

## Original Article

# Neutrophil to Lymphocyte Ratio (NLR) as an Inflammatory Marker in Predicting Severity in Acute Ischemic Stroke Patients

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**Background** : Inflammation plays an important role in Acute Ischemic Stroke (AIS). Chemokines and cytokines released from ischemic tissue and recruit peripheral circulating leukocytes mainly neutrophils into the brain which precipitate ischemic brain injury and increases stroke severity. Lymphocytes on the other hand represent the protective or regulatory component of inflammation which decreases due to increased release of cortisol in response to stress.

**Aims and Objectives** : To find the role of Neutrophil to Lymphocyte Ratio (NLR) in predicting the severity in patients of AIS.

**Materials and Methods** : This study included 100 patients of AIS admitted in Government Medical College and Hospitals, Kota with all relevant exclusion criteria. Peripheral blood sample was taken before initiating any treatment and CBC test was performed from which NLR was calculated. The ratio was then compared with healthy control group and also among patients of AIS .

**Results** : Mean value of NLR in AIS patients was 3.44 which was higher than NLR of control group which was 1.89 (p=0.001).

**Conclusion** : Thus, NLR is a cost effective, easy to calculate and newer inflammatory marker that can help in predicting severity of acute ischemic stroke score.

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**Key words** : Acute Ischemic Stroke (AIS), Neutrophil to Lymphocyte Ratio (NLR).

Hippocrates, the father of medicine, first recognized stroke over 2,400 years ago. At this time stroke was called apoplexy<sup>1,2</sup>. Stroke is the most common neurological disorder Worldwide and it is the most frequent of all the neurological disorders. Stroke is also known as Cerebrovascular Accident (CVA) derived from Greek word in the year 1599 which means 'StruckDown'<sup>3</sup>. It is the disease of developed nations.

According to the World Health Organization, 15 million people suffer from stroke worldwide every year. Of these, 5 million die and another 5 million are permanently disabled<sup>4</sup>.

Neutrophil to Lymphocyte Ratio (NLR) is an effortless and basic parameter that is readily obtained from the complete blood count, even in peripheral hospitals. Inflammation is regarded as a set of interactions between and among immune related cells such as lymphocytes, neutrophils which in turn lead to killing of tissues and destruction which is going on in stroke. One of the inflammatory markers in stroke

### Editor's Comment :

■ The Neutrophil to Lymphocyte Ratio (NLR) is a simple, accessible, and cost-effective inflammatory marker. An elevated NLR on admission is associated with greater stroke severity, worse outcomes and increased risk of complications like infarct expansion and mortality. NLR can be used as an adjunct to traditional markers and imaging to help guide early risk stratification and management in acute ischemic stroke patients.

is NLR and also has its relationship between many diseases like, myocardial infarction, COPD, chronic renal failure etc<sup>5-7</sup>.

Inflammatory cascade following Acute Ischemic Stroke (AIS) is an important pathological process in damaged brain tissue. The inflammatory process in acute ischemic stroke involves cytokines and chemokines released from ischemic tissues, promoting the accumulation of leukocytes to the ischemic areas. Among circulating leukocytes, neutrophils have been regarded as crucial mediators of ischemic injury. Accumulated neutrophils release free oxygen radicals, various inflammatory cytokines, and neurotoxic substances, all of which cause cellular necrosis and apoptosis in ischemic tissues. Lymphocytes, a type of leukocyte, are also known to be involved in inflammatory responses to Acute Ischemic Stroke (AIS). Low lymphocyte counts increase sympathetic activity and baseline cortisol

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levels, which can cause an increase in the production of inflammatory cytokines that aggravate ischemic injury. Therefore, increased total White Blood Cell (WBC) and Leukocyte Counts and reduced lymphocyte counts are associated with poor outcomes in various cardiovascular diseases<sup>8</sup>.

Earlier researchers have studied Neutrophil to Lymphocyte Ratio (NLR) and Mean platelet Volume (MPV) as prognostic marker in acute ischemic stroke separately. But we would like to study the combined effect of NLR and MPV in patients of acute ischemic stroke as prognostic marker.

#### AIMS AND OBJECTIVES

To study Neutrophil to Lymphocyte Ratio (NLR) in patients of Acute Ischemic Stroke.

