

EVALUATION OF HEMATOLOGICAL SCORING SYSTEM AND PLATELET INDICES IN NEONATAL SEPSIS

Pathology

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ABSTRACT

Neonates are easily prone for bacterial infection. Diagnosis of septicemia is difficult as the early signs of sepsis may be subtle and different at different gestational ages. Positive blood culture is considered the gold standard for confirmation of neonatal sepsis. But it does not provide timely diagnosis. The present study was done to evaluate the performance of hematological parameters in the form of HEMATOLOGICAL SCORING SYSTEM along with evaluation of PLATELET INDICES as a diagnostic and prognostic indicator of neonatal sepsis in correlation with clinical and serological profile in patients. The Analysis in our study found that all the seven hematological parameters showed higher mean value in the blood culture positive cases with I:T ratio (sensitivity=90%) and Immature PMN (sensitivity=85%) count both were found to be very sensitive indicators of neonatal sepsis and I:M ratio being the most specific (sp: 90%) indicator in early diagnosis of neonatal sepsis. The sensitivity, specificity, PPV and NPV of hematological scoring system with a cut-off score of 5 in predicting sepsis was 80.00%, 100%, 100% and 88.2% respectively. The platelet indices were also seen to have a role in the diagnosis of neonatal sepsis as increased MPV showed higher sensitivity. This study also shows that many parameters such as I:T ratio, I:M ratio, Total TLC, immature PMN counts were significantly associated with poor prognosis. Decreased plateletcrit and increased MPV both were associated with adverse outcome, plateletcrit being highly significant parameter in predicting mortality.

KEYWORDS

Hematological Scoring System, Platelet Indices, Neonatal sepsis, Infections, Blood Culture, PMN

INTRODUCTION

Neonatal Sepsis, neonatal septicaemia and sepsis neonatorum are terms that are used to describe the systemic response to infection in a newborn infant. As per the National Neonatal Perinatal Database 2002-2003, the incidence of neonatal sepsis is 30 per 1000 live births. Neonates are fragile and can deteriorate rapidly, so early diagnosis and prompt management is required. But the early clinical features of sepsis are often non-specific that makes it difficult for the physician to come to a definite diagnosis.³

Blood culture is considered 'GOLD STANDARD' for diagnosis of neonatal sepsis. However, its accuracy has been questioned because of spurious positive results. Also, increased cost and delayed reporting is a limiting factor for early diagnosis. Hence, we need to find parameters which will increase the sensitivity and specificity in early diagnosis of neonatal sepsis.

Various cheap but reliable laboratory tests have been evaluated for the diagnosis of systemic infection in neonates. There also have been studies showing significant changes in platelet indices (MPV, PDW, PCT) in patients with neonatal sepsis.²⁻⁷ The present study is to evaluate the usefulness of the seven hematological parameters of Rodwell HSS⁸ and platelet indices in early diagnosis of neonatal sepsis.

Hematological Scoring System*

Criteria	Abnormality	Score
Total WBC count	$\leq 5,000/\mu\text{l}$	1
	$\geq 25,000$ at birth	1

	$\geq 30,000$ —12–24 h	
	$\geq 21,000$ —Day 2 Onwards	
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	$\leq 150,000/\mu\text{l}$	1

The normal values are:

Total PMN count: 1800–5400

Immature: Total PMN ratio: 0.120

Immature: Mature PMN ratio: ≥ 0.3

Interpretation of hematological scoring system will be as

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

Platelet Indices

The platelet indices including platelet count, MPV (mean platelet volume); PDW (platelet distribution width) were performed as a part of the automatic complete blood count. The data will be analyzed using the mean and median values as applicable.

Normal Values of platelet Indices

Platelet Count (Analyzer calculated platelet number): 1.5–4.5 lac/cmm

Mean Platelet Volume (Analyzer calculated measure of thrombocyte volume): 7.0- 11.0 fL

Platelet distribution width (Indicator of volume variability in platelet size) : 9.0-17.0 fL

AIM AND OBJECTIVE

The Objective of the present study is to assess the diagnostic and prognostic value of seven parameters of Hematological Scoring System and Platelet Indices.

