



NEUTROPHIL LYMPHOCYTE RATIO IN STROKE: AN OBSERVATIONAL STUDY AT A TERTIARY TEACHING HOSPITAL IN JHARKHAND.

Medicine

Dr. Sita Paikra	Junior resident, Department of Medicine, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand.
Dr. Shivshankar Munda*	Junior resident, Department of Medicine, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand.*Corresponding Author
Dr. Chandrabhushan Sharma	Professor, Department of Medicine, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand.
Dr. Vikas Mardi	Junior resident, Department of Medicine, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand.

ABSTRACT

OBJECTIVES-This study was done to evaluate the role of Neutrophil Lymphocyte Ratio(NLR) as a prognostically important inflammatory marker in stroke patients. **MATERIALS AND METHOD**- Medical, demographic and clinical data of 100 stroke patients were recorded. Patients were grouped into two groups-AIS(acute ischemic stroke) and AHS (acute haemorrhagic stroke). AIS patients are further classified into 4 subtypes etiologically as great artery atherosclerosis, cardioembolic, lacunar and unknown origin. NIH stroke severity score(NIHSS) and admission NLR was calculated. The patient's outcome was recorded. Patients were followed up after 2 and 4 weeks. **RESULT**- NLR was more in AHS as compared to AIS, more in atherosclerotic type of AIS followed by cardioembolic and lacunar types respectively, more in dead patients and highest in patients with severe stroke and lowest in minor stroke. **CONCLUSION**- NLR may be used to predict the types, severity and prognosis of stroke.

KEYWORDS

Neutrophil Lymphocyte Ratio, Stroke, Nihss.

INTRODUCTION

A stroke or cerebrovascular accident is defined as "an abrupt onset of a neurological deficit that is attributable to a focal vascular cause."¹ The definition of TIA requires that all neurologic signs and symptoms resolve within 24 hrs without evidence of brain infarction on imaging. Stroke has occurred if the neurologic signs and symptoms last for >24hrs or brain infarction is demonstrated.¹ Inflammation play an important role in atherogenesis. Neutrophil and lymphocyte play an important role in inflammatory and atherosclerosis process which has been involved in the pathogenesis of stroke.² NLR is an easy to measure, and newly recognized biomarker in many inflammatory conditions.³ This ratio integrates the detrimental effects of neutrophilia (reflecting inflammation) and lymphopenia (reflecting physiological stress)⁴. So, this study was done to evaluate the role of NLR in assessment of types, severity and prognosis of stroke patients.

MATERIALS AND METHOD

100 stroke patients were studied at Department of Medicine, RIMS, Ranchi from 1st September 2017 to 31st August 2018. Diagnosis of stroke was confirmed by CT brain imaging in the emergency. Blood samples for the estimation of CBC was collected at the time of admission. Medical, demographic and clinical data of the patients were recorded by means of personal interview of patients and attendants after taking informed consent. Patients were grouped into two groups-AIS(acute ischemic stroke) and AHS (acute haemorrhagic stroke). AIS patients were further classified into 4 subtypes etiologically as great artery atherosclerosis, cardioembolic, small artery occlusion or lacunar and unknown origin. NIH stroke severity score was calculated. The patient's outcome / prognosis was recorded as either death in hospital or return home /discharge. NLR was calculated by dividing the absolute number of neutrophil and lymphocyte from the differential leukocyte count obtained at the time of admission and during follow up period at 2 and 4 weeks after discharge. (Reference values for neutrophil and leukocyte has been taken as 3000-6000 average 5400 and 1500-4000 average 2750 respectively). Patients were followed up after 2 and 4 weeks. Data were analysed using Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 23.0 software and the p-value <0.05 was considered as significant and <0.0001 as highly significant.

RESULTS

Table 1 shows the association of NLR and the type of CVA. NLR was more in AHS as compared to AIS (p <0.05).

NLR	AIS	AHS	p value
3.6-4	4	0	0.001
4.1-4.5	6	6	

4.5-5	4	14	
5.1-5.5	5	12	
5.6-6	4	1	
6.1-6.5	0	0	
6.6-7	3	0	
7.1-7.5	2	9	
7.6-8	2	2	
8.1-8.5	2	6	
8.6-9	7	5	
9.1-9.5	1	5	
TOTAL	40	60	

Table 2 shows the association of NLR and types of AIS. NLR was more in atherosclerotic type of AIS as compared to cardioembolic and lacunar types.(p <0.001)

NLR	ATHERO SCLEROTIC	CARDIO EMBOLIC	LACUNAR	p value
3.6-4	0	1	3	0.000
4.1-4.5	0	2	4	
4.6-5	3	1	0	
5.1-5.5	2	1	2	
5.6-6	2	2	0	
6.1-6.5	0	0	0	
6.6-7	0	3	0	
7.1-7.5	1	1	0	
7.6-8	1	1	0	
8.1-8.5	1	1	0	
8.6-9	7	0	0	
9.1-9.5	1	0	0	
TOTAL	18	13	9	

Table 3 showing mean NLR of dead and discharged patients. The mean NIHSS Score in dead patients was 34.6786 and that of discharged patients was 12.6786 and the difference was statistically significant (p value <0.0001)

	Dead patients	Discharge patients	p value
No. of patients	44	56	<0.0001
Mean	34.6591	12.6786	
Median	35	14	
Mode	36	14	
Std. deviation	2.70179	3.57317	
Minimum	29	4	
Maximum	35	20	

Table 4 shows association of NLR and NIHSS score. NLR was highest in patients with severe stroke followed by patients with severe to moderate to severe stroke and lowest in minor.(p<0.001).

