

Original research article

A correlation of neutrophil lymphocyte ratio on admission with functional outcome in acute cerebrovascular accident as short-term prognosis in a tertiary care hospital in Tiruchirappalli

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Abstract

Background: Cerebrovascular accident or stroke is defined as abrupt onset of focal neurological deficit that is attributable to vascular cause, accounting for second leading cause of global mortality. Inflammation is the key for atherosclerosis pathogenesis with neutrophil lymphocyte ratio being the indicator of systemic inflammatory response and serving as prognostic biomarker in ischemic events.

Methodology: A descriptive study was done among the cerebrovascular accident patients, excluding those with acute and chronic diseases of infective, inflammatory, hepatic and renal disease. History and clinical examination along with radio imaging was used for the diagnosis of CVA*. Neutrophil Lymphocyte Ratio was calculated on admission. The functional outcome of the patients was assessed using Modified Rankin Scale which was administered both during admission as well as at 7 days/discharge.

Results: 45 to 75 years was the age range of the study participants and majority 66% were males, remaining females, 96% presented with ischemic stroke only 4% had haemorrhagic stroke. Mean Modified Rankin Scale score of 3.3 ± 0.8 and 2.8 ± 1.3 was found at admission and day 7/discharge respectively. A highly significant positive correlation between the Neutrophil Lymphocyte ratio at admission and Modified Rankin Scale score at day 7/discharge was found. Majority of participants remained in static functional outcome group followed by improved group, as we measured outcome on day 7 or discharge whichever is earlier.

Conclusion: As Neutrophil Lymphocyte ratio is cost effective and easily obtainable inflammatory marker that can be used to predict short term prognosis in acute cerebrovascular accident patients.

Keywords: Ischemic stroke, hemorrhagic stroke, Modified Rankin Scale, functional outcome, CVA (CEREBRO Vascular Accident)

Introduction

Cerebrovascular accident or stroke is defined as abrupt onset of focal neurological deficit that is attributable to vascular cause. It accounts for second leading cause of mortality worldwide ^[1]. Globally 15 million people suffer from stroke on annual basis, of which death is seen in 5 million and another 5 million are left with permanent disability, causing a burden to family and community. Tobacco usage and high blood pressure are considered to be the most significant modifiable risk factors and smoking had contributed to 2/5th of death due to stroke ^[2]. Ischemic stroke accounts for 80%, which is caused by blockage and Hemorrhagic stroke accounts for 10 to 20%, caused by rupture of blood vessels ^[3]. Stroke patients may present with any of the symptoms like difficulty in walking, speaking and understanding, dizziness, loss of coordination and balance, numbness or paralysis, blurred or darkened vision, headache with nausea and vomiting ^[4]. There is a complex relationship between Lipids and cerebrovascular disease, though; there is a direct effect of cholesterol on ischemic stroke, particularly atherosclerotic disease. There is an increased risk of Intra cranial hemorrhage at low cholesterol levels, and there is evidence that low lipid levels also increase the risk of small vessel disease ^[5]. Few other studies have also shown the involvement of central nervous system in diabetes its is considered as one of the risk factor of ischemic stroke as it is associated with poor functional outcome, severe disability, higher mortality and higher frequency of recurrence. In both animals and humans with diabetes, there was a disturbance in cerebral blood flow, impaired cerebrovascular reactivity and damage to both intra and extra-cranial cerebral vessels observed. Cerebral atherosclerosis was also observed in a very early stage with increased severity in case of diabetic compared to non-diabetic, thus revealing a higher incidence of CVA ^[6, 7].

Atherosclerosis which is one of the causes of stroke is primarily limited to hypertension and hypercholesterolemia. Inflammation also plays a key role in pathogenesis of atherosclerosis. The most abundant white blood cell in circulation, the neutrophils, is suggested to have an association with atherosclerosis. This is due to the depletion of neutrophils during atherogenesis leading to control in macrophage migration. Neutrophil lymphocyte ratio (NLR) is an indicator of systemic inflammatory response and serving as prognostic biomarker in ischemic events^[8, 9]. Modified Rankin Scale (mRS) is measure of global disability, is widely applied for evaluating stroke patient functional outcomes^[10]. This study was aimed to determine the NLR on admission which serves as a short-term prognosis predictor, with the objective to determine the association between neutrophil lymphocyte ratio with the outcome of acute cerebrovascular accident.

