JPSIM Journal of Pakistan Society of Internal Medicine

Original Article

Neonatal Sepsis: Accuracy of Hematological Scoring System for Diagnosing Neonatal Sepsis

Fareeha Abbas,[1] Bushra Ahmad,[1] Sadia Shabir,[1] Khawaja Amjad Hassan[2]

[1]Mayo Hospital, Lahore, [2]Services Hospital, Lahore

Abstract

Objective: To find the diagnostic accuracy of hematological scoring system in early diagnosis of neonatal sepsis taking blood culture as gold standard.

Methods: After IRB approval, this Cross sectional study was done in the Department of Pediatric Medicine, Mayo Hospital/ KEMU Lahore, for 6 months (Apr-Oct 2018). After informed parental consent, information including age, sex and anthropometric data were recorded. The laboratory investigations were sent to laboratory of Mayo Hospital. Complete blood counts including TLC and platelets count were done using Sysmax method. Neonatal sepsis was labeled as positive or negative on hematological score system and blood cultures.

Results: The mean age of neonates was 14.20 ± 8.09 days. There were 60(60%) male and 40(40%) female babies. Mean weight and length of these babies were 3.05 ± 0.46 kg and 51.49 ± 1.41 cm. A total of 41(41%) babies had neonatal sepsis on hematological score and 38(38%) on blood culture. The Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value and Diagnostic Accuracy was 81.58%, 85.48%, 77.50%, 88.33% and 84.00% respectively.

Conclusion: Hematological scoring system has high diagnostic accuracy in diagnosing neonatal sepsis at earliest, taking blood culture as gold standard.

Keywords: Diagnostic accuracy, Hematological scoring, sepsis

How to cite this:

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): 46-50

Corresponding Author: Dr. Sadia Shabir **Email:** drsadiashabir@gmail.com

Introduction

Neonatal sepsis is systemic illness caused by bacteria, viruses or fungi, associated with hemodynamic disturbances and clinical features, causing severe morbidity and mortality.[1] Developing countries contribute to 98% of neonatal deaths globally, sepsis being causative for up to 30-50% of cases.

Sixty five percent of the global neonatal deaths contributed by just 10 countries, Pakistan ranks third amongst them. Annually 300,000 newborns die in our country, with neonatal mortality rate of 42 per thousand live births, contributing to 7% of total neonatal mortality worldwide.[2-6] National data about neonatal sepsis incidence in Pakistan is limited ranging from 1.3 to 3.8 per thousand live births.[7]

Neonatal sepsis has been subdivided as early onset or late onset according to time of onset. In early onset sepsis, clinical symptoms arise in initial seventy two hours of life while in late onset sepsis, symptoms arise from 4 to 28 days of life. In neonates signs and symptoms are non specific, causing difficulty in diagnosis. Infectious agents may arise from intra uterine and maternal flora, may be hospital or community acquired. Blood culture is taken as standard investigation for diagnosis, but results are often held up to 72 hours, false negative and false positive results are also there. For this reason empiric antibiotic therapy is often started to prevent lethal outcome of untreated sepsis. Antibiotics should be discontinued as soon as the results of culture would be available and depending upon clinical condition of newborn because unnecessary use of antibiotics can cause adverse side effects.[8] A number of new markers have been used in diagnosis of neonatal sepsis such as acute phase reactants, cell surface antigens, cytokines, chemokines, bacterial genomes, polymerase chain reactions alone or in combination. Previous studies have revealed that Hematological scoring system (HSS) by

Rodwell et al., is easy, practicable, radily available and cost effective 09-10 that uses total leukocyte count, total neutrophil count, platelet count and others.[12] The results of these tests are available within 1or 2 hour so antibiotics can be started judiciously.[11] Hematological scoring system in septic population has a sensitivity of 96%, specificity of 90%, PPV (86.7%) and NPV 86%. [12]

In past, studies have been conducted to determine the role hematological markers for neonatal sepsis. However, data regarding our population is lacking. So this study was devised to determine the role of hematological scoring system as a single rapid, reliable and cost effective marker for neonatal sepsis and to differentiate infected ones using simple modified hematological scoring system assigning 1 score each to abnormal total leukocytes count, polymorphs count, raised immature neutrophil count, raised immature to total neutrophil ratio, immature to mature neutrophil ratio greater than or equal to 0.3, platelet count equal or less than 150,000/mm^3, and marked degeneration in neutrophils. If mature polymorphs are not present on the peripheral smear then to accommodate for the low I: M ratio, an abnormal total count is given a score of 2 instead of 1. These results were helpful to diagnose cases of neonatal sepsis early and reliably.

