Reappraisal of the Haematological Scoring System (HSS) for early diagnosis of neonatal sepsis in a remote geographical location of North East India

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Abstract

Sepsis in newborns is one of the commonest clinical problems encountered by the paediatricians. It accounts for major cases of neonatal mortality and morbidity. The initial presentation of neonatal septicaemia may be subtle and therefore, it is important not only to recognize the neonates with septicaemia but also to identify the non-infected neonates. The primary objective of the clinician caring for infants at risk for neonatal infections is to identify all potential cases of bacterial diseases quickly and begin antibiotic therapy promptly. It is important, however, to determine which of these cases represent true infection and thus require a full course of antibiotics and which do not. Blood culture is the gold standard for diagnosis, but requires 48-72 hours for the final report. It is therefore necessary to have a method for early detection of neonatal sepsis for prompt initiation of antibiotic therapy. This study is designed to evaluate the haematological scoring system put forward by Rodwell for early diagnosis of neonatal septicaemia.

Keywords: Early diagnosis, Haematological scoring, Neonatal sepsis

Access this article online	
Quick Response Code:	Website: www.innovativepublication.com
	DOI: 10.5958/2394-6792.2016.00069.7

Introduction

Neonatal septicaemia is one of the commonest clinical problems encountered by the paediatricians. It accounts for major cases of neonatal mortality and morbidity and at the same time its diagnosis remains challenging.[1,2]

Most neonatal bacterial infections occur during the first week of life (early onset sepsis) and result from spread of micro-organisms colonising the maternal genital tract into amniotic cavity.[2] This clinical syndrome is characterised by signs and symptoms of infection with accompanying bacteremia in first month of life.[2]

The early signs of neonatal septicaemia may be subtle and it is important not only to recognise the neonates with septicaemia but also to identify the non-infected neonates. Early diagnosis of neonatal sepsis is critical because of its non-specific clinical picture, the illness progresses more rapidly than the adults and newborns, especially premature are prone to serious infections by organisms and the signs of these infections may be absent or minimal or hard to detect. Thus fatal septicaemia may occur with little warning.[1,2]

The primary objective of the clinician caring for infants at risk for neonatal infections is to identify all potential cases of bacterial diseases quickly and begin antibiotic therapy promptly. It is important, however, to determine which of these cases represent true infection and thus require a full course of antibiotics and which do not.[3]

Definite diagnosis of neonatal sepsis requires positive blood culture, a process which takes around 48-72 hours.[4] Blood culture facility is not available in remote health care delivery centres and since it is a time consuming process, there is a need for a rapid test for bacteremia, which is easy to perform and the reports of which can be made available to the paediatricians quickly.[5]

Rodwell et al gave a haematological Scoring System (HSS) for early diagnosis of neonatal sepsis in high risk infants.[6] This scoring system takes seven haematological parameters (Total WBC count, total polymorphonuclear (PMN) count, immature PMN count, immature/total PMN ratio, immature/mature PMN ratio, platelet count and degenerative changes in neutrophils) into account and assigns a score of one to each of the seven haematological findings. There is one exception; an abnormal total polymorphonuclear (PMN) count is assigned a score of 2 rather than 1 if no mature PMNs are seen on the blood smear. The total score thus ranges from 0-8, and it has been suggested that if the total score is less than 2, sepsis is very unlikely and if the score is more than 5 the likelihood of sepsis is very high. Though different studies have suggested the utility of HSS in making an early diagnosis of neonatal sepsis, the system is not being used in routine practice and there is a need to simplify and standardize the interpretation of this test.

Aims and Objectives

The objective of this study is to evaluate the diagnostic accuracy of total Haematological Scoring System and its individual seven components, for diagnosis of neonatal sepsis as evidenced by blood culture (definite neonatal sepsis), or by systemic inflammatory response (SIRS) (probable neonatal sepsis).