Methodology

A cross sectional descriptive study was done among patients with acute cerebrovascular accident admitted in a tertiary care hospital, Trichy. The study was done over a period of 3 months. Total enumeration sampling was done. All the patients above 18 years admitted in the institution during the study period presenting with both ischemic and hemorrhagic type of cerebrovascular accident within 3 days of symptom onset, and those who gave consent were included in the study. Among these those patients suffering from any acute or chronic infection, inflammatory or autoimmune disease, venous sinus thrombosis, hepatic and renal diseases were excluded from the study. Taking into consideration of the inclusion and exclusion criteria a total of 50 patients participated in our study. The study was started after obtaining the approval from the institutional ethical committee. The purpose of the study was clearly explained to the patients and an informed written consent was obtained from all the patients participating in the study. The right to withdraw from the study at any given point of time without any loss in care or penalty was explained to the patients. The diagnosis of acute stroke was done based on history and clinical examination of the patients and was confirmed with radio imaging in the day of admission. Neutrophil lymphocyte ratio was calculated from the complete blood count collected on the day of admission. Modified Rankin Scale was used to determine the functional outcome of the patient with score ranging from 0 to 6. For the purpose of classification in our study good functional outcome was said to be when the Modified Rankin Scale score is ≤ 2 and when the score of Modified Rankin Scale is ≥ 3 it was considered poor functional outcome. The scale was applied on day 1 to assess the functional outcome of the patient and was reassessed either on day 7 or at discharge, which ever was the earliest. The data collected was entered in MS Excel and analysis was done using SPSS software version 23. Mean and standard deviation was used to express the continuous variables and categorical variables were expressed using frequency and percentage. Spearman correlation was assessed between NLR & modified ranking score both at admission and on day 7/discharge.

Results

The range of age among the study participants was 45 years to 75 years. Of the total 50 study participant's majority 33(66%) were male. Of the total only 2(4%) patients presented with hemorrhagic stroke while all the rest 48(96%) had ischemic stroke.

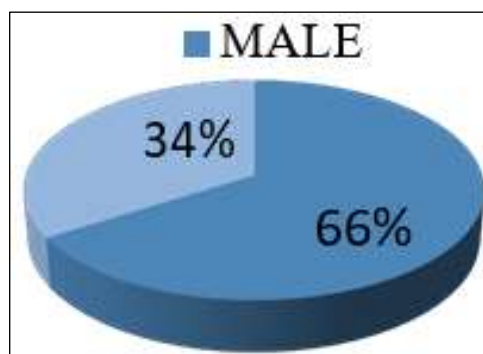


Fig 1: Distribution of male and female participants

Table 1: Frequency distribution of past history among the study participants.

Disease	Number	Percentage
Diabetes Mellitus	32	64%
Systemic Hypertension	28	56%
Dyslipidemia	9	18%

While assessing the personal history and past history of the study participants 28(56%) had history of smoking, 14(28%) gave history of consumption of alcohol and 3(6%) had previous history of stroke and 7(14%) had history of myocardial ischemia respectively.

In our study around 34(64%) of the participants presented with left hemiparesis and 14(28%) presented with right hemiparesis. Only 4(8%) of the participants showed clinical symptoms of posterior circulation stroke and the most common artery involved is the middle cerebral artery territory.

The mean value of Neutrophil lymphocyte ratio at admission was 7.7 ± 6.5 . Total of 15(30%) had $NLR < 5.27$ (54%) having NLR value of 5.1-10, 5(10%) participants with 10.0-20 NLR and 2(4%) with NLR value more than 20.1. Mean Modified Rankin Scale score of 3.3 ± 0.8 and 2.8 ± 1.3 was found at admission and day 7/discharge respectively.

Table 2: Assessment of Modified Rankin Scale during admission and at 7 days/discharge

Modified ranking scale score	At admission	At discharge
1. No significant disability	1(2%)	10(20%)
2. Slight disability	7(14%)	13(26%)
3. Moderate disability	22(44%)	10(20%)
4. Moderately severe disability	18(36%)	13(26%)
5. Severe disability	2(4%)	4(8%)

