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Original Research Article

Early Onset Neonatal Sepsis: Efficacy of CRP and Total Leucocyte Count as Screening Tests

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Abstract:

Purpose: To study the efficacy of CRP and various hematological parameters as screening tests in early onset neonatal sepsis.

Methods: A prospective case control study was done including 48 neonatal sepsis cases in study group and 42 cases in control group. For all cases CBC, ESR, C-reactive protein (CRP) and blood culture were performed. Mean CRP for both groups and cut off value of CRP for diagnosis was calculated using receiver operating characteristic curve. Quantitative variables were compared using independent t test & Mann Whitney U test.

Results: CRP levels were found to be higher in study group with than in control group ($p< 0.050$). Cutoff value of CRP for diagnosing neonatal sepsis was found to be 6.5mg/l with a sensitivity and specificity of 60% and 70% respectively. In this study mean total leucocyte count was 14193 ±SD 7208 for study group and 10861 ±SD 4274, which was higher statistically significant with p value of 0.008.

Conclusion: In this study, we found that CRP can be used as an immediate screening test for detection of early onset neonatal sepsis. Combination of CRP and TLC together have better efficacy in diagnosing early neonatal sepsis.

Keywords: CRP, Neonatal Sepsis, Acute phase reactant, CRP, platelets.

Introduction

Early-onset sepsis manifests from birth to 7 days, usually less than 72 hrs [1]. Neonatal mortality rate was 25.3 per 1000 live births as per National Neonatal Perinatal Database (NNPD) 2002-2003 Report. Even though neonatal sepsis has such a high mortality, but presentation is with nonspecific signs and symptoms like excessive cry, fever, refusal to feed, tachycardia, tachypnea, hypoglycemia, hypothermia, convulsions. These nonspecific presentations give rises to need of diagnostic and screening tests. [2,3]

Gold standard for diagnosis of neonatal sepsis is Culture and sensitivity, takes 48 to 72 hours [4][5], which is crucial period for appropriate treatment and cannot be wasted in waiting for report. To fill this gap various markers like C-reactive protein (CRP), Total Leucocyte count (TLC), Absolute Neutrophil Count (ANC), nRBC's, ESR and platelet count are used to support the diagnosis.

This study was undertaken to evaluate the efficacy of CRP and Hematological parameters like Total Leucocyte count (TLC), Absolute Neutrophil Count (ANC), ESR and platelet count as screening test in early onset neonatal sepsis.

C reactive protein: CRP produced in liver and levels of CRP increase at least by 25% in various inflammatory conditions, infection and neoplastic conditions.[6],[7],[8],[9],[10] It takes 6 to 8 hours to increase following any exposure to infection or any inflammation.

Total Leucocyte count (TLC): Leucocyte count- Total counts more than 30,000/µl and less than 5000/ µl are considered as abnormal. [11]

Erythrocyte sedimentation rate: The erythrocyte sedimentation rate measures rate of settling (sedimentation) of erythroblasts in anticoagulated whole blood.[6] The normal range for ESR in neonates is day of life plus 3mm/hr up to 15mm/hr. [12]

Platelet count: normal value is 1.5lac/ µl. Decreased platelet counts are associated with late onset sepsis. Mechanism causing thrombocytopenia in sepsis can be decreased production due to bone

marrow infection, increased destruction due to endothelial injury or sepsis related complications like DIC causing consumption of platelet.[13]

Materials and Methods

Clinically suspected cases of neonatal sepsis and hyperbilirubinemia, which were admitted in Neonatal Intensive Care Unit (NICU) of Shri B.M. Patil Medical College Hospital & Research Center, Vijayapura, were taken as cases and controls for this Prospective Case Control study from December 2017 to June 2019. Blood samples were collected in plain, EDTA and Citrate anticoagulated vacutainers for blood culture, CRP, CBC and coagulation profile respectively. Plain Sample blood was first inoculated in glucose broth and incubated for 48 hours and then streaked into Mc conkey agar for further growth.

Optimal cut off values of CRP for were defined by Youdens index. Sensitivity and specificity of these variables were performed using ROC curves. Categorical variables were compared using chi square test, quantitative variables were compared using independent t test & Mann Whitney U test. For all tests, significant value was achieved at $p<0.05$.

