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ASSESMENT OF HAEMATOLOGICAL SCORING SYSTEM IN EARLY DIAGNOSIS OF NEONATAL SEPSIS IN TERM AND PRE-TERM NEONATES

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ABSTRACT

Title: Assessment of haematological scoring system and its importance in early diagnosis of neonatal sepsis in term and pre-term neonates. **Background:** Systemic infection in the newborn is the commonest cause of neonatal mortality in developing countries. The objectives of our study was to evaluate the utility of haematological scoring system in early diagnosis of neonatal sepsis in pre-term and term neonates and to correlate these haematological parameters with blood culture results. **Material and methods:** This study wasconducted on all neonates during 1st week of life presenting in Neonatal ICU, MMIMSR, Mullana, Ambala. A total of 85 neonates with clinically suspicious sepsis were included and were simultaneously confirmed by blood culture. **Results:** The study showed 12 (14.1%) neonates with sepsis likely, 27 (31.8%) with sepsis suspected and 46 (54.1%) neonates with sepsis unlikely based on HSS. Overall sensitivity, specificity, PPV and NPV for HSS was 93.55%, 81.48%, 74.36% and 95.65% respectively. Highest sensitivity was observed for the parameter total PMN count i.e. 96.77% followed by degenerative changes with a sensitivity of 90.32%.

KEYWORDS: Haematological scoring system, neonatal sepsis.

INTRODUCTION

Systemic infection is the chief cause of neonatal mortality in the newborns especially developing countries.[1] On the other hand, it is seen that, the survivors of neonatal sepsis are susceptible to short- and long-term neurodevelopment associated morbidity.[2,3] Neonatal septicaemia is categorized by the presence of various clinical signs and symptoms accompanied by sepsis in the 1st month of life.[4] Above all the premature newborns are more susceptible to serious infections. Initiating the antibiotic therapy at birth has been a frequent practice. The decision to discontinuing the antibiotic therapy in these already weak neonates is often tricky and not easy. Thus, fatal septicaemia may occur with little warning.[5]

The present study is undertaken to assess the role of hematologic scoring system (HSS) in aiding an early diagnosis of neonatal septicaemia which can be cost effective, chiefly in developing countries like India. The current hematologic scoring system was first proposed by Rodwell, et al. in 1988.[6] These haematological scores are augmented by taking into account the clinical data and measurements collected by physicians such as body temperature, blood pressure and clinical presentation in defining the course of treatment, before the blood culture results are obtained. The HSS not only is a fast and easy means in diagnosis of neonatal sepsis but also has an advantage in its application to all neonates, including those who have received antibiotic therapy prior to sending blood sample for culture studies. Thus, the HSS is a convenient test to differentiate the infected from the non infected neonates. It has a high sensitivity and specificity, the certitude of sepsis being present increases with higher scores. Several studies in the past have been conducted to assess and analyse the significant and effective utilization of HSS, but not in this part of world.

MATERIAL AND METHODS

This study was a hospital based study of all neonates during 1st week of life which reported in Neonatal Intensive Care Unit of Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala. Total 85 neonates were included in the study. Term and pre-term neonates clinically suspected to have bacterial infection within 1st week of life, based on perinatal risk factors and clinical features were taken as the study group. All neonates were simultaneously confirmed by blood culture studies. Complete blood counts along with haematological score were done using

peripheral blood smears which were stained with leishman stain and were examined under oil –immersion lens of light microscope at a magnification of 1000X. Thus, all the peripheral blood smears were analyzed by the pathologist using haematological scoring system (HSS).

HSS includes

- White blood cell (WBC) count and its differential
- Platelet count
- Nucleated red blood cell count (to correct total WBCs count)
- Total WBC (white blood cell) count
- Total PMN (polymorphonuclear neutrophil) count
- Immature PMN count
- I:T PMN (immature to total polymorphonuclear neutrophil ratio)
- I:M PMN ratio (immature to mature polymorphonuclear neutrophil ratio)
- Degenerative changes in PMN
- Platelet count
- Assessment of degenerative and toxic changes in PMNs.

HSS assigns a score of 1 for each of seven findings significantly associated with sepsis: Abnormal total leukocyte count, abnormal total PMN count, elevated immature PMN count, elevated immature to total (I:T) PMN ratio, immature to mature (I:M) PMN ratio ≥0.3, platelet count ≤150,000/mm^3 and pronounced degenerative or toxic changes in PMNs. An abnormal total PMN count is assigned score of 2 instead of 1, if no mature polymorphs are seen on the peripheral smear to compensate for the low I:M ratio. **(Table 1).**

Table 1: Haematological scoring system (HSS)

Criteria	Abnormality	Score
Total WBC count	≤5000/µl ≥25000 at birth ≥30000-12-24 hrs ≥21000-day 2 onwards	 1 1
Total PMN count	1800-5400/mm^3 No mature PMN seen Increased/decreased	0 2 1
Immature PMN count	600/mm^3 Increased	0 1
I:T PMN ratio	0.2 Increased	0 1
I:M PMN ratio	≤0.3 ≥0.3	0 1
Degenerative changes in PMN	Toxic granules / cytoplasmic vacuoles	1
Platelet count	≤1.5 lakhs/µl	1

I:T=Abnormal immature to total neutrophil ratio; I:M=abnormal immature to mature neutrophil ratio; PMN=polymorphonuclear, WBC=white blood cell.

