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A Study of Validity of Haematological Parameters in the Diagnosis of Neonatal Sepsis

KEYWORDS: Sepsis,HSS,ANC

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ABSTRACT *Background:The current study is undertaken to study the validity of haematological parameters in the early diagnosis of neonatal septicemia using Rodwell"s scoring criteria which includes simple laboratory tests such as total leucocyte count (TLC),absolute neutrophil count (ANC),immature neutrophill count (I),immature to total neutrophil ratio (I:TNR),immature to mature neutrophil count ratio,platelet count and degenerative changes in neutrophils.*

Materials and methods: Infants were enrolled in the study if there were predisposing perinatal factors or if there was clinical suspicion of sepsis. The HSS assigns a score of one for each of the seven criteria found to be significantly associated with sepsis with one exception. An abnormal total count is assigned a score of 2 instead of 1, if no mature polymorphs are seen on the peripheral smear to compensate for the low I:M ratio. Sensitivity, specificity, positive and negative predictive values were evaluated for each of the seven criteria of HSS.

Results:From the present study it was found that out of 50 cases with culture proven sepsis, 42 (84%) infants had score ≥5, and 8 (16%) had scores 3-4.42 out of 50 cases which were culture positive,were also sepsis positive on HSS.HSS has a sensitivity of 84%, specificity of 77.15% .

Conclusion:Hematologic scoring system (HSS) should improve the efficiency of the CBC as a screening test for sepsis until a reliable diagnostic test is available.

INTRODUCTION

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life. Neonatal sepsis encompasses systemic infections of the newborn including septicemia, meningitis, pneumonia, arthritis, osteomyelitis and urinary tract infection of the newborn.[1]

When pathogenic bacteria gain access into the blood stream, they may cause overwhelming infection without much localization termed as septicemia or may get predominantly localized to the lungs resulting in pneumonia, or the meninges causing meningitis.[2]

Systemic bacterial infection during the first month of life have remained a major cause of infant morbidity and mortality despite the development of broad spectrum antibiotics.The incidence of neonatal sepsis according to the data from national neonatal perinatal database (NNPD,2002-2003) is 30 per 1000 live births.[3] Sepsis is most common in preterm and low birth weight neonates due to decrease immunity to combat bacterial infections but term babies are not exclusion from the infection.

Neonatal sepsis can be divided into two subtypes depending upon whether the onset of symptom is during first 72 hours of life or later.The term early onset neonatal sepsis refers to those infections which occur in first 72 hours of life.It is caused by organisms prevelant in the genital tract or in the labour room.The predisposing factors include low birth weight (LBW),prolonged rupture of membranes,foul smelling liquor,multiple per vaginum examinations,maternal fever,difficult or prolonged labour and aspiration of meconium.[2]

Late onset sepsis occurs after 72 hours of life.Infections are caused by the organisms thriving in the external environments of the home or the hospitals.The infection is often

transmitted through the hands of the care providers.The predisposing factors include LBW,lack of breastfeeding, poor cord care,superficial infections, aspiration of feeds and disruption of skin integrity with needle pricks and use of intravenous fluids.[2]

Blood culture is the Gold standard test for diagnosis of neonatal sepsis.[1]Although a positive culture is obtained in 30-75% of cases,it is time consuming procedure requiring 48-72 hours and and demands a well equipped laboratory. Institution of antibiotics before culture often increases the problem of unnecessary exposure to antibiotics and bacterial resistance.

The current study is undertaken to study the validity of haematological parameters in the early diagnosis of neonatal septicemia using Rodwell"s scoring criteria [4] which includes simple laboratory tests such as total leucocyte count (TLC),absolute neutrophil count (ANC),immature neutrophill count (I),immature to total neutrophil ratio (I:TNR),immature to mature neutrophil count ratio,platelet count and degenerative changes in neutrophils(toxic granules,cytoplasmic vacuoles etc.).

MATERIALS AND METHODS

In this prospective study,infants were enrolled if there were predisposing perinatal factors or if there was clinical suspicion of sepsis.

The study included three groups:

- Group 1—infants with sepsis with positive blood cul-

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tures.

