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Original Research Article

A prospective study of inflammatory biomarkers in neonatal sepsis at a tertiary level hospital

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ABSTRACT

Background: Sepsis in neonates is a syndrome which is characterized clinically by systemic symptoms or signs of infection and associated with bacteremia in the first 28 days of life. More than 40% of under-five deaths globally occur in the neonatal period, resulting in 3.1 million newborn deaths each year. Procalcitonin (PCT) is an early diagnostic tool for neonatal sepsis.
Methods: Present prospective cross- sectional observational study was conducted at NICU of Base hospital, Delhi Cantonment from 1st Dec 2016 to Jan 31st, 2018. Universal sampling technique was followed. SPSS version 21 was used for statistical analysis. A p-value of less than 0.05 was taken as significant.
Results: Out of the total 440 cases, 63% were males while rest 37% were females. Mean gestation age and birth weight of the babies was 35.6 weeks and 2.13 Kg respectively. Raised/ decreased Total Leucocyte Count (TLC) and raised pro calcitonin levels were seen in 23% and 19.8% cases respectively.
Conclusions: These results indicated that the sensitivity of procalcitonin was higher than TLC for the diagnosis of culture proven neonatal sepsis. Hence, PCT is a more sensitive and useful biomarker for the diagnosis of neonatal sepsis.

Keywords: Biomarkers, Neonate, Procalcitonin, Sepsis, Total leucocyte count

INTRODUCTION

Sepsis in neonates is a syndrome which is characterized clinically by systemic signs or symptoms of infection and associated with bacteremia in the first 28 days of life. It is still one of the significant causes of morbidity and mortality in neonates, despite of advances in health care system.[1] The majority of these deaths usually occur in low-income countries and almost 1 million of these deaths are attributed to infectious causes including neonatal sepsis, meningitis, and pneumonia.[2] The incidence of neonatal sepsis in India was 30/1000 live birth as per National Neonatal Perinatal Database.[3,4] The risk factors include lack of antenatal care, unsupervised or poorly supervised home deliveries, unhygienic and unsafe delivery practices and cord care, prematurity, low birth weight, lack of exclusive breast-feeding, and delays in recognition of danger signs in both mother and baby.[5]

Diagnosis and management of sepsis is a great challenge for neonatologists in NICUs. Clinical diagnosis of presentation is difficult due to non-specific signs and symptoms. In addition, laboratory diagnosis is time consuming. Thus, antibiotics are administered before culture results are obtained to reduce morbidity and mortality. This results in usage of variety of antibiotics for variable durations leading to the emergence of antibiotic resistant microorganisms.[6]

Understandably then, there has been significant interest in identification of specific biomarkers of neonatal sepsis.[7] Haematological indices are still being the most

extensively used in practice, currently in association with new markers for infection.[8] Research studies reported that PCT is an effective marker for sepsis as PCT levels rise earlier and return to normal levels more rapidly than other inflammatory markers.

The present research aimed to study the inflammatory biomarkers in neonates with clinical evidence of sepsis.

METHODS

It is a prospective cross- sectional observational study, conducted at NICU of Base hospital, Delhi Cantonment. This tertiary level hospital caters to the healthcare needs of large population of Armed forces, for the study period of thirteen months from Dec 1st, 2016 to Jan 31st, 2018.

Neonates, inborn or out born admitted in the NICU of our hospital were included in this study. Universal sampling technique was used for the selection of study subjects. All the neonates fulfilling the inclusion and exclusion criteria during the study period were included in the study after taking informed written consent from their legal guardians.

Inclusion criteria

- All neonates were included who have been admitted with a diagnosis of sepsis. Clinical diagnosis was based on general signs and symptoms and clinical experience of the pediatrician.

Exclusion criteria

- Major congenital malformation
- Life-threatening conditions like inborn errors of metabolism.
- Whose guardians refuse to give consent for the study.

After explaining the purpose of the study, informed written consent was taken from the guardians. All clinical information was abstracted from medical records. The blood samples of neonates suspicious of sepsis were sent to Department of Pathology, Base Hospital, Delhi cantt. A brief note of clinical history, physical findings and probable diagnosis was noted. In addition to that, TLC, procalcitonin and blood culture were measured for all included patients. TLC <5000 cells/mm^3 or >20000 cells/mm^3 were recorded as decreased or raised respectively. PCT value of >0.1 ng/ml was recorded as raised.

Statistical analysis

The quantitative data was represented as their mean±SD. Categorical and nominal data was expressed in frequency and percentage. Categorical data was analysed by using chi-square test. The significance threshold of p-value was set at <0.05. All analysis was carried out by using SPSS software version 21.

