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Research Article

Correlation Between Neutrophil-to-Lymphocyte Ratio and Severity Scores in Septic Patients Presenting to Emergency Department

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ABSTRACT

Objective: Sepsis is a life-threatening condition caused by a dysregulated immune response to infection, leading to organ dysfunction and high mortality rates. Early identification is crucial but challenging, particularly in vulnerable populations. The neutrophil-to-lymphocyte ratio (NLR) has emerged as a potential biomarker for assessing sepsis severity. This study evaluates the correlation between NLR and established severity scores, including Acute Physiology and Chronic Health Evaluation (APACHE) II and Sequential Organ Failure Assessment, to determine its usefulness in early risk assessment.

Methods: This prospective observational study was conducted in the emergency department of a tertiary care hospital, enrolling 64 patients based on predefined criteria. Data collection included medical history, physical examination, laboratory investigations, and radiological evaluations. Statistical analyses were performed using SPSS and R software, with significance set at $P < 0.05$.

Results: Among 64 patients, 23 (35.9%) had a NLR of ≥ 8, while 41 (64.1%) had an NLR of < 8, with a mean of 7.57. Patients with NLR ≥ 8 were more likely to require vasopressor support ($P = 0.009$) and had significantly lower mean arterial pressure ($P = 0.027$) and systolic blood pressure ($P = 0.041$). Higher inflammatory markers were noted in the NLR ≥ 8 group. Strong correlations were found between NLR and APACHE ($r = 0.80$), and between NLR and procalcitonin ($r = 0.81$).

Conclusion: This study highlights the NLR as a crucial biomarker for sepsis severity in emergency department patients. Elevated NLR correlates with critical severity scores and poorer hemodynamic status. It also suggests that NLR can enhance diagnostic accuracy, aiding timely interventions and improving outcomes in critical care.

Keywords: Neutrophil-to-lymphocyte ratio, procalcitonin, sepsis, APACHE II, SOFA

INTRODUCTION

Sepsis is a life-threatening syndrome characterized by organ dysfunction resulting from a dysregulated host response to infection.[1] Globally, sepsis affects an estimated 31.5 million individuals each year, with approximately 19.4 million progressing to septic shock and resulting in around 5.3 million deaths annually. In-hospital mortality rates for sepsis range from 17% to 26%.[2] The 2020 Global Burden of Sepsis study, conducted by the Institute for Health Metrics and Evaluation, reported 48.9 million incident cases in 2017, equating to 677.5 cases per 100.000 age-standardized population. Overall, sepsis accounted for 19.8% of global deaths, with 11.0 million fatalities in 2017.[3] In India alone, sepsis cases were estimated at 11.3 million, with 2.9 million sepsis-related deaths (297.7 per 100.000 population) in 2017.[4] These figures underscore the

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need for reliable and easily measurable biomarkers to facilitate early detection and risk assessment, particularly in low- and middle-income countries like India.[4]

Classic signs of infection and organ dysfunction, such as fever, productive cough, and dysuria, are commonly observed in sepsis. However, sepsis can also present with subtle or atypical symptoms, complicating diagnosis and delaying timely intervention.[5] Effective sepsis management relies on early and accurate identification of high-risk patients, often assessed through established scoring systems including the Acute Physiology and Chronic Health Evaluation II (APACHE II) and the Sequential Organ Failure Assessment (SOFA). Although widely used, these scoring systems are complex and may not always be feasible for rapid bedside assessment in emergency settings, creating a demand for simpler, more accessible tools in clinical practice.[6-9]

There is a growing need for simpler and more accessible tools to assess the severity of sepsis in clinical practice.[10] The inflammatory and immunological response plays a pivotal role in sepsis pathophysiology, driving efforts to identify reliable biomarkers that can enhance prognosis and guide management. While several biomarkers have been investigated, only a few are currently integrated into clinical practice.[11] Among these, the neutrophil-to-lymphocyte ratio (NLR), an easily calculable marker derived from a complete blood count, has garnered attention as a potential biomarker that reflects the immune dysregulation characteristic of sepsis. NLR has shown potential for predicting poor outcomes in various critical illnesses; however, its effectiveness as an independent predictor of mortality in sepsis, particularly in relation to the established severity scoring systems APACHE II and SOFA, remains underexplored. Hence, the present study aims to evaluate the association between NLR and APACHE II/SOFA scores in septic patients presenting to the emergency department (ED), with the objective of determining whether NLR can be used as a surrogate marker for disease severity and facilitate early risk assessment.

