

A Study on the Neutrophil Lymphocyte Ratio as a Predictor of Mortality in Patients with Acute Cerebrovascular Accident at Tertiary Care Center**K Leelaprasad Babu¹, Matta Sumathi², Bhaskararao Chavakala³, Tammana Chiranjeevi Venkatesh⁴, Chiyeti Yaswanth Kumar Reddy⁵, Nallamothe Sandeep Kumar⁶**¹Associate Professor, Department of General Medicine, GMC, Kadapa²Assistant Professor, Department of General Medicine, GMC, Kadapa³Assistant Professor, Department of General Medicine, GMC, Kadapa⁴Post Graduate, Department of General Medicine, GMC, Kadapa⁵Post Graduate, Department of General Medicine, GMC, Kadapa⁶Post Graduate, Department of General Medicine, GMC, Kadapa

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Conflict of interest: Nil

Abstract:

Background: Stroke is a growing public health problem which remains as a leading cause of mortality worldwide. Among different stroke subtypes, ischemic stroke (IS) is the most common type, constituting for around 80% of all strokes. The neutrophil-to-lymphocyte ratio (NLR) is an easily accessible marker of systemic inflammatory status, implying the balance between neutrophil and lymphocytes in the peripheral blood. Rise in NLR levels were reported to be linked with atherosclerotic events, acting as a prognostic predictor in coronary artery disease (CAD), peripheral arterial occlusive disease (PAD), and stroke. High NLR levels were associated with the severity of stroke, poor functional outcomes, and recurrent ischemic attacks.

Aim: To study neutrophil-lymphocyte ratio as a predictor of mortality in patients with acute cerebrovascular accident (CVA) at tertiary care center.

Patients and Methods: This was a Prospective Observational study conducted in 100 patients in the Department of General Medicine, GMC, GGH, Kadapa, India selected by Simple Random sampling.

Results & Conclusion: The present study showed a positive relation between raised NLR and mortality risk in stroke patients. Sensitivity, PPV, NPV and diagnostic accuracy of NLR in detecting mortality was 78.5%, 100%, 96.63% and 91.48% at a cut off value of 9.3. Early management is important, to reduce mortality and improve outcomes. NLR may help to select risky patients to start intervention on time. We conclude that higher NLR can predict post stroke mortality risk also.

Keywords: Ischemic Stroke, Hemorrhagic Stroke, Neutrophil to Lymphocyte Ratio.

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Introduction

Stroke is a growing public health problem which remains as a leading cause of mortality worldwide. [1] Among different stroke subtypes, ischemic stroke (IS) is the most common type, constituting for around 80% of all strokes. It is caused by atherosclerosis, especially intracranial atherosclerotic stenosis (ICAS), which has more prevalence among Africans, Asians, and Hispanics compared to Caucasians. [2,3]

Evidence implies that ICAS was linked to more risk of dementia, cognitive impairment, recurrence of stroke and death. [4-6] Pathogenesis of ICAS was not well-investigated. Previous studies proved that atherosclerosis is an inflammatory disorder that is mediated by the activation of inflammatory markers from various inflammatory cells, mainly

from macrophages and T cells, which release metalloproteinases, leading to the instability of atherosclerotic or rupture, ischemia, and infarction. [7,8] As ICAS is on the spectrum of atherosclerosis, inflammation is also a pathophysiological mechanism for the progression of ICAS and development of stroke.

The neutrophil-to-lymphocyte ratio (NLR) is an easily accessible marker of systemic inflammatory status, implying the balance between neutrophil and lymphocytes in the peripheral blood. [9] Rise in NLR levels were reported to be linked with atherosclerotic events, acting as a prognostic predictor in coronary artery disease (CAD), peripheral arterial occlusive disease (PAD), and stroke. [10-11] High NLR levels were associated

with the severity of stroke, poor functional outcomes, and recurrent ischemic attacks. [12,13] Large vessel occlusion patients with more NLR values had more risk of symptomatic intracranial hemorrhage (ICH) and mortality after thrombectomy. [14]

Even among healthy patients, increased NLR was proved to be linked to more burdens of ICAS. [15]. There is a relative paucity of literature investigating the underlying associations between admission NLR with initial severity and prognosis of ICAS. So, this study was done to evaluate the predictive capacity of NLR levels for short-term prognosis of patients with acute stroke (AIS).

Aim: To study neutrophil-lymphocyte ratio as a predictor of mortality in patients with acute cerebrovascular accident (CVA) at tertiary care center.

Objectives: To study the correlation between neutrophil-lymphocyte ratio and outcome of CVA, to study the risk factors and types of CVA, to follow up the patient for 30 days to know the mortality.

Patients and Methods: This was a Prospective Observational study conducted in 100 patients in the Department of General Medicine, GMC, GGH, Kadapa, India selected by Simple Random sampling.

Inclusion criteria: Patients aged above 18yrs and having clinical and Radiological (CT/MRI) confirmed diagnosis of stroke (CVA).

Exclusion criteria: Stroke due to trauma or malignancy or active infections /haematological diseases /immunosuppressive agents, Patients with previous history of stroke, Patients with incomplete or absent medical, demographic, clinical laboratory and radiological data.