Immature polymorphs include promyelocyte, myelocyte, metamyelocyte and band forms. Band cell is described as a PMN in which the nucleus is indented by more than one-half, but in which the isthmus between the lobes is wide enough to reveal two distinct margins with nuclear material in between. Degenerative changes include vacuolization, toxic granulations and Dohle bodies. Score of ≤2 was interpreted as sepsis unlikely; score 3-4: Sepsis is possible and ≥5 sepsis or infection is very likely. Minimum score that can be obtained is 0 and maximum score, 8. Sensitivity, specificity, positive predictive values and negative predictive values were calculated for each parameter. *P* value was calculated for different parameters. Data was compiled and statistically analyzed by using SPSS software.

RESULTS

In our study, out of total 85 neonates, 49 (57.6%) were males and 36 (42.4%) cases were females, respectively. Maximum number of cases i.e. 46 (54.1%) were observed on day 1 of birth followed by 21 (24.7%) cases and 11 (12.9%) cases on day 2 and day 3, respectively. Out of 31 neonates with proven sepsis (with positive blood culture), 11 (35.5%) cases had immature PMN count of ≤600 per mm3 and 20 (64.5%) cases had a PMN count of >600 per mm3. Majority of the neonates with proven sepsis (with positive blood culture) showed a TLC of >11000/mm^3. Majority i.e. 27 (87.1%) cases showed low platelet count of ≤1.5 Lakhs/mm^3 and 4 (12.9%) cases showed a platelet count of >1.5 lakhs/mm^3. According to the HSS scores allotted to all neonates, out of 31 proven sepsis cases (with positive blood culture), majority i.e.18 (58.1%) neonates were categorized as sepsis suspected followed by 11 (35.5%) neonates categorized as sepsis likely and only 2 (6.5%) neonates were categorized as sepsis unlikely. **(Table 2 & 3).**

Table 2: Distribution of neonates according to their age in days

Age in days	No. of cases	Percentage
1	46	54.1
2	21	24.7
3	11	12.9
4	3	3.5
5	1	1.2
6	3	3.5
Total	85	100.0

Table 4: HSS score versus blood culture results

Category of sepsis	Statistics	BC Results		Total
		Positive	Negative	
Sepsis Unlikely	No. of cases	2	44	46
	Percentage	6.5%	81.5%	54.1%
Sepsis suspected	No. of cases	18	9	27
	Percentage	58.1%	16.7%	31.8%
Sepsis Likely	No. of cases	11	1	12
	Percentage	35.5%	1.9%	14.1%
Total	No. of cases	31	54	85
	Percentage	100.0%	100.0%	100.0%

Table 5: Performance of individual haematological parameters

	Sensitivity	Specificity	Positive predictive value (PPV)	Negative predictive value (NPV)
Total WBC count	83.87%	48.15%	48.15%	83.87%
Total PMN count	96.77%	37.04%	46.88%	95.24%
Immature PMN count	64.52%	90.74%	80.00%	81.67%
I:M PMN ratio	3.23%	100.00%	100.0%	64.29%
Degenerative changes	90.32%	75.93%	68.29%	93.18%
Platelet count	87.10%	68.97%	60.00%	90.91%

DISCUSSION

Neonatal sepsis, sepsis neonatorum and neonatal septicaemia are terms that have been used to describe the systemic response to infection in newborn infants. Sepsis in newborn can be a devastating problem leading to morbidity and mortality. The inability of neonates to completely muster the minimum inflammatory response makes them more susceptible to bacterial invasion of the blood stream than older children and adults and the risks are even higher in preterm infants. Diagnosis of neonatal septicaemia may be difficult as the early signs of sepsis may be subtle and different at different gestational ages. Neonatal septicaemia is characterized by clinical signs and symptoms accompanied by bacteraemia in the 1st month of life.[2] Thenewborn especially the premature are more prone to serious infections. The properties of an ideal diagnostic biomarker include excellence in sensitivity and negative predicative value as well as excellent specificity and positive predictive value. Biomarker levels should change early in the disease course and remain altered for a period of time, to give an opportunity for clinicians to measure these biomarkers to optimize clinical management, monitor disease progress and guide antimicrobial treatment.[7] Discrimination between aetiologies of sepsis such as viral, bacterial, or fungal aetiology would be a valuable characteristic to assist clinicians in timely directed antibiotic therapy or antibiotic stewardship to avoid excess antibiotic use.

In our study, on overall evaluation of HSS, sensitivity was found to be 93.55%, specificity was 81.48%, PPV 74.36% and NPV as 95.65% respectively. Similarly, in the study of Saleem et al., HSS was found to have a sensitivity of 90%, specificity of 74.5%, Positive Predictive Value of 65.9% and Negative Predictive Value as 93.2%.[8] The results were again similar in the study of Kabeere et al. where HSS had a sensitivity of 85%, specificity of 86.67%, negative predictive value of 95.58% and a positive predictive value of 62.96% respectively.[9] **(Table 5).** The HSS increases the diagnostic accuracy of the complete blood cell count as a screening test for sepsis and simplifies and standardizes its interpretation.

SUMMARY AND CONCLUSION

Examination of peripheral blood film remains a very useful diagnostic tool in haematological assessment for distinguishing infected neonates from the non-infected neonates. HSS is a simple, quick, cost effective and readily available tool assisting in timely diagnosis of neonatal sepsis. Its major contribution is seen in making an early diagnosis of neonatal sepsis much before the blood culture results are available to the clinicians and required antibiotic treatment to the neonates can be initiated before, their health is compromised further. Hence, the HSS provides an effective guideline to make decisions regarding judicious use of antibiotic therapy, which will be life saving, provide early cure, reduced mortality, shorten the hospital stay and minimize the risk of emergence of resistant organisms due to misuse of antibiotics.

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