ISSN NO. 2320-5407

Journal homepage: http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

Study of hematological parameters in culture positive neonatal septicemia

Dr. Rahul Bhardwaj, Dr. Sanjay Chaudhari, Dr. Mauli Joshi, Dr. Het Thanky, Dr. Jayani Patel
Department of Pathology, Pramukh Swami Medical College, Karamsad, Gujarat, India.

Manuscript Info

Manuscript History:

Received: 15 December 2015
Final Accepted: 22 January 2016
Published Online: February 2016

Key words:
EONS- Early onset neonatal septicemia, LONS- Late onset neonatal septicemia, CRP- C reactive protein, HSS- Hematological scoring system

Corresponding Author
Dr. Sanjay Chaudhari, Dr. Mauli Joshi

Abstract

Context: Neonatal septicemia refers to a generalized bacterial infection confirmed by a positive blood culture in the first 4 weeks of life. Two types of neonatal septicemia: Early onset neonatal septicemia (EONS) and Late onset neonatal septicemia (LONS).

Aims and objectives: To evaluate variation in haematological parameters in neonatal septicemia; To study differences in parameters in EONS and LONS and its comparison with CRP for diagnosis.

Material and methods: A total of 60 neonates with culture proven septicemia were studied in Shree Krishna Hospital, Karamsad, for period of 12 months. Haemoglobin, total count, differential count, toxic granules, band cells, immature(I) and mature(M) neutrophils, total(T) neutrophil count, platelet count and CRP were performed. Haematological Scoring System (HSS), formulated by Rodwell et al was applied.

Results: Neonatal septicemia was more commonly seen in male sex (80%), preterm babies (55%) and low birth weight (<2.5 kg) babies (76.67%). Klebsiella pneumonia (28.3%) and Staphylococcus aureus (25%) were the predominant isolated pathogens. Total nine patients died and Klebsiella pneumoniae was the most common pathogen isolated.

Discussion: This study provides information on the value of several simple and cheap laboratory tests used singly or in combination to diagnose neonatal septicemia.

Conclusion: Various hematological 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 septicemia.

Introduction:-

Neonatal septicemia refers to a generalized bacterial infection confirmed by a positive blood culture in the first 4 weeks of life. Two types:

1. Early onset neonatal septicemia (EONS)
   – Within first 72 hours of life ;
2. Late onset neonatal septicemia (LONS)
   – 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 defense of the body even local infections tend to become generalized, resulting in neonatal septicemia which may be fatal.

The incidence of neonatal septicemia varies widely, being influenced by the quality of intrauterine life, host factors and environmental factors. Early onset septicemia is usually caused by bacterial flora of maternal birth canal, while late onset septicemia 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 septicemia 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.

Aims and objectives:-

- To evaluate the variation in haematological parameters in neonatal septicemia;
- To evaluate differences, if any, in the haematological parameters in EONS and LONS; and
- The diagnostic value of haematological parameters vis-à-vis C-reactive protein (CRP) in the diagnosis of sepsis.

Material and methods:-

A total of 60 neonates with culture proven septicemia were studied at the department of pathology, Shree Krishna Hospital, Karamsad, over a period of 12 months. For each patient, investigations like haemoglobin concentration, total leucocyte count, differential leucocyte 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. Haematological scoring system.

Parameter	Finding	Score
Total WBC count	≤5,000 per µl. ≥25,000 per µl at birth. ≥30,000 per µl at 12-24 hours ≥21,000 per 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 unikely
3 or 4	Sepsis is possible
≥ 5	Sepsis or infection is very likely

Results:-

In the present study, neonatal septicemia was more commonly seen in male sex (80%), preterm babies (55%) and low birth weight (<2.5 kg) babies (76.67%). 66.67% cases were of EONS and 33.33% cases were of LONS. Klebsiella pneumonia (28.3%) and Staphylococcus 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.