- Group 2—infants with probable infection with strong clinical history but negative blood cultures.
- Group 3—normal infants without any evidence of sepsis.

120 Newborn babies in age of 0 to 28 days which were admitted in the Department of Paediatrics were included in this study. After taking a careful history specified questionnaire was designed and the detailed information was recorded by the investigator.

With all aseptic precaution at least two ml of blood was withdrawn from suspected sepsis patients in within 24 hours of admission. 1 ml sample was anticoagulated with EDTA and using Sysmex XS-800i automated haematology analyzer, values of total leucocyte count (TLC) and platelets count were noted and counter checked . TLC and platelet count were also done by direct counting in a Improved Neubauer`s Chamber.

Peripheral blood smears were made and stained by Leishman stain. Differential

leucocyte counts (DLC), total neutrophil count(TNC), immature neutrophil count (I) (including band form), mature neutrophil count (M) were performed. IT (immature to total neutrophil) ratio and IM (immature to mature neutrophil) ratio were calculated. IT ratio is

calculated dividing the total immature count by total neutrophil count (including both mature and immature neutrophil count).

The peripheral blood smears of all newborns were analysed for early diagnosis of neonatal sepsis using the hematological scoring system of Rodwell et al. The HSS assigns a score of one for each of the seven criteria found to be significantly associated with sepsis with one exception. An abnormal total count is assigned a score of 2 instead of 1, if no mature polymorphs are seen on the peripheral smear to compensate for the low I:M ratio. Sensitivity, specificity, positive and negative predictive values were evaluated for each of the seven criteria of HSS.

CRITERIA	ABNORMALITY	SCORE
TOTAL WBC COUNT	≤5000/µl	
	≥25,000 at birth	1
	≥30,000 after 12-48 hours	1
	≥21,000 day 2 onwards	
TOTAL PMN COUNT	No mature 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 granules/cytoplasmic vacuoles	1
PLATELET COUNT	≤1,50,000	1

Normal values are:
Total PMN count 1800-5400
Immature PMN count 600
Immature:total PMN count 0.120

Interpretation:

Score	Interpretation
≤ 2	Sepsis is very unlikely
3 or 4	Probable sepsis
> 5	Sepsis or infection is very likely

RESULTS

Out of the 120 infants, based on clinical findings and laboratory data were classified into three categories: Sepsis (*n*=50), probable infection (*n*=25) and normal (*n*=45). [Table 1].Out of 50 cases with culture proven sepsis, 42 (84%) infants had score ≥5, and 8 (16.%) had scores 3-4.10 (40%) cases with probable infection had scores 3-4; 9 (36%) had score 5.7 (15.55%) of the normal infants had score 5 suggesting the presence of sepsis and 8 (17.77%) had scores 3-4 suggesting the possibility of sepsis in these cases. **[Table 1].**

42 out of 50 cases which were culture positive,were also sepsis positive on HSS.HSS has a sensitivity of 84%,specificity of 77.15%,PPV of 72.41%,NPV of 87.09 %.**[Table 2].**So haematological scoring system can be a usefull tool for the diagnosis of neonatal sepsis as it has a very good sensitivity.

Table no 1:Distribution of cases according to sepsis score

	Score 0-2(%)	Score 3-4(%)	Score >5(%)
Sepsis(50)	0	8(16%)	42(84%)
Probable sepsis(25)	6(24%)	10(40%)	9(36%)
Normal(45)	30(66.66%)	8(17.77%)	7(15.55%)
Total cases(120)	36	26	58

Table 2:Distribution of cases according to sepsis on blood culture and sepsis on haematological score

	Sepsis positive on blood culture	Sepsis negative on blood culture	Total
Sepsis positive on HSS	42(84%)	16(22.85%)	58
Sepsis negative on HSS	8(16%)	54(77.15%)	62
Total	50	70	12

Table 3: The performance of individual hematological parameter in diagnosing neonatal septicemia

Haematological parameters	Sensitivity (%)	Specificity (%)	Positive Predictive Value(%)	Negative Predictive Value(%)
Total WBC count	60	85.71	75	75
Total PMN count	90	65.71	65.22	90.19
Immature: PMN count	96	87.14	84.21	96.82
Immature: Total PMN ratio	92	88.57	85.19	93.94
Immature: Mature PMN ratio	58	92.85	85.29	75.58
Degenerative changes	70	62.85	57.37	74.58
Platelet count	64	81.3	71.11	76

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Out of the total 120 cases,66 (55%) cases were preterm and 54 (45%) cases were term.The study also showed male preponderance (60% males and 40% females).

