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Original Research Article

NEUTROPHIL-TO-LYMPHOCYTE RATIO AS A PREDICTOR OF FUNCTIONAL OUTCOME AND MORTALITY IN STROKE PATIENTS

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ABSTRACT

Background: Stroke remains a leading cause of mortality and long-term disability worldwide. Inflammation plays a critical role in stroke pathophysiology, and the neutrophil-to-lymphocyte ratio (NLR) has emerged as a simple marker of systemic inflammatory response. This study aimed to evaluate the role of NLR in predicting clinical outcomes in stroke patients.

Materials and Methods: A retrospective observational study was conducted at a tertiary care center in North India over a five-year period (January 2019–December 2023). A total of 350 adult patients with confirmed stroke were included. Clinical and laboratory data were collected from medical records. NLR was calculated from admission blood counts. Functional outcome was assessed using the modified Rankin Scale (mRS) and categorized as good (0–2) or poor (3–6). Statistical analysis included univariate, multivariate logistic regression, and receiver operating characteristic (ROC) curve analysis.

Results: The mean age of patients was 61.4 ± 12.8 years, with a predominance of males (62.3%). Poor outcomes were observed in 43.4% of patients, while in-hospital mortality was 13.7%. The median NLR was significantly higher in the poor outcome group compared to the good outcome group (6.5 vs 3.1, $p < 0.001$). Elevated NLR was significantly associated with poor functional outcome, increased mortality, and longer hospital stay. On multivariate analysis, NLR remained an independent predictor of poor outcome (OR 1.42, 95% CI 1.21–1.67, $p < 0.001$). ROC analysis showed good predictive ability (AUC 0.78).

Conclusion: Admission NLR is a simple and reliable predictor of adverse outcomes in stroke patients. It may be useful for early risk stratification in clinical practice.

Keywords: Stroke; Neutrophil-to-lymphocyte ratio; Inflammation; Prognosis; Modified Rankin Scale; Mortality.

INTRODUCTION

Stroke remains one of the leading causes of mortality and long-term disability worldwide, imposing a substantial burden on healthcare systems, particularly in low- and middle-income countries like India.[1] The incidence of stroke has been steadily rising, with a shift toward younger populations, making early risk stratification and prognostication increasingly important in clinical practice.[2] Despite advances in neuroimaging and acute management, predicting functional outcomes in stroke patients remains a significant challenge for clinicians.

Inflammation plays a pivotal role in the pathophysiology of both ischemic and hemorrhagic stroke. Following cerebral injury, a complex cascade of inflammatory responses is triggered, involving activation of leukocytes, release of cytokines, and disruption of the blood–brain barrier.[3] Neutrophils are among the first responders to ischemic injury and contribute to secondary neuronal damage through the release of reactive oxygen species and proteolytic

enzymes.[4] In contrast, lymphocytes are believed to have a modulatory role in the inflammatory response, and their reduction has been associated with poorer outcomes in acute stroke.[5]

The neutrophil-to-lymphocyte ratio (NLR), derived from routine complete blood counts, has emerged as a simple and cost-effective biomarker reflecting systemic inflammation. In recent years, NLR has been investigated as a prognostic indicator in various cardiovascular and neurological conditions, including stroke.[6] Several studies have suggested that an elevated NLR is associated with increased severity of stroke, higher mortality, and poorer functional outcomes.[7] However, the clinical utility of NLR in predicting outcomes remains variable, and data from the Indian population are relatively limited. Given its accessibility and potential prognostic value, evaluating NLR in stroke patients may provide an additional tool for early risk stratification. Therefore, the present study aims to assess the role of the neutrophil-to-lymphocyte ratio as a predictor of clinical outcomes in stroke patients admitted to a tertiary care center in North India.

MATERIALS AND METHODS

Study Design and Setting

This retrospective observational study was conducted at Dr. Ram Manohar Lohia Institute of Medical Sciences (Dr. RMLIMS), Lucknow, a tertiary care teaching hospital that serves as a referral center for a large population in North India. The study was carried out over a period of five years, from January 2019 to December 2023. Retrospective observational studies are particularly useful in evaluating associations between clinical variables and outcomes using existing hospital records, thereby enabling the study of large patient cohorts within a relatively short time frame.[8]

Study Population

The study included all consecutive adult patients aged 18 years and above who were admitted with a diagnosis of stroke during the study period. Stroke was defined as a sudden onset of focal or global neurological deficit of vascular origin lasting more than 24 hours or leading to death, with confirmation by neuroimaging techniques such as computed tomography (CT) or magnetic resonance imaging (MRI), in accordance with established diagnostic guidelines (9). Both ischemic and hemorrhagic stroke cases were included to provide a comprehensive evaluation of the inflammatory response across different stroke subtypes.