#### MATERIALS AND METHOD

The study was performed at the Government Medical College and attached groups of Hospitals Kota in year 2021-2022, after obtaining the approval of the Internal Ethical Committee of Government Medical College & Hospital, Kota and Informed written consent from all the patients considered for the study was procured before conducting the study.

**Study Design :** Hospital based prospective and observational study carried out on patients admitted and diagnosed as an Acute Ischemic Stroke.

**Study Place :** Department of medicine, Government Medical College & Associated Group of MBS Hospital, Kota (Rajasthan).

**Study Population :** patients with Acute Ischemic Stroke who had symptom onset within 7 days.

**Study Duration :** 2021-2022.

#### Inclusion Criteria :

(1) Patients of Age >18 years admitted in MBS Hospital, Kota diagnosed with Acute Ischemic Stroke

#### Exclusion Criteria :

- (1) Patients of Age <18 years.
- (2) Patients with other forms of stroke like ICH/SAH/post traumatic.
- (3) Patients with venous sinus thrombosis.
- (4) Serious ill/moribund patients.
- (5) Patients having hepatic or renal disease.
- (6) Systemic acute or chronic inflammatory or autoimmune or infectious disease, connective tissue diseases or prior myocardial infarction.
- (7) Individuals with missing data of lipid profile, monocyte count.
- (8) Pregnant patients.
- (9) Patient refusing to give informed consent for the study.

#### RESULT

Out of 100 subjects in the control group; 55 were males and 45 were females whereas in the study group of 100 subjects, 57 were males and 43 were females. Males were more than females with male to female ratio being 1.3:1. Thus, males are more prone to develop stroke as compared to female. The maximum number of patients were in the range of 50-59 years ie, 38 cases (38%) followed by in 60-69 years 35 cases (35%), in 70-79 years 15 cases (15%), in 40-49 years 8 cases (8%) and in  $\geq 80$  years of age group 4 cases (4%) so in 50-69 years cases 73%.

When the study group was compared on the basis of focal neurological deficit, maximum number of patients had either isolated left hemiparesis or isolated right hemiparesis amounting to 32% each. 17% of patients had right hemiparesis with cranial nerve palsy and 13% had left hemiparesis with cranial nerve palsy. Patients with the features of posterior circulatory stroke like vertigo, blurring of vision etc contributed 6% of the cases. ACS is 94% in compare to PCS is 6%.

Table 1 shows the comparison of control and study group on the basis of mean Neutrophil count at the time of admission. Mean Neutrophil count  $\pm$  SD of the cases in study group was  $4.472 \pm 1.1$  ( $10^3/\text{cu mm}$ ) which was higher than the mean value of  $3.4965 \pm 1.7$  ( $10^3/\text{cu mm}$ ) obtained in the control group and difference between the two was statistically significant with the p-value of 0.0001.

Table 2 shows the comparison of control and study group on the basis of mean total lymphocyte count. Mean Total lymphocyte count  $\pm$  SD of the cases in the study group was  $1.30 \pm 0.54$  ( $10^3/\text{cu mm}$ ) which was lower than the mean value of  $1.85 \pm 0.22$  ( $10^3/\text{cu mm}$ ) obtained in the subjects of control group and difference between the two values was statistically significant with the p-value of 0.0001.

Table 3 shows the comparison of control and study group on the basis of Neutrophil to Lymphocyte Ratio. Mean NLR  $\pm$  SD of all the cases in study group was  $3.44 \pm 2.56$  which was higher than the mean value of  $1.89 \pm 0.61$  obtained in the subjects of the control group

Table 1 — Comparison of Total Neutrophil Count in Control and Study Group

Neutrophil ( $10^3/\text{cu mm}$ )	Control group (n=100)	Acute Ischemic Stroke Group (n=100)
Mean	3.4965	4.472
SD	1.7	1.1
T	6.473	
P-value	0.0001	

Total Lymphocyte count (10 <sup>3</sup> /cu mm)	Control group (n=100)	Study group (n=100)
Mean	1.85	1.30
SD	0.22	0.54
T	9.432	
P-value	0.0001	

Neutrophil-to-lymphocyte Ratio	Control Subjects (n=100)	Acute Ischemic Stroke Subjects (n=100)
Mean	1.89	3.44
SD	0.61	2.56
T	2.32	
P-value	0.021	

and the difference between the two values was statistically significant with the p-value of 0.021.