MATERIALS AND METHODS

The present study was a prospective analysis of the hematological profiles of 100 neonates admitted in Guru Nanak Dev Hospital, Government. Medical College, Amritsar. Infants from 0-28 days with clinical suspicion of sepsis were enrolled in the study. The study included two groups:
Group 1 Infants with sepsis with positive blood cultures.
Group 2 Infants with probable infection with strong clinical history but negative blood cultures.

Under complete aseptic conditions, blood samples were obtained each sample was divided into 3 parts; first part in vacutainer tube for serological and biochemical tests, second part in EDTA tube, and the third part in sterile blood culture bottle. The EDTA blood sample were run on ERBA automated cell counter and Total leucocyte count, platelet count and platelet indices were obtained and corrected for nucleated red blood cells. Peripheral blood smears prepared within 1–2 h of venipuncture and stained with Leishman stain were examined under oil immersion light microscopy at a final magnification of ×1000 and Differential counts was performed after counting 200 cells. Sepsis work up included blood culture and routine blood counts with peripheral blood smear examinations. Since blood culture is considered as a gold standard test for diagnosis of sepsis, samples with positive blood cultures were considered as confirmed sepsis, hence blood culture was used as a yardstick for comparing various parameters of hematological scoring system in our study.

OBSERVATIONS

Table 1 Diagnostic Utility Of Various Hss Parameters In Neonatal Sepsis

Parameter	Sensitivity	Specificity	PPV	NPV	p-value
TLC	65.0%	71.6%	60.47%	75.44%	0.002
Total PMN Count	82.5%	41.67%	48.53%	78.12%	0.001
Immature PMN Count	85.00%	41.67	49.28%	80.67%	0.40
I:T ratio	90.00%	71.67%	67.92%	91.49%	0.001
I:M ratio	60.00%	90.00%	80.00%	77.14%	0.001
Degenerative Changes in neutrophils	85.00%	51.67%	53.97%	83.78%	0.001
Platelet Count	55.00%	75.00%	59.46%	71.43%	0.025
PLATELET INDICES					
MPV	80.00%	40.00%	47.06%	75.00%	0.001
PDW	72.5%	36.67%	43.28%	36.67%	0.004
PCT	47.50%	88.33%	73.08%	71.62%	0.001

Table 2 Hss Cut Off As A Predictor Of Neonatal Sepsis

HSS cut off	Sensitivity	Specificity	PPV	NPV	p-Value
1	100%	8.33%	42.11	100%	0.061
2	100%	31.67	49.38%	100%	0.001
3	100%	66.67%	66.67%	100%	0.001
4	95.00%	88.33%	84.44%	96.36%	0.001
5	80.00%	100%	100%	88.24%	0.001

Table 3 Correlation Of Hss Parameters, Hematological Score > 5 And Platelet Indices With Outcome

HSS Parameters	Score		OUTCOME		Chi-Square
			CURED	DEAD	
TLC	0	N and (%age)	49 (66.21%)	7 (26.92%)	12.056**
	1.0	N and (%age)	25 (33.78%)	19 (73.07%)	

