

ORIGINAL RESEARCH

Role of Neutrophil to Lymphocyte Ratio (NLR) and its Correlation with NIHSS (National Institute of Health Stroke Scale) for Prediction of Severity in Patients of Acute Ischemic Stroke

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ABSTRACT

Background: Cerebrovascular accident or stroke is the sudden onset of the neurological deficit from a vascular mechanism; 85% are due to vascular ischemia, while 15% are due to primary hemorrhage. Stroke is the third leading cause of death in the world and the most common cause of neurological disease in adults. Additionally, it is the third leading cause of disability-adjusted life-years (DALYs) worldwide.¹ Atherosclerosis plays an important role in the pathogenesis of stroke and inflammation is central in the initiation, progression and complications of atherosclerosis by mediating every stage of atheroma development. aim of the present study was to find out the role of Neutrophil to Lymphocyte ratio(NLR) in patients of acute ischemic stroke (AIS)and correlating with NIHSS for predicting the prognosis.

Materials and Methods: 46 ischemic stroke patients were included in the study. Blood sample analysis was done to calculate NLR ratio. Patients' NIHSS at first admission was also calculated. Multiple statistical analyses were used to analyze the statistical significance of NLR in poor prognosis.

Results: The age of the study population was between 30-80 years, with 19 males and 27 females. The NLR values were correlated with NIHSS in predicting th severity of AIS. There was a positive correlation between NLR, NIHSS and the severity of AIS(p<0.0001).

Conclusion: Neutrophil to Lymphocyte Ratio(NLR) is a simple, cost effective and easily obtainable novel inflammatory marker that may help in predicting the severity of disease and prognosis in terms of functional outcome as evidenced by its increased value in patients of acute ischemic stroke as well as its linear positive correlation with NIHSS score.

Keywords: Neutrophil Lymphocyte Ratio, National institutes of health stroke scale, Acute Ischemic Stroke.

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INTRODUCTION

Stroke or cerebrovascular accident is defined as an abrupt onset of focal neurological deficit that is attributable to vascular cause. It accounts for 80% to 85% of all cerebrovascular disease. Stroke is the second leading cause of death worldwide and third most common cause of disability-adjusted life years in the world.^[1] Post-ischemic inflammation plays an important role in various stages of cerebral ischemic injury, resulting from stagnant blood flow, activation of intravascular leukocytes and release of pro-inflammatory mediators from the ischemic endothelium, platelet granules, and brain parenchyma.^[2,3] Numerous studies confirmed that inflammatory response aggravated ischemic brain damage and neurological dysfunction.^[4] Previous researches suggested that leukocytosis on admission was associated

with stroke severity and poor clinical outcomes in acute ischemic stroke (AIS) patients.^[5] High neutrophil count and low lymphocyte count were regarded as correlation factors of unfavorable functional outcomes of acute cerebral infarction.^[5,6] Lymphocytes modulate the mononuclear cell phenotype and induce tissue inhibitor of metalloproteinase-1 expression that have key role in tissue healing.^[7,8] Experimental models have also revealed that lymphocytes exert anti-inflammatory response in atherosclerosis development. Studies have clearly demonstrated a negative correlation between lymphocyte counts and severity of coronary atherosclerosis.^[9, 10] High NLR as an inflammatory marker has been correlated with the poor prognosis in various diseases like Myocardial infarction, critical limb ischemia, end-stage renal failure, pulmonary embolism and various malignancies including breast, ovarian, pancreatic, hepatobiliary carcinoma and other solid tumors.^[10] This emerging marker has not been frequently studied with acute ischemic stroke; hence present study was done to find out the role of NEUTROPHIL to lymphocyte ratio(NLR) in patients of acute ischemic stroke and correlating with NIHSS for predicting the prognosis .

Objectives

The main objective of our study was to determine the value of Neutrophil to Lymphocyte ratio(NLR) in patients of acute ischemic stroke and correlate it with NIHSS score to predict the prognosis.

