lead to death[12]. An early assessment of sepsis is important because starting antimicrobial treatment promptly improves the outcome. The measure of blood culture positivity is used to diagnose septicaemia in both infants and adults. However, it does have its own specific limitations since it requires a well-equipped microbiological lab and the results acquired can take a minimum of 24-72 hrs. On average, out of the 7-13% of newborns evaluated for sepsis, only 3-8% are confirmed to have sepsis through culture testing[13-16]. Administering antibiotics prior to conducting a culture test frequently exacerbates the issue of unwarranted antibiotic exposure and the development of bacterial resistance. The importance of different screening tests, whether used alone or together, is noted. Several studies have indicated that the Haematological Scoring System (HSS) developed by Rodwell et al. is practical, straightforward, efficient, and cost-effective[17-19]. Therefore, this study aims to assess the importance of analyzing the blood characteristics for early detection of neonatal sepsis. This test is quick and can be performed before initiating antibiotic treatment for the newborn.

MATERIALS AND METHODS

The research was carried out in the Pathology Department of a tertiary care hospital in Haldia. All the newborns who were believed to have sepsis or had a maternal history of infection were included in the study. The information of these newborns was recorded and assessed at a later time. A few of these newborns did not show any symptoms but were checked for sepsis due to risk factors during childbirth, such as extended rupture of membranes, urinary tract infection in the mother, maternal fever above 38°C during childbirth, chorioamnionitis and profuse vaginal discharge. Newborns were not included if they had: a) significant birth defect; b) metabolic disorders present from birth; c) jaundice caused by the breakdown of red blood cells or respiratory distress syndrome (caused by a lack of surfactant). Every newborn was assessed by a pediatric resident who was working in the NICU or a neonatology fellow. They documented the indications and manifestations of the newborn, circumstances that may have contributed to their condition at birth and the clinical evaluation of the newborn. The sepsis investigation includes full blood counts, C-reactive protein (CRP) tests and blood culture with antibiotic susceptibility. A full blood count, including platelet count, total white blood cell count (WBC), and total neutrophil count (TNC). Absolute neutrophil counts (ANC) were determined based on the measured values. The standard values used were the reference values of the newborn hematological parameters from the study conducted by Manroe *et al*.[20]. Blood samples were taken prior to the start of antibiotic treatment. The pathologist, who was unaware of the infection status of the neonate, conducted the examination of the peripheral smear findings.

We allocated a single number to each of the four hematological parameters. The hematological scores utilized are displayed in Table 1. Infants were categorized into two groups based on the clinical findings and laboratory data: confirmed sepsis and suspected sepsis. A diagnosis of sepsis was confirmed based on positive results from a blood culture. Infants were categorized as having possible sepsis when the blood culture yielded negative results, but there was a significant clinical history indicating infection.

RESULTS

Analyzed were a total of 150 newborns with probable sepsis. Among 150 cases that were suspected of having a clinical condition, 60 newborns were confirmed to have a blood infection using a culture test, while 90 newborns were likely to have sepsis. An

Table 1: Hematological scores used in the study

Hematological test	Abnormality	Score
Increase or decrease WBC	= 5,000 mm3 or = 25,000mm3, 30,000mm3, 21,000 mm3 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*[20]
CRP = C reactive protein
ANC = Absolute neutrophil count

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 grams 4250 grams	Mean = 2170 ± 746
Gestational age	25 weeks -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 8	38	82
Increase or decrease ANC	38	80
CRP	25	88
Platelet count = 150,000 mm3	70	86

Normal values as defined by reference ranges of Manroe et al
8 = 5,000 mm3 or = 25,000mm3, 30,000mm3, 21,000mm3 at birth ,12-24 hrs and day 2 onwards respectively
= 1800 0r = 5400 ,14000 , 5400 at birth , 12- 48 hrs and 48 hrs onwards respectively

important discovery was the variation in the gender distribution of both groups. In the group of individuals suspected to have sepsis, 50% were male (n = 45) and 50% were female (n = 45). Among the infants in the confirmed septic group, 60% were male (36/60) and 40% were female (24/60). The premature babies accounted for 60% (54/90) of the group with probable sepsis, while the group with confirmed sepsis included 70% (42/60) of preterm neonates. The youngest was born after 25 weeks of gestation while the oldest was born after 41 weeks of gestation. The weight at birth varied from 730 grams to 4250 grams. The demographic characteristics of the newborns in the confirmed septic group are displayed in table 2.

An examination of the blood test results revealed that thrombocytopenia had higher levels of both sensitivity and specificity compared to other factors. Each test individually did not have adequate levels of sensitivity. The specific hematologic abnormalities of 150 infants that are strongly linked to sepsis are presented in table III. As shown in the table, the sensitivities of the different tests are below the desired level, but the CRP and thrombocytopenia have sufficient specificity. The C-reactive protein (CRP) was found to be positive in 25% (15 out of 60) of infants with confirmed sepsis and in 20% (18 out of 90) of infants with suspected sepsis, which is self-explanatory. Similarly, thrombocytopenia on its own was not an effective screening test for prediction. It was found in 42 out of 60 cases with confirmed sepsis, with a sensitivity of only 70%. The investigation indicated that the tests had low sensitivities but better specificities. The assays, when used together, can be an effective screening tool for ruling out sepsis.