PMN	0	N and (%age)	27 (36.48%)	5 (19.23%)	2.633
	1.0	N and (%age)	47 (63.51%)	21 (80.76%)	
IMMATU RE PMN	0	N and (%age)	36 (48.64%)	5 (19.23%)	6.883**
	1.0	N and (%age)	38 (51.35%)	21 (80.76%)	
I:T Ratio	0	N and (%age)	42 (56.75%)	5 (19.23%)	10.877**
	1.0	N and (%age)	32 (43.24%)	21 (80.76%)	
I:M Ratio	0	N and (%age)	58 (78.37%)	12 (46.15%)	9.514**
	1.0	N and (%age)	16 (21.62%)	14 (53.84%)	
Degenerative Changes	0	N and (%age)	36 (48.64%)	4 (15.38%)	8.870**
	1.0	N and (%age)	38 (51.35%)	22 (84.61%)	
Platelet Count	0	N and (%age)	57 (77.02%)	3 (11.53%)	34.381**
	1.0	N and (%age)	17 (22.97%)	23 (88.46%)	
HSS	>5	N and (%age)	12 (16.21%)	20 (76.92%)	32.585**
	<5	N and (%age)	62 (83.78%)	6 (23.07%)	
Platelet Indices			OUTCOME		Chi-Square
			CURED	DEAD	
MPV	AB	N and (%age)	44 (59.45%)	22 (84.61%)	5.426*
	N	N and (%age)	30 (40.54%)	4 (15.38%)	
PDW	AB	N and (%age)	48 (64.86%)	18 (69.23%)	.163
	N	N and (%age)	26 (35.13%)	8 (30.76%)	
PCT	D	N and (%age)	5 (6.75%)	16 (61.53%)	35.249**
	I	N and (%age)	5 (6.75%)	0 (0.0%)	
	N	N and (%age)	64 (86.46%)	10 (38.46%)	

**Significant P-value at .01
*Significant P-value at .05

Table shows correlation of various HSS parameters and platelet indices with outcome. It was observed that HSS parameters of TLC, Immature PMN count, I:T ratio, I:M ratio, degenerative changes ad platelet count were showing association with mortality with a significant (p-value 0.01). while total PMN count did not have any association with mortality.

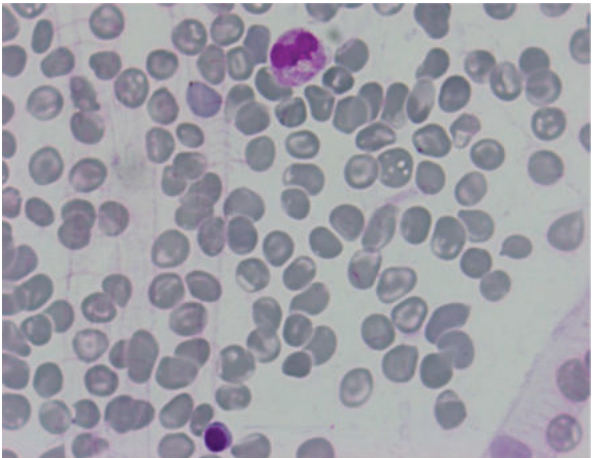


Figure 1: Microphotograph of Peripheral smear showing Thrombocytopenia with degenerative changes seen in neutrophil alongwith nRBC (Leishman stain 100X)

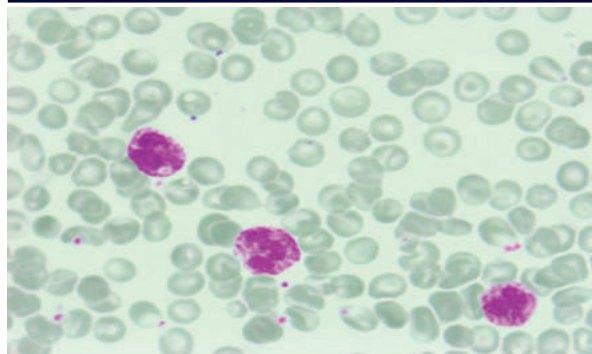


Figure 2: Microphotograph of Peripheral smear showing mature Neutrophils with Toxic granulation (Leishman stain 100X)

