e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 14(12); 514-519

Original Research Article

A Prospective Hospital-Based Study to Evaluate the Utility of the Hematological Scoring System (HSS) in the Early Diagnosis of Neonatal Sepsis

Akanksha Singh[1], Deepali[2]

[1]Tutor, Department of Pathology, Patna Medical College, Patna, Bihar, India
[2]Tutor, Department of Pathology, Patna Medical College, Patna, Bihar, India

Received: 15-10-2022 / Revised: 20-11-2022 / Accepted: 02-12-2022
Corresponding author: Dr. Deepali
Conflict of interest: Nil

Abstract

Aim: The aim of the present study was done to evaluate the utility of the hematological scoring system (HSS) in the early diagnosis of neonatal sepsis.

Methods: The prospective study was conducted in the Department of Pathology, Patna Medical College, Patna, Bihar, India for the period of six months. A total of 200 neonates in the department of pediatrics and neonatology were included in the study.

Results: A total of 200 neonates were classified into three categories, sepsis (n=90), probable infection (n=40), and normal (n=70), based on the clinical examination and laboratory findings. The total number of culture positive cases was 90 (45%) and culture was bacteriologically negative in 120 (60%) cases. The total number of preterm babies was 110 (55%) while 90 (45%) were term babies. Preterm babies were more affected by sepsis than term babies. There were 120 (60%) males and 80 (40%) females. Five (12.5%) of the normal neonates had score ≥5 suggesting the presence of sepsis, 15 (21.42%) had scores 3-4 suggesting possibility of sepsis, and 50 (71.42%) normal cases had scores ≤2 which suggested less likely sepsis in these cases.

Conclusion: Diagnosis of neonatal septicemia may be difficult as the early signs of sepsis may be subtle and different at different gestational ages. The HSS is a simple, quick, and cost-effective tool which can be used as screening test for early diagnosis of neonatal sepsis.

Keywords: Blood culture, Hematological scoring system, Neonatal sepsis

Introduction

Neonatal sepsis is a systemic illness caused by bacteria, viruses, or fungal infections. Furthermore, it is linked to hemodynamic alterations and clinical findings, as well as bringing substantial morbidity and mortality. [1] Neonatal sepsis is a clinical syndrome caused by systemic bacterial infection documented by a positive blood culture in the first 4 weeks of life. [2] It can be defined by positive blood and/or cerebrospinal fluid (CSF) culture. [3]

Sepsis occurring in the first 72 hours of life is defined as early-onset sepsis (EOS) and that occurring beyond 72 hours as late-onset sepsis (LOS). [1,4,5] According to the global burden of disease study 2016/2017, there are 1.3 million yearly incident cases of neonatal sepsis worldwide, resulting in 203,000 sepsis-attributable deaths. [6,7]

Probable sepsis includes clinical and laboratory findings which are consistent with bacterial infection but without a positive culture. Neonatal sepsis includes various systemic infections of the neonates such as pneumonia, meningitis, septicemia, arthritis, osteomyelitis, and urinary tract infections. [8] Systemic signs include lethargy, hypotonia, tachycardia, abdominal distension, fever, chest retractions, grunting, shock, apnea, pallor, jaundice, bradycardia, and increased ventilator requirements. Sepsis is more common in preterm and low birth weight neonates due to low immunity to combat bacterial infection.

Depending on the onset of symptoms, neonatal sepsis is classified into early-onset sepsis which presents at or before 72 h of life and late-onset sepsis which usually presents after 72 h of life. [9] Blood culture is the gold standard test for the diagnosis of neonatal sepsis which should be performed in all cases of suspected sepsis before starting antibiotics. [8] However, it is a time-consuming procedure requiring 48–72 h.

Blood culture is regarded as the gold standard test, but it takes around 48-72 hours. Further yield of blood culture is 30-70 %, so some neonates may be missed. [10] Furthermore, inability to exclude sepsis early results in the unnecessary exposure to antibiotics to the infants who do not have sepsis. Novel markers, like Interleukin-6, Interlukin-8, plasma elastase, are more sensitive early diagnosis but are not routinely available and are impractical for use in developing country like India. Leukopenia, toxic granules, immature neutrophil to total neutrophil ratio, thrombocytopenia, micro-ESR, C-reactive protein are some of the indirect markers of sepsis. These investigations are collectively referred to as sepsis screen. These investigations are rapid and available routinely. Presence of two or more of these in the background of clinical suspicion is positive sepsis screen.