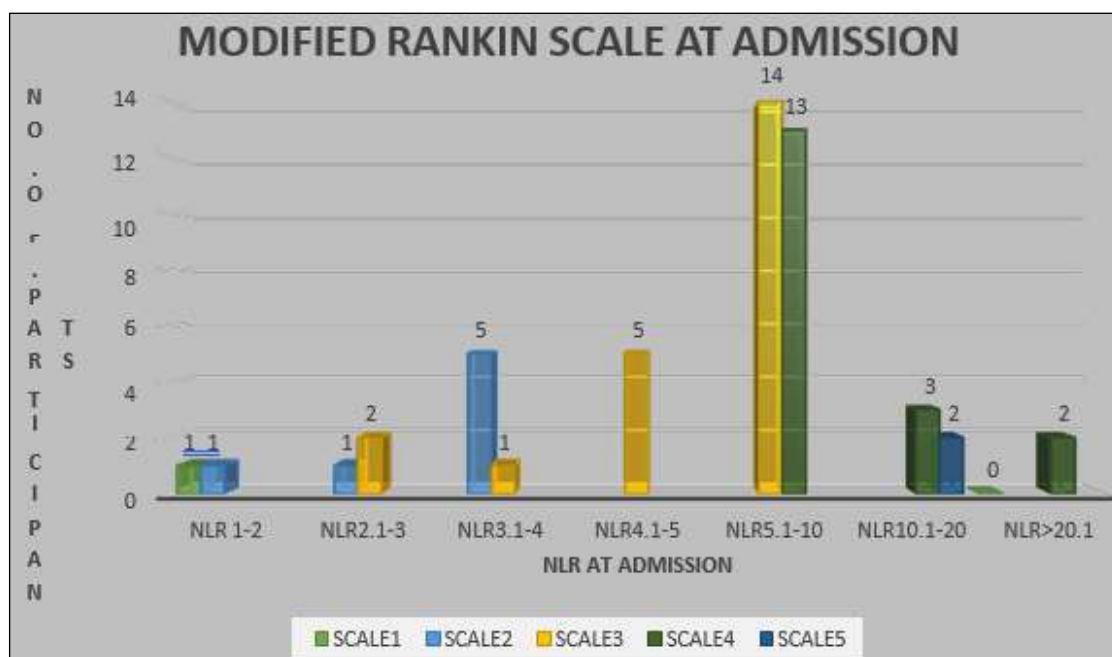


Fig 2: Distribution of Modified Rankin Scale score under each category of neutrophil lymphocyte ratio at admission

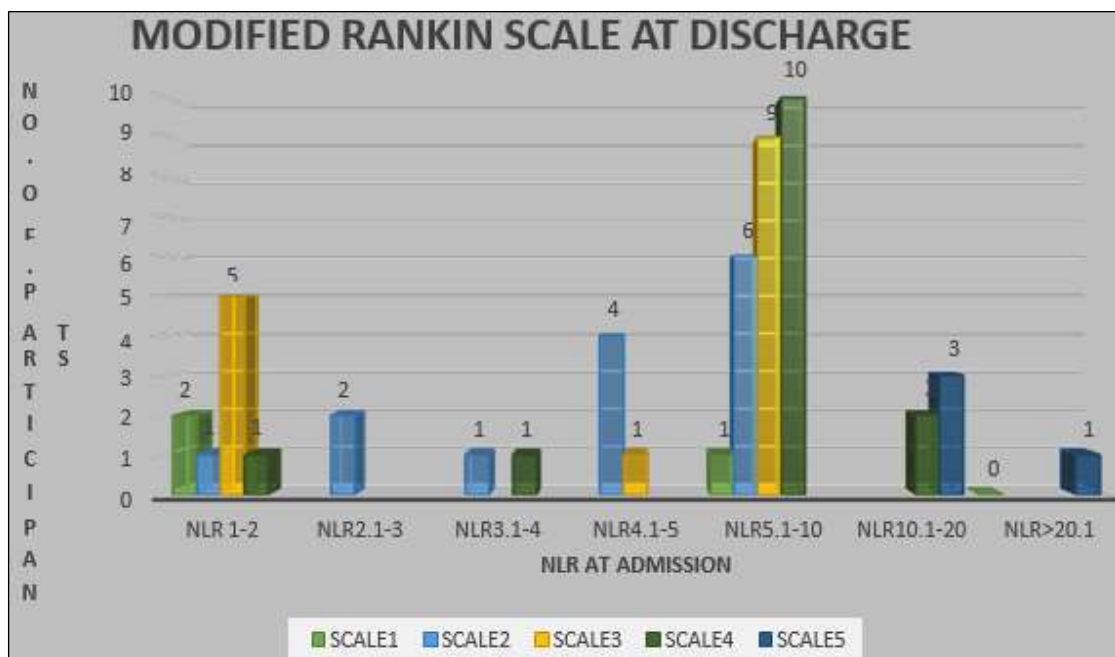


Fig 3: Distribution of Modified Rankin Scale score under each category of neutrophil lymphocyte ratio at 7 days/discharge

Spearman correlation was calculated as the distribution of NLR at admission, Modified Rankin Scale at admission and at 7 days/discharge was not distributed equally. This showed a highly significant positive correlation between the Neutrophil Lymphocyte ratio at admission and Modified Rankin Scale score at day 7/discharge with a value of 0.879 and 0.916 respectively.