Sample size: 36 cases in each group.

Inclusion Criteria:

- Neonatal cases with early signs of sepsis.
- Neonates born to mothers with premature rupture of membranes and fever.

Exclusion Criteria:

- Neonates with congenital anomalies.

Results

A total of 90 neonates were included, 48 in the study group and 42 neonates in the control group, with an age range of 1- 30 days who presented with signs and symptoms of sepsis. Among 48 suspected cases 18 cases were positive for various bacterial and viral infections. Most common bacterial infection was E. Coli followed by Klebsiella. Most common viral infection was CMV.

In this study, among 48 cases from study group 4 (8.34%) cases presented with total leucocyte count of <5000 cells/cumm, 42(87.50%) cases presented with total leucocyte count between5000 to 30000 cells/cumm, 2(4.16) cases presented with total leucocyte count above 30000 cells/cumm. In control group among 42, cases 4(9.52) cases presented with total leucocyte count of <5000 cells/cumm, and remaining 38(90.48%) cases presented with total leucocyte count between5000 to 30000 cells/cumm and none cases had total leucocyte count above 30000 cells/cumm.

Mean total leucocyte count was 14193 ±SD 7208 for study group and 10861 ±SD 4274, which was higher statistically significant with p value of 0.008.

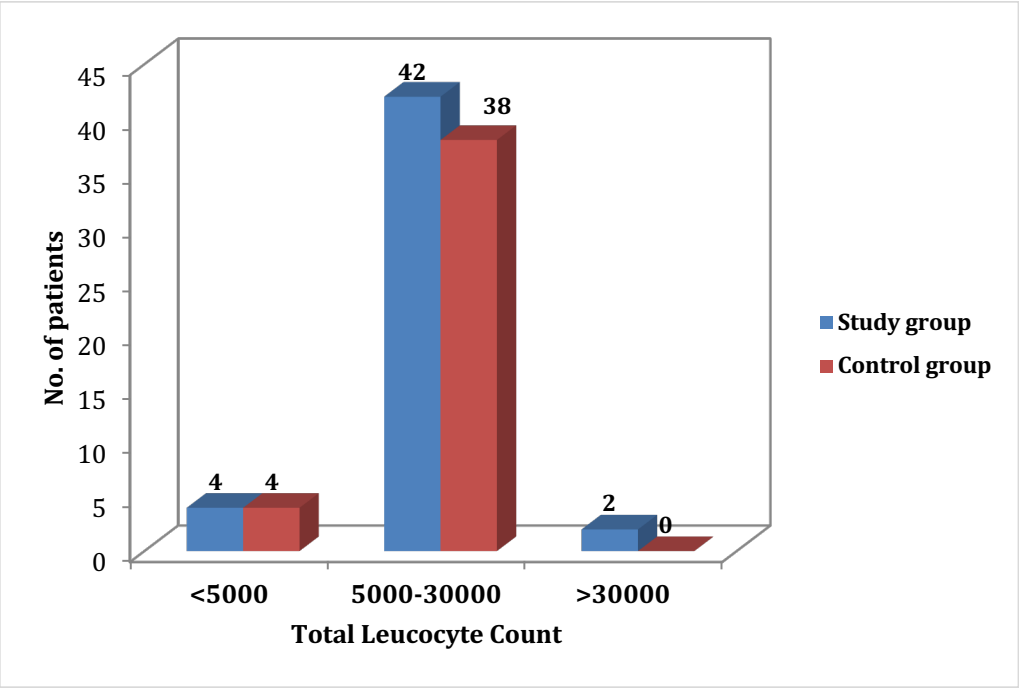

Figure 1: comparison of Total Leucocyte Count of patients between study & control group

In this study, mean value of CRP was 22.92 ±SD 24.45 for study group and 10.86 ±SD 13.69, which was higher and statistically significant with p value of 0.005.