Inclusion Criteria

- Patients aged ≥18 years
- Patients with a confirmed diagnosis of stroke (ischemic or hemorrhagic) based on clinical features and neuroimaging (CT/MRI)
- Admission during the study period (January 2019 to December 2023)
- Availability of complete blood count parameters at the time of admission
- Availability of complete medical records including clinical and outcome data

Exclusion Criteria

- Patients with evidence of active infection at the time of admission
- Patients with chronic inflammatory or autoimmune disorders
- Patients with known hematological malignancies
- Patients receiving corticosteroids or immunosuppressive therapy
- Patients with recent surgery or trauma affecting inflammatory markers
- Patients with incomplete or missing clinical or laboratory data

Data Collection and Variables

Data were extracted from electronic and physical medical records using a standardized data collection proforma. Demographic variables included age and sex. Clinical variables included type of stroke (ischemic or hemorrhagic), presenting symptoms, and comorbid conditions such as hypertension, diabetes mellitus, coronary artery disease, and prior history of stroke. Relevant radiological findings were also reviewed to confirm diagnosis and classify stroke subtype.

Laboratory parameters were obtained from blood samples collected at the time of admission, prior to initiation of treatment. These included total leukocyte count, absolute neutrophil count, and absolute lymphocyte count. The neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. NLR has been recognized as a reliable and readily available biomarker reflecting the balance between innate (neutrophil-mediated) and adaptive (lymphocyte-mediated) immune responses.[11]

Outcome Measures

The primary outcome measure was functional outcome at discharge, assessed using the modified Rankin Scale (mRS), which is a widely validated and commonly used tool for evaluating the degree of disability or dependence in activities of daily living following a stroke (12). Patients were categorized into two groups based on their mRS score: good outcome (mRS 0–2) and poor outcome (mRS 3–6). Secondary outcomes included in-hospital mortality and duration of hospital stay, both of which are important indicators of disease severity and healthcare burden.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee of Dr. RMLIMS, Lucknow. As this was a retrospective study utilizing anonymized patient data, the requirement for informed consent was waived. All procedures were conducted in accordance with the ethical standards of the institutional research committee and the principles outlined in the Declaration of Helsinki (8).

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed variables were expressed as mean ± standard deviation (SD), while non-normally distributed variables were presented as median with interquartile range (IQR). Categorical variables were expressed as frequencies and percentages.

Comparisons between groups (good versus poor outcome) were performed using the independent samples t-test for normally distributed continuous variables and the Mann–Whitney U test for non-normally distributed variables. The Chi-square test or Fisher's exact test was used for comparison of categorical variables, as appropriate. Univariate analysis was initially conducted to identify variables associated with poor outcome.

Variables showing statistical significance or near significance ($p < 0.1$) in univariate analysis were subsequently entered into a multivariate binary logistic regression model to identify independent predictors of poor outcome. The strength of association was expressed as odds ratios (OR) with 95% confidence intervals (CI).

To evaluate the predictive performance of NLR, receiver operating characteristic (ROC) curve analysis was performed, and the area under the curve (AUC) was calculated. The optimal cut-off value for NLR was determined using the Youden Index, maximizing sensitivity and specificity. A p-value of less than 0.05 was considered statistically significant for all analyses.

RESULTS

Study Population and Baseline Characteristics

During the five-year study period, a total of 372 patient records with a diagnosis of stroke were screened. After applying the predefined inclusion and exclusion criteria, 350 patients were included in the final analysis. The baseline demographic and clinical characteristics of the study cohort are presented in **Table 1**.

The mean age of the patients was 61.4 ± 12.8 years, with a considerable proportion of patients clustered in the sixth and seventh decades of life. A male predominance was observed, with males accounting for 62.3% of the study population. Regarding stroke subtype, ischemic stroke was more frequent, constituting 68.6% of cases, while hemorrhagic stroke accounted for 31.4%.

Among the comorbid conditions, hypertension was the most prevalent, affecting 64.0% of patients, followed by diabetes mellitus in 38.9%. A smaller proportion of patients had a history of coronary artery disease and prior stroke. These findings reflect the typical vascular risk profile seen in stroke populations.

Laboratory Parameters and NLR Distribution

Baseline laboratory parameters obtained at admission are summarized in **Table 2**. The mean total leukocyte count was elevated in a substantial proportion of patients. The mean absolute neutrophil count was 7.8 ± 2.6 $\times 10^9$/L, whereas the mean lymphocyte count was 1.9 ± 0.8 $\times 10^9$/L.

