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Haematological Profile As A Screening Tool For Neonatal Sepsis : A Hospital Based Study

¹Dr Neha Batra, Assistant Professor, Department Of Pathology, Veer Chand Singh Garhwali Medical Institute & Research Centre, Srikot, Srinagar Gharwal, Uttrakhand.

²Dr Deepa Hatwal, Associate Professor, Department Of Pathology, Veer Chand Singh Garhwali Medical Institute & Research Centre, Srikot, Srinagar Gharwal, Uttrakhand

³Dr Arvind Kumar, Assistant Professor, Department Of Pathology, AIIMS Rishikesh Uttarakhand

⁴Dr Sheela Chaudhari, Professor, Department Of Pathology, Veer Chand Singh Garhwali Medical Institute & Research Centre, Srikot,Srinagar Gharwal,Uttrakhand

⁵Dr S.K Barpanda, Associate Professor, Department Of Pathology, Veer Chand Singh Garhwali Medical Institute & Resarch Centre, Srikot, Srinagar Gharwal, Uttrakhand

Corresponding Author: Dr Deepa Hatwal, Associate Professor, Department Of Pathology, Veer Chand Singh Garhwali Medical Institute & Research Centre, Srikot, Srinagar Gharwal, Uttrakhand

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Abstract

Objective: The present study was undertaken to emphasize the role of hematological scoring system (HSS) in the early detection of neonatal sepsis.

Material And Methods: The study enrolled 100 neonates admitted in nicu with clinical suspicion of sepsis. The detailed perinatal history was recorded. Blood sample was taken for routine blood count , Esr and crp along with peripheral smear for each patient which was analysed using haematological scoring system that included total leukocyte count, total polymorphonuclear neutrophils (PMN) count, elevated immature PMN count, elevated immature: Total (I:T) PMN ratio, immature: Mature (I:M) PMN ratio ≥ 0.3 , platelet count $\leq 150,000/\text{mm}^3$ and pronounced degenerative or toxic changes in PMNs. Blood culture was taken as a standard test. Sensitivity, specificity, positive and negative predictive values (NPVs) were calculated for each parameter. **Results:** Out of the 100 infants, those in full blown sepsis were 40, probable sepsis category were 21 (n=21) and remaining were normal (n=39) asymptomatic.55% had positive blood culture. Of the total 46 (46%) were term and, 54 (54%) preterm. The study had 42(42%) males and 58 (58%) females. Maximum 57 (57%) neonates presented within the first 24 h of life. For sepsis and probable sepsis, I:T and I:M PMN ratio have highest sensitivity, specificity, positive predictive value and negative predictive value followed by total PMN count.

Conclusion: Haematological profile is a simple, easy, cheap and quick adjunct for the diagnosis of clinically suspected cases of neonatal sepsis.

Introduction

Septicaemia is a recognized cause of morbidity and mortality in the new-borns in the developing countries Neonatal sepsis is the response of neonates to any kind of infections.¹The incidence of neonatal sepsis in India is 30

per 1000 live-births (NNPD 2002-03). ² It can be early or late in onset. In early onset, maximum cases are observed within 24 h of life, remaining thereafter up to 7 days and 'late onset' follows after the first week¹. The clinical signs of neonatal sepsis are versatile and they have varying predictive values for the diagnosis of sepsis.

The most reliable diagnostic of neonatal sepsis, often referred to as the gold standard, is a blood culture test for bacteria. While this test is the most reliable available, it can take 48 hours to obtain the results. As a result, treatment must often begin before the results are known. An additional complication is the fact that the blood culture test can be negative for one in five subjects with sepsis.

Rapid diagnostic test(s) (sepsis screen test, the haematological scoring system) differentiate infected from non-infected infants neonate particularly in the early newborn period and have the potential to make a significant impact on survival of neonate so we conducted this study to access significance of the cost-effective markers tests for the diagnosis of early neonatal sepsis so that prompt treatment can be initiated and neonatal deaths can be minimized.

Objective

The present study was undertaken to emphasize the role of hematological scoring system (HSS) in the early detection of neonatal sepsis.

Materials and Methods

Study Design: Cross sectional study.

Source of Data: Neonates admitted to NICU of Hemwati nandan bahuguna hospital with clinical suspicion of sepsis from july 2016 to june 2018.

Sample Size: All the babies satisfying the inclusion criteria and admitted during the study period were included in the study. This came up to 100 newborns.

Inclusion Criteria: Neonates (<28 days) admitted to our NICU with clinical suspicion of sepsis.

Exclusion Criteria

- Neonates who received antibiotics before admission.
- Neonates with congenital malformations, birth asphyxia, inborn error of metabolism, hemolytic jaundice, gestational age < 33 weeks, respiratory distress syndrome (due to surfactant deficiency) were excluded.
- Neonates who underwent surgery.