The aim of the present study was done to evaluate the utility of the hematological scoring system (HSS) in the early diagnosis of neonatal sepsis.

Materials and Methods

The prospective study was conducted in the Department of Pathology, Patna Medical College, Patna, Bihar, India for the period of six months. A total of 200 neonates in the department of pediatrics and neonatology were included in the study.

Inclusion criteria

The study included all neonates with features of sepsis and those neonates having predisposing factors or history suggestive of sepsis.

Exclusion Criteria

Neonates born to known immunocompromised mother, with a suspicion of TORCH, malaria, congenital abnormalities, hemolytic jaundice, or inborn error of metabolism, who received antibiotics before taking blood for culture were excluded from the study.

Methodology

Informed consent was taken from the parents of all the neonates. Taking all aseptic precautions, 2 ml of blood was withdrawn from suspected neonates within 24 h of admission. One milliliter of sample was anticoagulated with EDTA and using Sysmex XS-800i automated hematology analyzer, values of TLC and platelet count were noted and counter checked. Another 1 ml of blood was collected in red Vacutainer and allowed to rest for 30 min. It was then centrifuged and the serum was obtained for CRP estimation. Peripheral blood smear (PBS) was also made from the collected sample and was stained by Leishman's stain. PBS was examined for immature neutrophils and degenerative changes in neutrophils. All PBSs were analyzed in the department of pathology, using HSS as proposed by Rodwell et al.

HSS assigns a score of 1 for each of the seven criteria found to be significantly associated with sepsis with the exception of score of 2 for an abnormal total polymorphonuclear neutrophils (PMNs) count.

Score	Interpretation
≤	Sepsis is very unlikely
3 or 4	Probable sepsis
≥	Sepsis or infection is very likely

Sensitivity, specificity, and positive predictive value (PPV) were calculated for each parameter. p value was also calculated for different parameters. Data were compiled and statistical analysis was done using the SPSS software.

Results

Table 1: Hematological scoring system

Criteria	Abnormality	Score
Total WBC count	≤5000/Ml ≥25,000 at birth ≥30,000 after 12–48 h ≥21,000 day 2 onward	1 1
Total PMN count	No mature PMN seen Increased/decreased	2 1
Immature PMN count	Increased	1
I:T PMN ratio	Increased	1
I:M PMN ratio	≥0.3	1
Degenerative changes in PMN	Toxic granules/cytoplasmic vacuoles	1
Platelet count	≤150,000	1

A total of 200 neonates were classified into three categories, sepsis (n=90), probable infection (n=40), and normal (n=70), based on the clinical examination and laboratory findings. The total number of culture positive cases was 90 (45%) and culture was bacteriologically negative in 120 (60%) cases. The total number of preterm babies was 110 (55%) while 90 (45%) were term babies. Preterm babies were more affected by sepsis than term babies. There were 120 (60%) males and 80 (40%) females.

Table 2: Distribution of cases according to sepsis score

Sepsis score	Score 0-2 (%)	Score 3-4 (%)	Score >5 (%)
Sepsis (90)	0	12 (13.34)	78 (86.66)
Probable Sepsis (40)	5 (12.5)	20 (50)	15 (37.5)
Normal (70)	50 (71.42)	15 (21.42)	5 (7.14)
Total	55	47	98

Five (12.5%) of the normal neonates had score ≥5 suggesting the presence of sepsis, 15 (21.42%) had scores 3-4 suggesting possibility of sepsis, and 50 (71.42%) normal cases had scores ≤2 which suggested less likely sepsis in these cases.