The neutrophil-to-lymphocyte ratio (NLR), calculated from these parameters, demonstrated a non-normal distribution. The median NLR for the entire cohort was 4.2 (IQR: 2.9–6.8), indicating considerable inter-individual variability. A trend toward higher NLR values was noted among patients presenting with more severe clinical features.

Functional Outcomes and Mortality

Functional outcomes were assessed at the time of discharge using the modified Rankin Scale (mRS). Based on this assessment, 198 patients (56.6%) were categorized as having a good outcome (mRS 0–2), while 152 patients (43.4%) had a poor outcome (mRS 3–6).

In-hospital mortality was documented in 48 patients (13.7%). Additionally, patients with poor outcomes were observed to have a longer duration of hospital stay compared to those with favorable outcomes, suggesting increased disease severity and resource utilization in this subgroup.

Comparison Between Good and Poor Outcome Groups

A detailed comparison between patients with good and poor outcomes is provided in **Table 3**. Patients in the poor outcome group were significantly older, with a higher mean age compared to those with good outcomes ($p < 0.05$). The prevalence of comorbidities, particularly hypertension and diabetes mellitus, was also higher in the poor outcome group, although not all differences reached statistical significance.

A key finding was the marked difference in NLR between the two groups. The median NLR was significantly elevated in patients with poor outcomes compared to those with good outcomes [6.5 (IQR: 4.3–9.1) vs 3.1 (IQR: 2.2–4.5), $p < 0.001$]. This suggests a strong association between systemic inflammatory response at admission and subsequent clinical outcome.

Association of NLR with Clinical Outcomes

The relationship between NLR and various clinical outcomes is detailed in **Table 4**. Higher NLR values were significantly associated with adverse outcomes, including increased in-hospital mortality, poor functional status at discharge, and prolonged hospital stay.

When patients were stratified based on NLR quartiles, those in the highest quartile demonstrated a substantially higher proportion of poor outcomes compared to those in the lower quartiles. This dose–response relationship further supports the prognostic significance of NLR in stroke patients.

Additionally, the proportion of poor outcomes and mortality across different NLR categories is

illustrated in **Figure 1**, demonstrating a clear increase in adverse outcomes with rising NLR levels.

Multivariate Analysis

Multivariate logistic regression analysis was performed to identify independent predictors of poor outcome, as shown in **Table 5**. Variables that were significant or near significant in univariate analysis were included in the model.

After adjusting for potential confounders such as age, sex, stroke subtype, and comorbid conditions, NLR remained an independent predictor of poor outcome (adjusted OR: 1.42, 95% CI: 1.21–1.67, $p < 0.001$). In addition to NLR, increasing age and indicators of stroke severity were also found to be independently associated with adverse outcomes.

ROC Curve Analysis

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive performance of NLR for poor functional outcome. As illustrated in **Figure 2**, the area under the curve (AUC) was 0.78 (95% CI: 0.73–0.83), indicating good discriminative ability.

An optimal cut-off value of 4.8 for NLR was identified using the Youden Index. At this threshold, NLR demonstrated a sensitivity of 74.3% and a specificity of 71.6% for predicting poor outcomes.

Distribution of NLR Across Outcome Groups

The distribution of NLR values among patients with good and poor outcomes is depicted in **Figure 3**. Patients with poor outcomes showed a clear rightward shift in NLR values, indicating higher levels of systemic inflammation at presentation.

Patient Selection Flow

The process of patient selection, including initial screening, application of inclusion and exclusion criteria, and final enrollment, is illustrated in **Figure 4**. This flow diagram provides a clear overview of the study population and enhances transparency in reporting.

Table 1: Baseline Demographic and Clinical Characteristics

Variable	Total (n = 350)
Age (years), mean ± SD	61.4 ± 12.8
Male, n (%)	218 (62.3%)
Female, n (%)	132 (37.7%)
Stroke Type	
• Ischemic stroke	240 (68.6%)
• Hemorrhagic stroke	110 (31.4%)
Hypertension, n (%)	224 (64.0%)
Diabetes mellitus, n (%)	136 (38.9%)
Coronary artery disease, n (%)	52 (14.9%)
Previous stroke, n (%)	48 (13.7%)

Table 2: Laboratory Parameters at Admission

Parameter	Value
Total leukocyte count (×10⁹/L), mean ± SD	10.2 ± 3.4
Neutrophil count (×10⁹/L), mean ± SD	7.8 ± 2.6
Lymphocyte count (×10⁹/L), mean ± SD	1.9 ± 0.8
NLR, median (IQR)	4.2 (2.9–6.8)