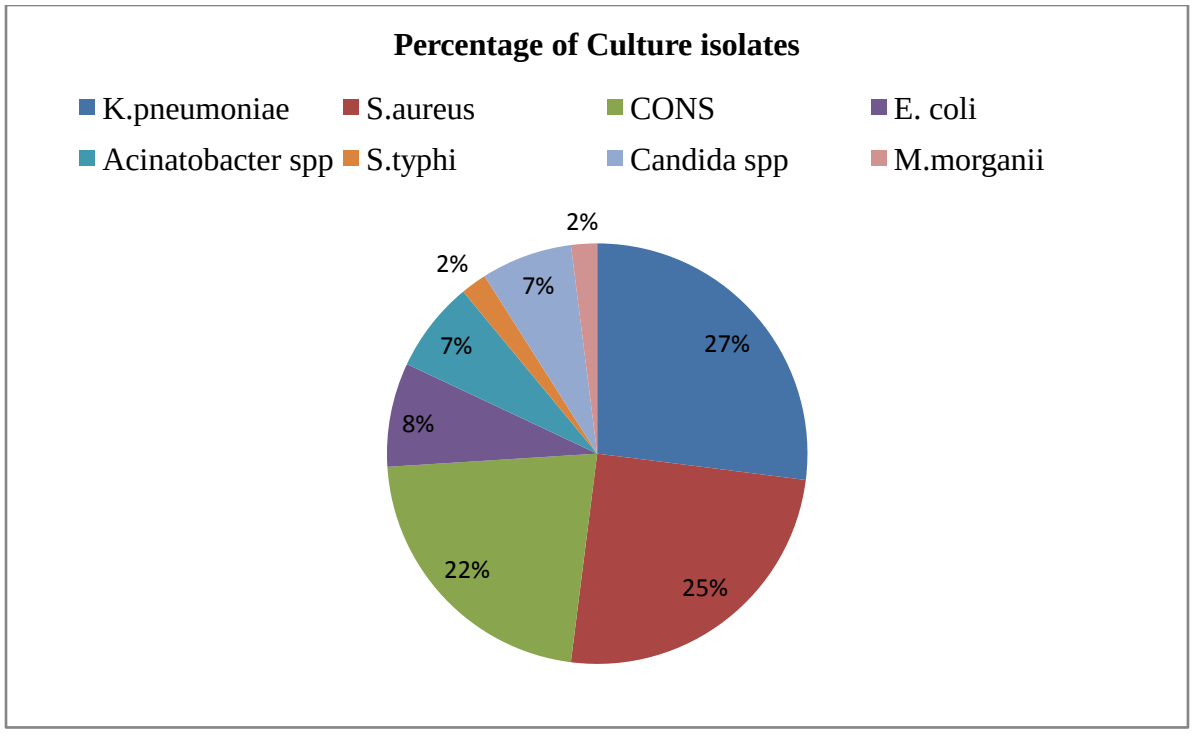

Figure 1: Percentage of culture isolates

Table 2: Mean, standard deviation (SD) & range of various hematological parameters in the study group.

Parameters	Cases(n=60) Mean	Cases(n=60) SD	Cases(n=60) Range
Hemoglobin (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	0.04-0.54
I/M ratio	0.27	0.20	0.05-1.18

In general, total neutrophil count, I/T ratio, platelet count and CRP had a higher positivity compared to other parameters.

Table 3: Hematological parameters in early and late onset septicemia

Parameters	Early onset (n=40) Mean ±SD	Late onset (n=20) Mean ± SD	Statistical significance
Hemoglobin (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 shows mean and standard deviation of the various hematological parameters in early and late onset septicemia.
(NS- not significant)

Table 4: Percentage positivity of various parameters in the study group

Test	Cut off	Percentage positive
CRP mg/L	≥6	73.33%
TLC($x10^3$/µl)	≤5,000 or ≥21,000	35%
Platelet($x10^3$/µl)	<150	60%
Total neutrophil count ($x10^3$/µl)	Early onset : <7.8 or 14.5 Late onset: <1.80 or >5.4	80% 70%
I/T ratio	≥0.16	71.67%
I/M ratio	≥0.30 ≥0.25	35% 50%

Table 5: Positivity of various parameters in EONS and LONS

Test	Cut off	Percentage positive in Early onset	Percentage positive in late onset
CRP mg/L	≥6	65%	90%
TLC($x10^3$/µl)	≤5,000 or ≥21,000	32.5%	40%
Platelet($x10^3$/µl)	<150	33.33%	80%
Total neutrophil count ($x10^3$/µl)	Early onset : <7.8 or 14.5 Late onset: <1.80 or >5.4	80%	70%
I/T ratio	≥0.16	60%	95%
I/M ratio	≥0.30 ≥0.25	25% 45%	55% 60%