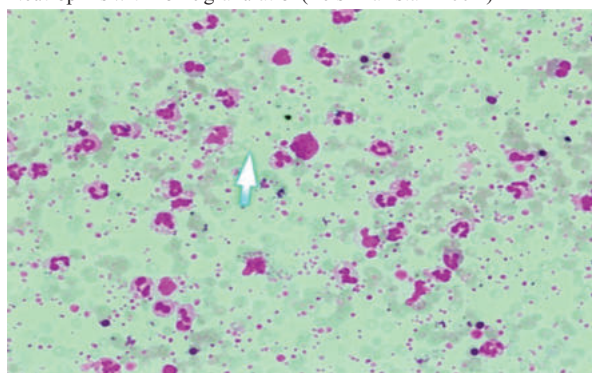


Figure 3: Microphotograph of Peripheral smear showing Leucocytosis (Leishman stain 40X)

RESULT

In the present study, sensitivity, specificity, PPV and NPV of seven parameters of Rodwel HSS and platelet indices were evaluated as a marker for the diagnosis of neonatal sepsis. Also these tests were evaluated for their prognostic value as well.

It was analysed that out of 100 clinically suspected neonates Blood culture positive sepsis was seen in 40% of cases only. Looking into the individual parameters of HSS, all the seven hematological parameters showed higher mean value in the culture positive cases. Raised I:T neutrophil ratio had a significant p value ($p < 0.001$), raised I:M neutrophil ratio had a significant p value ($p = 0.001$), degenerative changes had a significant p value ($p = 0.001$), decreased platelet count had a significant p value ($p = 0.02$) and total PMN count ($p = 0.001$) and total WBC ($p = 0.002$) had a significant p value. However, immature PMN count did not show significant p value.

32 out of 40 culture positive cases had ≥ 5 HSS score and showed sensitivity of 80%, specificity of 100%, positive predictive value of 100% and negative predictive value of 88.24%.

Various HSS parameters such as decreased platelet count, increased TLC, immature PMN count, I:T ratio, I:M ratio and presence of degenerative changes, can be used as a prognostic marker in neonatal sepsis as all these were associated with increased mortality. Also, total Hematological score of >5 was associated with poor prognosis.

Platelet indices also have a role in diagnosis of neonatal sepsis. MPV having sensitivity of 80% and specificity of 40%, PDW having sensitivity of 72.5% and specificity of 36.67% and PCT having sensitivity and specificity of 47.50% and 88.33% respectively. Hence platelet indices can also be used as an additional diagnostic tool especially in thrombocytopenic patients to evaluate neonatal sepsis.

DISCUSSION

Sepsis is one of the most common causes of neonatal mortality and is probably responsible for 30-50% of total neonatal deaths each year in the developing countries.^{9,10} The laboratory diagnosis of neonatal sepsis requires a microbiologic-clinical correlation.

In the present study, we included all the existing HSS parameters like total leucocyte count, total PMN count, immature PMN count, I/T

ratio, I/M ratio, degenerative changes in PMNs and platelet count along with platelet indices.

Elevated I:T ratio was found to be the most reliable indicator of sepsis in our study ($s = 90\%$) followed by immature neutrophil count ($s = 85\%$). This was similar to study done by Ghosh et al.¹¹ in which they concluded that an abnormal immature to total neutrophil (I:T) ratio followed by an abnormal immature to mature neutrophil (I:M) ratio were the most sensitive indicators in identifying infants with sepsis.

However, Narasimha et al found total PMN count to be most sensitive indicator with a sensitivity of 89.47% and specificity of 8.33%, followed by immature PMN count, I:M ratio and I:T ratio with a sensitivity of 78.94%, 73.68% and 63.15% respectively.⁸

In our study, I:M ratio was found to be a highly specific marker for neonatal sepsis with a specificity of 90.00%. This was similar to the study conducted by Makkar M where they found I:M ratio to be the highest specific parameter with a specificity of 97.2%.¹²

Degenerative changes in neutrophils, also found to be 85% sensitive parameter. A similar result was seen in the study of Cheng-hurd Liu et al where it was found that presence of degenerative changes in neutrophils in a patient of neonatal sepsis had a sensitivity of 81%.¹³

