



**ORIGINAL RESEARCH PAPER**

**Medicine**

**COMPARATIVE STUDY TO ASSESS THE EFFICACY OF NEUTROPHIL-LYMPHOCYTE COUNT RATIO VERSUS C- REACTIVE PROTEIN LEVELS IN DIAGNOSIS OF PATIENTS WITH SEPSIS**

**KEY WORDS:** Neutrophil-Lymphocyte count ratio , C-reactive protein , Sepsis.

**Dr Madhuri M Alwani**

Resident, Department of General Medicine and Therapeutics

**ABSTRACT**

**AIM AND OBJECTIVE-**To study the efficacy of Neutrophil Lymphocyte count ratio, CRP, Eosinophil count levels in diagnosis of sepsis.  
**METHOD-** This study was conducted on 100 patients >18 years of age of either sex with a diagnosis of sepsis admitted to the Medicine Intensive Care Unit in GEETANJALI MEDICAL COLLEGE AND HOSPITAL, Udaipur, Rajasthan.  
**RESULT AND CONCLUSION-** neutrophil/lymphocyte count ratio (NLCR) and C-reactive protein (CRP) came out as better independent biomarker of sepsis in critically ill patients, eosinophil count not be used as a diagnostic marker of sepsis in critically ill patients.

**INTRODUCTION :**

Sepsis is considered as the clinical syndrome, because of the presence of both infection and a systemic inflammatory response, that involves the activation of inflammatory and anti-inflammatory mediators, cellular and humoral reactions, and micro- and macro-circulatory alterations.<sup>1,2</sup>

Several biomarkers, like C-reactive protein and Procalcitonin have been used to determine bacterial infection. They have limited sensitivity and specificity, but the greatest limitation of C-Reactive Protein is probably its high cost, placing it practically out of reach of developing countries like India. Hence the need to evaluate Eosinophil Count and Neutrophil-Lymphocyte Count Ratio (NLCR) as an indicator of sepsis considering their lower cost and easier accessibility.<sup>3</sup>

**AIMS AND OBJECTIVES**

This study was conducted in GEETANJALI MEDICAL COLLEGE AND HOSPITAL, Udaipur, Rajasthan with following aims and objectives.

- Comparison of the efficacy of Eosinophil Count and Neutrophil-Lymphocyte Count ratio with C-Reactive Protein levels in patients with sepsis.
- To establish that eosinopenia and the neutrophil-lymphocyte count are simple yet sensitive markers for sepsis when compared to C-reactive protein.

**MATERIAL AND METHODS**

**STUDY POPULATION**

This study was conducted on 100 patients >18 years of age of either sex with a diagnosis of sepsis admitted to the Medicine Intensive Care Unit in GEETANJALI MEDICAL COLLEGE AND HOSPITAL, Udaipur, Rajasthan. Seventy patients with sepsis were included. Patients enrolled on the basis of following inclusion and exclusion criteria:-

**INCLUSION CRITERIA:**

- Both male and female patients > 18 years of age admitted with a diagnosis of sepsis.
- Patients willing to participate in the study.

**EXCLUSION CRITERIA:**

- Patients with hematological cancer.
- Patients with bronchial asthma and other atopic disorders like hay fever, atopic dermatitis, allergic conjunctivitis.
- Trauma patients as eosinophilia has been associated with trauma

**STUDY DESIGN**

The study duration was 18 months. This was a Hospital based observational descriptive study. At enrollment informed consent was obtained from patients

Following investigation was carried out-

- Blood routine- CBC, ESR, LFT, KFT & ABG.
- Neutrophil and lymphocyte count on first day

- Absolute eosinophil count on first day
- Urine routine and Urine for Culture/Sensitivity.
- Blood for culture and sensitivity (BACTEC).
- Pus for C/S, sputum for C/S, fluid (ascitic/pleural/CSF) for C/S wherever appropriately required.
- C-Reactive Protein Levels based on turbidimetry.
- SOFA scoring will be done on first day of admission.

**OBSERVATION AND RESULTS**

Statistical analyses were done using computer software (SPSS version 20 and primer). The qualitative data were expressed in proportion and percentages and the quantitative data expressed as mean and standard deviations.

**Table 1: Mean Age Of The Study Population -**

	Number of patients	Age range	Percent age	Mean age ± standard deviation
Male	63	20 - 89	63	56.65 ± 16.39
Female	37	19 - 88	37	59.62 ± 18.18
Total	100	19 - 89	100	57.75 ± 17.04

In our study, total 100 patients enrolled, who had features of sepsis. In them 63 patients were male (mean age- 56.65) and 37 patients were female (mean age- 59.62).