The blood culture was positive in 60 out of 150 (40%) of the infants suspected of sepsis. The most frequently found organism was group B Streptococcus (30%, n = 18), followed by Staphylococcus aureus (25%, n = 15), Acinetobacter (20%, n = 12) and E. coli (10%, n = 6). There were two isolates of Salmonella, as well as one each of Proteus vulgaris and Pseudomonas aeruginosa.

DISCUSSIONS

Neonatal sepsis, sepsis neonatorum and neonatal septicaemia are words that have been employed to characterize the body's overall reaction to infection in newborn babies. Neonate's limited ability to fully generate the minimum inflammatory response makes them more prone to bacterial invasion of the bloodstream compared to older children and adults. This danger is considerably greater for preterm newborns. The rate of neonatal sepsis in India is 30 per 1000 live births (NNPD 2002-03). Early identification and diagnosis of newborn septicaemia can be challenging due to the inconsistent and non-specific clinical symptoms associated with this illness[21].

While blood culture is often regarded as the most reliable method for diagnosing septicemia, it does require a well-equipped laboratory and can be time-consuming. An optimal diagnostic test for newborn sepsis should possess high sensitivity and specificity. Testing should be affordable, conveniently conducted and provide prompt findings. Several researchers have assessed a range of extremely responsive and provocative indicators. However, these options may not be suitable for underdeveloped countries due to their complexity and lack of practicality.

Manroe et colleagues in 1979 established a standard range for total neutrophil counts and indices of immature neutrophil count in newborns. The count

starts at 1800/mm3, increases to 7200/mm3 at 12 hours of age and then decreases to and remains at 1800/mm3 after 72 hrs of age. They also set the highest Immature: Total neutrophil [I:T] ratio, which is 0.16 for the initial 24 hours of life, which decreases to 0.13 for 60-120 hrs and subsequently to 0.12 for 5-28 days[22]. In the developing fetus, as well as in the adult, fully developed neutrophils are stored in the bone marrow and can also be detected in the liver and spleen. Universal findings include fatal bacterial sepsis, neutropenia and depletion of the neutrophil storage pool, as determined by bone marrow aspiration[23]. Liu CH and Lehan C regularly noticed degenerative alterations in neutrophils, such as vacuolization and toxic granulation, in neonates with culture verified sepsis. This test seemed to offer useful support in the early identification of newborn sepsis[24].

The current study assesses the effectiveness of the white blood cell count and the C-reactive proteins as an early indicator of newborn septicemia. This study was conducted because it is a straightforward and affordable test that may be performed even if the kid has received antibiotics. Although the blood culture is considered the most reliable method for identifying newborn sepsis, it is not easily accessible in our nation. On the other hand, the blood image test is available in all healthcare facilities. In a comprehensive analysis of the research literature on studies assessing the effectiveness of CRP and leukocyte indices, the authors discovered a broad spectrum of sensitivity (ranging from 17%-90%) and specificity (ranging from 31%- 100%)[25]. The main issue in newborn infections is determining which infants are sick, as well as identifying those who are not affected. This is challenging due to the non-specific clinical signs[26]. In this study, 90 children who were classified as likely having sepsis showed clinical signs of infection but did not have microbiologic evidence to confirm it. These are the newborns who present a challenge in terms of diagnosis and treatment because deadly infections have been documented even when blood cultures show no signs of infection[27]. Different assays are utilized as a diagnostic tool for neonatal sepsis[28]. The complete blood count with differential is commonly utilised, either alone or together with additional tests or clinical findings. The criteria developed by Manroe et al are considered to be the most dependable among the assessed published criteria. These criteria have been found to effectively identify nearly all newborns with sepsis or suspected sepsis. The benefit of the Haematological Scoring System is that it is simple and may be used for all infants, even those who have been given antibiotics.

Out of the various parameters examined, we discovered that none of them alone have the necessary sensitivity. This is in line with several studies that have found no significant correlation between the overall number of white blood cells or the total number of neutrophils and sepsis[29]. Our observations similarly align with those of Monroe *et al*, who have warned against just relying on neutrophil count without considering changes in the ratio of mature and immature neutrophils. In our investigation, we did not observe a strong association between the CRP and newborn sepsis. The sensitivity was just 25% with a specificity of 88%. There are contradictory findings on the CRP levels in the literature. Zeeshan and others,30 The study has also demonstrated limited predictive usefulness. In our study, the group with suspected sepsis had a 60% rate of premature births, whereas the group with confirmed sepsis had a 70% rate of preterm births. This may have been caused by weakened defence mechanisms and reduced levels of immunoglobulin G in premature newborns. The literature also confirms this discovery regarding the vulnerability of preterm infants to sepsis.

CONCLUSION

The Hematologic profile that we examined is a straightforward, fast and cost-efficient method in the early detection of newborn sepsis. However, its ability to accurately detect neonatal sepsis is not sufficient. The necessity of preventing sepsis must be recognised. It is important to prevent variables that increase the risk of newborn septicemia, such as premature birth and low birth weight. The use of aseptic procedures in delivery rooms and hospitals is also critical. Implementing a logical approach to antibiotic usage and following appropriate procedures for the use of antimicrobial drugs would help decrease the emergence of resistance, which is becoming a worldwide concern. Thus, it is unable to offer guidance for judgements on antibiotic treatment.

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