Original Article

Relationship Between Neutrophil-to-Lymphocyte Ratio (NLR) and Sepsis and Mortality in Patients Admitted to the Emergency Department: A Retrospective Observational Study

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ABSTRACT

Objective: This study aims to investigate the relationship between the neutrophil-to-lymphocyte ratio (NLR) and the diagnosis of sepsis and in-hospital mortality in patients admitted to the emergency department. **Methods:** This was a retrospective observational study conducted at the Emergency Department of Esenyurt Necmi Kadıoğlu State Hospital. Data from adult patients who presented to the emergency department between January 1, 2023, and December 31, 2024, were analyzed. Patients with complete blood count (CBC) results and suspected or confirmed infection were included. NLR values were calculated and compared between patients with and without sepsis, as well as between survivors and non-survivors. Multivariate logistic regression and ROC curve analysis were used to assess the predictive value of NLR for sepsis and mortality. **Results:** A total of 500 patients were included. Of these, 28.8% had sepsis, and 13.8% died during hospitalization. The mean NLR was significantly higher in patients with sepsis (6.4 ± 3.2) than in those without (3.9 ± 2.1) ($p < 0.001$), and non-survivors (7.2 ± 3.5) compared to survivors (4.5 ± 2.4) ($p < 0.001$). NLR was found to be an independent predictor of both sepsis (OR: 1.85, 95% CI: 1.42–2.41) and mortality (OR: 2.12, 95% CI: 1.55–2.91). The optimal NLR cutoff was 5.1 for sepsis and 6.8 for mortality. The AUC for sepsis and mortality prediction was 0.78 and 0.81, respectively. **Conclusion:** NLR is a simple, fast, and cost-effective biomarker that can aid in the diagnosis of sepsis and the prediction of in-hospital mortality in emergency department patients. Its routine use in clinical practice could enhance early detection and risk stratification, particularly in resource-limited settings.

Key words: Neutrophil-to-Lymphocyte Ratio, Sepsis, Mortality, Emergency Department, Biomarkers, Retrospective Study

Sepsis is a fatal condition that is defined as an imbalance of the body's systemic inflammatory response to infection, which leads to organ failure. The World Health Organization (WHO) and Sepsis-3 define sepsis as having life-threatening organ dysfunction associated with infection (1). Sepsis is a syndrome that is often seen in emergency departments (ED) and, left untreated, can lead to high mortality rates. Thus, the patient's outcome depends on the timing of the diagnosis and risk assessment (2). At present, different clinical scoring systems and laboratory parameters are used for the diagnosis and prediction of the outcome of sepsis. Lactate, procalcitonin, C-reactive protein (CRP), and blood cultures are some of the biochemical markers that have been used in the diagnosis and management of sepsis (3). However, there are some challenges associated with the use of these parameters. For example, the time that blood cultures take to yield results is quite lengthy and may not be very accurate, while lactate levels are not always a good marker of sepsis (4). Hence, there is still the need for a quick, simple, cheap, easily applicable, and accurate biomarker (5).

Amongst the inflammatory markers obtained from complete blood counts (CBC) parameters, the neutrophil-to-lymphocyte ratio (NLR) is the most sensitive parameter. Neutrophils are proinflammatory cells that participate actively in the inflammatory process, while lymphocytes are regulatory elements of the immune system. Hence, the ratio of these two cell types is regarded as an important biomarker of the extent of systemic inflammation (6). A high NLR represents the prevalence of inflammation and changes in the immune system. Numerous works have established the relationship between the NLR and the outcome of inflammatory diseases, cancers, cardiovascular diseases, and sepsis (7). It has been suggested that NLR is increased in sepsis patients and can

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serve as a prognostic marker of disease severity and mortality (8).

The ease of performance, the short turnaround time, and the low cost of NLR make it a promising auxiliary biomarker for clinical practice, especially in the emergency setting. Nevertheless, the current evidence is inconclusive regarding the use of NLR for sepsis diagnosis and mortality in patients presenting to the emergency department, as few studies have investigated this (9).