Materials and Methods

This is a prospective study which was conducted in a tertiary care referral hospital in Sikkim for a period of 2 months. All consecutive neonates (1-30 days) admitted to the hospital with a suspicion of neonatal sepsis were included in the study. The blood of all such neonates were collected and evaluated for haematological parameters and bacterial culture. A written consent was taken from parents of eligible neonates for this study.

Neonates who were severely jaundiced due to blood group incompatibilities were excluded from the study.

Haematological evaluation was done using Automated Cell Counter (for CBC) and Light microscopy with Manual Cell counter (for total PMN count, immature PMN count, mature PMN).

Blood culture was performed by BACTEC method using automated system VITEK-2 for identification and antimicrobial susceptibility of the organism.

Basic clinical information from hospital charts of eligible and consenting participants was taken. This clinical information included age, gender, presence of fever, heart rate, blood pressure, respiratory rate, oxygen saturation, presence of any infection.

Index Test

- Under complete aseptic conditions, 0.5-1 ml of blood sample was obtained by peripheral venepuncture.
- The samples were collected in tripotassium ethylene diamine tetra acetic acid containing non-siliconised vacutainer tubes.
- Peripheral blood smears were prepared immediately, stained with Leishman stain and examined under an oil immersion lens of light microscope at a magnification of x1000.
- Complete blood count was performed by Beckman Coulter ACT Diff5.
- Total PMN count, immature PMN count, mature PMN count were calculated on the basis of WBC count obtained by Cell counter and DLC obtained after examining.
- Degenerative changes in neutrophils like cytoplasmic vacuolations, toxic granulations, and presence of Dohle bodies were noted.
- Each haematological criterion was given a score based upon its presence and then the total score was calculated as shown in the following table.

Table 1: HSS criteria and respective scores

HSS criteria	Abnormality	Score
Total WBC count	<=5,000/microliter	1
	>=25,000/microlitre at birth >=30,000/microlitre-12-24hours after birth >=21,000/microliter-day 2 onwards	1
Total PMN count	No immature 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 granulations/cytoplasmic vacuoles	1
Platelet count	<-1,50,000 microlitre	1

Normal Values (according to Manore et al[7])
Total PMN count-1800-5400
Immature PMN count-600
I:T PMN ratio-0.120
I:M PMN ratio-<-=0.3

Results

The study included 40 cases. Based on clinical findings and laboratory data infants were classified into three categories (Table 2):

1. **Definite sepsis (10/40 cases):** The diagnosis of sepsis was made when there were positive findings on blood culture.

2. **Probable sepsis (6/40 cases):** Infants were classified as having probable infection when blood cultures were negative but there was a strong clinical history indicating infection. Certain high risk factors such as prolonged rupture of membranes, me-conium aspiration, prolong labour and maternal fevers were noted in these neonates. The infants presented with clinical features such as respiratory distress and grunting, apnea, lethargy, poor feeding/sucking, abdominal distension and shock.
3. **No sepsis (24/40 cases):** This group consisted of neonates with negative blood culture, who finally presented with feature of suspected sepsis or with associated risk factors. On further investigation they were found to be suffering from other disorders such as hyaline membrane disease, transient tachypnea of the new born and hypoglycemia.

Table 2: Distribution of cases based on presence of sepsis

Groups	No. of cases
Group 1-Definite Sepsis	10
Group 2-Probable Sepsis	6
Group 3-No Sepsis	24

The study had 17 males (56.6%) and 23 females (43.4%). There was predominance of preterm cases (70%) (Table 3).

