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Modified Hematological Sepsis Score in the Early Diagnosis of Neonatal Sepsis

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Author`s Contribution

[1,5]Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; Data Collection. [3,4]Active participation in active methodology [2,6]Drafting the work or revising it critically for important intellectual content, Final approval of the version to be published/Supervision

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ABSTRACT

Objective: To compare the diagnostic accuracy of modified hematological sepsis score (MHSS) with hematological sepsis score (HSS) in early diagnosis of neonatal sepsis taking blood culture as gold standard.

Methodology: This cross-sectional validation study was done at the Neonatology Department, Children Hospital of Pakistan Institute of Medical Sciences, Islamabad from 1-01-2020 to 30-06-2020 after ethical approval. A total of 80 neonates admitted to the neonatal unit with clinical manifestations suggestive of sepsis or maternal risk factors were enrolled using nonprobability convenient sampling. Babies were assessed in consultation with the senior neonatologist. After informed written consent, their blood samples were sent to the laboratory for blood complete picture, peripheral film and blood culture. Both MHSS and HSS were calculated. Specificity, sensitivity, positive predictive value (PPV) and negative predictive value (NPV) of MHSS were compared with that of HSS taking blood culture as the gold standard.

Results: Modified hematological sepsis score has a sensitivity and specificity of 84.21% and 75.41% respectively whereas its PPV and NPV are 51.6% and 93.8%. Compared to this, the hematological sepsis score has sensitivity, specificity, PPV and NPV of 78.9% and 67.21%, 42.6% and 91.11%, respectively.

Conclusion: Modified hematological sepsis score has increased sensitivity and specificity in early diagnosis of neonatal sepsis. The diagnostic strength of the modified hematological sepsis score is superior to that of the hematological sepsis score.

Keywords: Neonatal Sepsis, Modified Hematological Sepsis Score, MHSS, Hematological Sepsis Score, HSS, Blood culture.

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Introduction

Neonatal sepsis is a bloodstream infection in the first four weeks of life. It is accountable for significant mortality and morbidity.[1] It is the second most frequent cause of neonatal deaths with almost 24% of the deaths worldwide. Almost 1.7 million neonates suffer from sepsis globally, leading to 45% of the deaths under five years of age. Low-income and lower-middle-income countries face 99% burden of neonatal deaths.[2] In addition, sepsis attributes to increased financial burden with long periods of hospitalizations, intensive care unit admissions and expensive treatments. Pakistan has a high burden of neonatal sepsis leading to 7% of neonatal deaths. The high disease burden is caused by low birth weight which is due to many factors such as poor nutritional status of mothers, lack of antenatal care and higher rates of infections at birth.[3] The diagnosis of neonatal sepsis is always challenging for neonatologists due to nonspecific clinical manifestations and lack of specific tests that can help to diagnose sepsis. The gold

standard is blood culture, but it takes times a minimum of 48-72 hours, and the yield is low. On the other hand, the disease requires immediate aggressive management due to its rapid progression. It is not only important to recognize neonates with sepsis but also to identify those without disease.[4,5] Currently, biomarkers such as hematological indices have been introduced to aid in diagnosis.[4] The hematological sepsis score (HSS), introduced by Rodwell et al., consists of seven parameters with the range of 0-8. The parameters included in the HSS are total leucocyte count (TLC), absolute neutrophil count, immature neutrophils, immature to total neutrophils ratio (I:T ratio), immature to mature neutrophil ratio (I:M ratio), degenerative changes in neutrophils and platelet count. The likelihood of sepsis is high if the score is greater than 5.[5,6] According to Elsayed et al., HSS is simple & fast and differentiates between neonates with or without sepsis.[7]

After the Hematological Score, a modified hematological sepsis score (MHSS) was introduced to improve the specificity of the hematological score. In the modified score, the parameter of nucleated red blood cells (RBCs) was added. Two parameters: neutrophil band count and I:M ratio were removed as their pathogenic mechanism is the same as that of the other I:T. Literature has revealed that nucleated RBCs are significant in neonatal sepsis. Neutropenia is also an important diagnostic indicator of neonatal sepsis. Its score is increased from 1 to 2 in the modified score.[8]

It is very important to diagnose sepsis promptly as it causes irreversible problems in newborns. Treatment must be started as soon as sepsis is suspected without delay in waiting for laboratory reports, but at the same time, judicious use of antibiotics should be done to avoid antibiotic resistance. Due to delays in results of blood culture reports and a lack of resources in developing countries, physicians have to depend on certain other markers to treat sepsis. This study was done to compare the diagnostic accuracy of MHSS and HSS in neonatal sepsis in our setup taking blood culture as the gold standard. In Pakistan, research has been done evaluating the diagnostic accuracy of HSS[9,10] but none of the studies has compared the diagnostic accuracy of the modified hematological score with the hematological score. This would help us to use the modified hematological score as a diagnostic modality for neonatal sepsis as it is simple, fast and readily available.