MAIN POINTS

- Elevated neutrophil-to-lymphocyte ratio (NLR) levels were associated with significantly higher C-reactive protein (P = 0.002), serum lactate (P < 0.001), and procalcitonin levels (P = 0.006), suggesting their role as a surrogate marker for systemic inflammation and sepsis severity.
- NLR showed a strong correlation with Acute Physiology and Chronic Health Evaluation II (r = 0.80) and Sequential Organ Failure Assessment scores (r = 0.74), highlighting its potential as a reliable biomarker for assessing illness severity in septic patients, with higher NLR values indicating worse clinical outcomes.
- The respiratory tract was identified as the most common infection source (53.1%), followed by urinary infections (21.9%) and gastrointestinal infections (15.6%), underscoring the need for targeted antimicrobial strategies in septic patients presenting to the emergency department.
- Given its strong correlation with key inflammatory and severity markers, NLR emerges as a cost-effective, readily available biomarker that can enhance early risk stratification, guide clinical decision-making, and improve sepsis management in emergency and critical care settings.

MATERIAL AND METHODS

This study was approved by the Institutional Ethics Committee-Biomedical Research and Scientific Committee of Indraprastha Apollo Hospitals (approval no.: 152-20120-201-230554, date: 30.06.2022). Also, a written informed consent was obtained from the patient for study participation.

This prospective observational study was conducted over a period of 20 months in the ED of a tertiary care hospital, involving a total of 64 patients. Inclusion criteria were established based on the quick SOFA scores for patients aged over 18 years, which required a respiratory rate of ≥ 22 breaths per minute, altered mental status, systolic blood pressure (SBP) of ≤ 100 mmHg, and a serum lactate level greater than 2 mmol/L. Exclusion criteria included pregnant women, individuals under 18 years, prior antibiotic use for more than 24 hours, haematological disorders, chronic inflammatory conditions, recent steroid use, and chemotherapy or radiotherapy within the last three months.

Each patient underwent a comprehensive assessment that included detailed history- taking, demographic information such as age, sex, special habits, substance abuse, co-morbid conditions, and past medical history. A comprehensive physical examination was performed, using techniques such as inspection, palpation, percussion, and auscultation, guided by the patient's reported symptoms. Laboratory assessments included essential tests, arterial and venous blood gas analysis, complete blood count, serum creatinine levels, urinalysis, liver function tests (which encompassed albumin, serum glutamic oxaloacetic transaminas, serum glutamic pyruvic transaminase, bilirubin, and international normalized ratio), blood glucose measurements, C-reactive protein (CRP), procalcitonin, and serum lactate. Cultures were collected from all suspected infectious biological fluids, and the NLR was derived from the complete blood count results. Radiological evaluations, including abdominal ultrasound, echocardiography, electrocardiography, and chest imaging (chest X-ray or non-contrast computed tomography chest), were also performed. The sepsis severity scores SOFA and APACHE II were calculated upon admission for each patient.

Statistical Analysis

Data management involved meticulous checking of collected data in case record forms for completeness and accuracy. Descriptive statistics for categorical data are expressed as numbers and percentages, while mean ± standard deviation is used to express continuous data based on normal distribution.

After appropriate data filtration, the datasheet was analyzed using SPSS statistical software version 22.0 and R version 3.2.0. Chi-square (χ^2) test for categorical data and Student t-test for quantitative variables were performed to compare the time taken to receive scan reports. The means of two or more groups were compared using analysis of variance to determine any significant differences. A *P* value ≤ 0.05 was deemed statistically significant.

RESULTS

Of the 64 patients, 23 (35.9%) had an NLR of ≥ 8, whereas 41 (64.1%) had an NLR of < 8. The NLR values demonstrated a wide range, with a minimum value of 2.19 and a maximum value of 17.5 (Table 1). The age distribution analysis revealed that among 23 patients with an NLR of ≥ 8, 39.13% were aged 56-65 years, 30.43% were aged 46-55 years, and 21.74% were aged 66-75 years. In contrast, among 41 patients with an NLR of < 8, 34.15% were in both the 46-55 year and 56-65 year age groups, while 8.70% were aged over 75 years (*P* = 0.358). Regarding gender distribution, the NLR ≥ 8 group included 52.17% males and 47.83% females, whereas the NLR < 8 group included 56.10% males and 43.90% females (*P* = 0.764). Additionally, 47.8% of patients in the NLR ≥ 8 group required vasopressor support, which was significantly higher than the 17.1% in the NLR < 8 group (*P* = 0.009) (Table 2).

