

## Comparative Evaluation of the Predictive Value of Hematological Scoring System(HSS) and Acute Inflammatory Markers(Micro ESR and CRP) in Early Diagnosis of Neonatal Sepsis

Dr. Ayush Saxena<sup>1\*</sup>, Dr. Anshu Gupta Devra<sup>2</sup>, Dr. Kiranjot Kaur<sup>3</sup>, Dr. Devyani Pendharkar<sup>4</sup>, Dr. Kangana Sengar<sup>5</sup>

<sup>1\*</sup>Post Graduate Student, Department of Pathology, School of Medical Sciences And Research, Sharda University

<sup>2</sup>Professor and Head of Department, Department of Pathology, School of Medical Sciences And Research, Sharda University (Corresponding Author)

<sup>3</sup>Assistant Professor, Department of Pathology, School of Medical Sciences And Research, Sharda University

<sup>4</sup>Assistant Professor, Department of Pathology, School of Medical Sciences And Research, Sharda University

<sup>5</sup>Associate Professor, Department of Pathology, School of Medical Sciences And Research, Sharda University

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### ABSTRACT

**INTRODUCTION:** Neonatal sepsis is a major cause of morbidity and mortality in newborns globally, requiring prompt and precise diagnosis to ensure timely treatment and improve survival rates. The challenge lies in the nonspecific clinical signs and the delay in obtaining blood culture results. This study evaluates the diagnostic effectiveness of the Hematological Scoring System (HSS), rs, in comparison with acute inflammatory markers like Micro-Erythrocyte Sedimentation Rate (Micro-ESR) and C-Reactive Protein (CRP).

**AIM:** The aim of the study was to identify the most reliable method, either standalone or in combination, for diagnosing neonatal sepsis early.

**METHODOLOGY:** Study took into consideration 50 blood samples of suspected neonatal sepsis, which were then divided into groups(1,2,3) depending on their score and culture status. Performance analysis of hematological parameters constituting HSS, micro-ESR and CRP was calculated.

**RESULT:** Of the 7 parameters that constituted HSS Score, maximum correlation with culture positivity was noted with Immature Neutrophil Count and Immature to Total Neutrophil Ratio (100% each) followed by Immature to Mature Neutrophil Ratio (70%).

### 1. INTRODUCTION:

Sepsis neonatorum or neonatal septicemia, is a term used to describe a systemic inflammatory reaction in newborns brought on by bacterial infections during the first month of life. Neonatal sepsis affects roughly 2-3% of all live births, though the incidence varies. Newborns are especially vulnerable to infections because their immune systems are still developing, so early detection and treatment are essential[1,2]. In India, neonatal sepsis accounts for approximately 25% of all newborn deaths, with an estimated mortality rate of 26 deaths per 1,000 live births[3]. In order to improve outcomes and lessen the catastrophic effects of sepsis on infant health, early detection, timely treatment, and efficient infection control methods are vital, as this high fatality rate emphasizes[4]. A positive blood culture confirming the infection is the gold standard for diagnosing newborn sepsis but has some serious drawbacks as results are not available for at least 48 to 72 hours, which delays important treatment decisions[5]. Additionally, only 30–40% of blood cultures provide positive findings, which means that a sizable portion of illnesses might go undiagnosed. Furthermore, sepsis cannot be ruled out completely by a negative blood culture. These drawbacks emphasize the necessity of more clinical monitoring and diagnostic techniques to guarantee prompt and precise identification of newborn sepsis[5].

Hematological Scoring System (HSS)

To determine the risk of sepsis in newborns, the HSS employs a seven-point scoring system. The risk of infection is calculated by adding together the scores assigned to each parameter. According to studies, the HSS has a high sensitivity of 96%, which means that a significant percentage of infected infants are correctly identified[5].

## C-Reactive Protein (CRP)

CRP is an acute phase reactant with increased values signifying inflammation. It can be difficult to assess CRP dynamics in infants because of non-specific spikes during the first three days of life. Despite this, CRP is still a useful biomarker in clinical practice, for identifying bacterial infections after the first 48 hours.[6].