RESULTS

The present hospital based cross sectional study revealed the following results. Out of the total 583 admissions in NICU, sepsis was suspected in 440 i.e. 75.5%cases. A total of 440 samples were sent from these 440 patients with blood culture positivity rate of 23.18% (102 samples). Out of the 583 cases admitted in NICU, culture positive sepsis was seen in 102 cases (17.5%) (Table 1).

Table 1: Total Admissions, suspected sepsis cases and results of culture.

Variables	N
Total admissions	583
Suspected sepsis	440
No. of cultures sent	440
Culture positive	102 (23.18%)
Culture negative	338 (76.82%)

In the study population mean gestation age and birth weight of the babies was 35.6 weeks and 2.13 Kg respectively (Table 2).

Present study showed that out of the total 440 cases, 63% were males while rest 37% were females (Figure 1) and over half of the cases were pre-term birth (51.4%) (Table 3). Early onset sepsis was observed in 91.4% cases while late onset sepsis was observed in 8.6% cases (Table 4).

Raised/ decreased TLC and raised PCT levels were seen in 23% and 19.8% cases respectively (Table 5). Blood was the most common sample sent for culture report and its positivity rate was 23.18% (Table 6).

Out of the 102 culture positive cases, raised/ decreased TLC was seen in 46.1% as compared to only 16% culture negative cases. The sensitivity and specificity of TLC was 46.1% and 84% respectively with overall accuracy of 75.22% (Figure 2).

Table 2: Mean gestation age and birth weight.

Baseline characteristics	N	Mean	SD	Minimum	Maximum
Gestational age (wks)	440	35.6	3.92	25	42
Birth weight (kg)	440	2.13	0.79	0.650	4.20

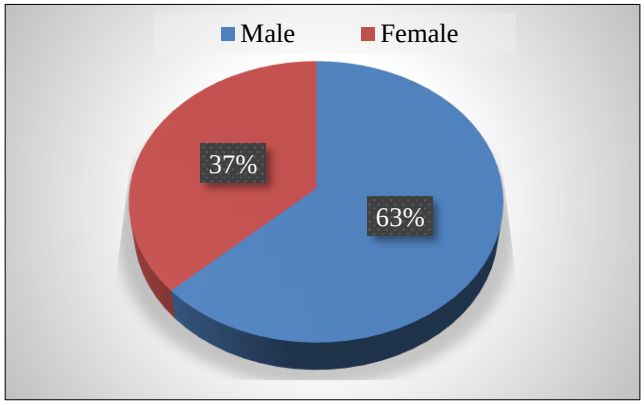

Figure 1: Distribution of subjects based on gender.

Table 3: Distribution of subjects based on gestation age.

Gestation age	N	%
Pre-term	226	51.4%
Term	214	48.6%
Total	440	100.0%

Table 4: Distribution of subjects based on Mode of onset of sepsis.

Type of Sepsis	N	%
EOS	402	91.4%
LOS	38	8.6%
Total	440	100.0%

Table 5: Distribution of subjects based on results of TLC and PCT.

Biomarkers	N	%
Increased/ Decreased TLC	101	23.0%
Increased PCT	87	19.8%

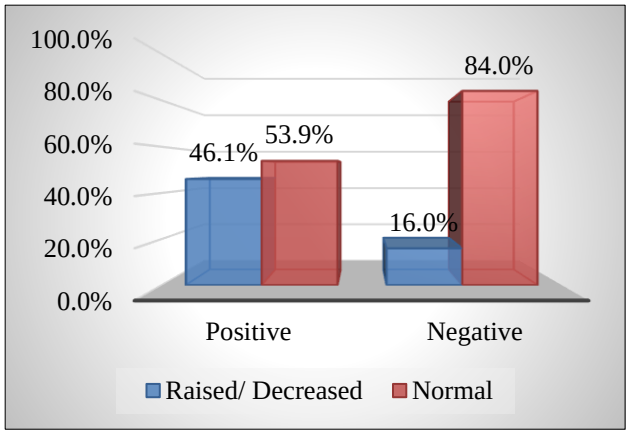

Figure 2: Comparison of TLC results with culture positivity.

Out of the 102 culture positive cases, raised PCT was seen in 58.8% as compared to only 8% culture negative cases. The sensitivity and specificity of PCT was 58.8% and 92% respectively with overall accuracy of 84.3% (Figure 3).

Table 6: Blood culture positivity of the neonates.