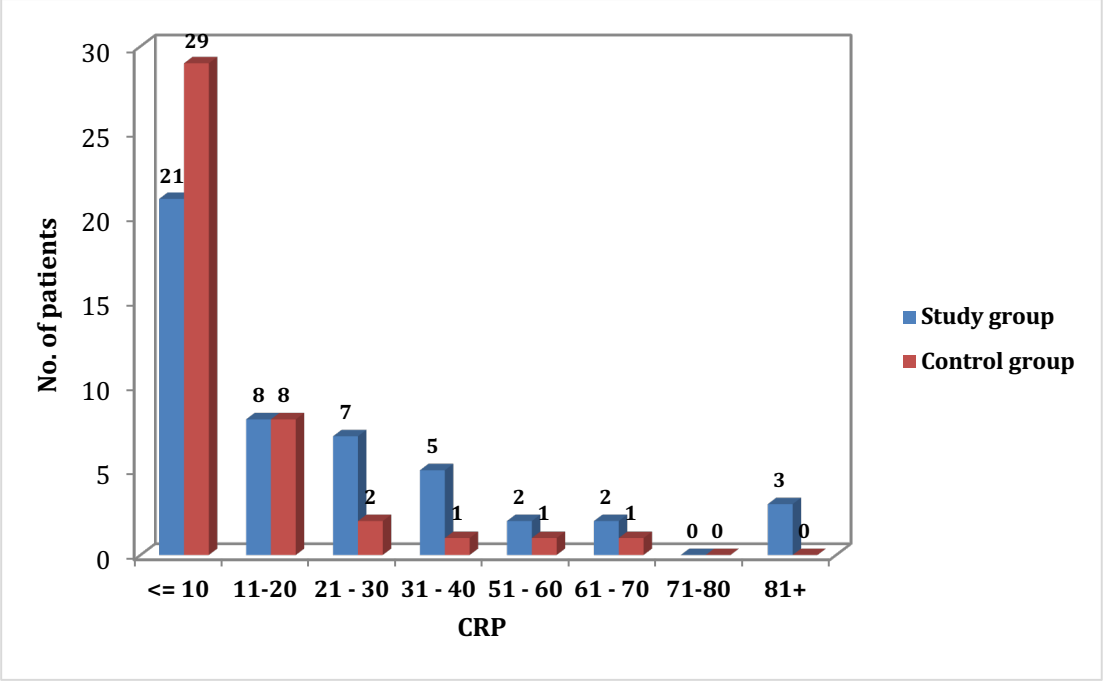

Figure 2: comparison of CRP of patients between study & control group

In this study, mean value of CRP was 22.92 ±SD 24.45 for study group and 10.86 ±SD 13.69, which was higher and statistically significant with p value of 0.005.

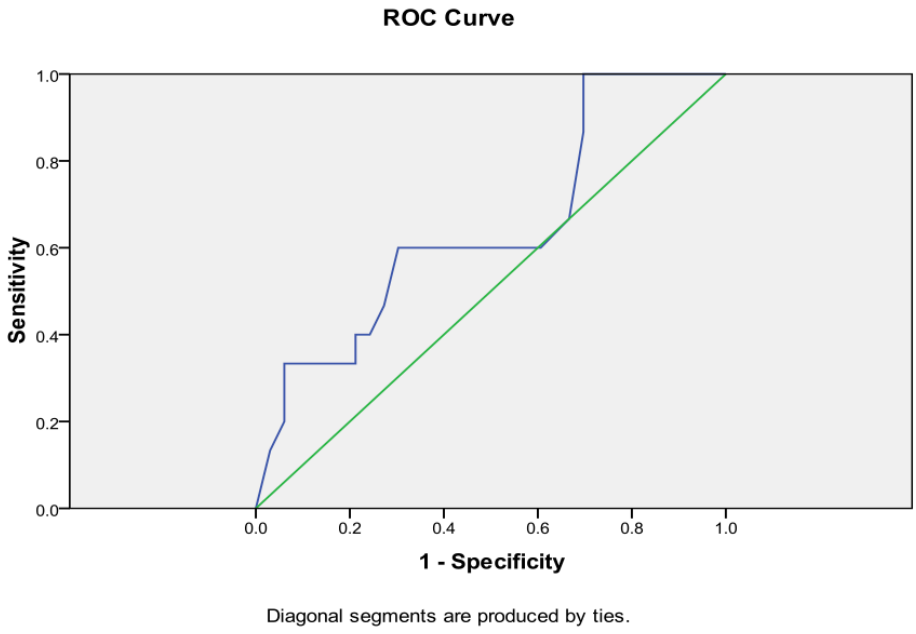

Figure 3: ROC curve of CRP in diagnosis of neonatal sepsis with all cases in study group

In this study, mean value of ESR was 7.79 ±SD 9.804 for study group and 6.29±SD 5.591, which was statistically not significant.

