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Evaluation of hematological scoring system in early diagnosis of neonatal sepsis

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Abstract

Neonatal septicemia was one of the major risk factors contributing to the high perinatal and neonatal mortality and morbidity. The definite diagnosis of septicemia was made by a positive blood culture which required a minimum period of 48-72 hours and yielded a positive result in 30-70% of cases. Hence there was a critical need for laboratory tests that aid in the rapid diagnosis of neonatal sepsis. We studied the Rodwell's hematological parameters including the various changes seen in the peripheral smears of 160 neonates clinically suspicious of having sepsis. Out of 160 infants, 28 (17.50%) cases with proven sepsis, 80 (50%) cases with probable sepsis and 52 (32.50%) as normal infants. 116 (72.5%) infants had early onset neonatal sepsis and 44 (27.50%) infants had late onset sepsis. The advantage of study was that these can be done rapidly even in small hospitals, allowing prompt treatment to neonates with sepsis and minimizing therapy. It can be good predictors of short term neonatal outcome and carries diagnostic and prognostic value.

Keywords: Neonatal Sepsis, Rodwell's Hematological Scoring System, HSS, Blood Culture, Peripheral Smear.

Introduction

Sepsis is defined as a systemic inflammatory response syndrome (SIRS) associated with infection diagnosed either on microbiological cultures or strong clinical evidence of infection.(1) Sepsis neonatorum is used to describe systemic response to infection in newborn.(2)

Neonatal infections currently cause 1.6 million deaths annually in developing countries. Sepsis and meningitis responsible for most of these deaths.(3) Neonatal sepsis is an important cause of neonatal morbidity and mortality; it is responsible for about 30-50% of total neonatal deaths in developing countries.(4) The incidence of neonatal sepsis according to the data from National Neonatal Perinatal Database (NNPD, 2002-03) is 30 per 1000 live births.(5) The newborn infants are more prone to bacterial invasion than the older children and adults due to weaker immune system.(6) The infection can be contracted either from mother via transplacental route, ascending infections, during passage through an infected birth canal or exposure to infected blood at delivery.(7)

Diagnosis of neonatal septicemia may be difficult as early signs are subtle and nonspecific, but its early detection is critical also, as the illness can be rapidly progressive and sometimes fatal.(7) Newer inflammatory markers such as interleukin-6, interleukin-8 and plasma elastase are highly sensitive and specific to diagnose neonatal sepsis and septic shock but they require sophisticated and expensive kits.(8) Blood culture is still considered as a gold standard for diagnosis of septicemia, however it is time consuming, requires well equipped set up and yield is low (8-73%).(9)

Therefore to avoid irrational use of antibiotics just based on clinical suspicion, various other reliable hematological laboratory tests giving quick results have also been evaluated. Among them complete blood count along with the various neutrophil parameters and C-reactive protein are most frequently used.

Considering above all drawbacks of blood culture the present study was done to evaluate and highlight the importance of simple, quick, cost effective hematological scoring system which may aid clinicians to reach a probable diagnosis, avoiding unnecessary use of antibiotics and decreasing death toll.

Material and Methods

This study was carried out in neonates clinically suspected to have sepsis or had maternal history of infection hospitalized to our institute. A Total of 160 cases were studied. A detailed clinical history was recorded with reference to age, sex, weight, maternal history and presenting complaints.

Inclusion criteria: All the neonates clinically suspected to have sepsis or had maternal history of infection.

Exclusion criteria: Neonates with

a. Major congenital anomalies
b. Inborn errors of metabolism, Hemolytic jaundice.

Methods

Sample collection was done under all aseptic precautions. 0.5–1 ml of blood sample was collected by peripheral venipuncture in vaccutainer tubes with trisodium EDTA as anticoagulant and 1-2 ml blood sample was collected in paediatric blood culture bottle. Collected samples were subjected for sepsis work up which involved complete blood count, along with peripheral smear examination for hematological scoring system and blood culture and sensitivity.

The total leucocyte count and platelet count were measured on Automated analyzers, Cellenium 19 (cell counter) and also confirmed on Peripheral smear.

Peripheral blood smear were prepared within a hour of collection, stained with Leishman stain and examined

under oil immersion. Smears were analyzed using Rodwell et al Hematological scoring system.(HSS)[10]

The HSS had assigned a score of one for each criteria found to be significantly associated with sepsis (Table 1) with one exception. An abnormal total count was assogned a score of 2 instead of 1, if no mature polymorphs were seen on the peripheral smear to compensate for the low Immature/Mature (I:M) ratio.

Table 1: Hematological Scoring system

Criteria	Abnormality	Score
Total WBC Count	<5000/cmm >25000 at birth >30000 12-24 hours >21000 Day 2 onwards	1 1 1 1
Total PMN Count	No mature PMN Increased/Decreased	2 1
Immature PMN Count	Increased	1
I:T PMN Ratio	Increased	1
I:T PMN Ratio	>0.3	1
Degenerative changes	Toxic-granules/ Cytoplasmic vacuoles	1
Platelet count	<150000/cmm	1

Peripheral Smear reporting: A differential leucocyte count was performed on Leishman stained blood smears by counting at least 200 cells to obtain the total neutrophil count (TNC), immature neutrophil count (IM), including bands and stabs; and mature neutrophil count (M). Immature polymorphonuclear (PMN) cells include promyelocyte, myelocyte, metamyelocytes and band form. A band was defined as a neutrophil in which the nucleus was indented more than one half, but in which isthmus between the lobes was wide enough to reveal two distinct margins with nuclear material between. Using these values, Immature/mature polymorphonuclear cell (I/M) and Immature/Total Polymorphonuclear cell (I/T) ratios were calculated.