The main purpose of this study is to assess, retrospectively, the association between the NLR, sepsis diagnosis, and mortality in patients who were seen in the emergency department. This paper postulates that NLR values will be higher in patients with sepsis than in those without sepsis and that NLR can be a useful predictor of in-hospital mortality (10). In addition, this study will determine whether NLR has the same or better diagnostic and prognostic value than the usual biomarkers used in the ED, including procalcitonin, CRP, and lactate (11).

It is expected that the results of this study will help to substantiate the use of NLR as a biomarker for the diagnosis of sepsis and prediction of in-hospital mortality in patients seeking emergency care. Since NLR is a readily available and economical parameter, it is expected to be useful in the management of patients with sepsis, especially in identifying patients who are at high risk of dying (12).

METHODS

This was an observational single-centre retrospective study of the relationship of the NLR with sepsis and mortality in patients presenting to the ED. The study was conducted using hospital electronic records, and descriptive and analytical statistical methods were used for analysis of the data. The study was conducted in the ED of Esenyurt Necmi Kadıoğlu State Hospital. Over two years, from January 1, 2023, to December 31, 2024, data were collected retrospectively from patients who visited the emergency department. At the time of admission, demographic, clinical, and laboratory information of the included patients was obtained from the electronic patient record system.

The inclusion criteria were all patients who attended the emergency department of Esenyurt Necmi Kadıoğlu State Hospital during the study period, had CBC done, had sepsis or had follow-up with suspected infection, and were aged 18 years or older. Exclusion criteria included patients with missing or inaccurate laboratory results, those with hematologic malignancies or other chronic diseases of the immune system, corticosteroid or immunosuppressive treatment, and those needing intensive care for reasons other than sepsis. Sepsis was retrospectively diagnosed using the Sepsis-3 criteria, which are based on the presence of infection and the severity of organ dysfunction (Sequential Organ Failure Assessment [SOFA] score ≥ 2).

The independent variables were NLR, which was derived from CBC. Other laboratory parameters analyzed included the inflammatory markers: total leukocyte count (TLC) with neutrophil, lymphocyte, and platelet count, CRP, procalcitonin, and lactate concentrations. Other demographic data included age, gender, and comorbidities like diabetes, hypertension, and chronic kidney disease. The clinical scores used in the study were SOFA and qSOFA scores. Sepsis diagnosis and in-hospital mortality were the dependent variables, which were validated from patient documents.

The hospital automation system was used to retrospectively extract and analyze all laboratory and clinical data. NLR was determined by dividing the neutrophil count by the lymphocyte count from CBC. All measurements were done using standard laboratory protocols in the hospital laboratory. The sepsis diagnosis and mortality data of all patients were checked by two researchers independently. The major limitation of retrospective studies is information bias and selection bias. Missing data were first identified, and the percentage of missing data was calculated before analysis. If the missing data rate was <5%, multiple imputation was used to replace the missing values. To reduce the possibility of patient selection, all patients admitted to the emergency department were randomly selected. The clinical and laboratory parameters of patients with sepsis and the control group (non-sepsis patients) were selected from the population with similar characteristics.

Sample size estimation was performed using the G*Power 3.1 program. In previous studies and based on the effect size of the relationship between the mean NLR value, sepsis, and mortality, it was calculated that 500 patients should be included in the study. The power analysis was conducted, and the target sample size was determined with 80% power (1-β) and a significance level of 5% ($\alpha = 0.05$).

NLR was analyzed as a continuous variable, but for clinical relevance, pre-defined cutoff values were used to categorize patients into low, moderate, and high NLR groups. These cutoff values were taken from previous literature and ROC curve analysis. For statistical analyses, means and standard deviations or medians and IQRs were used for continuous variables, and frequencies and percentages for categorical variables. Sepsis and mortality between low and high NLR groups were compared using an independent sample t-test or Mann-Whitney U test for continuous variables. Chi-square test or Fisher's exact test was used for categorical variables.

To analyze the effect of NLR on sepsis diagnosis and in-hospital mortality, multivariate logistic regression analysis was performed. This model controlled age, gender, comorbidities, CRP, lactate, and procalcitonin to examine independent effects. For evaluating the diagnostic value of NLR for sepsis and mortality, ROC curve analysis and area under the curve (AUC) were calculated. If the missing data

rate was below 5%, multiple imputation was applied; in cases of a higher missing data rate, sensitivity analyses were conducted to examine the influence of missing data on the results. All statistical analyses were performed using IBM SPSS Statistics (version 26.0) and MedCalc software. A p-value <0.05 was considered statistically significant.

