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Early Diagnosis of Neonatal Septicemia Through Hematological Parameters at a Tertiary Care Center in India

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ABSTRACT
Bacterial sepsis poses significant health risks to newborns, contributing substantially to both morbidity and mortality rates. The identification of probable sepsis involves clinical and laboratory findings indicative of bacterial infection in the absence of positive culture results. This study aims to investigate and ascertain the predictive utility of hematological parameters for early detection of neonatal sepsis within a tertiary care facility located in India. Conducted prospectively at a tertiary care teaching hospital in India, this research enrolled 145 neonates admitted to the neonatal intensive care unit. Neonates exhibiting clinical suspicion of sepsis or possessing predisposing perinatal factors were included. The study evaluated a hematological scoring system (HSS) alongside patients' clinical profiles and sepsis screening tests. Sensitivity, specificity, and positive predictive value (PPV) of each parameter were determined and analyzed. Among the 61 cases with culture-confirmed sepsis, 53 infants (86.88%) displayed a score of ≥5, while 8 infants (13.11%) scored 3–4. the HSS demonstrated a sensitivity of 85.94% and specificity of 77.62%, with a PPV of 75.16%. Males exhibited a higher susceptibility to sepsis compared to females. Given the absence of any singularly superior hematological parameter in predicting neonatal sepsis, the combination of these parameters, along with C-reactive protein, is advocated. The study concludes that HSS serves as a valuable tool in distinguishing infected neonates from non-infected ones.

INTRODUCTION

Neonatal sepsis manifests as generalized systemic features of infection, with probable sepsis characterized by clinical and laboratory findings consistent with bacterial infection but without a positive culture. It encompasses various systemic infections in neonates, including pneumonia, meningitis, septicemia, arthritis, osteomyelitis, and urinary tract infections. Systemic signs may include lethargy, hypotonia, tachycardia, abdominal distension, fever, chest retractions, grunting, shock, apnea, pallor, jaundice, bradycardia, and increased ventilator requirements. Preterm and low birth weight neonates are at higher risk due to lower immunity against bacterial infection. Neonatal sepsis is categorized based on symptom onset: early-onset occurring at or before 72 hours of life and late-onset typically presenting after 72 hours[1-3].

Although blood culture remains the gold standard for diagnosis, its time-consuming nature necessitates 48–72 hours for results[2]. This study aimed to investigate hematological parameters for early neonatal sepsis diagnosis, employing Rodwell's scoring criteria[4]. The criteria encompass total leukocyte count (TLC), absolute neutrophil count, immature neutrophil count (I), immature-to-total neutrophil ratio, immature-to-mature neutrophil count ratio (I:M), platelet count, and degenerative changes in neutrophils (e.g., toxic granules, cytoplasmic vacuoles). Additionally, C-reactive protein (CRP) evaluation was included. The study sought to assess the utility of the hematological scoring system (HSS) in early neonatal sepsis diagnosis.

MATERIAL AND METHODS

This prospective study was conducted at a tertiary care teaching hospital in India. A cohort of 145 neonates admitted to the departments of pediatrics and neonatology was enrolled. The inclusion criteria comprised neonates displaying signs of sepsis or possessing predisposing factors or a suggestive history of sepsis. Exclusion criteria encompassed neonates born to known immunocompromised mothers, those with congenital anomalies, hemolytic jaundice, inborn errors of metabolism, malaria, or suspected TORCH infections, and those who had received antibiotics prior to blood culture collection should be arranged alphabetically.

Blood samples, totaling 2 mL, were aseptically withdrawn within 24 hours of admission from suspected neonates. One milliliter of the sample was anticoagulated with EDTA for hematological analysis, including total leukocyte count (TLC) and platelet count using automated hematology analyzer. Simultaneously, 1 mL of blood was collected in a red Vacutainer, allowed to clot, centrifuged, and the obtained serum was utilized for C-reactive protein (CRP) estimation. Additionally, peripheral blood smears (PBS) were prepared from the collected samples, stained with Leishman's stain, and examined for immature neutrophils and degenerative changes in neutrophils by the department of pathology. The HSS, as proposed by Rodwell *et al*.[4], was employed, assigning a score of 1 for each of the seven criteria significantly associated with sepsis, with the exception of a score of 2 for an abnormal total polymorphonuclear neutrophils (PMNs) count if no mature PMNs were observed on the peripheral smear (Table 1). This action is undertaken in instances where no mature PMNs are observed on the peripheral smear to account for the diminished immature to mature (I: M) ratio.

Sensitivity, specificity, and positive predictive value (PPV) were calculated for each parameter, and p-values were determined for different parameters. Data were compiled and subjected to statistical analysis using SPSS software.

RESULTS

In our study, 145 neonates were categorized into three groups: sepsis (n = 61), probable infection (n=29), and normal (n = 55), based on clinical examination and laboratory findings. Among them, 82 (56.55%) were preterm babies, while 63 (43.45%) were term babies. Preterm babies were more affected by sepsis compared to term babies. Additionally, there were 88 (60.69%) males and 57 (39.31%) females in the study population. The distribution of cases according to sepsis score is provided in (Table 2).

