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Research Paper

Usefulness of routine haematological tests in neonatal septicaemia

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Abstract
Background: *Neonatal septicaemia refers to a generalized bacterial infection in the first four weeks of life. It can be divided into two types: Early onset neonatal septicaemia (EONS) and Late onset neonatal septicaemia (LONS). The diagnosis can be confirmed by blood culture examination, but various haematological tests can positively predict the diagnosis and the results are available immediately.*
Objective: *To evaluate variation in haematological parameters in neonatal septicaemia against blood culture results and to study the difference in results in EONS and LONS and its comparison with C-reactive protein (CRP) for diagnosis.*
Materials and Methods: *A total of 60 neonates with culture positive septicaemia were studied. Haematological tests like haemoglobin, total leukocyte count, differential leukocyte count, toxic granules, band cells, immature and mature neutrophils, total neutrophil count, platelet count, and CRP were performed. The Haematological Scoring System (HSS) formulated by Rodwell et al was used to calculate the cut off value for the diagnosis.*
Results: *Out of various haematological parameters, total neutrophil count (75%), ratio of immature to total neutrophils (I/T ratio) (71.7%) and platelet count (60%) were significantly positive in septicaemia. The Haematological score was ≥3 in 76.6% of newborns. The CRP was positive in 75% of cases. The combined sensitivity of HSS and CRP was 90%.*
Conclusions: *Various haematological parameters can be easily performed and when properly interpreted along with their cut off value, as suggested in the study, it can aid in early recognition of neonatal septicaemia against the culture examination. This will save time, money and many a times life of a neonate.*
Keywords: *Neonatal, septicaemia, haematological tests, C - reactive protein.*

Introduction

Neonatal septicaemia is a generalized bacterial infection confirmed by a positive blood culture in the first 4 weeks of life. It can be divided into early onset neonatal septicaemia (EONS), occurring within first 72 hours of life; and late onset neonatal septicaemia (LONS), occurring after 72 hours of life. Infections are a frequent and important cause of morbidity and mortality in the neonatal period. Infection may enter the body

through umbilicus, skin and mucosa. Due to poor immunological defence of the body even local infections tend to become generalized, resulting in neonatal septicaemia which may prove fatal. The incidence of neonatal septicaemia varies widely, being influenced by the quality of intrauterine life, host factors and environmental factors. Early onset septicaemia is usually caused by bacterial flora of maternal birth canal, while late onset septicaemia represents nosocomial infections by organisms that colonize infants in the nursery or lying in the ward.

The mortality from untreated sepsis can be as high as 50% and the outcome of sepsis depends on its early identification. The definitive diagnosis of septicaemia is made by a positive blood culture, but it takes 48- 72 hours. Therefore, other tests for identification of infection should be considered that can be performed rapidly in an hour or two, so that antibiotic can be used judiciously and thereby reducing the incidence of drug resistance and improving the survival rate of neonate. So, this study was undertaken to evaluate the variation in haematological parameters in neonatal septicaemia; to evaluate differences, if any, in the haematological parameters in EONS and LONS; and to assess the diagnostic value of haematological parameters vis-à-vis C-reactive protein (CRP) in the diagnosis of sepsis.

Materials and Methods

The study was done at a tertiary care hospital wherein a total of 60 neonates admitted in paediatric intensive care unit with culture proven septicaemia were included over a period of 12 months. The blood samples received in the Hematology section of the laboratory and were examined for various parameters. For each patient, investigations like haemoglobin concentration, total leukocyte count, differential leukocyte count, toxic granules in neutrophil, band cell, immature (I) and mature (M) neutrophils, total (T) neutrophil count, I/T ratio, I/M ratio, platelet count and CRP were performed. Also, haematological scoring was done according to 7 point Haematological scoring system (HSS) formulated by Rodwell et al [1] (Table 1). The p value was calculated to know whether the value for a particular parameter and the difference between EONS and LONS was significant or not.

Results

In the present study, neonatal septicaemia was more commonly seen in male sex (80%), preterm babies (55%) and low birth weight (<2.5 kg) babies (76.67%). Out of 60 neonatal septicaemias, 40(66.67%) cases were of EONS and 20(33.33%) cases were of LONS.

Klebsiella pneumonia (28.3%) and Staphylo-coccus aureus (25%) were the predominant isolated pathogens. In our study, 9 (15%) patients died and Klebsiella pneumoniae was the most common pathogen isolated in neonates who expired.

In the present study, total neutrophil count (T), I/T ratio, platelet count and CRP had a higher positive percentage compared to other parameters and the difference in HSS was significant between EONS and LONS.(Table 2,3,4)

In the present study HSS $\geq$3 was present in 76.6% of total cases of septicaemia. In early onset septicaemia 70% cases had HSS $\geq$3 while in late onset septicaemia HSS $\geq$3 was present in 90%.(Table 5)

Table 1. Haematological scoring system.