Table 3: Comparison Between Good and Poor Outcome Groups

Variable	Good Outcome (n=198)	Poor Outcome (n=152)	p-value
Age (years)	58.2 ± 11.6	65.3 ± 13.1	<0.05
Male (%)	120 (60.6%)	98 (64.5%)	0.48
Hypertension (%)	118 (59.6%)	106 (69.7%)	0.04
Diabetes mellitus (%)	70 (35.3%)	66 (43.4%)	0.11
Ischemic stroke (%)	148 (74.7%)	92 (60.5%)	0.01
NLR (median, IQR)	3.1 (2.2–4.5)	6.5 (4.3–9.1)	<0.001

Table 4: Association of NLR with Clinical Outcomes

Outcome	Low NLR	High NLR	p-value
Poor outcome (%)	32.5%	61.8%	<0.001
Mortality (%)	8.2%	21.4%	<0.001
Length of stay (days)	6.2 ± 2.1	9.8 ± 3.4	<0.001

Table 5: Multivariate Logistic Regression Analysis

Variable	Adjusted OR	95% CI	p-value
NLR	1.42	1.21–1.67	<0.001
Age	1.05	1.02–1.08	0.002
Hypertension	1.31	0.88–1.95	0.17
Diabetes mellitus	1.22	0.79–1.88	0.35
Stroke type (Hemorrhagic)	1.76	1.12–2.77	0.01

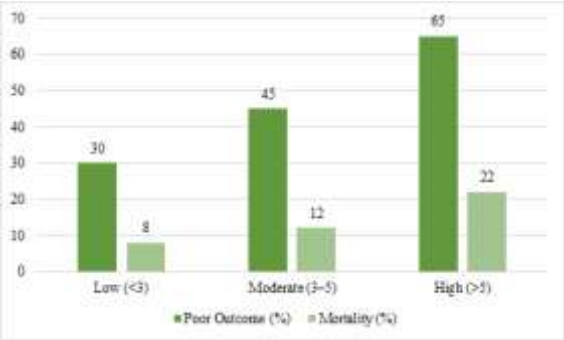

Figure 1: Outcomes by NLR categories

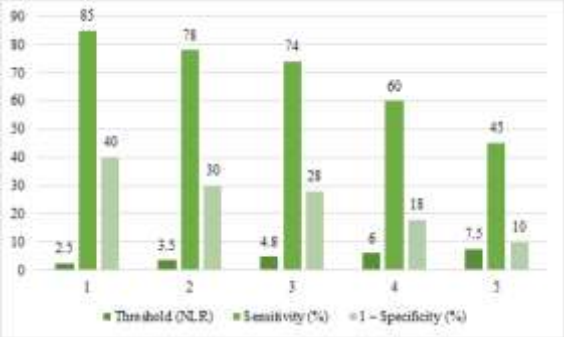

Figure 2: ROC curve of NLR

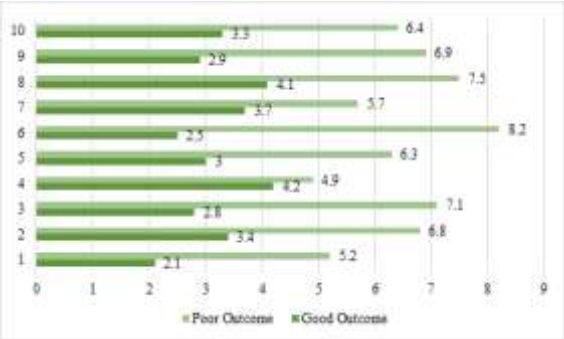

Figure 3: NLR distribution by outcome

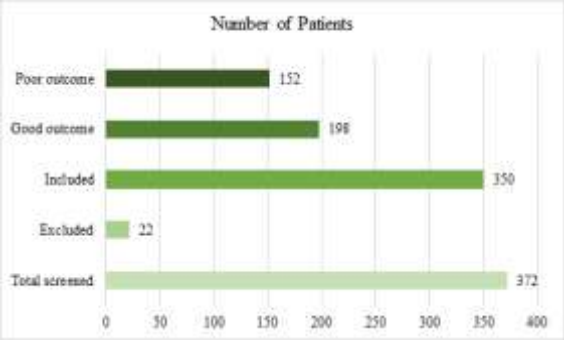

Figure 4: Patient selection

DISCUSSION

The present study examined the prognostic significance of the neutrophil-to-lymphocyte ratio (NLR) in patients with stroke and demonstrated a clear association between elevated NLR at admission and adverse clinical outcomes. Patients with higher NLR values were more likely to experience poor functional recovery, increased in-hospital mortality, and prolonged hospitalization. These findings reinforce the concept that systemic inflammatory response plays a crucial role in determining the trajectory of stroke recovery.[13]