## Erythrocyte Sedimentation Rate (ESR)

ESR is used widely as an indicator of inflammation and constitutes one of the acute phase reactants. A modified technique called micro or mini-ESR has been developed for use in neonatal care, where blood volume is constrained and the necessity of less invasive procedures is critical. Because this technique only requires a few drops of capillary blood, it can be used on neonates without the need for larger venous samples

**Aims and Objectives:** This study was conducted to compare the performance analysis of individual parameters of Hematological Scoring System (Rodwell et al) and acute inflammatory markers (Micro ESR and CRP) to assess the effectiveness of test/group of tests either singly or in combination for predicting neonatal sepsis.

To evaluate the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of individual parameters of the Hematological Scoring System considering positive blood culture as the gold standard.

To evaluate the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of Micro-ESR and CRP.

To compare HSS and acute inflammatory biomarkers to determine the most sensitive and most reliable test for early diagnosis of neonatal sepsis.

**Materials and Methods:** This was a prospective analytical study conducted in the Department of Pathology, in a tertiary care centre in western UP over a period of 1.5 years (May 2023 – November 2024). Total of 50 blood samples from suspected neonatal septicemic cases were evaluated for different hematological parameters constituting HSS along with MicroESR,CRP and blood culture

**Methodology:** All blood samples were received and processed by HORIBA Yumizen H2500 analyser. Values of Total Leucocyte Count (TLC) and Platelet Count were taken into account. Peripheral smears were prepared and stained with leishman stain. At least 200 leukocytes were counted for calculating differential leucocyte count, based on which values of total neutrophil count, mature and immature neutrophil count (including band forms) were calculated. The Immature to Total (IT) neutrophil Ratio and Immature to Mature (IM) Neutrophil ratio were also calculated. Smears were examined for degenerative/toxic changes in polymorphs like toxic granulations, Dohle bodies and cytoplasmic vacuolations.

Estimation of micro ESR was done at bedside by using pre-heparinized microhematocrit tube of 75 mm length with internal diameter of 1.1mm and external diameter of 1.5mm by heel-prick technique. Reading was noted after 1 hour and the normal range taken for Micro ESR was 1-15 mm in the 1st hour. 0.5ml of Blood sample for Serum CRP levels was collected in a Red-top pediatric (0.5ml) vial. Levels were measured by quantitative immunofluorescence method by ICROMA 2. The normal value for CRP taken was <5 mg/L. 1-3 ml of venous blood samples of all suspected cases was inoculated in a yellow coloured blood culture pediatric vial under complete aseptic conditions. HSS scoring system was applied and scores assigned to different parameters were assigned as given (Table 1).

The minimum score was 0 and maximum score was 8. After calculating the HSS, and taking into account status of the culture, the neonates were further grouped into 3 categories:- Group-1: HSS<2 and Culture negative (Unlikely Sepsis), Group-2: HSS 3 or 4 with positive or negative blood culture (Possible sepsis), Group-3: HSS >5 with positive or negative blood culture (Very likely sepsis).

**Statistical Analysis:** All the data analyzed was entered into MS Excel Sheet and IBM SPSS Software version 30, which was used for comparison and descriptive statistics showing the numeric data in frequency distribution with percentage and categorical data was shown by Tables and Pie Chart. Sensitivity, specificity, Positive predictive value (PPV) and Negative predictive value (NPV) was calculated for each parameter **Results:** The demographic characteristics as illustrated in table 2, indicated a significant predominance of neonates within the 0-7 days age group, comprising 92% of the total cases. Overall, males constitute 72% of the total population, while females account for 28%. M:F ratio was 2.5:1. Our study underscores a higher incidence of neonatal cases in the first week of life, with a notable male predominance across all age groups (Table 2).