MATERIALS & METHODS

Hospital based retrospective study was conducted on patients of acute ischemic stroke admitted in Department of Medicine, Siddaganga Medical College and Hospital from JAN 2022 to January 2023. All acute ischemic stroke patients who had symptom onset within 7 days of onset were included whereas patients with hemorrhagic stroke, venous sinus thrombosis, hepatic or renal disease, connective tissue disorders, autoimmune disease, sepsis, malignancy, psychiatric illness, moribund condition and unwillingness to participate in the study were excluded. The diagnosis of acute stroke was made on the basis of temporal profile of clinical syndrome, clinical examination and CT scan / MRI of brain. Severity of stroke was determined with the National Institute of Health Stroke Scale (NIHSS) in all patients at initial presentation. Stroke severity was grouped in minor stroke (1-4), moderate stroke (5-15), moderate to severe stroke (16-20) and severe stroke (21-42). For calculating NLR ratio, CBC (Complete Blood Count) test was performed by fully automated five part hematology analyzer available at our central laboratory, from which Neutrophil to lymphocyte ratio was obtained by dividing Neutrophil count by total lymphocyte count. This NLR ratio was then compared with the NIHSS severity score (calculated at the time of admission).

Statistical Analysis

Continuous variables were presented as mean±sd, categorical variables were expressed in frequency and percentages. Neutrophil to Lymphocyte ratio and severity of ischemic stroke including other variables using Graph Pad In Stat Version 3.10A value of $p > 0.05$ was considered as not significant and $p < 0.05$ was considered statistically significant.

RESULTS

The total number of patients were 46 with (19) males and (27) females. Smoking habits was observed in 15 patients, and 15 patients had a history of alcohol consumption. Diabetes mellitus was observed in 23 and 21 patients were hypertensive. Dyslipidemia was seen in 15 patients. 17 patients had cardiac disease and 26 patients had previous history of stroke. Table 1.

| Variables | Yes | No |
|-----------|-----|----|
| Smoking | 15 | 22 |

| | | |
|----------------------------|----|----|
| Alcohol | 15 | 22 |
| Diabetes Mellitus | 23 | 17 |
| Hypertension | 21 | 21 |
| Dyslipidemia | 15 | 20 |
| cardiac disease | 17 | 21 |
| previous history of stroke | 26 | 20 |

Table.1 Risk factor stratification

Table 1: Comparison of NIHSS score and Neutrophil to Lymphocyte ratio

| Parameters | NIHSS Score at Admission | P-value | NLR ratio | P-value |
|-----------------------------------|--------------------------|---------|----------------|---------|
| Gender | | | | |
| Male | 19.0 (14.0-24.0) | 0.024 | 3.4 (2.4-4.7) | 0.134 |
| Female | 27.0 (17.0-34.0) | | 4.0 (3.5-5.2) | |
| Outcome | | | | |
| Static/Deteriorated/Died | 28.0 (23.8-34.0) | <0.001 | 4.7 (3.6-5.1) | 0.009 |
| Improved | 17.0 (14.0-24.0) | | 3.2 (2.4-4.2) | |
| Diabetes Mellitus | | | | |
| No | 17.0 (11.5-26.0) | 0.331 | 3.6 (2.5-4.7) | 0.785 |
| Yes | 23.0 (15.0-28.3) | | 3.6 (2.6-4.8) | |
| Hypertension | | | | |
| No | 21.0 (16.5-28.0) | 0.572 | 3.7 (2.7-4.7) | 0.568 |
| Yes | 21.0 (13.5-28.0) | | 3.6 (2.4-4.8) | |
| Smoking | | | | |
| No | 22.0 (14.8-28.3) | 0.146 | 3.6 (2.6-4.7) | 0.250 |
| Yes | 15.0 (10.0-17.8) | | 2.7 (2.0-10.3) | |
| Alcoholism | | | | |
| No | 22.0 (14.8-28.3) | 0.146 | 3.6 (2.6-4.7) | 0.089 |
| Yes | 15.0 (10.0-17.8) | | 2.7 (2.0-3.3) | |
| Dyslipidemia | | | | |
| No | 20.5 (14.3-28.0) | 0.477 | 3.6 (2.6-4.7) | 0.233 |
| Yes | 15.0 (7.0-0.0) | | 2.6 (1.7-0.0) | |
| Cardiac Disease | | | | |
| No | 21.0 (13.5-28.0) | 0.930 | 3.6 (2.7-4.7) | 0.960 |
| Yes | 17.0 (15.0-26.0) | | 3.6 (2.4-5.4) | |
| Previous history of Stroke | | | | |
| No | 20.0 (14.0-27.0) | 0.261 | 3.6 (2.6-4.7) | 0.794 |
| Yes | 26.0 (14.5-35.8) | | 3.5 (2.5-4.4) | |

