Correlation of Procalcitonin with Hematological Markers in Patients with SIRS and Sepsis: An Observational Study

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ABSTRACT

Introduction : Systemic Inflammatory Response Syndrome (SIRS) represents an amplified immune response to diverse insults such as infection, trauma, surgery, or ischemia. When SIRS is associated with a suspected or confirmed infection, it is referred to as sepsis. Diagnostic criteria for SIRS include any two of the following: a white blood cell (WBC) count of ≥4000/μL or >10% immature band forms, a body temperature >38°C or <36°C, heart rate >90 bpm, respiratory rate >20/min, or a $PaCO_2$ level <32 mm Hg. While procalcitonin (PCT) serves as a reliable but costly biomarker for sepsis, more economical alternatives include total leukocyte count (TLC), absolute neutrophil count, and the neutrophil-to-lymphocyte ratio (NLR).

Objectives This study aimed to investigate the correlation between PCT and hematological markers such as TLC, neutrophil count, and NLR in patients diagnosed with SIRS, with and without confirmed infections, and to assess the utility of these markers in differentiating between non-infective SIRS and sepsis.

Methods: A total of 282 acutely ill adult patients meeting the SIRS criteria were enrolled. Within 12 hours of hospital admission, serum PCT levels, TLC, neutrophil counts, and blood cultures were obtained. Additional baseline investigations were also recorded.

Results: Of the 282 patients, 194 were classified under SIRS without infection (Group I) and 88 under sepsis (Group II). Statistically significant differences in age and gender distribution were observed between the two groups ($p < 0.05$). All four parameters—PCT, TLC, neutrophil count, and NLR—were significantly elevated in the sepsis group. Strong correlations were noted between PCT and the hematological markers, particularly with NLR and neutrophil count.

Conclusion: PCT remains the most accurate biomarker for diagnosing sepsis, but TLC, neutrophil count, and NLR also demonstrated significant predictive value. These readily available and affordable tests can be effective in identifying sepsis in resource-limited settings.

Keywords: *Procalcitonin, Systemic Inflammatory Response Syndrome, Sepsis, Neutrophil-to-Lymphocyte Ratio, Total Leukocyte Count, Hematological Markers*

1. INTRODUCTION

An elevated defensive reaction of the body to a harmful stressor, like infection, trauma, surgery, acute inflammation, ischemia, reperfusion, or malignancy, to localize and eliminate the endogenous or exogenous source of the injury, is known as systemic inflammatory response syndrome (SIRS). Sepsis is a term used for SIRS with suspected or documented sources of infection. It is characterized by the fulfilment of any two of the following conditions: white blood cell (WBC) count ≥4000/μL or >10% immature forms or bands; body temperature above 38°C or below 36°C; pulse rate above 90 beats per minute; tachypnea (respiratory rate greater than 20 breaths per minute); or partial pressure of CO_2 below 32 mm Hg.[1] A prompt clinical and laboratory diagnosis, along with appropriate therapeutic therapy, are critical factors that determine the prognosis and death rate of patients with this life-threatening illness. Procalcitonin (PCT) is one of the more complex and expensive lab indicators used to diagnose and prognosticate this disorder. Less expensive tests include total leukocyte count (TLC), neutrophil count, and neutrophil/lymphocyte ratio (NLR).[2] The complete blood counts (CBC) test, the most popular and straightforward laboratory test that offers a plethora of information about a person's health state, can be used to assess

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any one of these three assays. Usually, an increase in TLC indicates an infection or inflammation. In a similar vein, during an infection, the neutrophil count rises significantly and is typically correlated with the overall severity of the infection. Neither of the tests is specifically designed to detect infections. Due to delayed neutrophil apoptosis, the value of the neutrophil count in severe sepsis is restricted. Notably, a variety of stressors, including physical and psychological strain, physiological conditions like pregnancy and obesity,[3]

and some other illnesses like smoking, can cause neutrophilia.[4] Periodically, low TLC counts can also occur in sepsis. One consistent biomarker for sepsis that has surfaced is NLR. The equilibrium between neutrophil and lymphocyte numbers can be inferred from changes in NLR. NLR correlates with SOFA score, APACHE I, and sepsis severity scores, and has been demonstrated in multiple studies to be an early indicator of sepsis, regardless of the etiology of sepsis.[6–8] The effectiveness of PCT as a marker of bacterial infection and critical disease has been demonstrated by a wealth of research. A sensitive biomarker aids in treatment decision-making because positive bacteriological results can be attributed to contamination, while negative results do not rule out sepsis. We attempted to assess PCT's correlation with the other three sepsis biomarkers in the current study. These biomarkers can be easily obtained by simply doing a CBC count. These can be a cheaper alternative to costly tests and are done routinely in resource-poor settings as well.

