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Original Research Article

Modified hematological sepsis score in early diagnosis of neonatal sepsis

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ABSTRACT

Background: Diagnosis of neonatal sepsis at an early stage substantially reduces the mortality. The clinician often relies on laboratory parameters to support the clinical suspicion. As blood culture takes time and yield is low, hematological and biochemical parameters often guide to the diagnosis and management. Rodwell's Hematological sepsis score (HSS) has a reasonable sensitivity but low specificity. Some of the parameters included in that scoring system are repetitive of same pathogenic mechanism. A modified HSS was developed by the authors by removing the repetitive parameters, increasing the weightage for low neutrophil count and adding a new parameter - nucleated RBC. Objective of the study was to compare the diagnostic ability of the modified hematological sepsis score with Rodwell's hematological sepsis score.
Methods: Prospective analytical study conducted in a tertiary level hospital. Neonates admitted to NICU and had complete blood count done were included. Babies with clinical signs of systemic inflammatory response syndrome and evidence of organ dysfunction were considered septic. They were classified as proven sepsis if the blood culture was positive. All the samples were scored for both HSS and modified HSS. The sensitivity, specificity and other diagnostic ability tests were compared between the two scoring systems.
Results: Total of 75 neonates were enrolled. 25 of them had sepsis and three had blood culture positive. At a score of 3, the sensitivity and specificity of HSS was 80 and 70% and that of Modified HSS was 84 and 82% respectively.
Conclusions: Modified hematological score improves the specificity and likelihood ratios without decreasing the sensitivity in early diagnosis of neonatal sepsis.

Keywords: Hematological sepsis score, Modified hematological sepsis score, Neonate, Sepsis

INTRODUCTION

Neonatal sepsis has subtle and varied clinical presentation in the initial stages. Aggressive approach to diagnosis and management is the principle determinant of the prognosis. Early diagnosis of neonatal sepsis is the corner stone to reduce the case fatality rate.

Blood culture to identify the organism is the gold standard for the diagnosis. However, the yield is low due to several reasons such as low inoculum in the sample sent, inability of the laboratory to identify all the organisms and prior antibiotic usage.[1] Added to this is the delay in obtaining the results. The earliest result will be available after 48 hours of incubation of the blood sample. This period could be too late for the clinician to initiate any useful treatment.

Limitations of obtaining blood culture for treatment of septic neonates, has forced clinicians to use surrogate markers of sepsis for their initial management. Commonly requested tests are complete blood counts and CRP. Sepsis generally results in neutropenia, leukocytosis and thrombocytopenia. Immature neutrophils are released into the circulation leading to left shift.[2-5]

Rodwell et al studied individual parameters and developed hematological sepsis score (HSS) which combined different aspects of the blood picture to suggest sepsis.[6] A score of 3 had a sensitivity of above 80% in the later studies in diagnosing neonatal sepsis. Higher score of 5 further improved the diagnostic ability.[7-9]

In last few years nucleated RBCs are found to be elevated in stressed conditions.[10] Studies have reported the importance of nucleated RBCs in neonatal sepsis as well.[11,12] Study hypothesized that adding this parameter could improve the diagnostic ability of the score. We also hypothesized that removing two other parameters such as band count and immature to mature ratio which represents same pathological mechanism as immature to total ratio in the current form of HSS, wouldn't alter the diagnostic ability of the Hematological sepsis score. Several authors have highlighted the diagnostic ability of neutropenia to be higher than leukocytosis in neonatal sepsis.[13,14] Study observed that neutropenia was strongly associated with sepsis and hence deserved a higher weightage. Hence, we increased the weightage to two (instead of one in HSS) of this parameter to obtain the modified HSS (Table 1). Study set out to analyses if the modified HSS improved the specificity without altering the sensitivity in diagnosing neonatal sepsis.

Table 1: Components and weightage of hematological septic score (HSS) and modified HSS.

Parameter	Value	HSS	Mod HSS
Total leucocyte count	< 5000	1	2
	>25000 (at birth)	1	1
	> 30000 (12 - 24 hours)	1	1
	> 21000 (day 2 onwards)	1	1
	Normal	0	0
Total neutrophil count	No neutrophils	2	2
	Increased / decreased	1	1/2
	Normal (1800 - 5400/cumm)	0	0
Immature neutrophils	Increased	1	NA
	Not increased	0	NA
Immature: total neutrophil ratio (IT ratio)	> 0.2	1	1
	< 0.2	0	0
Immature: mature neutrophil ratio (IM ratio)	> 0.3	1	NA
	< 0.3	0	NA
Degenerative changes	Present	1	1
	Absent	0	0
Platelet count	<150000	1	1
	>150000	0	0
Nucleated RBC	> 5%	NA	1
	< 5%	NA	0

METHODS

Primary objective was to compare the diagnostic ability of the modified hematological sepsis score with Rodwell's hematological sepsis score. Study design was a prospective analytical study conducted in a tertiary health care facility. This study was conducted between January 2016 and December 2016. Neonates who were admitted to our NICU and had complete hemogram done. Babies who had congenital anomalies and severe congenital heart disease were excluded from the study.

Clinical data involved initial demographic data of all the subjects were obtained from the admission record. Babies who had hemogram done at the time of admission as the baseline investigation and did not develop any sepsis with in next 72 hours were considered as normal or no sepsis group.

One of the author who is a consultant neonatologist assessed the babies with suspected sepsis. Babies who had findings of systemic inflammatory response such as tachycardia, tachypnea, temperature instability, apnea etc. with one of the organ system being severely dysfunctional needing significant support such as respiratory support, inotropic support, renal failure etc. were diagnosed as probable (clinical) sepsis. Neonates with above features and had their blood culture showing growth were grouped as proven sepsis. In all these babies, intracranial hemorrhage was ruled out with bed side cranial ultrasound imaging. Other relevant investigations such as lumbar puncture, urine culture,

coagulation studies etc. was ordered as per the clinical indication.