In our study p value is found to be statistically significant in predicting the outcome in terms of static/deteriorated/died or improved by comparing NLR ratio and NIHSS score.

| | |
|--------------------|--------------|
| Sensitivity | 94% |
| Specificity | 67% |
| PPV | 54% |
| Variables | NIHSS |

| | |
|----------|-------|
| NPV | 96% |
| Accuracy | 75% |
| AUC | 84% |
| Cut Off | 20.50 |

In our study it is observed in comparison with NIHSS, the sensitivity is 94%,specificity is 67%,positive predictive value is 54%,negative predictive value is 96%,accuracy is 75%.

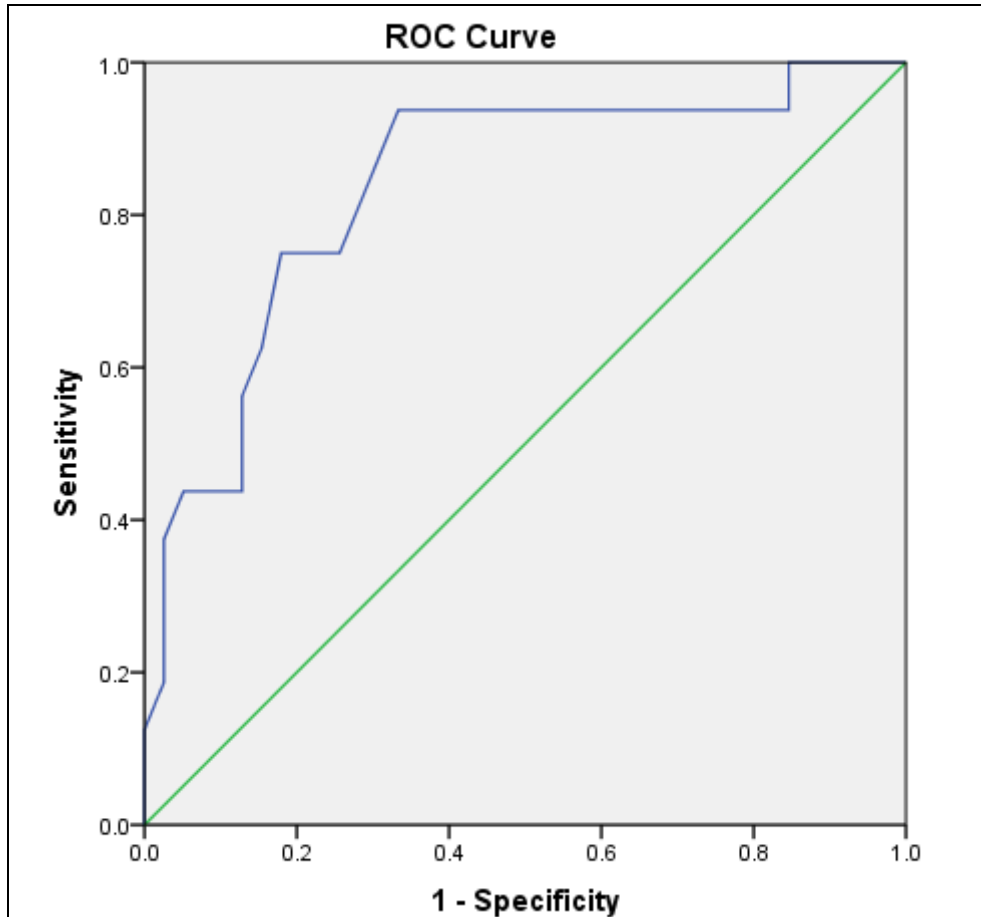


Fig. 3. Plotting of the receiver operating characteristic curve yielded an NIHSS cut-off value of 20.50 and an AUC of 84%, with a sensitivity of 94 % and a specificity of 67%

DISCUSSION

Stroke is the most common disabling and fatal disease in adults. More than 40% surviving stroke patients have neurological deficit symptoms and need to be cared for.^[13] The factors that affect the prognosis of the patients are the severity of stroke and old age. In addition, infection has a negative effect on the outcome, which plays an important role in extending hospital stay, worsening of neurological outcome, developing more serious complications and death.^[14,15]

Hence, this study evaluated the demographic, vascular risk factors, NLR. Lee H et al., demonstrated that measurement of NLR serially, and not only on admission but also on day four, predicts the prognosis and early treatment response.^[16] Kaushik R et al., demonstrated that a high NLR value at the end of late phase (day 5) had a poor outcome and prolonged duration of ICU stay and thus concluded that late phase value of this inflammatory biomarker is helpful in detecting the prognosis in sepsis.^[17]

Celikbilek A et al., found that the NLR levels were higher in patients with AIS when compared to the controls (p-value=0.001).^[12] Similarly in this study NLR levels were higher in patients with AIS. Zhao L et al., found that the NLR cut-off NLR value of 2.9 would mean a prolonged length of hospital stay.^[18] However, in this study, they have not mentioned about the length of hospital stay complications and prognosis. Günes M et al., also found a positive correlation between NLR (cut-off value of 4.43), length of hospital stay and morbidity. Although, in the present study, the patients were admitted for observation and to find out severity of AIS by correlating NIHSS and NLR levels despite no complications that might have reflected on the duration of hospital stay.