Total of 50 cases/samples were analysed for various hematological parameters and their corresponding scores assigned to calculate hematological scoring system (HSS). HSS score along with their culture status (positive/negative) was then taken into account and were further subdivided in one of the three groups (Table 3). Overall, only ten neonates 20% were culture-positive, while 40 neonates (80%) were culture-negative Group 1 HSS with score 2/3 consisted of 6% cases. All of them were negative for blood culture and hence were unlikely to be of septicemic etiology and were further excluded from performance analysis calculations Group 2 HSS with a score of 3/4 constituted 60% of the total cases (30/50), had 4 culture-

positive cases (13.3%) and 26 culture-negative cases (86.7%). This group segregates neonates with possible sepsis and likewise only a minority of cases were positive on culture. Group 3 accounted for 34% (17/50) and also had the highest proportion of culture-positive cases (6/17; 35.3%), while 64.7% were culture-negative. This segregates neonates in which sepsis is very likely and by our observation was also the group with maximum culture positivity.

We further analysed individual hematological parameters of HSS in group 2 and 3 with their culture status. Following observations were made (Table 4). In group 2 culture negative cases (n=26), TLC (TLC) abnormalities were noted in only 27% neonates. Total Neutrophil Count (TNC) were found to be abnormal in (80.7%) cases thus a significant proportion of neonates had abnormal neutrophil count in spite of normal TLC. Similarly, increased Immature Neutrophil Count was found in 21 (80.7%) neonates, suggesting a high incidence of neutrophil abnormalities despite negative cultures. The IT Neutrophil Ratio was elevated ( $>0.120$ ) in 24 cases (92.3%), making it the most frequently altered parameter. Of the seven parameters studied, total neutrophil count and IT ratio appear to be the most reliable indicators in decision-making for neonatal sepsis management, even in culture-negative cases. All the 26 patients exhibited normal MicroESR levels. CRP levels were normal in 88.5% abnormal in 11.5%.

In HSS group 2, only four cases were culture positive. TLC was normal in all cases, while Total Neutrophil Count abnormalities were present in 50%. Immature Neutrophil Count and IT Neutrophil Ratio were elevated in all 4 neonates (100%), suggesting their strong association with culture-positive sepsis. IM Neutrophil Ratio was increased in 50% of cases, and degenerative changes were seen in 50% as well. Thrombocytopenia ( $<150,000/\mu\text{L}$ ) was present in 25% of neonates. All four patients (100%) had normal MicroESR levels. CRP levels were abnormal in one patient (25%), while the remaining three (75%) had normal values.

HSS Group 3 with culture-negative sepsis. TLC was normal in 91% of cases, suggesting limited predictive value. Total Neutrophil Count was abnormal in all cases (100%), along with elevated Immature Neutrophil Count and IT Neutrophil Ratio, highlighting their strong association with sepsis, even in culture-negative cases (Table 5). IM Neutrophil Ratio was also increased in all neonates (100%), further supporting its diagnostic relevance. Degenerative changes were present in 91% of cases, reinforcing their significance in infection assessment (Table 5). These findings suggest that neutrophil abnormalities, especially IT and IM ratio, are highly sensitive markers for identifying neonatal sepsis, even in the absence of positive blood cultures. All 11 patients (100%) had normal MicroESR levels. CRP levels were normal in 10 patients (91%). HSS group 3 culture positive accounted for 6 cases. 100% exhibited an increased immature neutrophil count and an elevated IT neutrophil ratio, both of which are key indicators of infection-induced stress on the bone marrow. Similarly, 83.3% had an increased IM neutrophil ratio, reinforcing the presence of an inflammatory response. Among six patients, five (83.3%) had normal MicroESR levels, while one (16.7%) showed abnormal values.

Most frequently identified organism was Coagulase Negative Staphylococcus aureus, accounting for 40% of the cases. Acinetobacter was the second most common pathogen, found in 30% of cases. (Figure 6)