Table 3: Sex and term distribution of cases

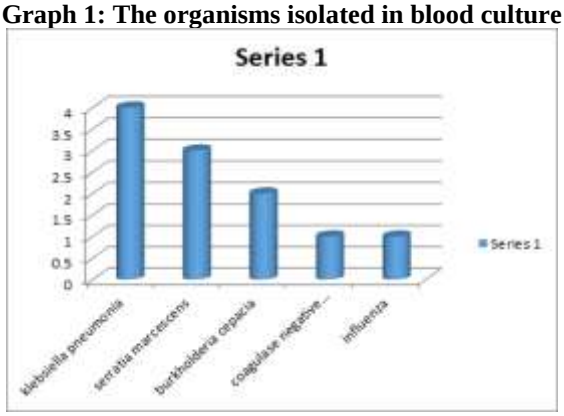
Cases	Males	Females
Term	8	11
Preterm	9	12

Table 4: Scores of each group

Groups	0-2	3 or 4	>=5
Sepsis (10 Cases)	1(10%)	1(10%)	8(80%)
Probable Sepsis (6 Cases)	2(33.3%)	3(50%)	1(16.6%)
No Sepsis (24 Cases)	15(62.5%)	7(29.16%)	2(8.3%)

It is noteworthy that 2 cases (8.3%) out of the 24 normal neonates had the score>=5 suggesting the presence of sepsis.

Graph 1: The organisms isolated in blood culture



Statistical Analysis

Performance of individual haematological findings was calculated-

1. Against definite sepsis, and no-definite sepsis groups (Table 6A)
2. Against definite-and-probable sepsis, and no-sepsis groups (Table 6B)

Table 6A: For definite sepsis and no-definite sepsis

Criteria	Sensitivity (%)	Specificity (%)	PPV	NPV	LR (+)	LR (-)
Total WBC Count	50	60	29.4	78.8	1.2	0.8
Total PMN Count	40	63	26.6	76	1.0	0.9
Immature PMN Count	80	90	72.2	93.10	8	0.2
I:T PMN Ratio	90	96.6	100	96.6	22.5	0.1
I:M PMN Ratio	60	93	75	87.5	8.5	0.4
Degenerative Changes	50	53	26.13	76.19	1	0.9
Platelet Count	50	66.6	33.3	80	1.4	0.7

PPV-Positive predictive value
NPV-Negative predictive value
LR (+)-Positive likelihood ratio
LR (-)-Negative likelihood ratio

From the above table, we see that

1. I:T PMN ratio(90%) was highly sensitive followed by immature PMN count(20%).
2. I:T PMN ratio(96.6%) was highly specific followed by I:M PMN ratio.
3. Positive predictive value was highest for I:T PMN ratio(100%) which was helpful in identifying neonates who really had sepsis.
4. Negative predictive value was highest with I:T PMN ratio(96.6%) which indicated that the neonates did not have the evidence of sepsis.
5. The goodness of fit was tested using Likelihood ratio test. I:T PMN was chosen the final model.

Table 6B: For definite-and-probable sepsis and no-sepsis group

Index Tests	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR (+)	LR(-)
Total WBC Count	55	66.6	50	66.6	1.61	0.68
Total PMN Count	37	66.6	42.8	61.5	1.08	0.95
Immature OMN Count	68	75	64.7	78.2	2.72	0.42
I:T PMN RATIO	75	87	80	84	5.76	0.28
I:M PMN RATIO	62	70	58.8	73.9	2.06	0.54
Degenerative Changes	31	58.3	33.3	56	0.73	1.18
Platelet Count	31	66.6	38.3	59.25	0.91	1.04

From the above table, we see that:

1. I:T PMN ratio (75%) was highly sensitive followed by immature PMN count(68%)
2. I:T PMN ratio(87%) followed by I:M PMN ratio was highly specific
3. Positive predictive value was highest with I:T PMN ratio and also the same in negative predictive value
4. The goodness of fitness was conducted and I:T PMN ratio once again was the fittest model

Assessment of cut-off points of 2 and 5

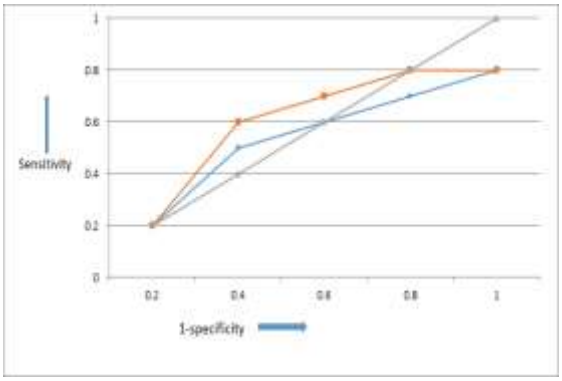
The higher the score the greater the certainty that sepsis was present.