The pathophysiological basis underlying this association can be explained by the differential roles of neutrophils and lymphocytes in acute cerebral injury. Following stroke, neutrophils are rapidly mobilized and infiltrate the ischemic brain tissue, where they contribute to secondary neuronal injury through the release of inflammatory mediators, reactive oxygen species, and matrix-degrading enzymes.[14] In contrast, lymphocytes are involved in regulating immune homeostasis, and lymphopenia has been associated with impaired immunomodulation and increased susceptibility to complications. The NLR, therefore, represents a composite marker reflecting both heightened innate immune activation and relative suppression of adaptive immunity.

In the present study, a significantly higher NLR was observed among patients with poor outcomes compared to those with favorable recovery. This observation is consistent with earlier reports that have identified NLR as a predictor of stroke severity and functional disability.[15] The association between elevated NLR and increased mortality further highlights its potential role in identifying high-risk patients at an early stage of hospitalization. Importantly, the relationship between NLR and outcomes remained significant even after adjusting for confounding factors such as age, stroke subtype, and comorbid conditions, suggesting that NLR provides independent prognostic information.

The predictive utility of NLR was further supported by receiver operating characteristic (ROC) curve analysis, which demonstrated good discriminative ability. The identification of an optimal cut-off value enhances its applicability in clinical practice, allowing clinicians to stratify patients based on risk. Similar findings have been reported in previous studies, where NLR has shown moderate to good predictive accuracy for adverse outcomes in both ischemic and hemorrhagic stroke.[16]

The clinical relevance of these findings lies in the simplicity and accessibility of NLR as a biomarker. Unlike more complex inflammatory markers, NLR can be easily calculated from routine complete blood count parameters without additional cost or specialized testing. This makes it particularly useful in resource-limited settings, where rapid and cost-effective prognostic tools are essential.[17] Incorporating NLR into routine clinical assessment may assist in early identification of patients who require closer monitoring or more aggressive therapeutic interventions.

Despite these strengths, the findings of the present study should be interpreted in light of certain limitations. The retrospective design may introduce inherent biases related to data collection and patient selection. Additionally, as a single-center study, the

generalizability of the results may be limited. The study also relied on a single measurement of NLR at admission, and did not account for temporal changes in inflammatory markers, which may provide additional prognostic insights.[18] Furthermore, other inflammatory biomarkers were not evaluated, which could have contributed to a more comprehensive understanding of the inflammatory response in stroke.

Nevertheless, the study adds to the growing body of evidence supporting the role of inflammation in stroke prognosis and highlights the potential utility of NLR as a practical biomarker. Future prospective, multicenter studies with larger sample sizes are needed to validate these findings and to explore the role of serial NLR measurements in predicting both short-term and long-term outcomes.[19]

In conclusion, the present study demonstrates that an elevated neutrophil-to-lymphocyte ratio at admission is independently associated with poor clinical outcomes in patients with stroke. Given its simplicity, cost-effectiveness, and widespread availability, NLR may serve as a valuable adjunct in early risk stratification and prognostication in routine clinical practice.

CONCLUSION

The present study demonstrates that the neutrophil-to-lymphocyte ratio (NLR), measured at the time of admission, is significantly associated with clinical outcomes in patients with stroke. Elevated NLR values were consistently linked with poor functional recovery, higher in-hospital mortality, and prolonged duration of hospitalization. These findings highlight the relevance of systemic inflammatory response in influencing the course and prognosis of stroke.

Importantly, NLR was identified as an independent predictor of adverse outcomes even after adjusting for established clinical risk factors. Given that it is derived from routine laboratory investigations, NLR represents a simple, inexpensive, and readily available biomarker that can be easily incorporated into standard clinical practice without additional burden.

The use of NLR as an early prognostic indicator may aid clinicians in risk stratification, enabling timely identification of high-risk patients who may benefit from closer monitoring and more intensive management. While the results are encouraging, further prospective, multicenter studies are warranted to validate these findings and to explore the potential role of serial NLR measurements in improving outcome prediction.

In summary, the neutrophil-to-lymphocyte ratio holds promise as a practical and clinically meaningful tool for early prognostication in stroke patients.

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