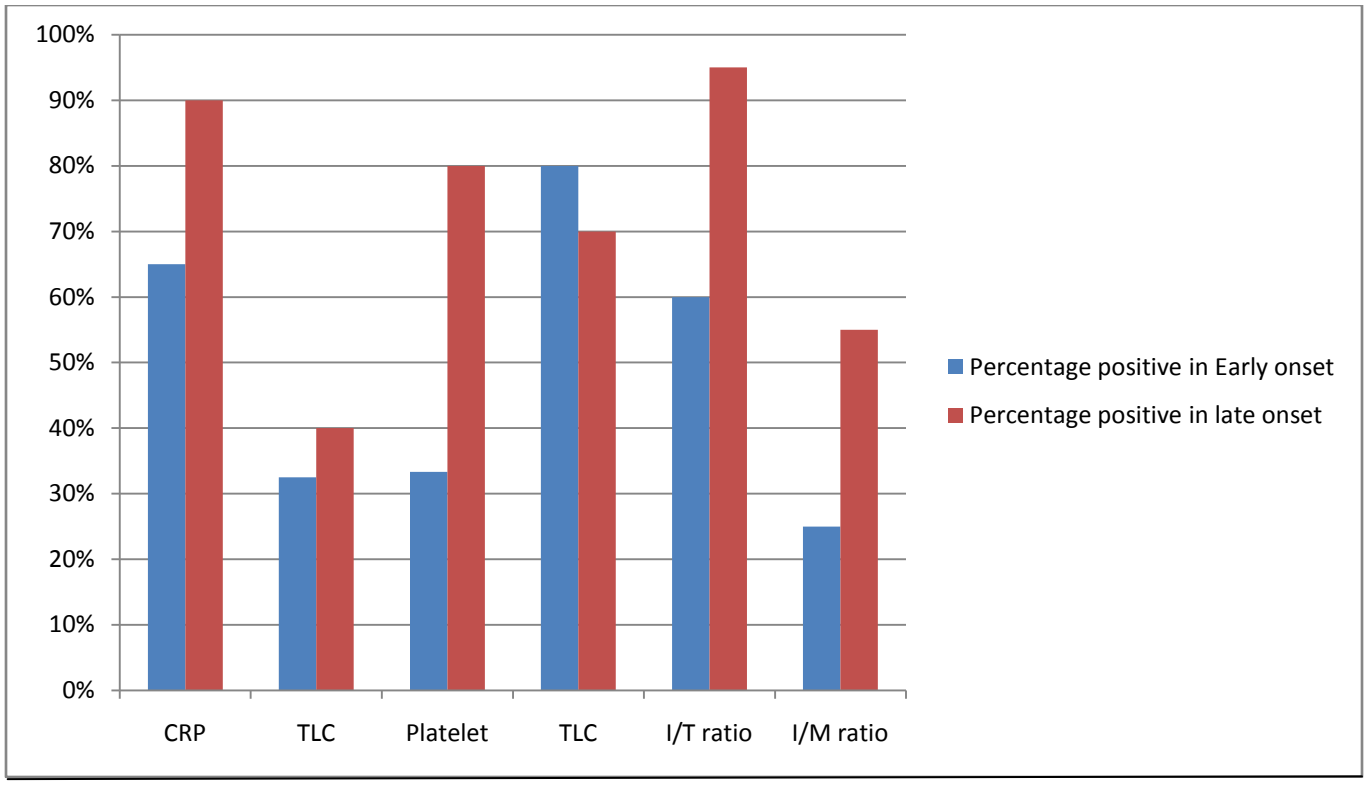

Figure 2: Positivity of various parameters in EONS and LONS

Table 6: Hematological score in EONS and LONS

	Total Mean ± 1SD	Early onset Septicemia mean±1SD	Late onset septicemia mean±1SD	Statistical significance
Hematological scoring	3.63±1.65	3.15±1.52	4.6±1.50	0.0011

Table shows statistically significant difference ($p<0.001$) of hematological score in early and late onset septicemia.

Table 7: Hematological score versus CRP in EONS and LONS

	Total cases(n=60)	Early onset septicemia (n=40)	Late onset septicemia(n=20)
Hematological score (≥3)	45(75%)	27(67.5%)	18(90%)
C-reactive protein(≥6 mg/dl)	44(73.33%)	26(65%)	18(90%)

Table shows no significant difference in Hematological score and CRP in early and late onset septicemia.

Table 8: Outcome

Outcome	No. of cases	Percentage
Discharged	51	85%
Expired	09	15%
Total	60	100%

Table shows 15% mortality rate in neonatal septicemia.