Mean value of platelet count was 2.02 ±SD 1.862 for study group and 1.99±SD 0.845, which was statistically not significant.

Mean value of absolute neutrophil count was 53.80±54.35for study group and 57.05±SD 15.174, which was statistically not significant.

Table 2: Comparison of variables between study and control group

Variables	Study group(n=48)		Control group(n=42)		Mann Whitney U test/Independent t test	P value
	Mean	±SD	Mean	±SD		
TLC	14193.13	7208.278	10861.43	4274.709	**t=** 2.705	P=0.008 HS
ANC	53.80	54.35	57.05	15.174	**t=** 0.828	P=0.410 NS
ESR	7.79	9.804	6.29	5.591	**t=** 0.671	P=0.505 NS
CRP	22.92	24.450	10.86	13.693	**U=** 660.50	P=0.005 HS
Platelet count	2.02	1.862	1.99	0.845	**U=** 839.00	P=0.169 NS
NS; Not significant HS: Highly significant						

Discussion

In present study the most common organism isolated was E coli followed by Klebsiella pneumonia. Similar findings were seen in Cortese F et al [14], Manroe et al[15] Chandna A et al[16] and Renolder B et al[17]. Most common viral infection was CMV.

Total WBC count in neonatal sepsis: In this study mean Total Leucocyte Count (TLC) was 14193 ±SD 7208 for study group and 10861 ±SD 4274, which was higher than control group having statistical significance with p value of 0.008.As per study done by Ahirrao BM *et a[18]* Total WBC count has lower sensitivity but higher specificity in detecting neonatal sepsis. It is because of wide normal range of WBC count between 5000-34000cells/cumm.

In this study total leucocyte count of less than 5000 cells/cumm ie; leucopenia cases and total leucocytes count more than 30000 cells /cumm ie; leucocytosis are considered as indicator for sepsis. In a study conducted by Das B *et al[5]* they found out that 54.5% of pod proven neonatal sepsis cases had leucopenia.

CRP in neonatal sepsis: In current study we found out that CRP was significantly elevated in study group than control group. Mean CRP level was 22.9±SD 24.450 for study group and 10.86 ±SD 13.693, which was higher than control group having statistical significance with p value of 0.005.

In a study conducted by Mondal *et al[19]* found out that CRP is most sensitive and is single best marker for detecting early onset Neonatal sepsis. Stephan E *et al*[20] found that CRP levels were most important parameter in guiding the duration of treatment with antibiotics of neonates with suspected sepsis.

In current study after comparing proven neonatal sepsis cases with our control population, on analysis of ROC curves we got cut off value of 6.5mg/l with sensitivity and specificity of 60% and 70%. This was comparable to study conducted by Guibourdenche J *et al*. Guibourdenche J *et al[21]* found that cut off value of 7.5mg/l for neonatal sepsis on analysis of ROC curves for CRP.

Khursid *et al*[22] observed CRP had sensitivity and specificity of 66% and 48%. In study conducted by Das B *et al*[5] got cut off value of 6 mg/l for neonatal sepsis. In a study by Morad et al., CRP showed a sensitivity (89.5%), a specificity (66.7%), a PPV (92.5%), a NPV (60.0%), and a significant accuracy 86.0% (p value = 0.001) [16].

Whereas individually, ANC, ESR and Platelet count were not helpful in diagnosing sepsis.

Conclusion

In this study, we found that CRP can be used as screening test for detection of early onset neonatal sepsis. Combination of CRP and TLC together have better efficacy in diagnosing early neonatal sepsis. These tests are rapid, economical and easy to perform. They aid in diagnosis of early onset neonatal sepsis but are not gold standard or help in deciding guidelines for antibiotic therapy.

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