In our study, Thrombocytopenia was found to be 55% sensitive and 75% specific. This was similar to the study of Narasimha et al where they found platelet counts to be a more specific test with a sensitivity of 47.36% and specificity of 75%.⁵

In present study different cut off values of HSS were used to evaluate its importance in early diagnosis of neonatal sepsis. The sensitivity, specificity, PPV and NPV of hematological scoring system with cut-off score of 5 in predicting sepsis was 80.00%, 100%, 100% and 88.24% respectively. Mohisra S. Elsayed and others in their study concluded, majority of neonates with sepsis had score ≥ 5 and sensitivity = 80% and specificity = 90%. Therefore, score of 5 is more specific and increases the likelihood of sepsis.¹⁴

It was also seen out that higher the score, more are the chances of sepsis and vice versa. In addition to these parameters we studied platelet indices as an additional diagnostic tool in neonatal sepsis. MPV in our data was increased in 68% of cases. Mittal et al. found, in their study, that MPV was increased in 70.7% of neonatal sepsis.¹⁵ Choudhary et al. also found a 70.9% increase in MPV value in sepsis cases.¹⁶

However, among culture positive neonates 32 out of 40 neonates had increased MPV with a mean of 11.95 ± 1.711 . The sensitivity and specificity of MPV in diagnosis of sepsis came out to be 80% and 40% respectively. This was in par with the study conducted by Majumdar A et al where they found that MPV was increased in cases of neonatal sepsis with a sensitivity and specificity of 84.9% and 33.7% respectively.¹⁷

Similarly, increased PDW showed a sensitivity and specificity of 72.5% and 36.67% respectively in this study. Guclu et al. in his study showed that MPV and PDW were significantly different between sepsis patients and control group.¹⁸

Plateletcrit (PCT) showed a sensitivity and specificity of 47.50% and 88.33% respectively. It was observed that plateletcrit was low in 18 out of 40 culture positive cases, with 1 culture positive case showed increased plateletcrit level. Contrary to this, Chandar V and others, in their study found that PCT in culture proven cases had sensitivity of 17% and specificity of 6.25%.¹⁹ Of the several platelet indices PCT is studied less often in neonatal sepsis.

This study also show that few hematological parameters such as I:T ratio, I:M ratio, Total TLC, immature PMN counts were significantly associated with poor prognosis, while total PMN did not show any association with outcome.

It was seen that out of 26 neonates who died, 23 had thrombocytopenia, 6 out of which had mild thrombocytopenia while and 17 had moderate to severe thrombocytopenia. This correlated well with other studies done by Philip et al., Rodwell et al., Speer et al., and Basu et al.^{2,10,20,21} Among platelet indices it was found Decreased plateletcrit and increased MPV both were associated with adverse outcome,

plateletcrit being highly significant parameter in predicting mortality. However, PDW did not show any association with prognosis in our study. Also, Sayez SZ and others, concluded in their study that PCT was significantly lower ($p < 0.001$) and MPV was significantly higher in non-survivor than survivors ($p = 0.004$).²²

Hence, HSS and platelet indices have both diagnostic as well as prognostic role in neonatal sepsis.

CONCLUSION

The hematologic scoring system is a simple, quick, cost effective, reliable and readily available test with high sensitivity and specificity in the early diagnosis of neonatal sepsis. So it can be very well used as a screening test for early diagnosis of neonatal sepsis. I:T ratio, I:M ratio, degenerative changes in neutrophils, immature PMN count, TLC and total PMN count can be viewed as regular parameters that can predict the neonatal sepsis.

In addition, we found that Platelet indices is also an additional, simple and quick test which can be used in conjunction with other existing tests for early diagnosis of neonatal sepsis.

Further, these indices and various other hematological parameters are a good prognostic marker for sick neonates presenting with sepsis. Hence monitoring the platelet counts, platelet indices and various parameters of HSS can also guide the clinicians to start for an aggressive treatment and readiness for prompt interventions if required

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