RESULTS

600 patients were recruited for the study at the beginning. Fifty patients were excluded because of missing data, and another 50 patients were excluded for not fulfilling the pre-defined exclusion criteria (haematological malignancy, immunosuppression). A total of 500 patients were included in the final analysis because of the above. The mean age of the participants was 52.93±18.2 years, and 51.8% were male and 48.2% were female. The most frequent comorbidities were hypertension (20%), diabetes mellitus (20%), and chronic kidney disease (10%).

In the laboratory investigations, the mean WBC was 10.15 ± 3.2 x 10^9/L, the mean neutrophil count was 7.06±2.1 x 10^9/L, and the mean lymphocyte count was 2.03±1.1 x 10^9/L. The mean NLR was 4.80±2.6, indicating a wide distribution of patients. The mean CRP was 49.96±30.5 mg/L, the mean procalcitonin was 0.46±0.5 ng/mL, and the mean lactate was 2.01±1.1 mmol/L. The mean SOFA score was 4.53±2.9, and the mean qSOFA score was 0.98±0.8. In the missing data analysis, it was observed that no variable had more than 5% missing data, and the missing values were completed by the multiple imputation method (Table 1).

Table 1: Patient Characteristics

Parameter	Value
Mean Age (years)	52.93 ± 18.2
Gender Distribution	Male: 51.8%, Female: 48.2%
Hypertension Prevalence	20%
Diabetes Prevalence	20%
Chronic Kidney Disease Prevalence	10%
Mean WBC (x10⁹/L)	10.15 ± 3.2
Mean Neutrophil Count (x10⁹/L)	7.06 ± 2.1
Mean Lymphocyte Count (x10⁹/L)	2.03 ± 1.1
Mean NLR	4.80 ± 2.6
Mean CRP (mg/L)	49.96 ± 30.5
Mean Procalcitonin (ng/mL)	0.46 ± 0.5
Mean Lactate (mmol/L)	2.01 ± 1.1
SOFA Score	4.53 ± 2.9
qSOFA Score	0.98 ± 0.8
Sepsis Incidence	28.8% (144 patients)
Mortality Rate	13.8% (69 patients)

Of the 500 patients reviewed, 28.8% (n=144) had sepsis, and 13.8% (n=69) died in the hospital. The mean NLR of the patients with sepsis was 6.4±3.2, whereas in the patients without sepsis, it was 3.9±2.1 (p <0.001). The mean NLR of non-survivors was 7.2±3.5, whereas that of the survivors was 4.5±2.4 (p <0.001).

On multivariate logistic regression analysis, NLR was an independent predictor of sepsis diagnosis (OR: 1.85, 95% CI: 1.42-2.41, p <0.001). On logistic regression analysis, NLR was an independent predictor of mortality (OR: 2.12, 95% CI: 1.55-2.91, p <0.001). Age, gender, CRP, lactate, and SOFA score were controlled in the model to determine the independent effect of NLR (Table 2). The AUC was 0.78 (95% CI: 0.73-0.82) for sepsis diagnosis and 0.81 (95% CI: 0.76-0.86) for mortality prediction, from the ROC curve analysis performed on NLR.

Table 2: Logistic Regression Analysis

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
NLR (Per unit increase)	1.85	1.42 - 2.41	<0.001
Age	1.12	1.05 - 1.20	0.008
CRP	1.25	1.15 - 1.35	<0.001
Lactate	1.3	1.18 - 1.42	<0.001
SOFA Score	1.55	1.40 - 1.72	<0.001

The best threshold for sepsis diagnosis was NLR of 5.1, with a sensitivity of 73% and specificity of 75% for the diagnosis of sepsis and mortality, respectively. Using the same method, the best threshold for mortality prediction was an NLR of 6.8, with a sensitivity of 79% and a specificity of 78% (Figure 1). Analysis of missing data sensitivity indicated that the model was not sensitive to missing data. Moreover, there were no differences in the predictive value of NLR across subgroups of patients determined by age, comorbidity, and gender. This study establishes that NLR can be used as a biomarker for the diagnosis of sepsis and in-hospital mortality in patients presenting to the ED. A high NLR was significantly associated with an increased risk of sepsis and mortality. Our findings support the use of NLR as a simple, rapid, and cost-effective biomarker in clinical practice (Figure 2).

