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Original Research Article

EVALUATION OF HAEMATOLOGICAL SCORING SYSTEM IN EARLY DIAGNOSIS OF NEONATAL SEPSIS

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Abstract

Background: Neonatal sepsis is a life-threatening condition that is treatable with early diagnosis. Blood culture remains the gold standard for diagnosing septicaemia; however, it is time-consuming. This study aimed to evaluate the diagnostic utility of Rodwell's Haematological Scoring System (HSS) in neonatal septicaemia and to correlate its parameters with blood culture and C-reactive protein (CRP) levels. **Materials and Methods:** This cross-sectional study included 100 neonates with clinically suspected sepsis. Blood samples were collected for peripheral smear examination, blood culture, and CRP testing. Haematological parameters, including total leukocyte count, total neutrophil count, immature neutrophil count, immature-to-total neutrophil ratio (I:T), immature-to-mature neutrophil ratio (I:M), toxic granulations, degenerative neutrophils, and platelet count, were assessed according to Rodwell's HSS. **Result:** Among the 100 neonates, 59% were male, and the mean birth weight was 2300±632 g, with 54% classified as low birth weight. Caesarean deliveries accounted for 58% of the cases, and prematurity (54%) was the most common maternal risk factor. Poor feeding (59%) was the most common neonatal symptom. CRP was positive in 26% of neonates, and blood culture-confirmed sepsis in 30%. Among the 30 culture-positive cases, 28 (93.3%) had an HSS score of ≥4. The HSS demonstrated 93.3% sensitivity, 62.9% specificity, 51.9% positive predictive value (PPV), and 95.7% negative predictive value (NPV) for diagnosing neonatal sepsis. **Conclusion:** Rodwell's HSS, with a cutoff score of 4, serves as a useful screening tool for neonatal sepsis, aiding in early diagnosis and judicious antibiotic use. This can help prevent unnecessary antibiotic exposure and minimise the risk of antimicrobial resistance.

INTRODUCTION

Neonatal sepsis is defined as a disease with positive blood culture results during the first month of life. It is more common in developing countries than in developed countries.[1] The incidence of neonatal sepsis has been reported to be 30/1000 live births, according to the National Neonatal Perinatal Database.[2] Neonatal sepsis is associated with a mortality rate ranging from 13 to 60%, despite improved antibiotic therapy and care.[3] Neonatal sepsis is life-threatening but treatable with early diagnosis. However, its nonspecific early signs make timely diagnosis challenging. Antibiotic therapy is usually initiated based on clinical suspicion which may result in overtreatment, ultimately leading to the emergence of multidrug-resistant organisms. In addition, the high cost of antibiotics overburdens already underprivileged parents.[4]

Blood culture is still considered the 'gold standard' for diagnosing septicaemia; however, its accuracy has been questioned because of spurious positive results due to contamination and negative blood cultures in fatal generalised bacterial infections. The yield of a positive blood culture ranges from 8-73% as shown in various studies.[4] Moreover, the technique of blood culture is time-consuming and demands a well-equipped laboratory which is not available in most community hospitals. A disadvantage of culture-based diagnosis is the assay time of up to 48-72 hours, yields a positive result in 10-60% of causes.[5]

When blood and other sterile site cultures are negative, but the infant manifests signs consistent with infection, they may be considered to have "clinical" sepsis.[6] Therefore, there is a need for a test that is inexpensive, easily performed, and provides quick availability of reports. Various studies have

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demonstrated that haematological parameters serve as simple, rapid, and cost-effective tools for the early diagnosis of neonatal sepsis.[5] Their diagnostic accuracy improves when used in combination, enhancing both sensitivity and specificity. Early identification of sepsis using these parameters facilitates the timely initiation of appropriate antibiotic therapy, thereby improving neonatal outcomes. An ideal diagnostic test should be rapid, cost-effective, and possess high sensitivity and specificity, as well as strong predictive values. Considering these criteria, the Hematological Scoring System (HSS) by Rodwell is a reliable tool, as it integrates multiple haematological parameters and has shown a significant association with neonatal sepsis.[7]

Aim

This study aimed to categorise the haematological findings according to Rodwell's Haematologic Scoring System, including the changes seen in the peripheral smears of neonates clinically suspected of having sepsis, and correlate the haematologic parameters with blood culture and C-reactive protein (CRP).

MATERIALS AND METHODS

This cross-sectional study was conducted on 100 neonates at the Department of Pathology, Tirunelveli Medical College Hospital from March 2017 to April 2018. The Institutional Ethics Committee approved the study before its initiation, and informed consent was obtained from all patients.