Majority of neonates with sepsis had score>=5 and sensitivity =80% and specificity =90%. So score of 5 is more specific and increases the likelihood of sepsis.

Table 7: Performance of scores-2 and 5

Scores	Sensitivity (%)	Specificity (%)
2	10	43
5	80	90

ROC analysis of cut-off points-2 and 5



Discussion

Sepsis in newborn can be a devastating problem leading to morbidity and mortality.[8] Inability to adequately exclude the diagnosis of neonatal sepsis can result in unnecessary and prolonged exposure to antibiotics.[3] Thus laboratory tests that assist the clinicians in diagnosis of infection in neonates have considerable relevance. It helps in the early intervention compared to the culture reports, which may take days for the result to become positive and thus saving the lives of many neonates.[2]

The scoring system is significant in other way also, regarding its easy availability, low cost, less time consuming and practically possible in all laboratories, which makes it convenient for any common man to get a high risk neonate tested and diagnosed in time.[9]

Narasimha et al[10] have written an extensive review on significance of HSS in early diagnosis of neonatal sepsis. They found that 100% infants with history of sepsis had scores >=5, 42% infants with history of probable infection had score>=5, 41% of normal infants and 27% of infants with probable infections had the score>=2 which implies that sepsis was unlikely in these cases. Hence, when the performance of individual haematologic finding was calculated, total PMN count came out to be the most sensitive test followed by immature PMN count. In terms of specificity, TLC was the most specific one followed by I:T ratio.

S Ghosh et al[11] also assessed the utility of HSS in diagnosis of neonatal sepsis and found that abnormal I:T ratio followed by I;M ratio were the most sensitive indicators in identifying infants with sepsis. These two criteria along with thrombocytopenia had high negative predictive value over 94%.The study also found that higher the score the greater the certainty of sepsis being present.

In our study, we have correlated the sensitivity, specificity, positive predictive value, negative predictive value of various parameters with different groups and also with other studies.

Elevated I:T PMN ratio was found to be the most reliable indicator of sepsis in our study, also in various studies like those done by Ghosh et al[11] and Narasimha et al[10]. It was followed by immature PMN count in terms of sensitivity. There was no significant role of degenerative changes in diagnosis in our study.

Also in our study, total PMN count had a limited role in sepsis screening as shown by Akenzua[12], who inferred that there were patients who had normal PMN count but the band forms are raised and elevation was often very late and inconsistent.

Manucha et al[9] wrote an extensive review on utility of haematological parameters and CRP in the detection of neonatal sepsis and found that C-reactive protein does not have any advantage over HSS, either as a single test or in combination. In this study, score>=3 had the maximum sensitivity with 86% and negative predictive value of 96%. A combination of CRP with haematological parameters decreased the sensitivity and negative predictive value of HSS.

KB Khair et al[13] reviewed the role of HSS, C-reactive protein and serum haptoglobin in early diagnosis of neonatal sepsis. Score>=4 was found with sensitivity of 100% and specificity 60%. C-reactive protein had sensitivity of 75% and specificity of 74%. Haptoglobin was not found significant ($p<0.05$) with sepsis and sensitivity was very low. But combination of score>=4 and CRP showed sensitivity of 75%, specificity 85%, positive predictive value 41% and negative predictive value 96%.