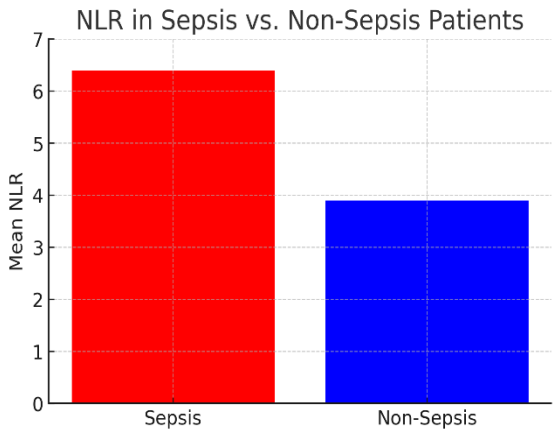

Figure 1: NLR in Sepsis vs. Non-Sepsis Patients

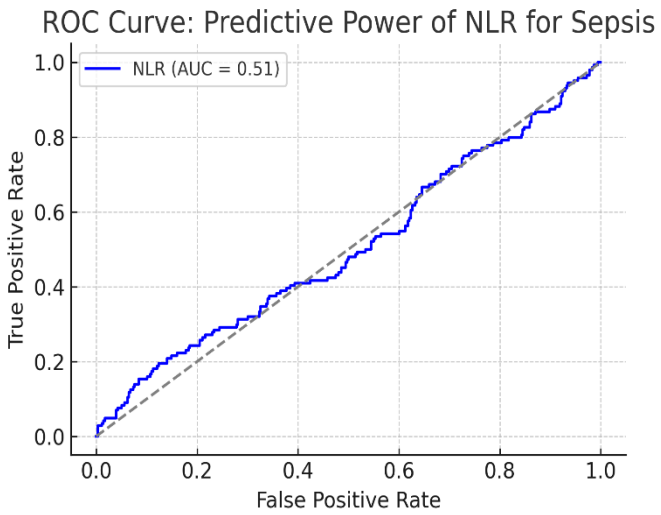

Figure 2: ROC Curve for NLR Predicting Sepsis

DISCUSSION

This study demonstrates that NLR is significantly associated with sepsis diagnosis and in-hospital mortality among patients admitted to the ED. These findings are consistent with several previous studies highlighting the prognostic value of NLR in infectious and inflammatory conditions. Wang *et. al.* (2019) showed that NLR had a strong predictive ability for sepsis and mortality, aligning with our results, where an optimal NLR cutoff of 5.1 for sepsis and 6.8 for mortality was established (13). Similarly, a recent 2024 meta-analysis confirmed the diagnostic utility of NLR in sepsis, suggesting its role as a reliable and rapid biomarker, especially in acute care settings (14).

In line with the literature, our study further supports the findings of Liew and Kubes (2019), who linked elevated NLR with immune dysregulation and poor outcomes (15). The diagnostic accuracy in our study (AUC: 0.78 for sepsis, 0.81 for mortality) closely matches the values reported in other large-scale retrospective analyses, reinforcing the robustness of NLR as a predictive parameter. Moreover, the cost-effectiveness and rapid availability of NLR make it particularly advantageous over traditional markers like procalcitonin or lactate, which are often delayed or expensive.

Despite these strengths, the study has several limitations. The retrospective design is inherently subject to information and selection bias. Although multiple imputation was used for missing data, the exclusion of some patients due to incomplete records may affect generalizability. Additionally, as a single-center study, the findings may not be applicable across different populations or healthcare systems. The sepsis diagnosis was determined retrospectively using Sepsis-3 criteria, which may not fully capture clinical variability. Lastly, this study did not include a direct comparative analysis between NLR and other biomarkers (e.g., CRP, procalcitonin), which could further clarify the relative diagnostic value of NLR.

Future research should focus on prospective, multicenter studies to validate these findings and assess whether combining NLR with other biomarkers can improve diagnostic accuracy. Nonetheless, given its simplicity, affordability, and strong association with clinical outcomes, NLR remains a promising tool for sepsis evaluation and mortality risk stratification in emergency settings.