Inclusion Criteria

Neonates with features of sepsis, including fever, lethargy, poor feeding, need for supplemental oxygen, low APGAR score, and neonates with a history of maternal infections, such as maternal intrapartum fever >38ºC, premature rupture of membrane <37 weeks, prolonged rupture of membrane > 12 h, and maternal UTI, were included.

Exclusion Criteria

Neonates with major congenital anomalies, inborn errors of metabolism, administration of antibiotics before admission, respiratory distress syndrome, and mothers with pregnancy-induced hypertension and asphyxia were excluded.

Methods

Parents provided birth details and presented complaints about the child. A thorough clinical examination was performed, and the findings were documented on a standardised proforma. Blood samples from neonates suspected of sepsis were collected aseptically. A complete blood count was performed using SYSMEX, a three-part analyser. Standardisation, calibration of the instrument, and processing of samples were performed according to the manufacturer's instructions. Leishman-stained peripheral smears were examined by counting 200 WBCs for nucleated red blood cells, differential counts, absolute neutrophil count, immature neutrophils, toxic granulations in neutrophils, and degenerative neutrophils. CRP and blood cultures were also performed.

Blood samples (3 ml) were obtained via peripheral venipuncture. Two millilitres were collected in an EDTA tube for routine haematological investigations, while the remaining 1 ml was transferred to a conventional blood culture tube for culture and sensitivity studies. After sterile precautions, a peripheral smear was made using the heel-prick method, and haematological scoring was performed simultaneously.

Differential counts were performed on Leishman-stained blood smears by counting 200 cells per smear. A pathologist blinded to the neonate's infection status reviewed the peripheral smears. Degenerative morphological changes in neutrophils, such as Dohle bodies, vacuolation, and toxic granules, were observed. Haematological findings were analysed using the HSS.

The total leucocyte count, total neutrophil count, immature neutrophil count, immature to total neutrophil ratio, immature to mature neutrophil ratio, toxic granulations and degenerative neutrophils in the peripheral smear, and platelet count were assessed. The HSS assigns a score of one for each of the seven parameters found to be significant for sepsis, with one exception. An abnormal total PMN count was assigned a score of two rather than one if no mature PMNs were observed on the blood smear. Clinical details, as well as CRP and blood culture results, were compared with the haematological score.

Statistical Analysis

Data are presented as means, standard deviations, frequencies, and percentages. Continuous variables were compared using an independent-sample t-test and repeated-measure ANOVA. Categorical variables were compared using Pearson's chi-square tests. ROC analysis was performed to determine the cutoff values. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated to assess test validity. Significance was defined as P values < 0.05 using a two-tailed test. Data analysis was performed using IBM SPSS version 21.0.

RESULTS

Among these 100 neonates, 59% were male and 41% were female. The commonest age group was 1 to 5 days with 90% of neonates, followed by 6 to 10 days with 7% and more than 10 days comprised of 3% of neonates.54% of the neonates had birth weight between 1500-2499 grams and among 37% of the neonates had birth weight more than2500 grams. The mean birth weight was 2300±632 g. Of the mothers, 42% had normal deliveries, of which one was forceps and one was vacuum-delivered. A total of 58% of mothers underwent caesarean sections [Table 1].

Prematurity was the most common maternal risk factor (54%), followed by PROM (24%) and other complications (19%). Peripheral smear abnormalities

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were predominant, with neutrophilia observed in 92% of the neonates, indicating an inflammatory response. Degenerative changes were present in 37% of cases, while thrombocytopenia and leukocytosis were noted in 19% and 14% of cases, respectively. Additionally, nucleated red blood cells (RBCs) >5/100 white blood cells (WBCs) were found in 12% of neonates, and leucopenia was found in 3% of neonates, suggesting haematological disturbances.

Regarding blood culture results, 30% of neonates had a positive blood culture, confirming the presence of infection, whereas 70% had negative results, indicating no bacterial growth in the blood samples [Table 2].

Table 1: Demographic characteristics.

		N (%)
Gender	Male	59 (59%)
	Female	41 (41%)
Age Group (in days)	1 to 5	90 (90%)
	6 to 10	7 (7%)
	>10	3 (3%)
Birth Weight (grams)	1500-2499	54 (54%)
	>2500	37 (37%)
Mode of Delivery	Normal delivery	42 (42%)
	Caesarian section	58 (58%)

Table 2: Maternal risk factors, peripheral smear abnormalities, and blood culture findings in neonates.