Recently, attention has been directed to the leukocyte cell surface antigens as the diagnostic markers of sepsis.[10] Neutrophil surface CD64 expression has also been studied. Variety of other rapid detection tests like DNA probes, automated blood culture system etc are available but HSS can still be used as a screening test for diagnosing sepsis and to differentiate infected neonates from non-infected neonates.[10] It has high sensitivity and specificity, the certainty of sepsis being present with higher scores.[14,15] However, the simplification and standardisation of interpretation of this global test is still required.[16]

Conclusion

Haematological Scoring System is a simple, feasible, quick, cost-effective tool which can be used as screening test for early diagnosis of neonatal sepsis to decrease death toll. It may aid the clinicians in identifying the sepsis cases to institute proper antibiotic therapy and prevent unnecessary exposure of neonates to antibiotics and hence thereby preventing the development of resistance to these drugs.

References

1. Barbara JS. Infection of the neonatal infant. In: Behrman RE, Kliegman RM, Jenson HB, Stanton BF. Editors. Nelson textbook of pediatrics. 20th edition. Philadelphia: WB Saunders Company; 2015.p.794-811.
2. Aggarwal R, Sakar N, Deorari AK, Paul VK. Sepsis in the newborn. Indian J Pediatr2001;68:1143-1147.
3. Rasul CH, Hassan MA, Habibullah M. Neonatal sepsis and use of antibiotic in a tertiary care hospital. Pakistan J Med Sci. 2007;23(1):78-81.
4. Sharma M, Yadav A, Yadav S, Goel N, Choudhary U. Microbial profile of septicemia in children. Indian j. 2008;5(4):01- 05.
5. Kuruvilla KA, Pillai S, Jesudason M, Jana AK. Bacterial profile sepsis in a neonatal unit in South India. Indian pediatrics. 1998;35:851-858
6. Rodwell RL, Leslie AL, Tudehope DI. Early diagnosis of neonatal sepsis using a hematologic scoring system. J Pediatr. 1988;112:761–7.
7. Manroe BL, Weinberg AG, Rosenfeld CR, Browne R. The neonatal blood count in health and disease. I. Reference values for neutrophilic cells. J Pediatr1979;95(1):89-98.
8. Gladstone IM, Ehrenkranz RA, Edberg SC, Baltimore RS. A ten-year review of neonatal sepsis and comparison with the previous fifty-year experience. Pediatr Infect Dis J. 1990;9:819–25.
9. Manucha V, Rusia U, Sikka M, Faridi MM, Madan N. Utility of haematological parameters and C-reactive protein in the detection of neonatal sepsis. J Paediatr Child Health. 2002;38:459–64.
10. Narasimha A, Harendra Kumar ML. Significance of Hematological Scoring System (HSS) in early diagnosis of neonatal sepsis. Indian J Hematol Blood Transfus. 2011;27:14–7.
11. Ghosh S, Mittal M, Jaganathan G. Early diagnosis of neonatal sepsis using a hematological scoring system. Indian J Med Sci. 2001;55:495–500.
12. Akenzua GI, Hui YT, Milner R, Zipursky A. Neutrophil and band counts in the diagnosis of neonatal infections. Pediatrics. 1974;54:38–42.
13. Khair KB, Rahman MA, Sultana T, Roy CK, Rahman MQ, Shahidullah M, et al. Role of hematologic scoring system in early diagnosis of neonatal septicemia. BSMMU J. 2010;3:62–7.

14. Basu S, Guruprasad, Narang A, Garewal G. Diagnosis of sepsis in the high risk neonate using a hematologic scoring system. Indian J Hematol Blood Transf. 1999;17:32–4.
15. Sharma A, Kutty CV, Sabharwal U, Rathee S, Mohan H. Evaluation of sepsis screen for diagnosis of neonatal septicemia. Indian J Pediatr. 1993;60:559–63.
16. Varsha, Rusia U, Sikka M, Faridi MM, Madan N. Validity of hematologic parameters in identification of early and late onset neonatal infection. Indian J Pathol Microbiol. 2003;46:565–8.