Methodology

This cross-sectional validation study was conducted at the Neonatology Department, Children's Hospital, Pakistan Institute of Medical Sciences, Islamabad, from January 1, 2020, to June 30, 2020. Ethical approval was obtained from the Institutional Review Board of Ref No. F.1-1/2015/ERB/SZABMU/392. A total of 80 neonates admitted to the neonatal unit were enrolled using nonprobability convenient sampling. Neonates had a history of maternal risk factors such as prolonged rupture of membranes (PROM) more than 18 hours, confirmed urinary tract infection (UTI) on urine culture, high maternal total leucocyte count (TLC), raised C reactive proteins (CRP), documented maternal fever more than 38 degree Celsius before labor or meconium stained liquor or presented with any of these clinical manifestations within 48 hours of admission: lethargy, tachypnea, refusal to feed, abdominal distention, hypothermia, tachycardia, apnea. The exclusion criteria were neonates with congenital malformations, life-threatening cardiopulmonary compromise, APGAR (appearance, pulse, grimace, activity and respiration) score < 5 at 5 minutes of birth, or evidence of immune hemolytic anemia

Babies were assessed in consultation with the senior neonatologist. The clinical signs were recorded, and any maternal risk factors were assessed and recorded in predesigned Performa. Clinical data involving demographic data was also recorded. After informed written consent, blood samples were taken through venipuncture by sterile procedure before administration of antibiotics and sent for blood complete picture (CP) and peripheral film to the Hematology section of the laboratory. Blood CP was done on Sysmex XN 1000. Peripheral blood film was reported by the Hematologist on Giemsa stained blood smear with a focus on nucleated RBCs, TLC, I:M, I;T, degenerative changes in neutrophil, and platelet count. Both MHSS and HSS were calculated on predefined Performa. The parameters of the HSS and MHSS score are depicted in Table 1.

Based on the modified hematological score, a score $\leq$2 is low risk, 3 or 4 is moderate risk and $\geq$5 is high risk for sepsis.[11]

3 ml of blood was aseptically introduced into blood culture bottle. Blood culture was followed at 48 hours and was considered positive if growth was identified, and if inoculated blood culture didn't show any growth till 7 days, then it was considered as negative.

Table I: Parameters of Hematological and Modified Hematological Sepsis Score.[8]

Parameter	Value	HSS	Mod HSS
Total leucocyte count	< 5000	1	1
	> 25000 (at birth)	1	1
	> 30000 (12 - 24 hours)	1	1
	> 21000 (day 2 onwards)	1	1
Total neutrophil count	No neutrophils	2	2
	Increased / decreased	1	1/2
	Normal (1800 - 5400 /cumm)	0	0
Immature neutrophils	Increased	1	1
	Not increased	0	0
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

The Statistical Package for the Social Sciences (SPSS) version 25 was used for analyzing data. Qualitative variables were presented using frequency/percentages and quantitative variables deviation were computed using mean/ standard deviation. The parameters of diagnostic accuracy were calculated using a 2 x 2 table as follows:

Table II: Comparison of HSS/ MHSS with Blood Culture for Diagnosing Neonatal Sepsis.

Index Test	Gold Standard Test	
MHSS/HSS	Blood Culture	
Positive	A (True Positive)	B (False Positive)
Negative	C (False Negative)	D (True Negative)

Results

Neonates had a mean age of 3.1 ± 1.5 days, with the majority of them 3-7 days of age (66.3%). The average gestational age was 36.75 ± 1.76 weeks ranging from 34 to 41 weeks. The gestational age was <37 weeks in 51.2% of the neonates. The average weight at birth was 2.68 ± 0.54 kg, the minimum and maximum weight being 1.3kg and 4.2 kg, respectively. The demographic variables of the neonates are shown in Table III.