Table 3: Correlation between NLR at admission and Modified Rankin Scale at day 7/discharge

	Spearman correlation	p value
Admission	0.879	<0.001
Day 7/discharge	0.916	<0.001

P value <0.001 is considered to be highly significant.

Table 4: Outcome of the patients depending on NLR at admission

NLR at Admission	No. of participants	Improved	Static	Detreated
1-2	2		2	
2.1-3	3	3		
3.1-4	6	6		
4.1-5	5	4	1	
5.1-10	27	10	17	
10.1-20	5		5	
>20.1	2			2

Discussion

In our study 66% of the participants were male, which was similar to a study done by Sethu Babu *et al.*, which showed 64.56% [3] of male participants. In a study done by Ying Y *et al.*, the age range of the participants were found to be 53-68 years [9], which was kind of similar to 45 years to 75 years observed in our study. Also the distribution of risk factors among the participants was observed to be 64% of diabetes, 56% of hypertension, 18% of dyslipidaemia, 56% smoking, 28% alcohol, 6% previous history of stroke and 14% of myocardial ischemia. These were a little deviated from the finding by Ying Y [9] of 77.8% hypertension, 34.5% diabetes mellitus, 45.8% dyslipidaemia, 14.5% of CAD, 43.4% smoking and 33.6% drinking and 19.27% of previous history of stroke [11] in a study done by Banerjee *et al.*, We observed that only 2(4%) patients presented with hemorrhagic stroke while all the rest 48(96%) had ischemic stroke, which was very similar to the data released in a fact sheet stating ischemic stroke accounts for 50%-85% and hemorrhagic for 1%-7% of all strokes [12]. The pooled data from all studies relating to stroke reveals 68-80% of ischemic and 20-32% of hemorrhagic stroke [13]. In a study done by Narra Lavanya *et al.*, the right hemiparesis 29% was most common than the left present in 25% while in contrast our study showed 64% of left hemiparesis and 28% of right hemiparesis [14]. 84% of our participants presented with poor functional outcome during admission and at the end of 7 days or at discharge only 54% had poor functional outcome which was almost similar to 42% [9] compared to 67.7% [3] poor functional outcome at 90 days, which was relatively higher. The mean NLR value at

admission in our study was 7.7 ± 6.5 compared to 5.34 ± 4.74 [3] in the study done by Sethu Babu *et al.*, As the NLR value increases there was also an increase in functional outcome scores, indicating poor outcome, this finding was much similar to the significant correlation established between NLR levels with severity of stroke and unfavourable short-term prognosis observed in a study done by Ying Y *et al.*, [9]. A similar finding was also observed in the study done by Jie Xue *et al.*, [15]. which showed the association of neutrophil to lymphocyte ratio with severity of stroke at admission and unfavourable functional outcome. The NLR was found to be a good predictor of functional outcomes which was highly significant [3], a similar result was observed in our study, where the spearman correlation between the NLR and the MRS scoring shows a highly significant positive correlation with values of 0.879 and 0.916 at admission and discharge respectively. Wenxia Li *et al.*, [16]., also showed that NLR has a significant association with poor prognosis of stroke patient, as high level of NLR was associated with 1.1 to 1.3 fold increase risk of poor outcome, thus serving as a potential biomarker. In the meta-analysis done by Jinzhao Wan *et al.*, [17]. It was concluded that the neutrophil-lymphocyte ratio plays a predictive role in short-term outcome following ischemic and hemorrhagic stroke. The phenomenon behind the association was also explained to be as, the inflammatory cells accumulated around the damaged parts in the course of stroke secretes cytokines, which in turn promotes the inflammatory response. This leads to cytokine storm causing secondary brain cell damage and migration of leucocytes. Neutrophils are fundamental subtypes of leucocytes, thus the neutrophils have an association with infarct volume, recurrent stroke risk and poor functional outcome. The role of lymphocyte which increases after a few days remains controversial, as few says it has a repairing and recovering effect, while others suggest that they are the source of pro-inflammatory cytokines having a negative role on ischemic brain damage. Thus, the ratio of neutrophil lymphocyte reflects on the trend of inflammation. Thus, a strong inflammatory response will have a negative impact on prognosis of stroke [18-21].

Conclusion

As Neutrophil Lymphocyte ratio is cost effective and easily obtainable inflammatory marker that can be used to predict short term prognosis in acute cerebrovascular accident patients. Patients admitted with CVA in Intensive care unit, multicentric, and in-depth research should be done over a long duration with follow up can be done, all these might serve as a strong substantiation for our results.

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