Study Objectives

To determine the relationship between procalcitonin and TLC, neutrophil count, and NLR in patients with SIRS without documented infection and SIRS with infection (sepsis).

To evaluate the TLC, neutrophil count, and NLR between SIRS without infection and sepsis.

2. MATERIALS AND METHODS

Data Source and Collection

All adult patients aged 18 years or more who presented to the emergency unit or were directly admitted to the intensive care unit (ICU) or wards, and who fulfilled the criteria of SIRS between January 2024 and October 2024 and gave consent for the study, were considered. Prior ethical approval of the research was obtained from the research ethical committee of the Muzaffarnagar Medical College.

Study Design

Observational cross-sectional study.

Sample Size and Sampling Method

According to a hospital-based study in North India, the prevalence of SIRS was found to be 23%. So, a sample size of 282 was taken.

Inclusion Criteria

All acutely ill, hospitalized medical patients aged 18 years or older, who presented to the emergency department or were directly admitted to the ICU or wards and fulfilled the inclusion criteria of SIRS or sepsis, were included. Consent was taken from the patient's attendant if the patient was not fit to give consent.

Exclusion Criteria

Unwilling patients

Individuals transferred from other hospitals or wards

Patients with untreated end-stage renal failure not on dialysis, medullary thyroid carcinoma, or islet cell tumors

Severe pancreatitis, post liver transplantation, severe and prolonged cardiogenic shock, or heat shock. Patients who were admitted to the department more than once during the inclusion period were counted only once, at the time of their initial admission, and not again during future admissions.

StudyThe serum PCT value, checked using the semiquantitative PCT test kit within 12 hours of admission to the hospital, was noted. A PCT value of ≥0.5 was considered significant, as per the manufacturer's instructions. TLC was measured by an automated hematology analyzer. Blood cultures were done using the automated BacT/ALERT BD system under strict aseptic precautions. All pertinent investigation reports were recorded, including blood investigations performed upon admission, such as CBC, LFT, KFT, and sugar, among others.

The demographic profile and medical examination findings of all the patients were registered. A detailed medical history, including comorbidities like hypertension (HTN), diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), pulmonary tuberculosis (PTB), malignancy, coronary artery disease (CAD), chronic kidney disease (CKD), chronic liver disease (CLD), cerebrovascular accident (CVA), etc., was noted along with the complete medical examination findings.

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The identification of a pertinent pathogen by microscopy, cultures in blood, urine, sputum, or tissue biopsy samples, or polymerase chain reaction, constituted the basis for documenting sepsis.

AnalysisPatients with confirmed SIRS were included in the study and divided based on negative and positive culture reports into group I and group II. All the data were analyzed using IBM SPSS 24. Mann–Whitney U tests were used to compare the medians of PCT, TLC, and NLR. The Chi-squared test was used to compare categorical variables. The correlation between PCT and the above-mentioned other three biomarkers of sepsis was determined with the help of Pearson's test.

ResultsOut of a total of 282 patients with SIRS, there was no documented infection in 194 patients (group I), whereas 88 patients had documented infection (sepsis group II). The difference between age and sex in both groups ($p < 0.05$) was found to be statistically significant. All four markers, PCT, TLC, neutrophils, and NLR, were significantly higher in the sepsis group (Table 1).

Table 1: Demographic profile and biomarkers in SIRS without infection and sepsis groups

	Group I (no sepsis) N = 194	Group II (sepsis) N = 88	p-value
Age (mean)*	43 (18–94)	45 (18–92)	0.0001 (Z score = 3.890)
Sex (M/F)*	103/22	22/66	0.0001 (Z score = 3.890)
PCTº	0.4 (0.4–10)	2 (0.4–10)	0.0002 (Z score = 3.719)
TLC	7.4 (1.51–58.6)	10.89 (1.69–29.16)	0.00143 (Z score = 3.188)
Neutrophil	79.5 (20–97)	83.5 (41–98)	<.00001 (Z score = 4.417)
NLR	5.7 (0.28–97)	8.4 (0.82–97)	0.01108 (Z score = 2.540)

*Chi-squared test; ºMann–Whitney U test

In Pearson's correlation analysis, except for PCT and WBC in sepsis, significant correlations were found between PCT and WBC, neutrophil count, and N/L ratio in both groups of SIRS (Table 2).