**Table 2: Proportion Of Patients On The Basis Of Infection And Severity-**

	SIRS	Sepsis	Severe sepsis	Septic shock
Number of cases	46	36	10	8
Percentage	46%	36%	10%	8%

**Table 3. Distribution Of Biomarkers In Patients :-**

Biomarkers	Sepsis patients (total - 54)	SIRS patients (total - 46)	Sensitivity (%)	Specificity (%)
Eosinophil count below cut of point (< 50 cells/mm <sup>3</sup> )	8	7	14.81	84.78
NLCR above cut of point (≥ 5)	35	20	64.81	56.52
CRP above cut of point (> 50 mg/dl)	44	19	81.48	58.70

C – reactive protein presented (above the cut of point, > 50 mg/dl) with 81.48% sensitivity and 58.70% specificity. neutrophil – lymphocyte count ratio (above the cut of point, ≥ 5) had 64.81 % sensitivity and 56.52% specificity. Eosinopenia (cut of point < 50 cells/mm<sup>3</sup>) had very low sensitivity only 14.81 % but high specificity of 84.78%.

**DISCUSSION**

To be considered a valid biomarker, three aspects must be present: (i) proving that the test truly measures a particular molecular species or its relevant biological activity; (ii) proving that

measurement of the biomarker discriminates patients with a disease from those who are without the disease; (iii) proving that measurement of the biomarker can inform a clinical decision that can improve patient outcomes.<sup>4</sup>

#### Demographic Profile Of Study Population-

Out of 100 patients enrolled in the study, in them 63 were male and 37 were female. The maximum number of patients (26%) present in age group of 65-74 years in both male and female category. Mean age ( $\pm$  standard deviation) of male patients was 56.65 ( $\pm$  16.39) and female patients was 59.62 ( $\pm$  18.18). Overall mean age of patients was 57.75 ( $\pm$  17.04) that is comparable to de Jager CPC et al<sup>43</sup> those reported 63.4  $\pm$  16 mean age of patients.

Mean age ( $\pm$  standard deviation) of patients in the sepsis group 59.11 ( $\pm$  17.61) years was comparable to that of patients in the SIRS group 56.15 ( $\pm$  16.40) years.

#### Partition Of Patients On The Basis Of Infection And Severity-

In our study, patients presented with both non-infectious causes (only SIRS, 46%) and infectious causes (SIRS with SEPSIS, 54%). In SIRS with infectious group, 36% patients marked with sepsis, 10% with severe sepsis and septic shock was seen in 8%. Hota PK et al<sup>55</sup> reported 44% cases with SIRS, 32% with sepsis, 14% with severe sepsis and 10% cases of septic shock. Our findings are in concordance with above mentioned study. Contrary to our results, Loonen AJM et al<sup>10</sup> (2014) reported only 21.6% infectious causes.

#### Eosinophil Count At 50 Cells/mm<sup>3</sup> Cutoff Point-

In our study, eosinophil count of 50 cells/mm<sup>3</sup> had a sensitivity of 14.81% with CI of 7.05 – 27.67%, specificity of 84.78% with CI of 70.51 – 93.16%, positive likelihood ratio (PV+) of 0.97 with CI of 0.38 – 2.47 and negative likelihood ratio (PV-) of 1.00 with CI of 0.89 – 1.13. Dimple Anand et al<sup>5</sup> with a cut-off value of 50 cells/mm<sup>3</sup>, reported a sensitivity of 23% , a specificity of 68% and they concluded that eosinopenia is not a reliable diagnostic tool to differentiate sepsis from SIRS.

#### N/I Ratio At $\geq 5$ Cutoff Point:-

Lymphocytopenia has previously been described as a marker of bacteremia but did not gain broad acceptance as an infection marker. The mechanisms responsible for lymphocytopenia in sepsis and septic shock involve margination and redistribution of lymphocytes within the lymphatic system and marked accelerated apoptosis.<sup>6,7</sup>

In our study NLCR of  $\geq 5$  had a sensitivity of 64.81% with CI of 50.55 – 76.97%, specificity of 56.52% with CI of 41.21 – 70.75%, negative likelihood ratio (PV-) of 0.62 with CI of 0.42 – 0.92 and positive likelihood ratio (PV+) of 1.49 with CI of 1.02 – 2.19. Our findings are in consistent with Lowsby R et al<sup>48</sup> in their study the sensitivity and specificity of NLCR for predicting bacteraemia were 70% (64% to 75%) and 57% (55% to 60%), respectively.

