Study of hematological parameters in the early diagnosis of neonatal sepsis in tertiary care center in Jharkhand

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ABSTRACT

Background: Bacterial sepsis is a major cause of morbidity and mortality in newborns. Probable sepsis is a clinical and laboratory finding consistent with bacterial infection without a positive culture. **Objectives:** The objectives of the study were to study and determine the predictive value of hematological parameters in the early diagnosis of neonatal sepsis at a tertiary care center in Jharkhand. **Materials and Methods:** This was a prospective study conducted from July 2016 to June 2017 in a tertiary care teaching hospital in Jharkhand. A total of 110 neonates admitted in neonatal intensive care unit of the hospital, with either clinical suspicion of sepsis or having predisposing perinatal factors for sepsis, were included in the study. In this study, hematological scoring system (HSS) along with clinical profile of patient and sepsis screening tests was studied. Sensitivity, specificity, and positive predictive value (PPV) of each parameter were studied and analyzed. **Results:** Out of 46 cases with culture-proven sepsis, 40 (86.95%) infants had score ≥5 and 6 (13.04%) had scores 3–4. HSS had a sensitivity of 86.95% and a specificity of 78.12%. HSS had PPV of 74.07%. Male babies were observed to be affected more than female babies. **Conclusion:** As no single individual hematological parameter is superior to other in predicting neonatal sepsis, a combination of these parameters in the form of HSS and C-reactive protein has been recommended. We conclude that HSS is a useful test to distinguish the infected from non-infected neonates.

Key words: *Antibiotic, Blood culture, Hematological scoring system, Neonatal sepsis*

Neonatal sepsis is the presence of generalized systemic features of infection. 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 [1]. 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 [2]. Blood culture is the gold standard test for the diagnosis of neonatal sepsis [1] which should be performed in all cases of suspected sepsis before starting antibiotics. However, it is a time-consuming procedure requiring 48–72 h.

The current study was undertaken to study the hematological parameters in the early diagnosis of neonatal sepsis using Rodwell's scoring criteria [3] which include laboratory tests such as total leukocyte count (TLC), absolute neutrophil count, immature neutrophil count (I), immature-to-total neutrophil ratio, immature-to-mature neutrophil count ratio, platelet count and degenerative changes in neutrophil (toxic granules, cytoplasmic vacuoles, etc.), and evaluation of C-reactive protein (CRP). This study was done to evaluate the utility of the hematological scoring system (HSS) in the early diagnosis of neonatal sepsis.

MATERIALS AND METHODS

This was a prospective study done in the departments of pediatrics and pathology in a tertiary care teaching hospital in Jharkhand from July 2016 to June 2017. A total of 110 neonates in the department of pediatrics and neonatology were included in the study. The study included all neonates with features of sepsis and those neonates having predisposing factors or history suggestive of sepsis. 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. The study was approved by the ethical committee of the institute and 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. This is done if no mature PMNs are seen on the peripheral smear to compensate for the low I: M (Table 1).

Score	Interpretation
≤2	Sepsis is very unlikely
3 or 4	Probable sepsis
≥5	Sepsis or infection is very likely

Minimum score: 0, Maximum score: 8

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

A total of 110 neonates were classified into three categories, sepsis (n=46), probable infection (n=22), and normal (n=42), based on the clinical examination and laboratory findings. The total number of culture positive cases was 46 (41.84%) and culture was bacteriologically negative in 64 (58.18%) cases. The total number of preterm babies was 62 (56.36%) while 48 (43.63%) were term babies. Preterm babies were more affected by sepsis than term babies. There were 66 (60%) males and 44 (40%) females.

The distribution of cases according to sepsis score is given in Table 2. Four (9.52%) of the normal neonates had score ≥5 suggesting the presence of sepsis, 8 (19%) had scores 3–4 suggesting possibility of sepsis, and 30 (71.4%) normal cases had scores ≤2 which suggested less likely sepsis in these cases.

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. Out of 44 cases with reactive CRP, 30 (66%) cases were culture positive while 14 (22%) were culture negative. The sensitivity of CRP test was 66% and specificity was 78%. PPV of the CRP test was 68.18%. White blood cells (WBCs) count had sensitivity of 60.86% and specificity of 90.62%. PPV was 82.35%. This result was statistically significant. Platelet count showed sensitivity of 81.25%, PPV was 71.42% 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=0.0018 (Table 3).

Table 1: Hematological scoring system

Criteria	Abnormality	Score
Total WBC count	≤5000/μL	1
	≥25,000 at birth	1
	≥30,000 after 12–48 h	
	≥21,000 day 2 onward	
Total PMN count	No mature PMN seen	2
	Increased/decreased	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

I:T: Immature-to-total neutrophil ratio, I:M: Immature-to-mature neutrophil ratio, ANC: Absolute neutrophil count, PMN: Polymorphonuclear neutrophil, WBC: White blood cell

Table 2: Distribution of cases according to sepsis score

Sepsis score	Score 0–2 (%)	Score 3–4 (%)	Score >5 (%)
Sepsis (46)	0	6 (13.04)	40 (86.95)
Probable sepsis (22)	4 (18.18)	10 (45.45)	8 (36.36)
Normal (42)	30 (71.4)	8 (19)	4 (9.52)
Total cases (110)	34	24	52

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

Investigations	Sensitivity (%)	Specificity (%)	PPV (%)
Total leukocyte count	60.86	90.62	82.35
I:T ratio	92	89	85.71
I:M ratio	58	92.18	84.37
Platelet count	65.21	81.25	71.42
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

PMN: Polymorphonuclear neutrophil, I:T: Immature-to-total neutrophil ratio, I:M: Immature-to-mature neutrophil ratio, PPV: Positive predictive value

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 [4].

In the present study, the distribution of cases according to sepsis score showed accuracy of 86.96%. This result was consistent with the studies by Rodwell *et al*. (96%), Narasimha and Harendra Kumar (100%), and Makkar *et al*. (83.33%) [3,5,6]. 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*. [7] 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*. [8] observed that hematological score ≥3 had a sensitivity of 86% and NPV of 96%. In our study, there were 66 (60%) male and 44 (40%) were female which are similar to the observation made by other authors also [9,10].

In the present study, 46 (41.81%) cases were culture positive. Sugandhi *et al*. observed culture positivity in 42.5% of cases, Namdeo *et al*. in 50% of cases, and Khatua *et al*. found culture positivity in 59.8% of cases [11-14]. 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% [5].

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 81.25%, and PPV of 71.42% which was consistent with other studies. Shiraji *et al*. [15] found that thrombocytopenia was 61% sensitive and 82% specific. Speer *et al*. [16], Rodwell *et al*. [3], and Basu *et al*. [17] 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 [18] observed sensitivity of 61% and specificity of 76% for CRP values. Wagle *et al*. [19] found CRP values to be 62% sensitive and 87% specific. Chan and Ho [20] observed CRP as 56% sensitive and 72% specific. The study had a few limitations such as the sample size was small and it was not a case–control study.

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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