Amongst the all seven haematological parameters immature PMN count was found to be highest sensitive(96%) followed by immature:total PMN ratio (92%),total PMN (90%),degenerative changes (70%).Immature:mature PMN was found to be highly specific test with a specificity of 92.85% followed by immature:total PMN ratio. Immature:mature PMN has highest positive predictive value (85.29%) whereas total PMN has highest negative predictive value (96.82%).**[Table 3]**

DISCUSSION

Septicemia is the commonest cause of neonatal mortality and morbidity.[5] Early diagnosis of neonatal septicemia is still a great challenge. For early diagnosis of neonatal septicemia a hematologic scoring system (HSS) of Rodwell are preferable because it includes all parameters. Haematological parameters should accurately predict the presence or absence of infection and be reliable.[6]

The definitive diagnosis of septicemia is made by a positive blood culture, which requires a minimum of 48-72 hours, yields a positive result in 10-60% of cases. Blood culture remains the gold standard for diagnosis of neonatal sepsis, yet it is important to develop effective screening tools which can presumably diagnose or exclude neonatal sepsis at the time of presentation and that is why this study was carried out. The early diagnosis of neonatal septicemia is primarily based on clinical evaluation but laboratory diagnosis requires a microbiologic-clinical correlation. Many babies were treated empirically with antibiotics for several days while waiting for bacteriologic culture for suspected infection. In this study 41.67% neonates were considered as proven sepsis by blood culture. However suspected sepsis groups (58.33%) comprises a difficult diagnostic group and could not be ignored, because fatal infection had been reported in other study in the presence of negative blood culture[7].

Early diagnosis of neonatal septicemia is still a great challenge. For early diagnosis of neonatal septicemia a hematologic scoring system (HSS) of Rodwell was introduced in the past. It included hematological parameters and showed that such score could accurately predict the presence or absence of infection and be reliable[4].

Among the included cases of suspected sepsis, the predominance of male may be due to the factors regulating the synthesis of a globulin are situated on the X chromosome leading male gender less immunologically protected than the females.

Preterm and very low birth weight babies are more susceptible to infection due to low

level of IgG and lower defense mechanism. Premature rupture of membrane (PROM) for >24 hours has to be an important risk factor in neonatal septicemia.This study shows that HSS has a sensitivity of 92%,specificity of 82.86%, PPV of 79.31% and NPV of 72.41%.Munazza Saleem et.al.[8] also found that the HSS was having a sensitivity of 90%, specificity of 74.5%, Positive Predictive Value was 65.9% and Negative Predictive Value was 93.2%.Manucha V et.al.[9] observed that a haematological score > or = 3 had a sensitivity of 86% and NPV of 96%.

Total leukocyte count (TLC) has a sensitivity of 60%, specificity of 85.71%, with PPV 75% and NPV 75% which were consistent with others like Makkar et.al.[10] , Khair et.al[11] .In this study total PMN count has a sensitivity of 90% and a specificity of 65.71% which is consistent wiyh studies like Khair et. al[11] and Narasimha et. al.[12].Immature PMN count is found to be of highest sensitivity (96%).Khair et. al.[11] and Makkar et. al.[10] found it to be 83% and 96.87% sensitive respectively.Immature:total PMN is 92% sensitive and 88.57% specific which is consistent with Namedo et. al.[13] and Buch et. al.[14].Immature:mature PMN count is a highly specific test (specificity 92.85%) which is similar to other studies like Khair et. al.[11]

Neonates with sepsis develop thrombocytopenia, possibly because of increased platelet destruction, sequestration secondary to infections, failure in platelet production due to reduced megakaryocytes or damaging effects of endotoxin[15]. In this study we found thrombocytopenia has sensitivity of 64%, specificity 81.45%, PPV 71.11% and NPV 76%. This parameter could be used as an early but nonspecific marker for sepsis. These results were consistent with other studies like Khair et.al[11],Speer et al.[16] .Rodwell et al.[4], Philip et al.[17],and Basu et al.[18] Shiraji et.al.[19] also found that thrombocytopenia is associated with neonatal sepsis.