**Discussion:** The comparative analysis of hematological parameters and inflammatory markers across different studies highlights varying degrees of sensitivity, specificity, PPV, and NPV in detecting neonatal sepsis. In the present study, the Immature Neutrophil Count and Immature to Total Neutrophil Ratio demonstrated the highest sensitivity (100%) with a negative predictive value (NPV) of 100%, making them effective screening tools for ruling out sepsis. However, their low specificity (13.51% and 5.4%, respectively) limits their utility as standalone diagnostic markers. Total Neutrophil Count showed moderate sensitivity (40%) and low specificity (10.81%), contrasting with Priyanka T et al. (2018) and Amir N et al. (2023), where higher specificity was observed. Platelet Count in the present study exhibited moderate sensitivity (60%) and specificity (78.4%), aligning closely with Priyanka T et al. (2018). Micro ESR displayed poor sensitivity (10%) but perfect specificity (100%), reinforcing its limited diagnostic role. C-Reactive Protein (CRP) emerged as a reliable marker, with sensitivity (60%) and specificity (89.2%), supporting its use in conjunction with other hematological parameters (Table 7). **Conclusion:** Of the 7 parameters that constituted HSS Score, maximum correlation with culture positivity was noted with Immature Neutrophil Count and Immature to Total Neutrophil Ratio (100% each) followed by Immature to Mature Neutrophil Ratio (70%). This suggests that even if culture status is unknown, if above parameters are abnormal, the probability of neonatal septicemia is very high. The analysis of these 3 parameters can therefore help the clinicians in predicting neonatal septicemia.

**Table 1: Hematological Scoring System**

Criteria	Abnormalities	Score
1.Total leukocyte count (TLC)	≤5000/μl	1
	≥25000 at birth	1
	≥30000-12-24 hrs	1
	≥21000 day 2 onwards	1
2.Total Neutrophil Count	1800-5400	0
	No mature PMN seen	2
	Increased / Decreased	1
3.Immature Neutrophil count	600	0
	>600 (Increased)	1
4. Immature: Total (I:T) Neutrophil Ratio	0.120	0
	> 0.120 (Increased)	1
5. Immature :Mature(I:M) Neutrophil Ratio	<0.3	0
	≥0.3 (Increased)	1
6. Degenerative changes in neutrophils	Toxic granules / cytoplasmic vacuolations	1
7. Platelet Count	≤ 150000/μl	1

**[Table/Fig-1]:** Haematological scoring system (Rodwell RL et al.,)

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

**[Table/Fig-2]:** Interpretation of Score.

**Table 2: Demographic Characteristics**

Age	Total	Male	Female
<b>0 - 7 Days</b>	46(92%)	34(73.9%)	12(26.1%)
<b>8 - 14 Days</b>	3(6%)	2(66.66%)	1(33.33%)
<b>15 - 21 Days</b>	1(2%)	0	1(100%)
<b>22 - 30 Days</b>	0	0	0
<b>Total</b>	<b>50</b>	<b>36(72%)</b>	<b>14(28%)</b>

**Table 3: Overall Group Division**

HSS GROUP	Total Cases	Culture Positive	Culture Negative	Percentage
<b>GROUP 1</b>	3(6%)	0	3(100%)	<b>100% Culture Negative</b>
<b>GROUP 2</b>	30(60%)	4(13.3%)	26(86.7%)	<b>Positive - 13.33% Negative - 86.66%</b>
<b>GROUP 3</b>	17(34%)	6(35.3%)	11(64.7%)	<b>Positive - 35.3% Negative - 64.7%</b>
<b>Total</b>	<b>50</b>	<b>10(20%)</b>	<b>40(80%)</b>	

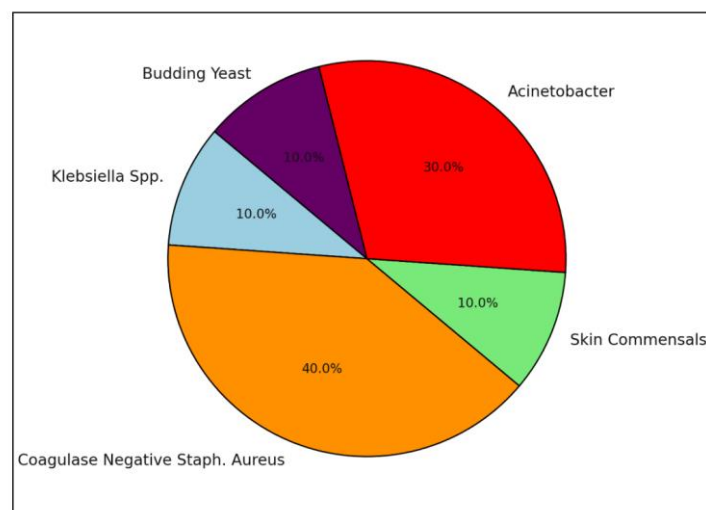
**Table 4: HSS Group-2 with Blood Culture Negative**