Mean arterial pressure (MAP) was significantly lower in patients with an NLR of ≥ 8 (mean 62 mmHg) compared to those with an NLR of < 8 (mean 76 mmHg; *P* = 0.027). SBP also demonstrated a significant difference, with patients having an NLR of ≥ 8 exhibiting a mean SBP of 92 mmHg, whereas those with an NLR of < 8 had a mean SBP of 108 mmHg (*P* = 0.041). Although the diastolic blood pressure showed a trend towards significance (*P* = 0.08), it did not reach statistical significance. Laboratory assessments in the NLR ≥ 8 group indicated significantly elevated CRP levels (mean 41.30 mg/L vs. 22.24 mg/L; *P* = 0.002), serum lactate levels (mean 6.88 mmol/L vs. 3.66 mmol/L; *P* < 0.001), and serum procalcitonin levels (mean 16.47 ng/mL vs. 6.93 ng/mL; *P* = 0.006) as compared to those in the NLR < 8 (Table 3).

The median APACHE score among 21 patients with an NLR of ≥ 8 was 13 (range: 8-28), indicating a higher severity of illness compared to those with an NLR of < 8 (n=41), whose median APACHE score was 9 (range: 3-18). Similarly, the median SOFA score was significantly elevated in the ≥ 8 NLR group was 8 (range: 6-11) versus 4 (range: 2-9) for the < 8 NLR group (Table 4).

Regarding the source of infection, the majority of patients had respiratory infections, accounting for 53.1% (n=34) of the cohort. 21.9% (n=14) had urinary infections, while 15.6% (n=10) had gastrointestinal tract (GIT) infections (Table 5).

The NLR had a strong correlation with the APACHE score (*r* = 0.80), SOFA score (*r* = 0.74) and serum procalcitonin (PCT) levels (*r* = 0.81). Also, NLR showed a moderate correlation with serum lactate levels (*r* = 0.64), but a weaker correlation with CRP (*r* = 0.45) and white blood cell (WBC) count (*r* = 0.28) (Table 6).

DISCUSSION

This prospective observational study was conducted on 64 patients to evaluate the correlation between NLR and severity scores such as APACHE II and SOFA in septic patients presenting to the ED. In our study, the respiratory system was the most commonly affected, accounting for 53.1% of cases, followed by the urinary system (21.9%) and the GIT (15.6%, n=10). Our findings align with those of Rehman et al.[12] who reported pneumonia as the most common source of sepsis in 44.0% (n=74) of patients, followed by urinary tract infections (26.2%, n=44), soft tissue/skin infections (19%, n=32), and intra-abdominal infections (5.4%, n= 9), and central nervous system infections (4.8%, n=8). Similarly, Velissaris et al.[13] observed that the most frequent origins of sepsis were pulmonary (36.8%, n=42), urinary (23.6%, n=27), surgical (15.7%, n=18), abdominal (10.5%, n=12), cutaneous (7.14%, n=10), and unknown sources (4.3%, n=5).

We observed that patients with elevated NLR exhibited lower MAP and SBP, suggesting they may experience greater hemodynamic instability or severity of illness. Additionally, higher neutrophil counts and CRP levels were observed in patients with elevated NLR, indicating a more pronounced inflammatory response. This aligns with the understanding that

Table 1. The Quantitative Values of the Neutrophil-to-Lymphocyte Ratio Among Study Participants

Parameter	Value
NLR ≥ 8	23 (35.9%)
NLR < 8	41 (64.1%)
Minimum	2.19
Mean	7.57
Median	6.86
Maximum	17.5

NLR, neutrophil-to-lymphocyte ratio.