Table 2: Table showing the correlation of PCT with other markers of sepsis

	Sepsis	Without sepsis
PCT and WBC	$rs = 0.2025, p$ (2-tailed) = 0.0559)	$rs = 0.2425, p$ (2-tailed) = 0.0006
PCT and neutrophil	$rs = 0.2175, p$ (2-tailed) = 0.01428	$rs = 0.2710, p$ (2-tailed) = 0.0001
PCT and N/L ratio	$rs = 0.2515, p$ (2-tailed) = 0.0183)	$rs = 0.2762, p$ (2-tailed) = 0.0003

To determine the cutoff values for the parameters PCT, TLC, neutrophil count, and NLR in the diagnosis of SIRS, a study of the area under receiver operating characteristic curves (AU-ROC) was conducted. Statistical significance was defined as values of $p < 0.05$

PCT had moderate sensitivity and high specificity, TLC and NLR had moderate sensitivity and specificity, and neutrophil count had moderate sensitivity and poor specificity to detect sepsis (Table 3).

Table 3: Table showing the cutoff value, sensitivity and specificity of all the four biomarkers of sepsis

Diagnostic test	Cutoff value	AUC	95% CI	p-value	Sensitivity	Specificity
PCT	6.00	0.638	0.565–0.711	0.000	44.3%	82%
TLC	7.35	0.618	0.546–0.691	0.001	70.5%	50%
Neutrophil	72.50	0.572	0.497–0.648	0.062	73.9%	26%
NLR	6.48	0.615	0.543–0.687	0.002	64.8%	56%

$p < 0.05$

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3. DISCUSSION

Our study, along with numerous others,[9–12] revealed that procalcitonin, WBC, neutrophil, and NLR values were considerably greater in patients with sepsis. However, one study hypothesized that PCT alone could be a good indicator of sepsis. Numerous studies have indicated that WBC counts are a poor predictor of sepsis and show little correlation with sepsis status, particularly in the elderly.

Aging-related reductions in phagocytosis and cell regeneration capacity may be the cause of this. In our investigation, there was a strong correlation between NLR and sepsis, or culture positivity. While the results were similar to many studies that identified a substantial correlation between NLR and sepsis, they differed from the few studies that found no significant association. The observed contradictory outcomes may be ascribed to differences in the research population, sample volume, or technique. These biomarkers are especially significant as treatment initiation at arrival may have a role in lowering the yield of culture positivity.

In correlation analysis, an insignificant correlation was found between PCT and TLC count in sepsis, which was similar to a few studies. It was in contrast to one study where a significant correlation between the two was observed. One such study revealed an insignificant correlation between PCT and all three markers. This particular study found that there was a significant correlation ($p < 0.001$) between PCT and WBC, CRP, and NLR, with respective values of 0.2332, 0.2245, and 0.2582.

Klebsiella pneumoniae was the second most frequently isolated organism in culture, after another gram-negative infection, *Escherichia coli*. This was comparable to numerous other reports. Our study has shown that PCT was the best parameter to diagnose sepsis and was even better than NLR. This outcome is different from a prior study, which found NLR to be superior to PCT. We found that TLC or NLR has the ability to predict sepsis, which is comparable to PCT, whereas neutrophil count has poor specificity. According to one study, NLR can predict the severity of sepsis ten times better than the absolute neutrophil count. As per our research, an NLR cutoff of 6.48 might also be used as a predictor of sepsis, similar to a study that showed NLR >7 was associated with a fatal outcome in sepsis patients and that it can be employed as a prognostic marker in patients with sepsis.

Due to its high sensitivity and specificity in predicting sepsis, PCT fared better on ROC curve analysis than the other three biomarkers, particularly the neutrophil count. In lieu of PCT for the diagnosis of sepsis, TLC and NLR have been shown to have intermediate sensitivity and specificity in predicting sepsis.

4. LIMITATION OF THE STUDY

This is a hospital-based study, so the true prevalence of SIRS in the community cannot be known. False negative values of the inflammatory markers or culture can occur due to technical or procedural errors or when the infection remains confined to a tissue or organ with no systemic manifestations. False positive tests can be present in certain conditions that could not be ruled out in those patients.

5. CONCLUSION

PCT is the best biomarker to predict sepsis and it correlated significantly with TLC, neutrophil count, and NLR in SIRS without infection, and with neutrophil count and NLR in sepsis in our study. Secondly, TLC and NLR are also good predictors of sepsis and can diagnose sepsis in resource-poor settings.

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