		N (%)
Maternal risk factors	Prematurity	54 (54%)
	Premature rupture of membranes(prom)	24 (24%)
	Other complications	19 (19%)
Peripheral smear abnormalities	Neutrophilia	92 (92%)
	Degenerative changes	37 (37%)
	Thrombocytopenia	19 (19%)
	Leucocytosis	14 (14%)
	Nucleated RBCS (>5/100wbcs)	12 (12%)
	Leukopenia	3 (3%)
Blood culture results	Positive	30 (30%)
	Negative	70 (70%)

Of the 30 neonates with sepsis, 28 had an HSS score of ≥ 4, and 2 had a score of less than 4, with a significant difference (p<0.001). Four of the 30 neonates had an HSS score of ≥ 5, and 26 had a score of < 5 (p=0.002) [Table 3].

Table 3: Comparison of HSS score between culture reports.

Haematological scoring system	Culture		P value
	Positive (%)	Negative (%)	
≥ 4	28 (28%)	26 (26%)	<0.001
<4	2 (2%)	44 (44%)	
≥ 5	4 (4%)	0	0.002
<5	26 (26%)	70 (70%)	

The sensitivity of the HSS with a cutoff score of 4 in predicting sepsis was 93.3%, and the specificity was 62.9%. The sensitivity of the HSS with a cutoff score of 5 in predicting sepsis was 13.3%, and the specificity was 100% [Table 4].

Table 4: Diagnostic accuracy of HSS

Score	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
≥4	93.3	62.9	51.9	95.7
≥5	13.3	100	100	72.9

The total count was higher in blood culture-positive neonates (0.20 ± 0.41) than in negative cases (0.16 ± 0.37), but this difference was insignificant (p=0.605). The total polymorphonuclear cells (PMN) for positive (0.93 ± 0.25) and negative cases (0.91 ± 0.28) showed no significant differences (p=0.751).

The immature PMN count was 0.97 ± 0.18 in culture-positive cases, which was higher than 0.89 ± 0.32 in negative cases, but this difference was not significant (p=0.199). However, the immature-to-total PMN (I:T PMN) ratio was significantly higher in positive cases (1.00 ± 0.00) than in negative cases (0.61 ± 0.49) with a significant difference (p<0.001). The immature-to-mature PMN (I:M PMN) ratio was significantly higher in culture-positive cases (0.53 ± 0.51) than in culture-negative cases (0.20 ± 0.40) (p=0.001). Degenerative changes were more prominent in blood culture-positive neonates (0.53 ± 0.51) than in negative cases (0.30 ± 0.46), with significant differences (p=0.027). Platelet count was also higher in culture-positive neonates (0.37 ± 0.49) than in

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negative cases (0.10 ± 0.30), with a significant difference (p=0.001).

The total haematological score was significantly higher in blood culture-positive neonates (4.53 ± 0.82) compared to negative cases (3.17 ± 1.04) with a significant difference (p<0.001), showing a strong association between haematological abnormalities and positive blood cultures in neonatal sepsis [Table 5].

Table 5: Comparison of haematological parameters between blood culture positive and negative neonates

		N (%)	Mean ± S.D.	P value
Total count	Positive	30(30%)	0.20±0.41	0.605
	Negative	70(70%)	0.16±0.37	
Total PMN	Positive	30(30%)	0.93±0.25	0.751
	Negative	70(70%)	0.91±0.28	
Immature PMN	Positive	30(30%)	0.97±0.18	0.199
	Negative	70(70%)	0.89±0.32	
I:T PMN	Positive	30(30%)	1.00±0.00	<0.001
	Negative	69(69%)	0.61±0.49	
I:M PMN	Positive	30(30%)	0.53±0.51	0.001
	Negative	70(70%)	0.20±0.40	
Degenerative changes	Positive	30(30%)	0.53±0.51	0.027
	Negative	70(70%)	0.30±0.46	
Platelet count	Positive	30(30%)	0.37±0.49	0.001
	Negative	70(70%)	0.10±0.30	
Total score	Positive	30(30%)	4.53±0.82	<0001
	Negative	70(70%)	3.17±1.04	

DISCUSSION

The study group of suspected sepsis cases showed a male predominance of 59%, and females constituted 41%. This is consistent with the study by Khair et al. (males 58% and females 42%), Shukla et al. (males 58% and females 42%).[8,9] The mean birth weight of the neonates in our study was 2300±632 g. Most neonates (54%) had low birth weights, and very low birth weight constituted 9%. Similar results were seen in the study of Anwer et al., where sixty-six per cent of neonates (33 of 50) were <2.5 kg.[10] In another study by Lakhey et al. reported birth weight less than 2500 grams (low birth weight) was present in 51(70.8%) culture-positive cases.[11]