Discussion:-

This study provides information on the value of several simple and cheap laboratory tests used singly or in combination to diagnose neonatal septicemia.

The cellular and humoral immunity improves with increasing maturity of neonate. This may explain the higher incidence of early onset septicemia.

Incidence of septicemia 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 septicemia 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 septicemia was found to be disproportionately higher compared to gram positive septicemia[5].

Hematological parameters:-

Hemoglobin: The lower mean value of hemoglobin concentration recorded in late onset septicemia as compared to early onset septicemia could be because of fall in hemoglobin concentration, which is expected to occur in the normal cause of events as the neonate matures[6].

Total leukocyte count: It has been of little clinical use in diagnosis of neonatal septicemia because of wide variation in values and overlap in normal and abnormal values.

Total neutrophil count: Neutropenia has been found to occur more commonly in neonates with septicemia as compared to neutrophilia. But neutropenia alone as a sign of septicemia can be misleading as it can also occur in some other conditions such as PIH , asphyxia neonatorum, isoimmune neutropenia , congenital neutropenia and in certain inborn errors of metabolism[7]. Possible cause attribute to this phenomenon is an imbalance between factors that stimulate granulopoiesis (colony stimulating factors) and those that inhibits granulocyte production such as lactoferrin and transferrin. In septicemia neutropenia occurs probably because of increased adherence to altered endothelial cells as well as increased utilization at the site of infection.

The neutrophil left shift is commonly used as an adjunct to early diagnosis of septicemia. In this study absolute immature neutrophil count, absolute band cell count, I/T and I/M ratio were used for its quantification. In response to infection more neutrophils are released from the marrow and more immature cells reach the blood, a process referred to as a left shift. Neutrophil ratios are more commonly abnormal during neonatal septicemia than the absolute band count. I/T ratio offer both practical and theoretical advantage over I/M ratio because in severe infection there may be few or no mature neutrophils in the circulation.

In view of the above, neutrophil factors should be used with caution as an independent indicator of septicemia. The hematological response may vary with both gestational and postnatal ages and with the time interval between the onset of infection and blood sampling apart from the perinatal events.

Platelet count: In this study 60% neonates had platelet count less than 150 X 10^3/µl. Thrombocytopenia might occur in neonatal septicemia in response to the products of microorganisms. These products cause platelet clumping and adherence leading to platelet destruction. Thrombocytopenia may be a presenting sign and can last as long as 3 weeks.

Hematological scoring system: It permits objective assessment of hematologic changes and could standardized the interpretation. It saves time for busy clinicians. It has high sensitivity and specificity, the certainty of septicemia being present with increasing scores.

In present study HSS≥3 was present in 75% of total cases of septicemia. Thus HSS could provide a guideline regarding decisions of antibiotic therapy.

C-reactive protein: According to results 90% cases of LONS are positive for CRP and 65% cases of EONS are positive for CRP. So CRP is best single test that can be used in early diagnosis of LONS.

Comparison between Hematological score versus CRP: In the present study hematological score is equivalent to CRP in early onset septicemia (67.5% and 65%) and late onset septicemia(90% in both).

Conclusion:-

Various hematological parameters can be easily performed and when properly interpreted along with their cut off value, as suggested in the study, can aid in early recognition of neonatal septicemia. While individual parameters have their limitations, combination of parameters certainly improve their usefulness.

References:-

1. Rodwell R, Leslie AC, Tudehope DI. Early diagnosis of neonatal sepsis using a hematologic scoring system. J Pediatr 1998; 112:761.
2. Kuruvilla A, Jadusason M, Pillai S. Bacteriological profile of sepsis in neonatal unit in south India. Indian Pediatr 1988;35:851-857.
3. Khatua SP, Das AK, Chatterjee BD, Khatua S, Saha A. Neonatal septicemia, Indian J Pediatr 1986;53:509.
4. Chacko B, Inderpreet S. Early onset neonatal sepsis. Indian J Pediatr 2005; 72:23-26.
5. Vesikari T. Neonatal septicemia. Arch of Dis 1985; 60:542-546.
6. Manucha V, Rusia U, Faridi MMA and Madan N. Utility of hematological parameters and C-reactive protein in the detection of neonatal sepsis. Indian J Pathol Microbiol 2003; 46(4):565-68.
7. Engle WD, Rosenfeld CR. Neutropenia in high risk neonates. J Pediatr 1984; 105:982.