CONCLUSION

As no single individual hematological parameter is superior in comparison to another in predicting neonatal sepsis, a combination of these parameters in the form of HSS has been recommended.We concluded that the hematologic scoring system are useful test to distinguish the infected from non infected infants.These are simple, quick, cost effective and readily available tool with high sensitivity and specificity in the early diagnosis of neonatal sepsis.In our study HSS may provide a 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 as well as will minimize the risk of emergence of resistant organism due to misuse of antibiotics.

REFERENCES

1. Shankar M J, Agarwal R and Deorari AK (2008). Sepsis in the new born. Indian Journal of Pediatrics 75 (3) 261- 270.
2. O P Ghai,Vinod K Paul,Arvind Bagga,Essential Pediatrics,Seventh Edition,2010;136.
3. Department of Pediatrics (2002-03), National Neonatal Perinatal Database. [online] New Delhi: All India Institute of Medical Sciences; NNPD nodalcenter.Available:http://www.newbornwhocc.org/pdf/HRRC_Report_2002-03.pdf (no dates).
4. Rodwell RL, Leslie AL, Tudehope DI. Early diagnosis of neonatal sepsis using a hematologic scoring system. J Pediatr 1988;112:761-7.
5. Sharma M, Yadav A, Yadav S, Goel N, Chudhary U. Microbial profile of septicemia in children. Indian j. 2008; 5(4) : 01-05.
6. Fowlie PW, Schmidt B. Diagnostic tests for bacterial infection from birth to 90 days-A systametic review. Arch Dis Child Fetal Neonatal. 1998; 78 : 92-98.
7. Comparison of broad range 16 S r DNA PCR to conventional blood culture for diagnosis of sepsis in the newborn. Egyptian J Med Human Genetics 2013; 14(4):403-11.
8. Munazza Saleem, Kiran Israr Shah, Sehrish Mukhtar Cheema, Matloob Azam, Hematological Scoring System for Early Diagnosis of Neonatal Sepsis, Journal of Rawalpindi Medical College (JRMC); 2014;18(1):68-72.
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.

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10. Makkar M, Gupta C, Pathak R, Garg S, Mahajan NC. Performance evaluation of hematologic scoring system in early diagnosis of neonatal sepsis. J Clin Neonatol 2013;2:25-9.
11. 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.
12. 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.
13. Namedo UK,Singh HP,Rajput VJ,Khuswaha JS.Haematological indices for early diagnosis of neonatal septicemia.Indian Paediatrics 1985;22:287-292.
14. A.C. Buch, V. Srivastava, Harsh Kumar and P.S. Jadhav, Evaluation Of Haematological profile in early diagnosis of clinically suspected cases of Neonatal Sepsis, International Journal of Basic and Applied Medical Sciences ISSN: 2277-2103 (Online), 2011 Vol. 1 (1) September-December, pp.1-6.
15. Arif SH, Ahmad I, Ali SM, Khan HM. Thrombocytopenia and bacterial sepsis in neonates. Indian J Hematol. Blood Transfus 2012;28(3):147-51.
16. Speer CP, Gahr M, Schröter W. Early diagnosis of neonatal infection. Monatsschr Kinderheilkd 1985;133:665-8.
17. Philip AG, Hewitt JR. Early diagnosis of neonatal sepsis. Pediatrics 1980;65:1036-41.
18. 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.
19. Haider Shirazi,Sadia Riaz,Rida Tahir, Role of the Hematological Profile in Early Diagnosis of Neonatal Sepsis, Ann. Pak. Inst. Med. Sci. 2010; 6(3): 152-156.