NLR	MINOR (1-4)	MODERATE (5-15)	MODERATE TO SEVERE (16-20)	SEVERE (21-42)	TOTAL	p value
3.6-4	3	1	0	0	4	0.000
4.1-4.5	0	10	2	0	12	
4.5-5	0	18	0	0	18	
5.1-5.5	0	14	2	0	16	
5.6-6	0	2	4	0	6	
6.6-7	0	0	0	3	3	
7.1-7.5	0	0	0	11	11	
7.6-8	0	0	0	4	4	
8.1-8.5	0	0	0	8	8	
8.6-9	0	0	0	11	11	
9.1-9.5	0	0	0	7	7	
TOTAL	3	45	8	44	100	

Table 5 showing association of NLR and NIHSS score and the mean NLR at the time of admission, after 2 and 4 weeks of discharge are 6.29, 4.67 and 4.47 respectively and the difference among them was statistically highly significant. (p<0.001)

	At the time of admission	2weeks after discharge	4weeks after discharge	p value
No. of patients	100	56	56	<0.0001
Mean	6.29	4.67	4.47	
Median	5.50	4.75	4.50	
Mode	5.00	5.00	4.30	
Std. deviation	1.75	0.52	0.51	
Minimum	3.8	3.65	3.50	
Maximum	9.5	5.65	5.40	

DISCUSSION

100 patients of stroke were selected and assessed during hospital stay and upto 4 weeks of follow up period.

The most common age group in the present study was 61-80 years followed by 41-60 years comprising 42% and 40% respectively and mean age was 58.51years. 15% of patients were under the age of 40years in the present study. The incidence of male and female patients was 60% and 40% respectively.

NLR was more in AHS as compared to AIS and was statistically significant. (p <0.05). S. Gokhan et al⁵ showed that NLR level in patients with TIA was significantly lower than those of AIS and AHS groups (p < 0.001) and it may be used as a simple and easy to measure marker for prediction of short-term prognosis and in-hospital mortality in both ischemic and haemorrhagic stroke patients. Simona Lattanzi et al⁶ also found that in patients with acute intracerebral hemorrhage, higher neutrophils, lower lymphocytes, and higher NLRs predicted worse 3-month outcome. Guo et al⁷ found that an increasing trend in the NLR was observed after stroke, and the NLR was higher in patients who developed PH or sICH at 3–6, 12–18, and 36–48 h after IVT (P < 0.01) than in those without PH or sICH. Yaming Sun et al⁸ also found the same result that higher admission NLR are associated with larger hematoma volume and more serious stroke.

Present study showed 45% of AIS was of atherosclerotic type followed by cardioembolic (32.5%) and lacunar type (22.5%). NLR was more in atherosclerotic type of AIS as compared to cardioembolic and lacunar types and is statistically highly significant (p <0.001) followed by cardioembolic and lacunar types respectively. Gokhan et al⁵ found that among AIS subgroups, NLR level was significantly higher in group with great artery atherosclerosis or atherothrombosis compared to other groups (p < 0.001). Tokgoz et al⁹ showed that the NLR was higher in both the atherosclerotic and cardioembolic stroke subgroups than the lacunar infarct subgroup. I Lakhani¹⁰ that increased NLR predicted atherosclerotic type of AIS. Rodriguez et al¹¹, Buck et al¹², Guven et al¹³ found the lowest leukocyte count in lacunar stroke.

Our study shows out of total patients, 44 (44%) patients died and 56 (56%) survived. NLR was more in dead patients as compared to discharged patients(p <0.001).S. Gokhan et al⁵ showed that NLR was significantly higher in patients who died (p < 0.001). Simona Lattanzi

et al⁶ found that higher neutrophils, lower lymphocytes, and higher NLRs predicted worse 3-month outcome. Jing Zhang et al¹⁴ showed that higher NLR was associated with poorer functional outcome at 3 months.Raymond Farah et al¹⁵ found that neutrophil to lymphocyte ratio is a good predictive factor of stroke and stroke prognosis. Meyung Kug Kim et al¹⁶ showed that the NLR was significantly higher in the poor outcome group. Ugur Lök, Umut Gülaçtı et al¹⁷ found that higher NLR is associated with an increased mortality rate in patients with AIS and NLR ratios were higher among the patients who later expired than among the patients who were discharged (p=0.011). Darmawan O et al¹⁸ showed that NLR median was higher in poor outcome group(p =0.018).