Table 3: Sensitivity, specificity, and PPV of each test

Investigations	Sensitivity (%)	Specificity (%)	PPV (%)
Total leukocyte count	60.80	90.60	82.38
I:T ratio	92	89	85.75
I:M ratio	58	92.18	84.37
Platelet count	65.25	81.29	71.49
Degenerative changes in PMN	70	62.5	51.14
Immature PMN count	96	87.50	84.61
PMN count	91.3	65.64	65.62

In our study, HSS had a sensitivity of 86.95% and specificity of 78.12%. HSS had PPV of 74.07% and $p < 0.0001$. White blood cells (WBCs) count had sensitivity of 60.80% and specificity of 90.60%. PPV was 82.38%. This result was statistically significant. Platelet count showed sensitivity of 81.29%, PPV was 71.49% and $p<0.0001$. Cells with degenerative changes showed sensitivity of 70% and specificity of 62.5%. PPV of the test was 51.14% and $p=0.0016$.

Discussion

Neonatal sepsis is one of the most common causes of neonatal mortality and morbidity. However, its early diagnosis is challenging. Blood culture is the gold standard test for diagnosing sepsis, but it has low sensitivity and delay in the culture reports that lead to injudicious use of antibiotics. HSS including blood parameters serves as useful tool in the early diagnosis and management of neonatal sepsis. [11]

Neonatal sepsis is defined by systemic infections in first 28 days of life. [10] Preterm birth complications and infections are the largest contributors to the neonatal mortality. The incidence of neonatal sepsis according to the data from National Neonatal Perinatal Database (NNPD, 2002-03) is 30 per 1000 live births. Mortality due to sepsis can be prevented by early diagnosis, rational use of antibiotics and aggressive supportive care. [12] However, early recognition is difficult as the sign and symptoms of early sepsis are non-specific. Blood culture is regarded as the gold standard test, but it takes around 48-72 hours. Further yield of blood culture is 30-70 %, so some neonates may be missed. [11]

In the present study, the distribution of cases according to sepsis score showed accuracy of 86.95%. This result was consistent with the studies by Rodwell et al. (96%), Narasimha and Harendra Kumar (100%), and Makkar et al. (83.33%). HSS had a sensitivity of 86.95%, specificity of 78.12%, PPV of 74.06%, and net present value (NPV) of 89.2%. Saleem et al. also found that the HSS was having a sensitivity of 90%, specificity of 74.5%, PPV of 65.9%, and NPV of 93.2%. Manucha et al. observed that hematological score ≥3 had a sensitivity of 86% and NPV of 96%. [13] In our study, there were 132 (60%) male and 88 (40%) were female which are similar to the observation made by other authors also.

In the present study, 90 (45%) cases were culture positive. Sugandhi et al. [14] observed culture positivity in 42.5% of cases, Namdeo et al. [15] in 50% of cases, and Khatua et al.[16] found culture positivity in 59.8% of cases. In our study, increased or decreased WBC count had a sensitivity of 60.86%, specificity of 90.62%, and PPV of 82.35% which was consistent with other studies. Makkar et al. found that increased or decreased WBC count had a sensitivity of 56.2% and specificity of 91.71%. [17]

Thrombocytopenia is associated with poor prognosis in neonatal sepsis. In the present study, 30 of 46 culture-positive cases had

thrombocytopenia with a sensitivity of 65.21%, specificity of 81.29%, and PPV of 71.49% which was consistent with other studies. Shiraji et al. [18] found that thrombocytopenia was 61% sensitive and 82% specific. Speer et al. [16], Rodwell et al. [19], and Basu et al. [20] also found thrombocytopenia to be associated with neonatal sepsis.

In our study, CRP had a sensitivity of 66%, specificity of 78%, and PPV of 68.18%. Mathers and Pohlandt [21] observed sensitivity of 61% and specificity of 76% for CRP values. Wagle et al. [22] found CRP values to be 62% sensitive and 87% specific. Chan and Ho observed CRP as 56% sensitive and 72% specific. [23,24]

Conclusion

Diagnosis of neonatal septicemia may be difficult as the early signs of sepsis may be subtle and different at different gestational ages. The HSS is a simple, quick, and cost-effective tool which can be used as screening test for early diagnosis of neonatal sepsis. It is applicable to all infants, including those who have received antibiotic therapy before evaluation and simplifies the interpretation of hematologic profile.

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