Methods

This cross-sectional study (after approval from IRB) was carried in the Department of Pediatric Medicine, King Edward Medical University/ Mayo Hospital Lahore for 6 months duration. Non probability consecutive sampling method was used and a sample size of 100 was calculated. Neonates of either gender, aged 1-28 days of life admitted with the diagnosis of suspected sepsis (presence of any sign favoring high index of suspicion of serious bacterial infection: (fits, respiratory rate > 60 breaths/min, severe chest in drawings, temperature > 37.7ºC or < 35.5ºC, lethargy or unconsciousness, inability to feed/suck, bulging fontanel, pus discharge from the ear, grunt /nasal flaring, redness around umbilicus) were enrolled in study. Neonates who received prior antibiotic therapy, those with gross congenital anomalies or born <28weeks of gestation or birth weight <1000 grams were excluded. After getting informed parental consent, data was recorded on structured questionnaire, including age, gender, anthropometric and systemic details. Under aseptic measures 1 ml blood from patients of suspected sepsis was anti-coagulated with EDTA and 1 ml blood was collected in blood culture bottles and 1 ml blood for CRP before the start of antibiotic therapy. The laboratory investigations were sent to Pediatric Hematology laboratory of Mayo Hospital. Complete blood counts including total leukocyte count and platelets count was done using Sysmax method. Peripheral blood smear was made and stained with Leishman stain and analyzed using hematological scoring system of Rodwell et al. for Differential leukocyte counts (DLC), total neutrophil count 50(TNC), immature neutrophil count (I), mature neutrophil count (M) was performed. Immature to total neutrophil (IT) ratio and immature to mature neutrophil (IM) ratio was calculated. IT ratio was by calculated dividing the total immature count to total neutrophil count (including both mature and immature neutrophil count) and degenerative changes in neutrophils. Neonatal sepsis was labeled as positive or negative on hematological score system and blood cultures (as per operational definition).

Data analysis was done using SPSS Version 20.0. Categorical variables like gender were depicted as frequency and percentages. Quantitative data like age, length and weight were presented as mean ±S.D. Data was stratified for age, gender and weight. Two by two contingency table was used to calculate performances of individual hematological parameter in diagnosing specificity, sensitivity and diagnostic accuracy of hematological markers using blood culture as gold standard taking p value ≤ 0.05 as significant.

Results

The mean age of neonates was 14.20 ± 8.09 days. A total of 46(46%) neonates were < 14 days old and 54

Table 1: *Comparison of Neonatal sepsis Diagnosis based on hematological score and blood culture with respect to Age groups (days)*

Age (Days)	Neonatal Sepsis as per Hematological Score	Neonatal Sepsis as per Blood Culture		Chi-square	p-value	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
<14	Yes	Yes	No	34.809	<0.001	95.24	92.00	90.91	95.83	93.48
		20	2							
	No	1	23							
14-28	Yes	11	7	10.989	0.001	64.71	81.08	61.11	83.33	75.93
	No	6	30							

(54%) were 14-28 days old. There were 60(60%) male and 40(40%) female babies with higher male to female cases. The mean weight and length of these babies was 3.05±0.46 kg and 51.49±1.41 cm respectively. There were 26(26%) neonates who were low birth weight and 74(74%) neonates had normal birth weight.

A total of 40(40%) babies had neonatal sepsis on hematological score and 38(38%) neonates had neonatal sepsis on blood culture. There were 31 true positive, 53 true negative, 9 false positive on hematological score and 7 false negative on hematological score but confirmed on blood culture for neonatal sepsis. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy turned out to be 81.58%, 85.48%, 77.50%, 88.33% and 84.00% respectively.

Table 2: *Comparison of Neonatal Sepsis Diagnosis Based on Hematological Score and Blood Culture with Respect to Gender*

Gender	Neonatal Sepsis as per Hematological Score	Neonatal Sepsis as per Blood Culture		Chi-square	p-value	Sensitivity	Specificity	PPV	NPV	Diag. Accuracy
		Yes	No							
Male	Yes	21	5	28.864	<0.001	84.00	85.71	80.77	88.24	85.00
	No	4	30							
Female	Yes	10	4	14.879	<0.001	76.92	85.19	71.43	88.46	82.50
	No	3	23							

Table 3: *Comparison of Neonatal Sepsis Diagnosis Based on Hematological Score and Blood Culture to Weight (kg)*

Weight (kg)	Neonatal Sepsis as per Hematological Score	Neonatal Sepsis as per Blood Culture		Chi-square	p-value	Sensitivity	Specificity	PPV	NPV	Diag. Accuracy
		Yes	No							
Low Birth Weight	Yes	8	3	9.458	0.002	80.00	81.25	72.73	86.67	80.77
	No	2	13							
Normal Birth Weight	Yes	23	6	34.873	<0.001	82.14	86.96	79.31	88.89	85.14
	No	5	40							

