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Original Research Article.

Assessment of Correlation of Haematological Profile and Early Onset of Infections in Neonates

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ABSTRACT

Background: Because of lack of specific clinical and laboratory findings, early diagnosis of neonatal septicemia is often difficult. Antibiotics are administered on suspicion of neonatal sepsis as early as possible whereas it takes some time to get reports from blood culture. To devise a way to early diagnosis and reduce the irrational use of antibiotics, several rapid haematological tests have been evaluated. This objective behind the study was to correlate the role of haematological parameters to early onset septicaemia in neonates and to establish it as a reliable indicator.

Materials and Methods: A prospective study of haematological parameters of 300 neonates with clinically suspected sepsis was performed. These parameters were evaluated statistically based on the standard reference values.

Results: Band cells, Increase/ decreased WBCs, neutropenia, I/M ratio, I/T ratio, Thrombocytopenia, Toxic granules were found to have good specificity and sensitivity. Most of the patients had two or more positive tests. Hematological scoring system had the sensitivity: 95.8%, specificity:73.8%, Positive predictive value:41%, Negative predictive value: 98.9%.

Conclusion: It is concluded that the haematological parameters can provide an early clue for diagnosis of early onset septicaemia in neonates. Hematological scoring system if established can act as a rapid adjunct to diagnose and help in early intervention thereby decreasing neonatal morbidity and mortality.

Keywords: Early Neonatal Sepsis, Diagnosis, Haematological, Mortality.

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INTRODUCTION

Systemic infection of a newborn with nonspecific systems along with bacteremia is referred to as neonatal sepsis.[1] It is a broad term for clinical syndrome in which circulatory compromise occurs in first four weeks of life in newborns due to presence of bacteria in blood.[2] It encompasses infections and clinical presentation of septicaemia, pneumonia, osteomyelitis and urinary tract infection in neonates.[1] It is one of the leading cause of neonatal deaths. It accounts for 5 million of total neonatal deaths per year in developing countries making up around 30 to 50 percent of neonates in developing countries.[1] In India, the incidence of neonatal sepsis is approximately 30 per 1000 live births.[3] Early onset septicaemia is different from late one in being encountered from bacteria before and during delivery. Late onset may be acquired through different reasons like from nosocomial or community sources.[4] As wide variety of bacteria maybe involved with a rapid spread of infection in neonates, the diagnosis and treatment often becomes difficult.[1,2] Therefore, an early recognition of bacteria and institution of antibacterial therapy as early as possible is imperative for favourable prognosis. This is possible through application of haematological markers which may aid in screening and early diagnosis. The results can be obtained even before the results of blood culture come.[1] Thus the present study was taken to evaluate and correlate haematological profile and early onset of infection in neonates.

MATERIALS AND METHODS

This prospective study was carried out at M.Y. Hospital, Department of paediatrics, M.G.M. Medical College, Indore, Madhya Pradesh, India over a period of one year. After ethical clearance from institutional ethics committee, the study was

started on 300 neonates. The enrolment was based on detailed history, clinical signs and symptoms of infection and thorough physical examination. Neonates who underwent surgery, who had already received antibiotics, who had congenital defects and who did not survive the complete work up were excluded from study.

Following investigations were done:

i) Hb ii) T & D iii) Band Cell Count

iv) Thrombocyte

v) Blood Culture: Cases were confirmed by positive blood culture

Total (TLC) and Differential Counts (DLC)

All the samples were collected within 24 hours of delivery from antecubital or femoral vein with full aseptic precautions. EDTA was used for anticoagulation. Blood smear was made and immediately mixed in methanol and within 2-3 min. 10-15 drops of buffer solution (sodium dihydrogen phosphate, potassium dihydrogen phosphate, distill water) were put and kept for 1 min. The solutions were mixed by gently blowing by pipette. After 10 min, the smear was washed with tap water. The slide was then dried and observed under high power objective and then oil immersion lens. The cells were then counted in 100 squares.

Toxic Granules

These were identified as coarse darkly stained granules irregularly distributed throughout the cytoplasm of the neutrophils.

Band Cells

Graunulocytes with sausage of band form nucleus were identified as band cells. The chromatin was coarse resembling that of the most mature cells. The abundant cytoplasm with the nucleo cytoplasmic ratio was about l to 2.

Shift to Left – Shift to Right

This labeling was done as per the Arneth's classification 'Shift to the left' meant an increase in single and bilobed (and thus younger forms) form while ' shift to right' implied an increase in the older forms.

Hematological Scoring System

A score of '1' is given to 7 items (I/T ratio, I/M ratio, abnormal no. of leukocytes, neutropenia, presence of immature cells, thrombocytopenia, presence of dohle bodies or toxic granules). A total score of 3 or more is considered to be screen positive.

Blood Culture

Blood samples were collected within 24 hours of birth. There was no antibiotic administration before collection of samples. Blood cultures were then prepared under fully aseptic conditions.