The most common clinical manifestation was tachypnea (23.8%) followed by lethargy (15%) and poor feeding (13.8%). Thirteen (16.3%) children had no such clinical manifestation, but they had maternal risk factors. The most common maternal risk factor was premature rupture of membranes (20%) and meconium-stained liquor (17.5%). These findings are presented in Table IV.

Table III: Demographic Variables of the Neonates. (n = 80)

Number of Cases	N(%)
Age (Days)	
<3 days	20(25%)
3-7 days	53(66.2%)
>7 days	7(8.8%)
Gender	
Male	44(55%)
Female	36(45%)
Gestational Age	
<37 weeks	41(51.2%)
>37 weeks	39(48.8%)
Birth Weight	
<1.5 kg	2(2.5%)
1.5-2.5 kg	32(40%)
>2.5 kg	46(57.5%)

Table IV: Clinical Manifestations of Neonates and Maternal Risk Factors. (n=80)

Clinical Manifestation	N (%)
Tachypnea	19(23.8%)
Lethargy	12(15%)
Poor feeding	11(13.8%)
Poor perfusion	8(10%)
Abdominal distention	10(12.5%)
Apnea	4(5%)
Hypothermia	8(10%)
No clinical manifestations	13(16.3%)
Maternal Risk Factors	
PROM > 18 hours	16(20%)
Meconium-stained liquor	14(17.5%)
UTI	10(12.5%)
Raised CRP	8(10%)
Raised TLC count	12(15%)
Maternal fever before delivery	9(11.3%)
No Risk factors	11(13.8%)

Blood culture revealed growth in 19(23.8%) cases. The most common organism isolated was Klebsiella in 8(42.1%) babies followed by Pseudomonas in 7(36.8%) babies, Escherichia coli in 2(10.5%) babies and Staphylococcus aureus in 2(10.5%) babies. A 2 x 2 table showing the relation of HSS with blood culture is given below:

Table V: Relation of HSS with Blood Culture in Neonatal Sepsis.

HSS	Blood Culture		Total
	Positive	Negative	
Positive	15	20	35
Negative	4	41	45
Total	19	61	80

The sensitivity of the Hematological sepsis score was 78.95% and specificity was 67.21%. The PPV, NPV, LR+, LR- and diagnostic accuracy were 42.86%, 91.11, 2.41%, 0.31 and 70%.

Modified hematological score was positive in 31(38.8%) neonates, with the score of 0-2 in 10(32.3%) neonates, score 3-4 in 17(54.8%) neonates and score >5 in 4(12.9%) neonates. A 2 x 2 table showing the relation of MHSS with blood culture is given below:

Table IV: Relation of MHSS with Blood Culture in Neonatal Sepsis.

MHSS	Blood Culture		Total
	Positive	Negative	
Positive	16	15	31
Negative	3	46	49
Total	19	61	80

The sensitivity of the Modified Hematological sepsis score was 84.21%, specificity was 75.41%, PPV was 51.61%, NPV was 93.88%, LR+ was 3.42, LR- was 0.21 and diagnostic accuracy was 77.5.

Discussion

Neonatal sepsis is a life-threatening condition associated with disability, deaths and financial constraints. Early identification and management can decrease mortality and improve the prognosis.[12] Neonatal sepsis still remains a challenge for pediatricians to correctly diagnose sepsis and commence treatment as early as possible.[13] The confirmatory test for the diagnosis is blood culture which takes considerable time and is positive in only 30-70% of the neonates. Hematological sepsis score and later on, modified hematological sepsis score were introduced due to the dire need for diagnostic parameters for neonatal sepsis.[14]

In our study, neonates had a mean age of 3.1 ± 1.5 days. The age was 5.5 days in another study.[8] On the other hand, a study done at Mayo Hospital, Lahore reported an average age of 14.20 ± 8.09 days.[9] In our study, 66.3% of the neonates were 3-7 days of age. In another study, 77.7% of the neonates were 1-5 days old.[15] Most of the neonates were males (55%) in our study. In another study from Pakistan, 60% of the neonates were males.[9] There were 58.3% and 64% males in two other studies.[8,15] In contrast, in a study done in Egypt, 54.9% of the neonates were females.[16] Our results showed that the average weight at birth was 2.68±0.54 kg. The average weight was 2.3 kg in another study.[15] The mean birth weight was low (1.76 kg) in a study by Krishnamurthy et al. and 3.05±0.46 kg in a study by Abbas et al.[8,9] Our results showed that 57% of the babies had normal birth weight whereas, 43% had low birth weight. Sharma et al. reported normal weight in 47.2% of the neonates and low weight in 52.8% of the neonates.[15] The average gestational age was 36.75 ± 1.76 weeks in our study. Similarly, the median gestational age was 36 weeks in a study.[8]