Parameters Assessed: Demographic data: Age, gender, Presence of HTN, DM, dyslipidemia, coronary artery disease, Smoking, BMI, NLR ratio, Outcome of stroke, Mortality: In hospital or upto 1 month, Type of stroke, Duration of hospitalization

Statistical Analysis: The data collected was entered in Excel 2023 and analysis was carried out using statistical software called SPSS version 26. P value <0.05, was considered as statistically significant. Frequencies, percentages were also used.

Unpaired students t-test was used to test the difference between continuous variables between two groups. Continuous variables were assessed using mean and SD.

Chi square test was used to find factors associating with stroke.

Results

Table 1: Patient Demographic Data

	HS	IS
Age Parameters		
Obs	24.0000	76.0000
Mean	59.4583	57.6842
Std Dev	9.9213	9.6860
	t value 0.78	p value 0.4386
Female	11	28
Male	13	48
BMI		
Obs	24.0000	76.0000
Mean	27.5417	26.6447
Std Dev	1.8877	2.2133
	t value 1.79	p value 0.0767

Table 2: Patient Past history

	HS	IS	Chi-Squared test
Smoking			
NO	20	61	0.4501
Yes	4	15	
Diabetes Mellitus			
No	14	53	1.0728
Yes	10	23	
Hypertension			
No	14	52	0.8272
Yes	10	24	
Coronary Heart Disease			

No	17	59	0.4622
Yes	7	17	
Dyslipidemia			
No	17	49	0.3288
Yes	7	27	

Table 3: Patient Parameters

	HS	IS
Hospital Stay		
Obs	24.0000	76.0000
Mean	5.7917	6.2895
Std Dev	1.8645	1.7113
	t value -1.22	p value 0.2269
NLR		
Obs	24.0000	76.0000
Mean	6.1167	5.7051
Std Dev	3.1635	2.9430
	t value 0.59	p value 0.5588

Table 4: Mortality

	HS	IS	Chi-Squared test
Mortality at Hospital			
No	22	69	0.3411
Yes	2	7	
Mortality at 1 Month			
No	24	73	0.9767
Yes	0	3	

NLR in predicting death: Sensitivity, Specificity, PPV, NPV and diagnostic accuracy of NLR in detecting mortality was 78.5%, 100%, 100%, 96.63% and 91.48% at a cut off value of 9.3.

Table 5: NLR and Relation to various parameters

Gender & NLR				
Group	Obs	Mean	Std Dev	t Value
Female	39.0000	5.9613	3.0006	0.42
Male	61.0000	5.7033	2.9977	
Smoking & NLR				
No	81.0000	5.5411	2.9265	P – 0.00
Yes	19.0000	6.9368	3.1279	
Diabetes Mellitus & NLR				
No	67.0000	5.5731	2.6969	-1.10
Yes	33.0000	6.2724	3.5001	
Hypertension & NLR				
No	66.0000	5.0680	2.5190	-3.64
Yes	34.0000	7.2324	3.3271	
Coronary Heart Disease & NLR				
No	76.0000	5.2301	2.7912	-3.62
Yes	24.0000	7.6208	2.9067	
Age & Mortality				
No	90.0000	57.7444	9.6169	P – 0.00
TN	1.0000	58.0000	Na N	
Yes	9.0000	61.7778	11.1443	

Discussion

On interpretation of study results and comparison with other studies: There is no significant difference in mean age, gender difference, difference in mean BMI, in between two groups of patients. There is no significant difference in the

presence of Smoking, Diabetes, Hypertension, Coronary Heart disease, dyslipidemia, in between two groups of patients. Overall smoking was seen in 19%, diabetes in 33%, HTN in 34%, CAD was seen in 24%, dyslipidemia in 34%.

There is no significant difference in mean duration of hospital stay in between two groups of patients. There is no significant difference in mean NLR in between two groups of patients. There is no significant difference in mortality in hospital in between two groups of patients. Mortality was seen among 9 patients. There is no significant difference in mortality rate at 1 month in between two groups of patients in the current study. 3% of patients died in 1 month. Sensitivity, specificity, PPV, NPV and diagnostic accuracy of NLR in detecting mortality was 78.5%, 100%, 100%, 96.63% and 91.48% at a cut off value of 9.3. There is no significant difference in mean gender & NLR in the current study. There is significant difference in mean smoking & NLR in the current study. There is no significant difference in mean DM & NLR in the current study. There is significant difference in mean HTN, CAD & NLR in the current study. There is no significant association in gender & mortality in the current study. There is no significant difference in mean age & mortality in the current study.

Age and gender: In the current study, mean age was 58 years. There is no significant difference in the mean age in between patients with ischemic or hemorrhagic stroke. Males were more common compared to females and there is no significant difference in gender in between two groups (patients with IS and HS) In the study of Fu-Liang Zhang, 54 among 4052 patients included with stroke, the mean age was found to be 54 years. The prevalence of stroke increased with age. Stroke was significantly higher in men than in women. This finding was similar to the current study finding. Mahdi Habibi [16] conducted a retrospective hospital-based study at Gorgan. In the study of Song Q [17] the mean age was 64.13 years and most of the patients- 63.5% were males.