In this study, the NLR values and NIHSS score positively correlated with the severity of AIS. The higher the NLR and NIHSS score the worse was the outcome. Overall, if the NLR and NIHSS values were high at the day of admission, the outcome was poor. Similarly, Celikbilek et al., also concluded that a NLR can be used as a predictive biomarker for worse outcome in AIS.^[12] Cai W et al., found that NLR positively correlated with higher NIHSS and infarct sizes, and determined that $NLR > 12.1 \pm 4.5$ had a poor prognosis.^[22] Brooks SD et al., also found a significant relationship between $NLR \geq 5.9$, poor outcome, and death at 90 days.^[9] All the three above-mentioned studies reported a statistically significant correlation between NLR values and overall prognosis of AIS.

CONCLUSION

Neutrophil to lymphocyte ratio (NLR) is a simple, cost effective and easily obtainable novel inflammatory marker that may help in predicting the severity of disease and prognosis in terms of functional outcome as evidenced by its increased value in patients of acute ischemic stroke as well as its linear positive correlation with NIHSS score. This ratio can be obtained even at primary health set ups and may be used for decision making in urgent referral of the patient for better outcome. Though, more studies are needed to validate our results, our study completely support the routine calculation of this ratio that may add to risk stratification of patients with acute ischemic stroke.

Limitation of Study Despite

1. The sample size of our study was small involving only single centre
2. Owing to lack of long term follow up for our patients, we cannot comment whether Neutrophil to lymphocyte ratio is a useful predictor of long term prognostic outcome in patients with AIS or not.
3. Our study was carried out in a tertiary centre where the cases are either serious or referred. Our study may thus be biased towards more serious cases.

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