Sample	Culture		%	Total
	Positive	Negative		
Blood	102	338	23.18%	440

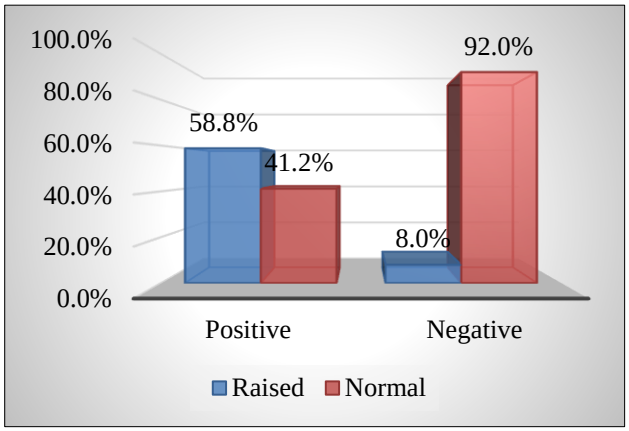

Figure 3: Comparison of PCT results with culture positivity.

DISCUSSION

Neonatal sepsis is one of the most common causes of neonatal deaths especially in developing countries. It is a life threatening emergency and any delay in treatment may result is death. The present research aimed to study the inflammatory biomarkers in neonates with clinical evidence of sepsis.

During the study period, a total of 583 children were admitted in NICU and sepsis was suspected in 440 i.e. 75.5% cases. A total of 440 samples were sent from these 440 patients with culture positivity rate of 23.18%. Out of the 583 cases admitted in NICU, prevalence of culture proven sepsis was seen as 17.5% (102 cases). Similar observations were also made by other authors as well. Jyoti et al, and Oomen et al, observed the culture positivity rate of the suspected samples as 19.2% and 23.35% respectively.[9,10]

In this study, 63% were males and 37% were females with male to female ratio of 1.7:1. In the study conducted by Vaidya et al, Male: Female ratio was 1.6:1.[11] Anitha Sharma et al, also reported male predominance with 37 out of 50 cases (74%) were males.[12]

In present study, over half of the cases with suspected sepsis were pre-term birth (51.4%). Similar reports have been made by other workers. In the study conducted by K.K. Anand et al, 62.1% of neonates were preterm.[13] Galhotra et al, also observed about 55% of preterms in suspected septicemia cases.[14]

Septicaemia was more common in low birth weight neonates (62%) as compared to the normal weight neonates (38%) with mean weight of 2.13 Kg. K.K. Anand et al, reported 81.3% of neonatal septicemia cases were below 2200 gms.[13] According to study conducted by K. Chug et al, the mean birth weight of septicaemic neonates was 1.84 kgs.[15]

In present study, early onset sepsis was observed in 91.4% cases while late onset sepsis was observed in 8.6% cases. In a study by Muley et al, 66.7% cases were of early onset septicemia (EOS) and 33.3% were of late onset septicemia (LOS).[16] Jyothi P et al, also observed early onset sepsis cases to be three times higher than late-onset sepsis.[9] Galhotra P et al, also observed that majority of the neonates presented with early onset sepsis (82.4%) as compared with late onset sepsis (17.5%).[14]

Raised/ decreased total leucocyte counts were seen in 23% cases. Out of the 102 culture positive cases, raised/decreased TLC was seen in 46.1% as compared to only 16% culture negative cases. The sensitivity and specificity of TLC was 46.1% and 84% respectively with overall accuracy of 75.22%. Study conducted by Basu R et al, showed that altered TLC was observed to have a sensitivity and specificity of 54.6% and 50% respectively.[17] Arif S et al, in another similar study observed sensitivity and specificity of TLC as 75% and 57% respectively.[18]

Results were also similar to another study conducted by Berger et al, who reported that abnormal TLC had high sensitivity i.e. 67% and 74% respectively for the detection of Neonatal sepsis.[19] Contrary to this, Ahmed et al, reported low sensitivity of TLC 39.3% for blood culture proven sepsis group.[20]

Raised procalcitonin levels were seen in 19.8% cases. Out of the 102 culture positive cases, raised PCT was seen in 58.8% as compared to only 8% culture negative cases. The sensitivity and specificity of PCT was 58.8% and 92% respectively with overall accuracy of 84.3%. Maamouri G et al, in their study found that the Sensitivity, specificity of procalcitonin in all patients were 92 and 89 percent respectively.[21] Adib et al, in their study also observed PCT has 70% sensitivity and 80% specificity 80% as a marker for the early diagnosis of neonatal sepsis.[22]

CONCLUSION

the sensitivity of procalcitonin was higher than TLC for the diagnosis of culture proven neonatal sepsis. Hence, PCT is a more sensitive and useful biomarker for the diagnosis of neonatal sepsis. This finding supports the usefulness of PCT to establish an early diagnosis of neonatal sepsis. We recommend further studies in a large number of populations to confirm the role of PCT in the diagnosis of neonatal sepsis.

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