Hematological data

0.5 ml of venous blood sample collected in EDTA vacutainer (BD pediatric) was received in the hematology lab. After the initial formalities, the sample was analyzed with 6-part cell counter (Sysmex XN 1000). A thin smear was made with the same sample and stained with Leishman stain. Blood picture was studied by one of the author with emphasis on nucleated RBC, immature to total leucocyte ratio, immature to mature ratio and degenerative changes in the neutrophils. This was a pilot study. To detect an improvement in specificity by 10% from 70 to 80 % we needed 50 cases. We had a total of 75 subjects recruited during the study period

Statistical analysis

The data was tabulated and initial analysis was done on analyze- it for Microsoft excel 4.65.2.

RESULTS

We recruited a total of 75 subjects. 50 did not have any sepsis and served as control. 25 neonates had sepsis which ranged from systemic response syndrome to multi organ dysfunction. Three out of 25 (12%) sepsis babies had growth in the blood culture. Out of them two had early onset sepsis and one had late onset sepsis. Sixteen percent of the babies in sepsis group had early onset and rest had late onset sepsis.

The minimum and maximum gestation in No sepsis group was 29 and 39 weeks and that in sepsis group was 28 and 41 weeks respectively. The minimum and maximum birth weight in No sepsis group was 760 and 3200 grams and that in sepsis group was 1120 and 4200 grams respectively. The baseline characteristics of this study subjects is depicted in Table 2. There was no significant difference between the birth weight, gestation, age at diagnosis, gender and maturity between no sepsis and sepsis group.

Table 2: Baseline characteristics.

Parameter		No sepsis	Sepsis	P value
		Median (IQR)	**Median (IQR)**	
Birth weight (grams)		2280 (1553 - 2675)	1760 (1433 - 2875)	0.823*
Gestation (weeks)		35 (31.8 - 38)	36 (30.4 - 38)	1*
Age (days)		3 (1 - 6)	5.5 (3.8 - 13.5)	0.302*
		n (%)	n (%)	
Gender	Male	37 (74)	16 (64)	0.263#
	Female	13 (26)	9 (36)	
Gestational maturity	Term	29 (58%)	15 (60%)	0.685#
	Preterm	21 (42%)	10 (40%)	
* Mann whitney U test, # chi square test.				

Table 3: Comparison of diagnostic ability between HSS and modified HSS (cut off score 3).

	HSS	Mod HSS
Sensitivity	0.80	0.84
Specificity	0.70	0.82
Positive predictive value*	0.57	0.70
Negative predictive value*	0.88	0.91
Positive likelihood ratio	2.66	4.60
Negative likelihood ratio	0.28	0.19

*PPV and NPV - incidence of neonatal sepsis is 0.35 in our unit.

At a cut off score of 3, the sensitivity of HSS in diagnosing sepsis was 80% which marginally improved to 84% with modified HSS. There was a 12% improvement in specificity with modified HSS compared to HSS. In study unit, the incidence of neonatal sepsis is 35%. Considering this, the positive predictive value improved from 57% to 70% with modified HSS. There was a nearly two-fold improvement in likelihood ratios as well. Table 3 compares the diagnostic ability of both HSS and modified HSS.

DISCUSSION

Neonatal Sepsis is a devastating condition with a case fatality rate ranging from 30 to 50%.[15,16] Early recognition and treatment can reduce the case related mortality to 10%. Blood culture which is the gold standard for diagnosis is difficult to obtain and has a very low sensitivity due to various preanalytical and analytical issues and is not available during the therapeutic window.[1] PCR for detection of antigen is currently gaining acceptance but are quite expensive.[17] CRP and Procalcitonin are biochemical markers of neonatal sepsis

in routine use which has better value in following the progress of the disease.[18] Complete blood count and peripheral blood picture is an early and commonly sought investigations by the clinicians when sepsis is suspected in neonates. Changes in various components of blood count and blood picture makes it one of the dependable early aid to diagnosis and management of neonatal sepsis. Rodwell suggested a comprehensive scoring system using blood counts and blood picture.[6] The diagnostic usefulness of Rodwell's hematological scoring system and its individual components have been extensively studied and found invaluable.[7-9] The study has reinforced this fact.

However, certain components of HSS appear repetitive due to same pathogenetic mechanism. For example, raise in immature neutrophil count invariably increase the score by 3 in the current form of HSS. Apart from that, neutropenia which is very common and more sensitive in diagnosis of sepsis has a similar score as leukocytosis which is frequently seen in neonates due to non-specific reasons.[13,14] Recent recognition of role of nucleated RBCs in neonatal sepsis deserves its inclusion in diagnosis of sepsis. The modified HSS designed by us have incorporated the above facts.

The Modified HSS proposed by us have shown to be similarly sensitive to HSS in diagnosing neonatal sepsis. Improvement in specificity by more than 10% will help the clinician to be more confident of the diagnosis. Another interesting statistic is the likelihood ratios. The positive likelihood ratio has increased from 2.66 to 4.6 which implies the generalizability of this score to various neonatal population. Combining the modified HSS with other biochemical marker may drastically improve the diagnosis of neonatal sepsis.

The proposed modified HSS is the intervention of the authors based on the pathophysiological concepts which has shown to be an advancement over Rodwell's HSS. This score is yet to be validated in a bigger study. More importantly, the diagnostic ability of this modified score must be assessed in neonates with soft signs of sepsis where the diagnostic dilemma is highest.

CONCLUSION

Modified hematological score improves the specificity and likelihood ratios without decreasing the sensitivity in neonatal sepsis.

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