Table 4 depicts the comparison of Acute Ischemic Stroke group and control group on the basis of demographic and biochemical profile including risk factors. The Mean  $\pm$  SD of all subjects in control and Acute Ischemic Stroke study group was obtained including age (61.33 $\pm$ 10.965; 60.79 $\pm$ 13.86) years,

Neutrophil-to-lymphocyte Ratio	Control Group (n=100)	Acute Ischemic Stroke Group (n=100)
Male (%)	55	57
Age (year)	61.33 $\pm$ 10.965	60.79 $\pm$ 13.86
Hypertension, n(%)	44	50
Smoker, n(%)	30	40
Alcoholic, n(%)	26	35
Diabetes mellitus, n(%)	25	36
HB (gm/dl), n(%)	11.63 $\pm$ 1.22	12.57 $\pm$ 1.69
B Glucose (mg/dL) (R)	148.97 $\pm$ 87.75	196.33 $\pm$ 92.26
B Urea (mg/dL)	30.87 $\pm$ 6.51	39.57 $\pm$ 16.72
S Creatinine (mg/dL)	0.984 $\pm$ 0.162	1.19 $\pm$ 0.40
Total cholesterol (mg/dL)	190.2 $\pm$ 31.29	198.48 $\pm$ 62.71
S Triglyceride (mg/dL)	127.66 $\pm$ 35.64	145.96 $\pm$ 55.04
Neutrophil count (10 <sup>3</sup> /cu.mm)	3.4965 $\pm$ 1.7	4.472 $\pm$ 1.1
Lymphocyte count (10 <sup>3</sup> /cu.mm)	1.85 $\pm$ 0.22	1.30 $\pm$ 0.54
Neutrophil to Lymphocyte Ratio	1.89 $\pm$ 0.69	3.44 $\pm$ 2.56

	Control Group (Mean $\pm$ SD)	Study group at the Time of Admission (Mean $\pm$ SD)	t value	p value
Neutrophil Count (10 <sup>3</sup> /cu.mm)	3.4965 $\pm$ 1.7	4.472 $\pm$ 1.1	6.473	0.0001
Lymphocyte count (10 <sup>3</sup> /cu.mm)	1.85 $\pm$ 0.22	1.30 $\pm$ 0.54	9.432	0.0001
Neutrophil to Lymphocyte Ratio	1.89 $\pm$ 0.61	3.44 $\pm$ 2.56	2.32	0.021

Hb (11.63 $\pm$ 1.22; 12.57 $\pm$ 1.69) gm/dl, B Glucose (148.97 $\pm$ 87.75; 196.33 $\pm$ 92.26) mg/dl, B Urea (30.87 $\pm$ 6.51; 39.57 $\pm$ 16.72) mg/dl, S Creatinine (0.984 $\pm$ 0.162; 1.19 $\pm$ 0.40) mg/dl, Total cholesterol (190.2 $\pm$ 31.29; 198.48 $\pm$ 62.71) mg/dl, Triglyceride (127.66 $\pm$ 35.64; 145.96 $\pm$ 55.04) mg/dl, Neutrophil count (3.4965 $\pm$ 1.7; 4.472 $\pm$ 1.1) 10<sup>3</sup>/cu mm, Lymphocyte count (1.85 $\pm$ 0.22; 1.30 $\pm$ 0.54) 10<sup>3</sup>/cu mm and Neutrophil to Lymphocyte Ratio (1.89 $\pm$ 0.61; 3.44 $\pm$ 2.56) respectively.

Table 5 clearly highlighted that the mean Neutrophil count, mean lymphocyte count and mean Neutrophil to mean Lymphocyte Ratio in study group was 4.472 $\pm$ 1.1x10<sup>3</sup>/cu mm, 1.30 $\pm$ 0.54x10<sup>3</sup>/cu mm and 3.44 $\pm$ 2.56 respectively which was higher than the mean control values of 3.4965 $\pm$ 1.7 x10<sup>3</sup>/cu mm, 1.85 $\pm$ 0.22 x10<sup>3</sup>/cu mm and 1.89 $\pm$ 0.61 respectively and the difference was statistically significant in both control and Acute Ischemic Stroke Study group with the p-value of 0.021.