Discussion

Early diagnosis and effective treatment is the best way to decrease neonatal sepsis related mortality and morbidity. Blood culture is gold standard diagnostic tool for neonatal sepsis, but the results are delayed up to 24-48 hours, and sensitivity is also affected by blood volume, prior antibiotic use and bacterial load.[13]

Hematological scoring system (HSS) of Rodwell, comprising of deranged leukocyte count, total neutrophil count, increased band cell, high IT ratio, raised immature to mature neutrophil (IM) ratio, low platelet count, and degeneration in neutrophils[9], is a helpful aid to differentiate the septic from the non-septic infants and results are also readily available. Its high sensitivity and specificity would made the certainty of sepsis being present with higher scores[13]. In our study, 40 babies had neonatal sepsis on hematological score out of which 31 were true positive, while 7 were false negative on HSS but confirmed on blood culture as neonatal sepsis. The sensitivity, specificity and diagnostic accuracy turned out to be 81.58%, 85.48% and 84.00% respectively.

Previously Rodwell et al proved HSS as having sensitivity as (96%) and specificity as (90%), values being higher than our's.[9] Jacob et al demonstrated that HSS score of 3 or more has the sensitivity as 87% and specificity as 85% in establishing diagnosis of sepsis, results being in agreement with ours[14]. In a neonatal sepsis study in Egypt, HSS showed the sensitivity of (95%) and recognized >90% of neonates with clinical impression of sepsis.[15] The diagnostic accuracy of HSS was much more (85.1%) as compared to the individual maximum diagnostic accuracy of parameters, like 74.46% for the total neutrophil count.[16]

Blood culture was positive in 38(38%) newborns in our study, the results being consistent with those of Samanta et al which demonstrated positive blood culture in 39.6% cases.[17] In current study the mean age of neonates was 14.20±8.09 days (range 1-28 days). The result of another study had showed that the mean age of participants was

13 days 18. There were 60(60%) males in our study who were clinically suspected sepsis, while out of 31 true positive cases neonatal sepsis, males constituted 21/31 (67.7%) and females 10/31(32.2%) with higher male to female ratio similar to the results of other studies which showed 71% male and 28% female babies[19] and 62% male and 38% female babies respectively[20] who presented with sign and symptoms of sepsis. The x-linked immunoregulatory factor might be responsible for predominance of male gender with septicemia.[21,22] In contrast to other studies by Swadkar M and Debroy A showed female predominance among neonates.[18,23]

Yadav et al have showed higher positivity of blood cultures in low birth weight newborns (62.7%) as compared to those with normal birth weight, results not being consistent with ours where 10/38(26.4%) babies with blood culture proven sepsis were with low birth weight and 28/38(73.6%) were with normal weight.[24]

All the newborns with clinical impression of sepsis whose blood culture turned out to be positive, had hematological scoring system score > 5 showing sensitivity of hematological scoring system for confirmed sepsis as 100%, while in patients with score less than 2, sepsis is less likely, with score 3-4, sepsis is probable and with score more than 5 ,sepsis is very likely.[18]

Conclusion

It is concluded that diagnostic accuracy of hematological scoring system is high in establishing neonatal sepsis diagnosis, taking blood culture as gold standard. Hence, in future this scoring system can be used to diagnose the neonatal sepsis that can help for better prognosis of patients after early diagnosis and timely treatment.

Limitations of the Study

Preterm neonates born at less than 28 weeks gestation and those with very low birth weight were not entertained in study because some parameters of HSS can also affected by disease process other than sepsis also. Comparison of HSS with other sepsis markers like CRP, Procalcitonin was not done in study due to cost issues but it is a way forward for further studies to be carried out in this aspect.