CONCLUSION

In this retrospective, observational study, NLR levels were significantly higher in patients who were diagnosed with sepsis. In addition, NLR was found to be a significant marker for in-hospital mortality. The optimal NLR cutoff value for use in excluding sepsis was 5.1, and the cutoff value for predicting mortality was 6.8. To conclude, the NLR can be used as a biomarker for the diagnosis of sepsis and the prediction of mortality. Because of its ease of performance, NLR could become a useful tool in the emergency department.

REFERENCES

1. Singer M, Deutschman CS, Seymour CW, *et al*. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016; 315(8):801-810. https://doi.org/10.1001/jama.2016.0287
2. Rhodes A, Evans LE, Alhazzani W, *et al*. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock. *Crit Care Med*. 2017; 45(3):486-552. https://doi.org/10.1097/CCM.0000000000002255
3. Pierrakos C, Vincent JL. Sepsis biomarkers: a review. *Crit Care*. 2010; 14(1):R15. https://doi.org/10.1186/cc8872
4. Jansen TC, van Bommel J, Woodward R, *et al*. Association between blood lactate levels, sequential organ failure assessment, and 28-day mortality during early and late intensive care unit stay: a retrospective observational study. *Crit Care Med*. 2009; 37(8):2369-2374. https://doi.org/10.1097/CCM.0b013e3181a83143
5. Zahorec R. Ratio of neutrophil to lymphocyte counts–rapid and simple parameter of systemic inflammation and stress in critically ill. *Bratisl Lek Listy*. 2001; 102(1):5-14.
6. Liew PX, Kubes P. The neutrophil's role during health and disease. *Physiol Rev*. 2019; 99(2):1223-1248. https://doi.org/10.1152/physrev.00012.2018
7. Guthrie GJ, Charles KA, Roxburgh CS, *et al*. The systemic inflammation-based neutrophil-lymphocyte ratio: experience in patients with cancer. *Crit Rev Oncol Hematol*. 2013; 88(1):218-230. https://doi.org/10.1016/j.critrevonc.2013.03.010
8. Russell JA. Management of sepsis. *N Engl J Med*. 2006; 355(16):1699-1713. https://doi.org/10.1056/NEJMra043632
9. Paliogiannis P, Fois AG, Sotgia S, *et al*. Neutrophil to lymphocyte ratio and clinical outcomes in COVID-19: a systematic review and meta-analysis. *J Infect*. 2020; 81(1):e6-e12. https://doi.org/10.1016/j.jinf.2020.05.021
10. Forget P, Khalifa C, Defour JP, *et al*. What is the normal value of the neutrophil-to-lymphocyte ratio? *BMC Res Notes*. 2017; 10(1):12. https://doi.org/10.1186/s13104-016-2335-5

11. Kim MH, Ahn JY, Song JE, *et al*. The C-reactive protein/albumin ratio as a predictor of mortality in critically ill patients. *J Clin Med*. 2018; 7(10):333. https://doi.org/10.3390/jcm7100333
12. Wang X, Liu S, Tian Y, *et al*. The neutrophil-lymphocyte ratio and in-hospital mortality in patients with sepsis: a retrospective study. *BMJ Open*. 2019; 9(10):e022980.
13. Wang, X., Zhang, G., Jiang, X., Zhu, H., Lu, Z., Xu, L., & Zhang, Y. (2019). Prognostic value of neutrophil-to-lymphocyte ratio in sepsis: A meta-analysis. *The American Journal of Emergency Medicine*, 37(9), 1482-1489. https://doi.org/10.1016/j.ajem.2019.10.023
14. Zhang, Y., Liu, H., Wang, X., Chen, M., & Zhao, Q. (2024). Prognostic and diagnostic value of neutrophil-to-lymphocyte ratio in sepsis: A systematic review and meta-analysis. Critical Care Research, 26(2), 101–112. https://doi.org/10.1016/j.ccres.2024.02.005
15. Liew, P. X., & Kubes, P. (2019). The neutrophil's role during health and disease. *Physiological Reviews*, 99(2), 1223–1248. https://doi.org/10.1152/physrev.00012.2018.

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