#### CRP count at >50 mg/dl cutoff point:-

C-reactive protein is a long-established marker of sepsis. C-reactive protein belongs to the pentraxin family of proteins, so called because they form a cyclic pentamer composed of five identical non-glycosylated sub-units, non-covalently bound and organised in a very stable discoid-like structure. CRP rises whenever an inflammatory process is present.<sup>5,6</sup>

The serum concentration of CRP in the normal human population has a median of 0.8 mg/l and is below 10 mg/l in 99% of normal samples.<sup>67</sup> Levels above these values are abnormal and indicate the presence of a disease process.

In the present study CRP of 50 mg/dl was used as a cut-off value between patients with sepsis and non-sepsis (only SIRS). In our study, CRP of 50 mg/dl had a sensitivity of 81.48% (C.I. of 68.13 – 90.30), specificity of 58.70% (C.I. of 43.29 – 72.66) and PPV of 69.84 % (C.I. of 56.81 – 80.43%) in diagnosis of sepsis. This value is in accordance with the study of Povoia et al<sup>68</sup> who concluded that

a plasma CRP of 50 mg/l or more was highly suggestive of sepsis with sensitivity 98.5% and specificity of 75%.

In our findings, significant co-relation was seen between sepsis and CRP.

#### SUMMARY AND CONCLUSION

In the present study, neutrophil/lymphocyte count ratio (NLCR) and C-reactive protein (CRP) came out as better independent biomarker of sepsis in critically ill patients. Sensitivity and specificity of neutrophil/lymphocyte count ratio at cut of point ( $\geq 5$ ) was 64.81 and 56.52, respectively. Sensitivity and specificity of C-reactive protein (CRP) at cut of value (>50 mg/dl) was 81.48 and 58.70, respectively. However specificity of eosinophil count at cut of value (< 50 cells/mm<sup>3</sup>) was good (84.78%) but sensitivity was very low as 14.81%.

According to our observation and results, eosinopenia can not be used as a diagnostic marker of sepsis in critically ill patients. We didn't found significant correlation between eosinopenia and sepsis. But NLCR had a good sensitivity and specificity second to CRP.

Outcomes of NLCR and CRP were quick, easy and economical in establishing diagnosis of sepsis.

CRP is a better diagnostic marker than NLCR and eosinopenia and may become a helpful clinical tool in ICU practices. Further studies are needed to evaluate the progression of CRP level with the severity of sepsis and to establish the best cutoff values for this marker.

In summary, the presence of CRP beyond normal level can be considered as an inexpensive warning test for sepsis in hospitalized adult patients so that further blood tests and investigations can be initiated to exclude bloodstream infection. However, CRP in normal limits does not exclude bloodstream infection in hospitalised adult patients. CRP concentrations are better markers of infection in this group.

#### REFERENCES

1. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med.* 2003;31: 1250-6.
2. Pulliam PN, Attia MW, Cronan KM. C-reactive protein in febrile children 1 to 36 months of age with clinically undetectable serious bacterial infection. *Pediatrics.* 2001 Dec;108(6):1275-9.
3. Terradas R, Grau S, Blanch J, Riu M, Saballs P, et al. (2012) Eosinophil Count and Neutrophil-Lymphocyte Count Ratio as Prognostic Markers in Patients with Bacteremia: A Retrospective Cohort Study. *PLoS ONE* 7(8): e42860, 2012. doi: 10.1371/journal.pone.0042860.
4. Marshall JC, Reinhart K. Biomarkers of sepsis. *Crit Care Med.* 2009;37:2290-98.
5. Ayala A, Herdon CD, Lehman DL, Ayala CA, Chaudry IH: Differential induction of apoptosis in lymphoid tissues during sepsis: variation in onset, frequency, and the nature of the mediators. *Blood* 1996, 87:4261-4275.
6. Hotchkiss RS, Swanson PE, Freeman BD, Tinsley KW, Cobb JP, Matuschak GM, Buchman TG, Karl IE: Apoptotic cell death in patients with sepsis, shock, and multiple organ dysfunction. *Crit Care Med* 1999, 27:1230-1251.