Euodia P Guinmapang et al¹⁹ found that the group with low NLR (<5.9) had mostly minor to moderate strokes, while those with higher NLR (>5.9) had a higher proportion for moderate and moderate to severe stroke. Xue J et al²⁰ showed that neutrophil-to-lymphocyte ratio is associated with stroke severity on admission, primary unfavorable functional outcome, and recurrent ischemic stroke in patients with acute ischemic stroke. Giede-Jeppe A, Bobinger T, Gerner S.T et al²¹ found that patients associated with high NLR (≥8.508 = above 75th-percentile) showed the worst neurological status on admission(p< 0.001).Raymond Farah et al¹⁵ also showed that NLR was higher in patients with moderate/severe stroke compared with those with minor stroke. The findings of the present study were comparable with the results of the studies done by the names mentioned above.

CONCLUSION-NLR was significantly high in AHS, atherosclerotic type of AIS, more severe stroke and dead patients.Thus, it may be used to predict the types, severity and prognosis in patients with both acute ischemic and hemorrhagic stroke.

REFERENCES

1. J.Larry Jameson et al, 2016;Harrison's Principles of Internal Medicine, 19:2559
2. Rodriguez-Yanez M,Castillo J.2008; Role of inflammatory markers in brain ischemia, Curr Opin Neurol 21:353-357
3. Lee et al,2013; Prognostic significance of neutrophil lymphocyte ratio and platelet lymphocyte ratio in advanced gastric cancer patients treated with FOLFOX chemotherapy, BMC Cancer 13: 350-360
4. Shouyu Wang et al,2011; The neutrophil lymphocyte ratio is an independent prognostic indicator in patients with bone metastasis, Oncology letters 2: 735-740
5. S.Gokhan et al,2013; Neutrophil lymphocyte ratios in stroke subtypes and transient ischemic attack, European Review for Medical and Pharmacological Sciences 17:653-657
6. Simona Lattanzi et al,2016; Neutrophil-to-Lymphocyte Ratio Predicts the Outcome of Acute Intracerebral Hemorrhage, Stroke 47(6) 1654-1657
7. Guo et al,2016; Dynamic change of neutrophil to lymphocyte ratio and hemorrhagic transformation after thrombolysis in stroke, Journal of Neuroinflammation 13:199
8. Yaming Sun et al,2017; Neutrophil to lymphocyte ratio and the hematoma volume and stroke severity in acute intracerebral hemorrhage patients, The American Journal of Emergency Medicine 35(3): 429-437.
9. Serhat Tokgoz et al,2014; Is Neutrophil Lymphocyte Ratio Predict to Short-term Mortality in Acute Cerebral Infarct Independently from Infarct, Journal of Stroke and Cerebrovascularaccidents 23(8)2163-2168
10. I Lakhani,2018; Predictive value of neutrophil-to-lymphocyte ratio for stroke-related outcomes: a systematic review and meta-analysis, European Heart Journal,39(1) 1
11. Rodriguez et al, 2008; Role of inflammatory markers in brain ischemia, Curr Opin Neurol 21:353-357
12. Brian h. Buck et al, 2008; Early Neutrophilia is associated with volume of ischemic tissue in acute stroke, American Heart Association Stroke 39:355-360
13. Guven et al, 2010; Effect of neutrophil and lymphocyte counts in ischemic infarcts and its its etiology and prognosis, J Neurol Sci 27: 311-318
14. Jing Zhang et al,2017; Prognostic role of neutrophil- lymphocyte ratio in patients with acute ischemic stroke,Medicine,Baltimore, 96(45) 8624.
15. Raymond Farah et al, 2018; Mean platelets volume and neutrophil to lymphocyte ratio as predictors of stroke, J Clin Lab Anal,32
16. Meyung Kug Kim, 2017; Neutrophil to Lymphocyte Ratio Predicts Short-Term Functional Outcome in Acute Ischemic Stroke, ARC Journal of Neuroscience Volume 2, Issue 3, 30-37
17. Ugur Lök, Umut Gülaçtı et al, 2016; The Predictive Effect of the Neutrophil-to-Lymphocyte Ratio (NLR) on the Mortality of Acute Ischemic Stroke and its Subtypes: a Retrospective Cross-Sectional Study, Eurasian J Emerg Med 15: 69-72
18. Darmawan, O et al,2017 ; High neutrophil lymphocyte ratio as predictor of poor outcome in patient with acute ischemic stroke in Sanglah General Hospital Denpasar O, Journal of the Neurological Sciences, 945–1128
19. Euodia P Guinmapang et al, 2017;The association of neutrophil-lymphocyte ratio with the 30-day mortality among patients with acute ischemic stroke, Journal of neurological disorders,5(2)44-45
20. Xue J et al,2017; Neutrophil-to-Lymphocyte Ratio Is a Prognostic Marker in Acute Ischemic Stroke, J Stroke Cerebrovasc Dis,26(3)650-657
21. Giede-Jeppe A, Bobinger T, Gerner S.T et al, 2017; Neutrophil-to-Lymphocyte Ratio Is an Independent Predictor for In-Hospital Mortality in Spontaneous Intracerebral Hemorrhage, J Stroke Cerebrovasc Dis,44:26-34