## DISCUSSION

Atherosclerosis, especially intracranial atherosclerosis, is an intrinsic abnormality in the development of ischemic stroke. Inflammation and lipid abnormalities has been proposed as the main constituents of the pathophysiology of atherosclerosis development and progression.

In this study we evaluated mean Neutrophil to Lymphocyte Ratio (NLR) and Mean Platelet Volume (MPV) in patients of Acute Ischemic Stroke by comparing with age and sex matched control subjects. An attempt was made to find out the association between NLR and smoking, alcohol consumption, hypertension, diabetes mellitus. The Neutrophil to Lymphocyte Ratio (NLR) is a parameter of inflammation that is easy to obtain and has been proposed as an independent useful prognostic marker to predict the mortality and prognosis of some cardiovascular and neurologic diseases. Many studies have demonstrated that peripheral leucocyte levels increase following cerebrovascular ischemia and postulated that the initial peripheral leucocyte count following a stroke can help to predict stroke severity.

It has been supposed that the leucocyte count at the time of admission is predictive of the likelihood of AIS and the impact of any resulting neurologic disability on daily living activity.

100 patients of Acute Ischemic Stroke and 100 age and sex matched

control subjects were included in our study. Although the control subjects were free from Acute Ischemic Stroke, some of them were having risk factors for ischemic stroke and it can be expected that they represented a stage in the initiation and progression of ischemic stroke.

#### NLR and Acute Ischemic Stroke :

In our study, mean Neutrophil to Lymphocyte Ratio (NLR), which is obtained by dividing absolute Neutrophil count by Lymphocyte count, was  $3.44 \pm 2.56$  in Acute Ischemic Stroke patients, which was significantly higher than the mean NLR value of  $1.89 \pm 0.61$  obtained in control subjects. Another study by Celikbilek, *et al*/2013 showed that high NLR levels are associated with increased infarct volume and mortality.

The Neutrophil to Lymphocyte Ratio (NLR) is a parameter of inflammation<sup>4</sup> that peripheral leucocyte levels increase following cerebrovascular ischemia, and postulated that the initial peripheral leucocyte count following a stroke can help predict stroke severity. It has been supposed that the leucocyte count at the time of admission is predictive of the likelihood of AIS and the impact of any resulting neurologic disability on daily living activity .

#### NLR and Hypertension :

Hypertension is the major risk factor for Acute Ischemic Stroke in our study. We have tried to study the correlation between NLR and hypertension in both controls and cases. The NLR values of our cases were  $3.44 \pm 2.56$  in hypertensive patients and were  $3.25 \pm 1.95$  in non hypertensive patients. The NLR ratio in hypertensive controls and non-hypertensive controls were  $1.89 \pm 0.61$  and  $1.81 \pm 0.52$  respectively. This showed that there was a slight rise in values of NLR in hypertensive population but this was statistically non significant in our study.

A study conducted by Celik, *et al*<sup>9</sup>, found that the NLR values were significantly higher in the hypertensive group than in the control group. A similar finding was obtained in the study by Aydin, *et al*<sup>10</sup>. In their study found that NLR value was higher in hypertensive patients compared to controls and also added to their conclusion that asymptomatic organ damage in primary hypertension was higher in patients with high NLR values.

The statistically insignificant NLR value in hypertensive patients in our study may be due to the

fact that there may be some other risk factors of atherosclerosis like diabetes, smoking etc in the non hypertensive group too, which can cause a rise in their NLR value there by not making a statistically significant difference in NLR values between hypertensive and non-hypertensive group. Also in this study we have not considered the duration and control of hypertension which may also have interfered with the NLR value of the patients. Our study was conducted in a small group of 100 stroke patients, this low number of cases may have further influenced the observation.

#### CONCLUSION

NLR is a simple, cost effective and easily obtainable novel marker that may help in predicting the severity of disease as evidenced by its increased value in patients of acute ischemic stroke.

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