Data Collection

Institutional Ethical committee clearance was taken prior to the study . All the babies underwent sepsis screen and blood culture. Blood samples were obtained under strict aseptic precautions from peripheral venepuncture in all neonates within 24 h of admission, before initiation of antibiotic therapy.Peripheral blood smears were prepared within 1-2 hr of venipuncture, stained with Leishman stain and examined under oil immersion light microscopy at a final magnification of ×1000. The sepsis work up included blood culture and routine blood counts along with the hematologic score. Total leucocyte count was obtained using sysmex 5 part automated analyser with standard calibration and corrected for nucleated red blood cells. Differential counts were performed on Leishman stained smears and about 100 cells were counted. The peripheral blood smears of all newborns from birth up to 1 week were analyzed 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 (Table 1) with one exception. An abnormal total count is assigned a score of 2 instead of 1, if no mature polymorphs are seen in the peripheral smear to compensate for the low I:M ratio. Statistical Analysis that is senitivity, specificity, positive and negative predictive

values were evaluated for each of the seven criteria of HSS. Data was compiled and statistically analyzed by using SPSS software for chi square test and p value <0.05 was considered as significant. Sepsis screen included following tests: Total Leucocyte Count (TLC), absolute Neutrophil Count (ANC), Platelet Count (PC), Immature: Total Neutrophil ratio (I: T ratio), Erythrocyte Sedimentation Rate (ESR), C-reactive protein (CRP)tests. CRP was estimated using Latex agglutination slide test.

Under strict aseptic measures samples of blood (2ml.) for culture and sensitivity were collected, these 2ml. of blood were added to a bottle containing (18ml.) Brain-Heart infusion broth. One ml. of blood was collected in a tube without EDTA and was used for estimation of C-reactive protein (CRP) by latex agglutination technique. The cut off values of the studied parameters for positive tests were:C-reactive protein (CRP) > 6mg./l, Erythrocyte Sedimentation Rate (ESR) > 15mm/hr. , Platelets count < 150000/cmm., White Blood cells Count (WBCs) < 5000/cmm. Or >20000/cmm., Absolute Neutrophil Count (ANC)-an age adjusted normal reference range was used and neutrophilia and neutropenia were considered abnormal, Immature to Total neutrophils ratio (I /T) ratio > 0.2 considered abnormal(3)

Results

The study was conducted on 100 neonates presenting with clinical features suspected of neonatal sepsis. based on clinical findings and laboratory data were classified into three categories, the confirmed cases of neonatal sepsis with positive blood culture were labeled as group-A, symptomatic neonates having clinical diagnosis of sepsis but negative blood culture were labeled as group-B and normal asymptomatic neonates, who served as control, were labeled as group-C. Out of the 100 infants,:neonates in full blown sepsis were 40,those in probable infection category were 21 (n=21) and remaining were normal (n=39) asymptomatic.

Of the total46 (46%) were term and 54 (54%) preterm. The study had 42(42%) males and 58 (58%) females. Maximum 57 (57%) neonates presented within the first 24 h of life [Table 2]. Proven sepsis was confirmed by blood culture in 55% of the neonates. coagulase negative staphylococcus are the most common organism isolated followed by escherischia coli. acinatorbacter spp. and enterobacter spp.

Table-1 Haematological scoring system

1	Total wbc count	≤5,000/µl	
		\geq 25,000 at birth	0
		≥30,000—12-24hrs	1
		≥21,000—day2	
		onwards	
2	Total pmn count	Increased or	1
		decreased	
3	I:T PMN ratio	<0.20	0
		Increased	1
4	I:M PMN ratio	0.3≤	0
		0.3≥	1
5	Degenerative	Toxic	1
	changes in PMN	granules/cytoplasmic	
		vacuoles	
6	Platelet count	≤1.5 lakhs/µl	1

Table	2:	Demographic	and	maternal	data	of	the	study
group								

Parameters		Frequency
Age (days)	0-7	49
8-14		28
15-21		11
>21 day	S	12
Sex		

Male	e	42
Fema	lle	58
Gestation		
Pret	erm	54
Ter	m	46
Mode of delivery		
No	ormal	42
Cae	esarean	58
Weight Norr	nal	45
Low birth weight		55

Table-3hematological scores of neonates of present

Study

haematologi	sepsis(n=4	probable	normal(n=3
cal score	0)	infection(n=2	9)
		1)	
0-2	-	6	32
3-4	18	11	6
≥5	22	4	1

wbc – white blood cells; pmn – polymorphonuclear neutrophils; I:T pmn ratio – immature

Total ratio; I:M pmn ratio – immature: Mature polymorph ratio

Discussion

HSS offers a rational approach in the diagnosis of neonatal septicemia and thus prevent the prolong antibiotic usage. However Clinical parameters cannot be ignored, as in our study.