Parameter	Result	Score
Total WBC count	≤5,000/µl ≥25,000/µl at birth ≥30,000/µl at 12-24 hours ≥21,000 /µl at day 2 onward	1
Total PMN count($x10^9$/L)	Early onset : <7.8 or >14.5 Late onset: <1.80 or >5.4	1
Immature PMN count ($x10^9$/L)	Early onset:<0.5 or >14.5 Late onset:>0.6	1
Immature-to-total PMN(I/T) ratio	Early onset >0.16 Late onset:>0.12	1
Immature-to-mature(I/M) PMN ratio	≥0.3	1
Degenerative changes in PMNs	≥3+ for toxic granulation	1
Platelet count	≤1,50,000 per µl	1

Interpretation

Score	Interpretation
≤ 2	Sepsis is very unlikely
3 or 4	Sepsis is possible
≥ 5	Sepsis is very likely

Table 2: Haematological parameters in neonates with septicaemia

Parameters	Cases(n=60) Mean	Cases(n=60) SD	Cases(n=60) Range
Haemoglobin (g/dl)	14.32	3.56	6.5-24.1
TLC($x10^3$ /µl)	11.92	8.18	1.6-37.8
Platelet($x10^3$ /µl)	141.30	102.45	15-409
Total neutrophil count ($x10^3$ /µl)	6.42	5.24	0.4-21.3
Mature neutrophil count($x10^3$ /µl)	5.33	4.44	0.32-17.8
Immature neutrophil count($x10^3$ /µl)	1.08	1.006	0.08-4.6
Band cells($x10^3$ /µl)	0.91	0.87	0.08-4.6
I/T ratio	0.197	0.10	0.004-0.54
I/M ratio	0.27	0.20	0.05-1.18

Table 3: Haematological parameters in early and late onset neonatal septicaemia

Parameters	Early onset(n=40) Mean ± SD	Late onset(n=20) Mean ± SD	Statistical significance
Haemoglobin (g/dl)	15.09 ± 3.62	12.78 ± 3.04	0.0115
TLC($x10^3$ /µl)	13.60 ± 8.92	8.56 ± 5.18	0.0076
Platelet($x10^3$ /µl)	159.55 ± 101.94	104.80 ± 95.70	0.047
Total neutrophil count ($x10^3$ /µl)	7.47 ± 5.52	4.34 ± 3.96	0.0152
Mature neutrophil count($x10^3$ /µl)	6.28 ± 4.68	3.4 ± 3.21	0.0075
Immature neutrophil count($x10^3$ /µl)	1.17 ± 1.08	0.91 ± 0.82	NS(0.29)
Band cells($x10^3$ /µl)	0.97 ± 0.91	0.78 ± 0.76	NS(0.40)
I/T ratio	0.17 ± 0.10	0.24 ± 0.10	0.0261
I/M ratio	0.24 ± 0.20	0.34 ± 0.20	NS(0.088)

Table 4: Positivity of various parameters in EONS and LONS

Test	Cut off	Percentage positive in EONS	Percentage positive in LONS
CRP mg/L	≥ 6	67.5%	85%
TLC ($x10^3$ /µl)	≤ 5,000 or ≥ 21,000	45%	70%
Platelet ($x10^3$ /µl)	< 150	52.5%	80%
Total neutrophil count ($x10^3$ /µl)	Early onset: < 7.8 or > 14.5 Late onset: <1.80 or > 5.4	77.5%	75%
I/T ratio	Early onset≥ 0.16 Late onset ≥ 0.12	50%	90%
I/M ratio	≥ 0.30	22.5%	45%

Table 5: Haematological score in EONS and LONS

	Total (Mean ± 1 SD)	Early onset septicaemia (mean ± 1 SD)	Late onset septicaemia (mean ± 1 SD)	Statistical significance
Haematological score	3.63 ± 1.65	3.15 ± 1.52	4.6 ± 1.50	0.0011

Table 6: Haematological score and CRP in EONS and LONS

	Total cases (n=60)	Early onset septicaemia (n=40)	Late onset septicaemia (n=20)
Haematological score (≥ 3)	46 (76.66%)	28 (70%)	18 (90%)
C-reactive protein (≥ 6 mg/dl)	45 (75%)	26 (65%)	19 (95%)
Haematological score (≥ 3) or C-reactive protein (≥ 6 mg/dl)	54 (90%)	35 (87.5%)	19 (95%)

Discussion

This study provides information on the value of several simple and cheap laboratory tests used singly or in combination to diagnose neonatal septicaemia. The cellular and humoral immunity improves with increasing maturity of neonate. This may explain the higher incidence of early onset septicaemia. Incidence of septicaemia was higher in males than in females. This is possible because the factors regulating the synthesis of immunoglobulin are situated on the x-chromosome [2]. Incidence of septicaemia was higher in low birth weight babies. This is because low birth weight babies have low IgG levels as well as impaired cellular immunity and hence is more susceptible to infection [3]. Incidence were higher in preterm babies because their lack of inherent defensive mechanisms as well as underdeveloped cellular and humoral immunity [4].

The frequencies of infection by various organisms vary from one institution to another and even year to year in the same institution. In India gram negative bacilli predominantly Klebsiella spp. E.coli and in gram positive cocci, staphylococcus spp. are common. The mortality rate in gram negative septicaemia was found to be disproportionately higher compared to gram positive septicaemia [5].

Various studies done by different authors emphasize the importance of HSS and CRP in the early diagnosis of neonatal septicaemia. [1, 6 ,7, 8]

The sensitivity of HSS to detect neonatal septicaemia was 76.66%, whereas that of CRP was 75%. The combined (HSS + CRP) sensitivity was 90 %. Ghosh et al found HSS ≥3 in 90% of septicaemic cases.[7]. Zawar et al reported that 91% of cases had positive CRP.[9]. Berger et al found that after 3 days of life (late onset septicaemia) CRP was the best single test in early diagnosis of neonatal septicaemia.[10]

Both HSS and CRP are better predictor of late onset neonatal septicaemia. Both the tests are cheap and the results are available in a short time. The combined predictive value of HSS and CRP is higher overall compared to individual value.

Other newer biomarkers for sepsis like Procalcitonin, CD 11b, CD 64, IL-6, and IL-8 are more sensitive and specific but are not within the reach of lot many people. Blood culture examination is the gold standard for the diagnosis but it takes 48 to 72 hours and the time is very crucial in the treatment of neonatal septicaemia.

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