Table 2. Baseline and Clinical Characteristics of Participants

Parameters	NL ratio		Chi-square test	*P* value
	≥ 8 (n, %)	< 8 (n, %)		
Age (years)				
≤ 45	0 (0.00)	5 (12.20)	4.370	0.358
46-55	7 (30.43)	14 (34.15)		
56-65	9 (39.13)	14 (34.15)		
66-75	5 (21.74)	7 (17.07)		
> 75	2 (8.70)	1 (2.44)		
Gender				
Female	11 (47.83)	18 (43.90)	0.090	0.764
Male	12 (52.17)	23 (56.10)		
Vasopressor needed				
Yes	11 (47.8)	7 (17.1)	6.786	**0.009**
No	12 (52.2)	34 (82.9)		

NL, neutrophil-to-lymphocyte.

Table 3. Blood Pressure and Lab Investigations at the Time of Admission

	NL ratio		*P* value
Parameters	**≥ 8**	**< 8**	
Mean arterial pressure			
Mean	62	76	
Median (range)	67 (46-84)	79 (56-90)	**0.027**
Systolic blood pressure			
Mean	92	108	
Median (range)	98 (60-114)	110 (70-130)	**0.041**
Diastolic blood pressure			
Mean	62	66	
Median (range)	58 (40-72)	68 (52-88)	0.08
Serum total bilirubin			
Mean	1.41	1.57	
Median (range)	1.4 (0.8-3.2)	0.9 (0.7-2.6)	0.66
Serum creatinine			
Mean	1.64	1.13	
Median (range)	1.3 (0.5-5.3)	1.4 (0.4-3.44)	0.24
Platelet			
Mean	119100	122100	
Median (range)	115000 (26000-211.200)	128000 (26000-345.000)	0.10
Total leukocyte count			
Mean	19216	16378	
Median (range)	18300 (8000-30100)	15500 (11000-34000)	0.167
Neutrophil			
Mean	18626	11795	
Median (range)	17500 (7000-31700)	12100 (2600-31700)	**0.018**
Lymphocyte			
Mean	1721	1867	
Median (range)	1740 (840-2530)	2100 (680-2600)	0.855
C-reactive protein			
Mean	41.30	22.24	
Median (range)	26 (18-84)	14 (6-72)	**0.002**
Serum lactate			
Mean	6.88	3.66	
Median (range)	6.5 (3.9-14)	2.98 (1.8-11)	**< 0.001**
Serum procalcitonin			
Mean	16.47	6.93	
Median (range)	15.35 (11.65-34)	6.2 (5.5-26)	**0.006**

NL, neutrophil-to-lymphocyte.

Table 4. Disease Severity Score Among Participants

Parameters	NL ratio	
	≥ 8	< 8
APACHE score		
Median (range)	13 (8-28)	9 (3-8)
SOFA Scale		
Median (range)	8 (6-11)	4 (2-9)
Glasgow Coma Scale		
Median (range)	14 (4-15)	14 (3-15)

NL, neutrophil-to-lymphocyte; APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment.

Table 5. The Source of Infection Identified in the Participants

System	n	%
Respiratory	34	53.1
Urinary	14	21.9
GIT	10	15.6
Others	6	9.3
Total	64	100.0

GIT, gastrointestinal tract.

Table 6. Spearman's Correlation Between NLR and Other Parameters

Scale	Co-relation coefficient (r)
	NLR
APACHE	0.80
SOFA	0.74
Serum procalcitonin	0.81
Serum lactate	0.64
C-reactive protein	0.45
WBC count	0.28

NLR, neutrophil-to-lymphocyte; APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment; WBC, white blood cell.

NLR serves as a marker of systemic inflammation. Moreover, serum lactate levels were significantly higher in the elevated NLR group, which may indicate tissue hypoperfusion or a more severe metabolic derangement commonly associated with critical illness. Elevated procalcitonin levels in this group further suggest an increased risk of bacterial infection and sepsis. In contrast, no significant differences were found in serum total bilirubin, serum creatinine levels, or platelet counts between the groups. These findings are consistent with those reported by Shalaby et al.[14], who reported significant differences in MAP, SBP, neutrophil levels, serum creatinine, and platelet count across NLR groups. Similarly, a study by Liang and Yu[15] indicated that levels of serum creatinine, inflammatory markers (CRP, PCT, NLR), PCT, and total bilirubin were significantly higher in patients with severe bloodstream infections and sepsis compared to those in the non-critical group ($P < 0.05$).