RESULTS

The results of the haematological tests and their correlation for early onset septicaemia (EOS) were as follow:

Table 1: Band cells and EOS

Screening test	Culture positive	Culture negative	Total
Positive	30(10%)	50(16.6%)	80(26.6%)
Negative	18(6%)	202(67.3%)	220(73.3%)
Total	48(16%)	252(84%)	300(100%)

Sensitivity: 62.5%; Specificity: 80.15%; Positive predictive value: 37.5%; Negative predictive value: 91.8%

Table 2: Increased/decreased TWBC and EOS

Screening test	Culture positive	Culture negative	Total
Positive	24(8%)	24(8%)	48(16%)
Negative	24(8%)	228(76%)	252(84%)
Total	48(16%)	252(84%)	300(100%)

Sensitivity: 90.4%; Specificity: 50%; Positive predictive value: 90%; Negative predictive value: 90.4%

Table 3: Neutropenia and EOS

Screening test	Culture positive	Culture negative	Total
Positive	38(12.6%)	76(25.3%)	114
Negative	10(3.33%)	176(58.6%)	186
Total	48(16%)	252(84%)	300

Sensitivity: 79.1%; Specificity: 69.8%; Positive predictive value: 33.3%; Negative predictive value: 94.6%

Table 4: I/M ratio and EOS

Screening test	Culture positive	Culture negative	Total
Positive	45	3	48
Negative	3	249	252
Total	48	252	300

Sensitivity: 93.75%; Specificity: 98.8%; Positive predictive value: 93.75%; Negative predictive value: 98.8%

Table: 5 I/T ratio and EOS

Screening test	Culture positive	Culture negative	Total
Positive	43(14.33%)	126(50%)	169
Negative	5(1.6%)	126(50%)	131
Total	48(16%)	252(84%)	300

Sensitivity: 89.5%; Specificity: 50 %; Positive predictive value: 25.4 %; Negative predictive value: 96.1%

Table 6: Thrombocytopenia and EOS

Screening test	Culture positive	Culture negative	Total
Positive	38(5%)	101(47.33%)	139
Negative	10(11%)	151(36.66%)	161
Total	48(16%)	252(84%)	300

Sensitivity: 79.1%; Specificity: 59.9%; Positive predictive value: 27.3%; Negative predictive value: 93.7

Table 7: Toxic granules and EOS

Screening test	Culture positive	Culture negative	Total
Positive	36	43	79
Negative	12	209	221
Total	48	252	300

Sensitivity: 75%; Specificity: 83.33%; Positive predictive value: 45.5%; Negative predictive value: 94.5%

Table 8: Hematological scoring system

Screening test	Culture positive	Culture negative	Total
Positive	46(15.3%)	66(22%)	112
Negative	2(0.6%)	186(62%)	188
Total	48(16%)	252(84%)	300

Sensitivity: 95.8%; Specificity: 73.8%; Positive predictive value: 41.0%; Negative predictive value: 98.9%

DISCUSSION

Bacteremia is a common cause of mortality and morbidity among neonates. It has been suggested that a combination of hematological and biochemical tests may provide a more rapid and accurate diagnosis of bacteremia and use of a septic 'screen' may reduce amount of antibiotic use.[1,5]

As there is immaturity of both cellular and hum oral immune systems in neonates, the susceptibility to infection and its rapid spread is more in newborns.[6] Because of functional immaturity newborns usually fail to keep pace with the process of WBC destruction and usually presents with leucopenia. Parida reported 25% of cases having leucopenia.[7] In Namdeo series of 50 cases, 40% had leucopenia.[8] Kite reported that predictive value of leucopenia is poor (27%) but it may be high or low in 89% of newborns having bacteremia.[9] Chandra et al found it less sensitive, highly specific and moderately predictive.[10]

According to literature band cell count is specifically significant in first week of life. Kite et al, Chandra et al and Kennedy et al found it significantly changed in infective states.[8,10,11] A rise in band cells count shows migration of white blood cells from their storage compartment irrespective of stage of maturation. Namdeo et al reported that B/N ratio significantly alters in septicemia.

Toxic granulations showed not only association with septicemia state but it has also been incriminated as bad prognostic sign.[12] It has been suggested that toxic granulations may be a result of defective function and decreased bacteriological activity.

For the purpose of present study newborns were considered infected only when there was positive bacteriological evidence. Sensitivity and positive predictive value of rapid diagnostic parameters had been evaluated in relation to bacteriological septicemia. Band cells (Sensitivity:62.5, Specificity: 80.15%, Positive predictive value: 37.5%, Negative predictive value: 91.8%, Increase/ decreased WBCs (Sensitivity: 90.4%, Specificity:50%, Positive predictive value:90%, Negative predictive value: 90.4%), neutropenia (Sensitivity: 79.1%, Specificity: 69.8%, Positive predictive value:33.3%, Negative predictive value: 94.6%),I/M ratio (Sensitivity: 93.75%, Specificity: 98.8%, Positive predictive value: 93.75%, Negative predictive value: 98.8%), I/T ratio (Sensitivity: 89.5, Specificity: 50%, Positive predictive value: 25.4%, Negative predictive value: 96.1%), Thrombocytopenia (Sensitivity: 79.1%, Specificity: 59.9%, Positive predictive value: 27.3%, Negative predictive value: 93.7%), Toxic granules (Sensitivity: 75%, Specificity: 83.33%, Positive predictive value: 45.5%, Negative predictive value: 94.5%) were considered useful hematological indices for early diagnosis of neonatal septicemia. Most of the patients had two or more positive tests. In this study, Hematological scoring system had the sensitivity: 95.8%, specificity: 73.8%, PPV:41%, NPV: 98.9%. This data is supported by Robyn, Rodwell, Anton L. Leslie, David, Tudehope. They found that likelihood of sepsis with score $\geq$ 3 was 31%. With score < 2 likelihood of sepsis absent was 99.[12]

CONCLUSION

The combination of haematological tests and haematological scoring system with clinical profile is helpful in early diagnosis as well as treatment of neonatal sepsis. Haematological profile may be used as a simple, easy, cheap and quick / rapid adjunct for the diagnosis of clinically suspected cases of early neonatal sepsis.

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