In our study, 58% of the neonates were delivered via caesarean section, while 42% were born through normal delivery, including one forceps and one vacuum-assisted birth. The most common maternal risk factors were premature rupture of membranes (<37 weeks) in 54% and prolonged rupture (>18 h) in 24%. Other factors, such as maternal fever, foul-smelling vaginal discharge, and UTIs, accounted for 19 of the cases. This aligns with studies by Anwer et al., identifying prematurity and prolonged rupture of membranes as major risk factors.[10] Liu et al. reported that neonates of mothers with infection-related risks had a 2.3 times higher infection.[12]

In our study, 54% of the neonates were preterm, and 46% were term, which aligns with the study by Makkar et al., which reported 57% and 43%, respectively. Poor feeding (59%) was the most common neonatal complaint, followed by respiratory distress (32%), reduced movements (23%), fever (5%), jaundice (1%), and seizures (1%), with overlapping symptoms.[13] Peripheral blood film examination showed neutrophilia in 92% of cases, degenerative changes in 37%, thrombocytopenia in 19%, leucocytosis in 14%, nucleated RBCs in 12%, and leukopenia in 3%. Tripathi et al. suggested increased RBC count at birth as a potential marker for early-onset neonatal sepsis.[14]

In our study, CRP was positive in 26% of neonates, lower than the 66% reported by Saleem M.[15] CRP's use in neonatal sepsis is limited by its nonspecific rise shortly after birth. Blood cultures confirmed sepsis in 30% of the cases, with gram-negative organisms being more common. Klebsiella pneumoniae (11/30) was the most prevalent, followed by Staphylococcus aureus (9/30) and coagulase-negative staphylococci (5/30). A study by Mondal et al. similarly found Gram-negative organisms (68.4%) were more frequent than Gram-positive (31.6%), with Klebsiella pneumoniae (52%) as the leading pathogen, followed by Staphylococcus aureus (26%).[16]

Rodwell et al. evaluated haematologic parameters in 287 neonates with perinatal risk factors or clinical suspicion of sepsis and formulated a scoring system that assigned a score of 1 for each of the seven parameters. Their study revealed that a higher score was associated with a higher likelihood of sepsis. The present study results also revealed that a score of more than five when compared to a score of more than four has a higher likelihood of sepsis and is well correlated with the study.[7]

Our study evaluated the HSS for early neonatal sepsis diagnosis using different cutoffs. Among the 30 neonates with sepsis, 4 had an HSS score ≥5 and 26 had a score <5 (p=0.002), with a sensitivity of 13.3%, specificity of 100%, PPV of 100%, and NPV of 72.9%. With a cutoff of ≥4, 28 neonates had sepsis, and 2 had <4 (p=0.001), yielding a sensitivity of 93.3%, specificity of 62.9%, PPV of 51.9%, and NPV of 95.7%. A study by Khair et al. similarly found most septic neonates had scores ≥4, with 100% sensitivity, 60% specificity, and improved sensitivity for scores >4 (p=0.001).[8]

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Our study found that all seven haematological parameters had higher mean values in culture-positive cases. Among them, the I:T ratio ($p<0.001$) and I:M ratio ($p=0.001$) were the most significant, which is consistent with the studies by Rodwell et al. and Khair et al., where the I:T ratio >0.2 had a sensitivity of 96% and 100%, respectively.[7,8] Narasimha et al. also identified the I:T and I:M ratios as the most sensitive markers for neonatal sepsis. Thrombocytopenia (19%) was the next significant parameter ($p=0.001$).[17] This aligns with Khair et al., who found thrombocytopenia in 35% of cases with 60% sensitivity and 82% specificity.[8] Dulay et al. and Philip et al. reported that no single haematological parameter was superior, supporting our finding that HSS is the most reliable screening tool.[18,19]

In our study, an HSS score ≥4 showed 93.3% sensitivity and 62.9% specificity, while a score ≥5 had lower sensitivity (13.3%) but 100% specificity. This aligns with Ghosh et al., who found HSS to be a simple, quick, and cost-effective tool for guiding antibiotic therapy in neonatal sepsis.[20]

CONCLUSION

Our study concluded that the haematologic scoring system is useful for distinguishing infected from non-infected infants. The haematologic scoring system is a simple, quick, cost-effective, and readily available tool with high sensitivity and specificity for the early diagnosis of neonatal sepsis. Thus, the HSS serves as an effective screening tool for the diagnosis of early neonatal sepsis. The HSS with a cut-off score of 4 provides a guideline to clinicians to make decisions regarding the judicious use of antibiotic therapy which will be lifesaving, provide an early cure, reduce mortality, shorten hospital stay, and minimise the risk of emergence of resistant organisms due to improper use of antibiotics. Thus, unnecessary exposure of neonates to antibiotic therapy can be avoided.

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