The findings of the present study indicate that patients in the elevated NLR group had a higher median APACHE score compared to those in the lower NLR group, suggesting a greater overall severity of illness. Similarly, the SOFA scores were significantly higher in the NLR ≥ 8 group, reflecting a more pronounced degree of organ dysfunction and systemic response to critical illness. In contrast, the Glasgow Coma Scale were comparable between the two groups, indicating no significant difference in neurological status. Shalaby et al.[14] reported those patients with severe sepsis or septic shock have significantly higher APACHE II score ($P = 0.001$) and higher SOFA score on admission ($P = 0.014$) in patients with NLR > 10 compared to the NLR < 10.

The Spearman's correlation analysis revealed a strong positive correlation between the NLR ratio and both the APACHE II score ($r = 0.80$) and SOFA score ($r = 0.74$), indicating that higher NLR ratios are associated with increased severity of illness and greater organ dysfunction. Serum PCT exhibited a similarly strong correlation with the NLR ratio ($r = 0.81$), underscoring its association with infection and inflammation markers. Serum lactate showed a moderate correlation ($r = 0.64$), while CRP ($r = 0.45$) and WBC count ($r = 0.28$) demonstrated weaker correlations, reflecting varying degrees of association between these parameters and the NLR ratio. These findings are consistent with Liang and Yu[15], who reported positive correlations of NLR, CRP, and PCT levels with disease severity in sepsis patients ($r = 0.468$, 0.456, and 0.670, respectively; $P < 0.001$). Similarly, Velissaris et al.[13] demonstrated that NLR was positively correlated with sepsis severity scores [(SOFA, $r = 0.497$, $P < 0.001$; APACHE II, $r = 0.411$, $P = 0.003$; Simplified Acute Physiology Score II (SAPS II), $r = 0.445$, $P = 0.001$)] and total WBC count ($r = 0.531$, $P < 0.001$).

Total WBC count also correlated with the SOFA, APACHE II, and SAPS II scores.[16] Drăgoescu et al.[16] found significant correlations between NLR and both presepsin ($r = 0.56$, $P < 0.001$) and the SOFA score ($r = 0.65$, $P < 0.001$), supporting the utility of NLR as a prognostic tool in sepsis, comparable to markers like presepsin and SOFA score.

Study Limitations

Several limitations of this study warrant consideration. As a single-centre observational study with a limited sample size, there is a potential for residual confounding, underscoring the necessity for future multicentre studies that incorporate larger sample sizes and a broader range of variables. The implementation of stringent exclusion criteria excluded patients with abnormal baseline WBC counts, which may have omitted individuals with significant comorbidities that could impact the study's findings. Additionally, the NLR was calculated without differentiating between lymphocyte subtypes, and intraday variations in cell counts were not accounted for, as only the initial measurement of the day was utilized.

CONCLUSION

This study emphasizes the NLR as an important biomarker for assessing sepsis severity in ED patients. Elevated NLR levels correlate strongly with critical severity scores like APACHE II and SOFA, reflecting the overall condition of septic patients. Higher NLR values are associated with poorer hemodynamic status, along with increased inflammatory markers such as CRP and PCT. The study also identifies the respiratory tract as the predominant source of infection, which has significant implications for clinical management. Furthermore, the strong correlation between NLR and serum PCT levels suggests that NLR could enhance diagnostic accuracy and prognostic assessments, thereby contributing to timely interventions aimed at reducing mortality in sepsis patients. Overall, NLR is presented as a cost-effective and readily available tool that may assist clinicians in quickly evaluating sepsis severity, guiding timely disposition, and improving patient outcomes in critical care settings. Future research should continue to explore the clinical implications of NLR alongside other inflammatory markers to refine its application in sepsis management.

Ethics

Ethics Committee Approval: This study was approved by the Institutional Ethics Committee-Biomedical Research and Scientific Committee of Indraprastha Apollo Hospitals (approval no.: 152-20120-201-230554, date: 30.06.2022).

Informed Consent: A written informed consent was obtained from the patient for the study participation.

Footnotes

Author Contributions

Concept Design – R.A., R.P., U.P.; Data Collection or Processing – R.A., R.P., U.P.; Analysis or Interpretation – R.A., R.P.; Literature Review – U.P.; Writing, Reviewing and Editing – R.A.

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