Table 1: The Hematological scoring system (HSS)

Parameter	Score
TLC ≤5000/µL	1
TLC ≥25,000 at birth	1
TLC ≥30,000 after 12–48 h	
TLC ≥21,000 day 2 onward	
No mature PMN seen	2
Total PMN count Increased/decreased	1
Immature PMN count Increased	1
I:T PMN ratio Increased	1
I:M PMN ratio ≥0.31	1
Degenerative changes in PMN (Toxic granules/cytoplasmic vacuoles)	1
Platelet count ≤150,000	1
Score	**Interpretation**
≤2	Sepsis-very unlikely
3 or 4	Probable sepsis
≥5	Sepsis/infection-very likely
Minimum Score	0
Maximum Score	8
≤2	Sepsis-very unlikely

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 patients according to the sepsis score

No. of cases as per Sepsis score						Interpretation	Total cases
0-2		3-4		>5			
n	%	n	%	n	%		
0	0.00	8	5.52	53	36.55	Sepsis	61
5	3.45	13	8.97	11	7.59	Probable Sepsis	29
39	26.90	11	7.59	5	3.45	Normal	55

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

Investigations	Sensitivity (%)	Specificity (%)	PPV (%)
Degenerative changes in PMN	72	61.8	50
I:M ratio	60	92.5	85
I:T ratio	90	88	86
Immature PMN count	95	88	82.5
Platelet count	64.5	82	70.8
PMN count	91.8	66.2	64.8
Total leukocyte count	62.5	89.2	80.5

Regarding the diagnostic performance, the HSS demonstrated a sensitivity of 85.94% and specificity of 77.62%, with a PPV of 75.16%. and p-value less than 0.0001. The sensitivity of the CRP test was 67.68% with a specificity of 77.15% and a PPV of 67.56%. WBC count had a sensitivity of 62.5% and specificity of 89.2%, with a PPV of 80.5%. These results were statistically significant, and others are shown in (Table 3).

DISCUSSION

Neonatal sepsis stands as a significant contributor to neonatal mortality and morbidity, posing challenges in its early detection. While blood culture remains the gold standard for diagnosis, its limited sensitivity and delayed reporting often result in indiscriminate antibiotic use. HSS, incorporating blood parameters, offer a valuable approach for the timely identification and management of neonatal sepsis[5].

Our investigation revealed an 87.69% accuracy in categorizing cases based on sepsis score distribution, aligning with prior findings by Harendra Kumar and Narasimha, Makkar et al., and Rodwell *et al*.[4,6,7]. The HSS exhibited a sensitivity of 85.94% and specificity of 77.62%, with a positive predictive value (PPV) of 75.16%. Correspondingly, Saleem *et al*.[8] reported a sensitivity of 90%, specificity of 74.5%, PPV of 65.9%, and negative predictive value (NPV) of 93.2% for HSS. Manucha *et al*.[9] noted a sensitivity of 86% and NPV of 96% for a hematological score ≥3. Our study population comprised 60.69% male and 39.31% female participants, consistent with observations from other studies[10,11].

Regarding culture results, 42.06% of cases were culture-positive in our study. This finding echoes similar rates reported by Sugandhi *et al*. (42.5%), Namdeo *et al*. (50%), and Khatua *et al*. (59.8%)[12-15]. Furthermore, alterations in white blood cell (WBC) counts demonstrated a sensitivity of 62.5% and specificity of 89.2%, with a PPV of 80.5%, consistent with previous research. Makkar *et al*.[7] similarly reported a sensitivity of 56.2% and specificity of 91.71% for changes in WBC counts.

Thrombocytopenia emerged as an indicator of poor prognosis in neonatal sepsis, with 30 out of 46 culture-positive cases exhibiting thrombocytopenia in our study. This finding demonstrated a sensitivity of 64.5%, specificity of 82%, and PPV of 70.8%, consistent with prior investigations by various authors[16-18].

In our study, C-reactive protein (CRP) displayed a sensitivity of 67.68%, specificity of 77.15%, and PPV of 67.56%. These values are in line with observations by Mathers and Pohlandt[19] (sensitivity 61%, specificity 76%), Wagle *et al*.[20] (sensitivity 62%, specificity 87%), and Chan and Ho[21] (sensitivity 56%, specificity 72%). Nonetheless, our study faced limitations, including a small sample size and the absence of a case-control design.

CONCLUSION

Diagnosing neonatal septicemia can be challenging due to subtle and varying early signs across different gestational ages. The Hematological Scoring System (HSS) offers a simple, rapid, and cost-effective screening tool for early detection of neonatal sepsis. It is applicable to all infants, even those who have received prior antibiotic therapy, and simplifies the interpretation of hematologic profiles.

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