Conflict of Interest: *None*

Funding Source: *None*

References

1. Ozmeral Odabasi İ, Bulbul A. Neonatal Sepsis. Med Bull Sisli Etfal Hosp 2020;54(2):142-58.
2. National Institute of Population Studies Pakistan, ICF International. Pakistan Demographic and Health Survey 2017–18. Islamabad and Rockville: NIPS, ICF; 2019
3. World Health Organization. Neonatal and perinatal mortality: country, regional and global estimates. Geneva: WHO; 2006.
4. Bhutta ZA, Ministry of Health Pakistan and United States Agency for International Development. Maternal and Child Health in Pakistan: Challenges and Opportunities. 1st ed: Oxford University Press; 2004.
5. Jalil F. Perinatal health in Pakistan: a review of the current situation. Acta Pediatrica. 2004;93(10):1273–9.
6. Khan A, Kinney MV, Hazir T, Hafeez A, Wall SN, Ali N, et al. Newborn survival in Pakistan: a decade of change and future implications. Health Policy Plan. 2012; 27 (Suppl 3):72–87.
7. Sheikh AN, Sajjad A, Hanif S. Neonatal sepsis: An evaluation of bacteriological spectrum, antibiotic susceptibilities and prognostic predictors at Civil Hospital, Karachi. Pakistan Paediatr J 2014; 38(3): 143–55.
8. Bromiker R, Elron E , Klinger G. Do neonatal infections require a positive blood culture? Am J Perinatol 2020; 37(S 02): S18-S21
9. Rodwell RL, Leslie AL, Tudehope DI. Early diagnosis of [6]Neonatal sepsis using a hematologic scoring system. J Pediatric.1988;112(7):761-67.
10. Rodwell RL, Taylor KM, Tudehope DI, Gray PH. Hematologic [7]scoring system in early diagnosis of sepsis in neutropenic newborns. Pediatr Infect Dis J. 1993;12(5):372-76.
11. Supreetha M, Alva S, Shivendra V, Kariappa T. Evaluation of neonatal septicaemia using hematological parantelers. Int J Recent Sci Res. 2015;6(2):2775-8
12. Moshira S. Elsayed; Alaaeldin A. Hassan; Alaa M. Hashim and Yasser T. Kassem. "The role of Hematological Scoring System (HSS) in early diagnosis of Neonatal Sepsis". Annals Neonatol J. 2021;3(1): 85-106
13. Bhalodia MJ, Hippargi SB, Patil MM. Role of hematological scoring system in diagnosis of neonatal sepsis. J Clin Neonatol 2017; 6(2):144-7.
14. Jacob SJ, Suman FR, Sharma D, Shalini SCN, Ninan B, Varadarajan S et al. Evaluation of Various Diagnostic Markers for Early Detection of Neonatal Sepsis. J Med Surg Pathol. 2018;3(3):1000163-5.
15. Derbala SG, Handoka NM, Hasan BBE, El-Sayed HF. Performance of Hematological Scoring System for Early Diagnosis of Neonatal Sepsis in a Neonatal Intensive Care Unit of a Developing Country. Infect Dis Med. 2017; 3 (4): e 429
16. Adhikari B, Paudyal P, Upadhyaya P, Agrawal J, Khanal B. Use of hematological parameters as an early screening tool for neonatal sepsis. J Pathol Nep. 2021;12(2): 1848-53.
17. Samanta M, Biswas C, Pal NK, Sarkar S, Goswami A, Hazra A et al. Performance of SNAPPE-II score in neonatal sepsis: an experience from a tertiary care center. Turkish J Pediat. 2020;62(2):191-8.

18. Sawadkar M, Dharwadkar A, Gore C, Chandan-wale S, Buch A et al. Hematological scoring system and its significance in of early Diagnosis of neonatal sepsis.; Saudi J Pathol Microbiol, Feb. 2020; 5(2): 108-14.
19. Priyanka T,Hemalata. Basic hematological scoring system - Is it the most accurate Neonatal Sepsis predictor? Nat J Lab Med. 2018;7(3): PO29-PO33
20. Ahirrao B, Dravid N, Ahirrao M, Gadre A, Gondane S et al. Diagnostic Utility of Hematological Scoring System (HSS) with Clinicopathological and Bacteriological Evaluation in Early Diagnosis of Neonatal Sepsis. Ann Pathol Lab Med.2017; 4(6):721-6.
21. Swarnkar K, Swarnkar M. A study of early onset neonatal sepsis with special reference to sepsis screening parameters in a tertiary care centre of rural India. Internet J Infect Dis. 2012;10(1):1-10.
22. Draz NI, Taha SE, Abou-Shady NM. Comparison of broad range DNA PCR to conventional blood culture for diagnosis of sepsis in the newborn. Egyptian J Med Human Genetics. 2013;14(4):403-11.
23. Debroy A, Joshi, D, Sinha T. Reappraisal of the Haematological Scoring System (HSS) for early diagnosis of neonatal sepsis in a remote geographical location of North East India. Indian J Pathol Oncol. 2016; 3(3): 366-371.
24. Yadav NS, Sharma S, Chaudhary DK. Bacteriological profile of neonatal sepsis and antibiotic susceptibility pattern of isolates admitted at Kanti Children's Hospital, Kathmandu, Nepal. BMC Res.2018;11(1):1-6.