Parameters	HSS Score 0 (Normal)	HSS Score 1 (Abnormal)	Total
1. TLC	19(73.07%)	7(26.92%)	26
2. Total Neutrophil Count	5(19.23%)	21(80.76%)	26
3. Immature Neutrophil Count	5(19.23%)	21(80.76%)	26
4. IT Neutrophil Ratio	2(7.69%)	24(92.31%)	26
5. IM Neutrophil Ratio	17(65.38%)	9(34.62%)	26
6. Degenerative Changes	16(61.5%)	10(38.5%)	26
7. Platelet Count	23(88.5%)	3(11.5%)	26

**Table 5: HSS Group 3 with Negative Blood Culture**

Parameters	HSS Score 0 (Normal)	HSS Score 1 (Abnormal)	Total
1. TLC	10(91%)	1(9%)	11
2. Total Neutrophil Count	0	11(100%)	11
3. Immature Neutrophil Count	0	11(100%)	11
4. IT Neutrophil Ratio	0	11(100%)	11
5. IM Neutrophil Ratio	0	11(100%)	11
6. Degenerative Changes	1(9%)	10(91%)	11
7. Platelet Count	6(54.54%)	5(45.45%)	11

**Figure 6: Percentage distribution of Microorganisms isolated in cultures.**



**Table 7: Comparison of Sensitivity(%), Specificity(%), Positive Predictive Value(%) and Negative Predictive Value (%) of various hematological parameters with other studies.**

	STUDIES	Sensitivity(%)	Specificity(%)	PPV(%)	NPV(%)
TLC	Present Study (2025)	20	78.4	20	78.4
	Priyanka T et al. (2018)	23.63	71.27	35.83	-
	Amir N et al. (2023)	77.8	72.1	63.1	84.1
TOTAL NEUTROPHIL COUNT	Present Study (2025)	40	10.81	11.11	45.45
	Priyanka T et al. (2018)	52.75	91.04	80	73.94
	Amir N et al. (2023)	44.4	96.7	89.3	74
IMMATURE NEUTROPHIL COUNT	Present Study (2025)	100	13.51	23.8	100
	Priyanka T et al. (2018)	55.49	92.91	84.17	75.45
	Amir N et al. (2023)	66.7	23	34.6	52.9
IMMATURE TO TOTAL NEUTROPHIL RATIO	Present Study (2025)	100	5.4	22.22	100
	Priyanka T et al. (2018)	35.82	72.76	39.17	59.09
	Amir N et al. (2023)	88.9	71.1	65.4	91.3
IMMATURE TO MATURE NEUTROPHIL RATIO	Present Study (2025)	70	46	26	85
	Priyanka T et al. (2018)	25.8	74.1	26.5	60.2
	Amir N et al. (2023)	88.9	88.5	82.5	92.8
DEGENERATIVE CHANGES	Present Study (2025)	60	46	23.07	63
	Priyanka T et al. (2018)	45.6	86.19	69.17	70
	Amir N et al. (2023)				
PLATELET COUNT	Present Study (2025)	60	78.4	42.8	87.9
	Priyanka T et al. (2018)	34.62	78.73	52.5	63.94
	Amir N et al. (2023)	88.9	44.3	49.4	86.7
MICRO ESR	Present Study (2025)	10	100	100	80.4
	Priyanka T et al. (2018)	-	-	-	-
	Amir N et al. (2023)	100	70.5	-	-
C-REACTIVE PROTEIN	Present Study (2025)	60	89.2	60	89.2
	Priyanka T et al. (2018)	-	-	-	-
	Amir N et al. (2023)	100	80.3	-	-



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