In our study, 51.2% of the neonates were premature. In another study, 40% of the neonates were premature.[8] In contrast, in a study, 76.5% of the neonates were premature.[16] Our study revealed PROM in 20% and meconium-stained liquor in 17.5% of the cases. The most frequent risk factor in mothers was PROM reported in 27.5% of cases.[16] In a study, prematurity was present in 50.9%, PROM in 43.5% and meconium-stained liquor in 13% of the cases.[15] The most common clinical manifestation was tachypnea (23.8%) followed by lethargy (15%) and poor feeding (13.8%) in our study. The most common clinical manifestations in neonates were lethargy (48.1%) and refusal to feed (36.1%) in another study.[15] Tachypnea was the most common presentation in a study.[17] In a study, 72.5% of the neonates presented with respiratory distress syndrome.[16] In our study, 23.8% of the neonates had positive blood cultures. Another study reported positive blood culture in 38% of the neonates.[9] In our study, Klebsiella was isolated in 42.1% of babies followed by Pseudomonas in 36.8%, Escherichia coli in 10.5% and Staphylococcus aureus in 10.5% of the babies. In a study by Padhy et al., Klebsiella was found in 52% and E. coli in 18% of the blood cultures[18] Coagulase-negative Staphylococcus was present in 25.71% of the neonates followed by Staphylococcus aureus (20%), Klebsiella pneumoniae (17.14%), Acinetobacter species (11.42%), Candida species (11.42%) and E. coli (8.57%) in another study.[15]

Our study revealed that the sensitivity of MHSS was 84.21% which was better than that of HSS (78.95%). Similarly, the specificity of MHSS was 75.41% and HSS was 67.21% at a cutoff of 3. The PPV and NPV of HSS were 42.86% and 91.11%, respectively whereas, the PPV and NPV of MHSS were 51.61% and 93.88%, respectively. Ibrahim et al. compared the sensitivity and specificity of HSS and MHSS. Their specificity was almost the same at a cutoff >1 but MHSS has a higher sensitivity of 76.5% as compared to MHS (72.6%).[16] Another study comparing HSS and MHSS scores revealed better sensitivity (84% versus 80%) and specificity (82% versus 70%) with MHSS. The PPV and NPV of MHSS were also better than HSS.[8] Padhy et al.

found that at the cutoff of 3, HSS had a sensitivity of 71% and specificity of 54%. The diagnostic accuracy of MHSS was significantly better than the hematological score with 68% sensitivity and 61% specificity.[18] A study done in Pakistan reported 81.58% sensitivity, 85.48% specificity, 77.50% PPV, 88.33% NPV and 84% diagnostic accuracy of HSS.[9] Another study from Pakistan reported that HSS has a sensitivity of 90%, specificity of 74.5%, PPV of 65.9% and NPV of 93.2%.[10] According to the study by Sharma et al., the hematological sepsis score has a sensitivity of 94.28%, specificity of 73.34%, PPV of 64.70% and NPV of 96.49% at the cutoff of 2. Whereas, at the cutoff of 3, the sensitivity, specificity, PPV and NPV of HSS were 82.85, 91.78, 82.85 and 91.78, respectively.[15] The sensitivity of 100%, specificity of 80.9%, PPV of 100% and NPV of 14.3% of hematological sepsis score were reported by Varughese et al.[17]

Conclusion

Modified hematological sepsis score has increased sensitivity and specificity for the diagnosis of neonatal sepsis. The diagnostic strength of the modified hematological sepsis score is superior to that of the hematological sepsis score. Keeping in view the burden of neonatal infections and resultant high mortality rates in Pakistan, the modified hematological sepsis scoring should be used as a diagnostic modality for neonatal sepsis.

RECOMMENDATIONS OF THE STUDY: For future reference and validation, the hematological predictive scores must be studied in multicenter health facilities with a bigger sample size.