Degenerative changes such as toxic granulation, Dohle bodies, and cytoplasmic vacuolization were also examined. Blood culture: One mililitre of blood was inoculated aseptically into 20ml of glucose broth for culture and sensitivity.

The diagnosis of sepsis was made when there were positive findings on blood culture. Infants were classified as having probable sepsis when the blood culture was negative, but there was a strong clinical history of infection. Infants were considered to be normal when blood culture was negative and there was no strong clinical evidence of infection.

Statistical Analysis

The data collected was statistically analysed and sensitivity, specificity, PPV(Positive Predictive Value) and NPV (Negative Predictive Value) for each of the hematological parameter was evaluated.

Results

The present study was conducted on 160 neonates who clinically presented with symptoms of sepsis.
Neonates in present study were classified according to the age and gender:

Age (in days)	Males	Females	Total
<3	70	46	116
>3	30	14	44
Total	100	60	160

Frequently presenting clinical features in infants were refusal to feed in 53 (33.13%) and fever 26 (16.25%), while premature rupture of membrane in 38 (23.75%) was most commonly associated maternal risk factor in our study.

Total score categories and blood culture findings were compared. Of 28 culture positive cases 20 (74.42%) were with score >5 and 8 (28.75%) with score 3-4. Out of 132 culture negative cases 79 (59.84%) were with score 0-2 and 48 (36.36%) were having score 3-4.

Discussion

Neonatal sepsis, sepsis neonatorum and neonatal septicemia are terms that are used to describe the systemic response to infection in the newborn infant.[6]

Monroe devised a criteria which used three parameters of total PMN count, immature PMN count and I:T ratio.[11] Whereas in this study we used hematological scoring system with more indices.

In our study we evaluated performance of individual hematological parameters in diagnosing neonatal sepsis. The sensitivity of total polymorphonuclear count for diagnosing sepsis was maximum i.e., 96.43%, followed by immature polymorphonuclear count and I:M ratio with sensitivity 89.29% and 85.71% respectively. Degenerative changes in neutrophils were highly specific 95%, followed by I:T ratio and total leucocyte count 84.09% and 83.33% respectively. Positive predictive value was highest i.e. 60% in degenerative changes in neutrophils. Negative predictive value was more than 90% in parameters like Total PMN count, immature PMN count and I:M ratio.

Not a single individual parameter is superior in comparison to another in predicting neonatal sepsis, a combination of these parameters in the form of HSS has been recommended.

Hematological score interpretation was categorized into three categories:
Score 0-2: Sepsis unlikely
Score 3-4: Sepsis is possible
Score >5: Sepsis or infection very likely

The higher the score of HSS, the greater was the likelihood of sepsis. The HSS increases the diagnostic accuracy of the complete blood count as a screening test for sepsis and simplifies and standardizes its interpretation. The early diagnosis of neonatal sepsis

with the help of HSS may provide a guideline to decisions regarding antibiotic therapy and thereby minimizes the risk of emergence of resistant organisms due to misuse of antibiotics.

In study done by Aparna Narasimha et al, about 50 peripheral blood smears of all newborns collected were analysed for neonatal sepsis using the HSS of Rodwell et al. (J Pediatr 112:761–767,1988). Analysis in their study found that an abnormal immature to total neutrophil ratio (I:T) followed by an abnormal immature to mature neutrophil ratio (I:M) were the most sensitive indicators in identifying infants with sepsis. The higher the score, the greater was the likelihood of sepsis. A score ≤2 suggests that sepsis was unlikely.[6] Total PMN count (89.47%) was highly sensitive followed by Immature PMN count (78.94%) in identifying infants with sepsis. Total leucocyte count (TLC) (91.66%) followed by Immature: Total PMN ratio (75%) and platelet counts (75%) were highly specific tests helpful in diagnosing sepsis. The positive predictive value was high for Immature: Total PMN ratio (88.88%) followed by platelet count (85.71%) which was helpful in identifying infants who really had sepsis. Negative predictive value was high in degenerative changes (40%) along with I:T PMN ratio which indicated that the infants did not have any evidenceof sepsis.[6]

In prospective cross sectional study done by Saleema Munazza et al in 120 newborns, the mean age of participants was 12.4 ± 7.3 days, of which 54.1% were male. Most neonates (52.4%) were in the age group up to 10 days and 61% were preterm. The HSS was found to have a sensitivity of 90%, specificity of 74.5%, Positive Predictive Value was 65.9% and Negative Predictive Value was 93.2%.[1]

Analysis of the hematologic profiles (Majumdar A et al) in the light of the HSS found that an abnormal immature to total neutrophil (I:T) ratio followed by an abnormal immature to mature neutrophil (I:M) ratio were the most sensitive indicators in identifying infants with sepsis. The study also found that the higher the score the greater the certainty of sepsis being present. The score ≥ 4 was more reliable as a screening tool than any individual hematological parameter.[12]

Conclusion

Hematological scoring system is sensitive, simple, quick, cost effective and readily available tool for early diagnosis of neonatal sepsis.[1,6,12] It may aid the clinicians in early diagnosis of neonatal sepsis and unnecessary exposure of infants to antibiotics can be avoided.

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