Features of sepsis were more commonly seen in pre-terms (57%) than in full-term infants (43%) This is because, preterm are more susceptible to infections than are the terms, which is due to their poor immune system, low levels of immunoglobulins and low weight at birth ⁴. *Rod well RR et al (1988)* enrolled 287 neonates in a study, who had predisposing perinatal factors or clinical suspicion of sepsis ,also Premature rupture of membrane (PROM) for >24 hours has to be an important risk factor in neonatal

septicemia because PROM poses risk of ascending infection to the fetus. Since the scoring system is easily available, accessible, cost effective, less time consuming and a practical test, most infants can be diagnosed in an early stage thus avoiding mortality and morbidity.⁵ Ghosh S. et al (2001) studied the hematologic profiles of 103 new born infants according to the scoring system of Rodwell's et al for the early detection of sepsis in high risk infants. They found it to be a simple, quick and cost effective tool which could provide a guideline to decisions regarding antibiotic therapy. Leucocytosis is not a sensitive marker for diagnosing sepsis, on the other hand specificity was found to be good i.e 91% which was consistent with other studies⁶. The reason for this high specificity but low sensitivity might be due to time interval between the onset of bacterernia and sampling ⁷.Dulay et al (2008) studied neonatal hematological indices and assessed sepsis categorization in all 68 neonates. Laboratory criteria were based on modification of the criteria of Rodwell et al. He found that Early-Onset Neonatal Sepsis (EONS) and WBC count and absolute neutrophil count (ANC) were not significant. In contrast, the associations with absolute band count (ABC), hematocrit, hemoglobin, bandemia, lymphocytes and I/T ratio continued to remain significant.⁸ Shirazi et al (2010) studied 138 neonates with suspected sepsis. They evaluated the usefulness of white blood cell count and C-reactive protein as an early indicator of neonatal septicemia.⁹ Narasimha A, Harendra kumar (2011) analysed 50 peripheral blood smears of newborns for neonatal sepsis using HSS of Rodwell et al. criteria. They found that an abnormal immature to total neutrophil ratio (I: T), followed by an abnormal immature to mature neutrophil ratio (I: M), were most sensitive indicators in the diagnosis of neonatal Sepsis.¹⁰ In neonatal sepsis, probably because of utilization at the infection site and adhesion to endothelial cells,

neutropenia is a more common finding than neutrophilia [11]. Berger et al. recommended a value $<4 \times 109/L$ (sensitivity 78%, PPV 25%) to detect early onset sepsis [12].In the present study, ANC <1750/mm3 had a sensitivity of 66% and a PPV of 81% in detection of sepsis. In our study, the total PMN count had a limited role in sepsis screening. This finding correlated well with the study done by vinay BS etal.(13) Elevated I:T ratio was found to be the most reliable indicator of sepsis in our study, and also in various other studies like those done by Ghosh et al and Philip AGS et al, immature PMN count and I:T PMN ratio was also a very sensitive indicator of neonatal sepsis. Degenerative changes in the PMNs made no significant contribution in the diagnosis, in this study. Moreover the presence of toxic granules indicates the production of unusual PMNs during infection and stress induced leucopoiesis. They are never seen in healthy babies. Their presence invariably indicates sepsis, but their count is not always increased.^{6,7} Thrombocytopenia was frequently associated with sepsis and indicated poor prognosis. This is thought to be due to increased platelet destruction, sequestration secondary to infections, failure in platelet production due to reduced megakaryocytes or damaging effects of endotoxin^{.14}In this study we found thrombocytopenia in 35% cases with sensitivity of 77%, specificity 65%, PPV 45% and NPV 55%. This correlated well with various other studies such as done by Makkar, et al^1 . In resource deficient places, where even a blood culture is not possible, this haematological scoring system, is a boon in rapid and effective diagnosis regardless of other expensive, less feasible tests such as DNA probe and fluorometric detection systems etc.Our study also correlates with study done by Makkar et al that higher score favours full blown septicemia.

Conclusion

In our study, certain parameters in heamatological scoring system like i/t PMN ratio and i/m PMN ratio have proven to be highly sensitive and specific in early detection of sepsis and differentiating full blown sepsis from probable sepsis patient so that unnecessary institution of antibiotics to the neonate is prevented and simultaneously development of resistance to the particular antibiotic can be avoided. Also Hss is an effective alternative to time consuming methods like culture etc and for initiating prompt treatment.

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