References

1. Mahmoud AH, Parekh R, Dhandibhotla S, Sai T, Pradhan A, Alugula S, et al. Insight into neonatal sepsis: an overview. Cureus. 2023 Sep 19; 15(9):e45530. doi: 10.7759/cureus.45530.
2. Mezgebu T, Ossabo G, Zekiwos A, Mohammed H, Demisse Z. Neonatal sepsis and its associated factors among neonates admitted to the neonatal intensive care unit in Wachemo University Comprehensive Specialized Hospital, Southern Ethiopia, 2022. Front Pediatr. 2023 Jul 3; 1 1:1184205. doi: 10.3389/fped.2023.1184205.
3. Bhatti ZI, Nawaz K, Mahmood R, Bhatti SZ. Indicators of neonatal sepsis in Pakistan. P JMHS. 2021; 15(3):629-32.
4. Celik IH, Hanna M, Canpolat FE, Mohan Pammi. Diagnosis of neonatal sepsis: the past, present and future. Pediatr Res. 2022 Jan; 91(2):337-350. doi: 10.1038/s41390-021-01696-z.
5. Bromiker R, Elron E, Klinger G. Do Neonatal infections require a positive blood culture? Am J Perinatol. 2020 Sep; 37(S 02):S18-S21. doi: 10.1055/s-0040-1714079.
6. Joshi D, Padma SK, Shetty JK, Goel S, Hidangmayum A. utility of hematological parameters in early diagnosis of neonatal sepsis in comparison to C-reactive protein. J Health Allied Sci NU. 2024; 14:174-7. doi: 10.1055/s-0043-1768593.
7. Elsayed M, Hassan A, Maklad AMH, Kasem Y. The role of hematological scoring system (HSS) in early diagnosis of neonatal sepsis. Ann Neonatol J. 2021; 3(1):85-106. doi:10.21608/anj.2021.140120.
8. Krishnamurthy V, Thandaveshwar D, Doreswamy SM. Modified hematological sepsis score in early diagnosis of neonatal sepsis. Int J Res Med Sci. 2017 Aug; 5(8):3573-7.
9. Abbas F, Ahmad B, Shabir S, Hassan KA. Neonatal Sepsis: Accuracy of hematological scoring system for diagnosing neonatal sepsis. J Pak Soc Intern Med. 2023; 4(1): 46-5.
10. Saleem M, Shah KI, Cheema SM, Azam M. Hematological scoring system for early diagnosis of neonatal sepsis. JRMC. 2014 Jun; 18(1). Available from: https://www.journalrmc.com/index.php/JRMC/article/view/391.
11. Bhalodia MJ, Hippargi SB, Patil MM. Role of hematological scoring system in diagnosis of neonatal sepsis. J Clin Neonatol. 2017; 6(3):144-7. doi: 10.4103/jcn.JCN_158_15.
12. De Rose DU, Ronchetti MP, Martini L, Rechichi J, Iannetta M, Dotta A, et al. Diagnosis and management of neonatal bacterial sepsis: current challenges and future perspectives. Trop Med Infect Dis. 2024 Aug 28; 9(9):199. doi: 10.3390/tropicalmed9090199.
13. Procianoy RS, Silveira RC. The challenges of neonatal sepsis management. J Pediatr. 2020; 96(S1):80-6. doi: 10.1016/j.jped.2019.10.004.
14. Sawadkar MM, Dharwadkar A, Gore CR, Chandanwale S, Buch A. Hematological scoring system and its significance in early diagnosis of neonatal sepsis. Saudi J Pathol Microbiol. 2020 Feb; 5(2):108-14. doi: 10.36348/sjpm.2020.v05i02.012.
15. Sharma R, Bombeshwar V, Varma R, Neral A, Gupta C. Role of Modified Rodwell's Haematological Scoring System in early diagnosis of neonatal sepsis: a study in tertiary care centre of Central India. IJPCR. 2024; 16(5); 539-43.
16. Ibrahim MMM, El -Sewefy DA, Ibrahim MJA, Pessar SA. Diagnostic evaluation of hematological sepsis score and presepsin in neonatal sepsis. Iran J Ped Hematol Oncol. 2021; 12(2):101-13. doi: 10.18502/ijpho.v12i2.9075.
17. Varughese PM. Modified hematological sepsis score: an easy and cost effective measure to combat neonatal septicemia. Int J Res Med Sci. 2020 Feb; 8(2):517-23. doi: 10.18203/2320-6012.ijrms20200228.
18. Padhy S, Thandavehwara D, Doreswamy SM, Krishnamurthy V. Sepscore - An improved armament in the diagnosis of neonatal sepsis. JCDR. 2023; 17(4): EC05-EC07. doi: 10.7860/JCDR/2023/59408.17710.