Smoking and BMI: 19% Patients were smokers in the current study. Most of the patients had normal BMI. There is no significant difference in mean BMI between two groups of patients in the current study. In the study of X Yi, [18] smoking was seen in 139 patients of 524 patients with stroke. Overweight and obese individuals were 355 out of 524 patients. These results show stroke patients usually having High BMI and smoking as addiction. Smoking was seen in 8% stroke patients in the study of Mahdi Habibi. [16]

Comorbidities and type of stroke: There is no significant difference in the presence of DM in between two groups of patients in the current study. Overall diabetes was seen among 33% of patients. There is no significant difference in the presence of HTN in between two groups of patients in the current study.

Overall HTN was seen among 34% of patients. There is no significant difference in the presence of CAD in between two groups of patients in the current study. Overall, CAD was seen among 24% of patients. There is no significant difference in dyslipidemia between two groups of patients in the current study. Overall dyslipidemia was seen among 34% of patients. 76% patients suffered from ischemic stroke in the current study. This indicates that ischemic stroke was more common compared to hemorrhagic stroke.

Ischemic heart disease was seen in 20.5% patients. Dyslipidemia was seen in 22.1% patients. 66% cases were of ischemic stroke and 33% were of hemorrhagic stroke. Ischemic stroke preponderance is similar to the current study findings. In the study done by Putaala [19] done in 2012, patients with 1st episode of ischemic stroke aged 15 to 49 years were included. In contrast, in our study patients of both ischemic and hemorrhagic stroke were included. Data was taken from hospital-or population-based prospective registries.

According to Kumar HH, et al. it is stated that the association between diabetes and stroke is not clearly established. They stated that there is no consistent association between them. Many studies have contradicting reports for confirming association between diabetes and stroke. Similar observation confirmed in the study by HN Harsha Kumar, there is no statistically significant association between diabetes and ischemic stroke.

NLR ratio in detecting outcomes: Inflammation plays a vital role in the development of AIS. Lymphocytes potentiate cerebral inflammation and brain injury in ischemic and hemorrhagic strokes. Neutrophil lymphocyte ratio reflects the immune status and the degree of inflammatory infiltration. NLR is a time dependent variable in stroke patients. It increases with time in 1st few days.

The study of Tokgoz S, [20] is a retrospective study that included 255 patients with acute infarction who got admitted in 24 hours of symptom onset. Ours is cross sectional study that included 100 patients. Duration of follow-up was done for 60 days, in contrast to the current study. 71 of 255 patients expired during the follow-up period.

The association between NLR and stroke recurrence was significant only at the 3-month follow-up before adjustments. But no correlation was found between NLR and hemorrhagic transformation during hospitalization. More NLR in 1st 24 hours after admission was linked to more risks of short- and long-term adverse clinical outcomes in ischemic stroke patients, irrespective of etiology.

Sharma et al [21] conducted a meta-analysis and found that Lower admission NLR was linked with

favorable functional outcomes (3-month modified Rankin Scale and early neurological improvement). High admission NLR was significantly associated with mortality, ICH, symptomatic ICH (sICH), and stroke associated infection or pneumonia. Higher delayed NLR was also significantly associated with sICH, ICH, and mortality. Outcomes varied across different RT group. In the study of Kakhki RD, [22] 180 patients with acute ischemic stroke and hemorrhagic stroke were included. Patients were divided into 2 groups basing on NLR score. NLR was significantly higher in ischemic stroke patients compared to hemorrhagic stroke patients. Patients with NLR of less 5 had a significant decrease in infectious diseases, in ischemic stroke group. The NLR had no associations with mortality rate. It was positively correlated to WBC and RBC, CRP, ESR, and HTN. The study concluded that NLR, along with other clinical and laboratory parameters, may be used to assess stroke type and predict patient susceptibility to infectious diseases like pneumonia.

He L Wang [23] included 606 patients with AIS. ROC analysis was done to know cut off value of NLR in detecting post-stroke infections. Results showed that cut point of NLR for PSI was $NLR \geq 5.79$. Patients with PSI have more NLR, more age, more NIHSS score, more % of nasogastric tube feeding and urinary catheter. Authors concluded that high NLR can predict infections among AIS patients.

Chen et al [24] did a retrospective analysis on patients treated with recombinant human tissue plasminogen activator and/or mechanical thrombectomy (MT) for acute ischemic stroke at Wenzhou Medical University, China, between January 2018 and December 2020. Blood samples were collected upon hospital admission and on day 1 post-stroke.

Conclusion

The present study showed a positive relation between raised NLR and mortality risk in stroke patients. Sensitivity, PPV, NPV and diagnostic accuracy of NLR in detecting mortality was 78.5%, 100%, 96.63% and 91.48% at a cut off value of 9.3. Early management is important, to reduce mortality and improve outcomes. NLR may help to select risky patients to start intervention on time. We conclude that higher NLR can predict post stroke mortality risk also.

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