Neutrophil to Lymphocyte Ratio among Acute Ischaemic Stroke Patients

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ABSTRACT

Introduction: Finding potential prognostic indicators for Acute Ischaemic Stroke (AIS) may help to increase the accuracy with which outcomes can be predicted, and implementing early therapies may help to improve the prognosis as well. Recently, Neutrophil Lymphocyte Ratio (NLR) was shown to predict short-term outcome in patients with AIS.

Aim: To determine whether NLR is useful in detecting length of stay, complications in the hospital and three months outcome of a patient admitted with AIS.

Materials and Methods: This was a prospective cohort clinical study that was conducted in the Department of General Medicine, Mahatma Gandhi Medical College and Research Institute, a tertiary care hospital, Pillaiyarkuppam, Puducherry, India where 62 AIS patients were enrolled between December 2019-May 2021. All the routine blood investigations and NLR was calculated during admission and on day five, The patients were followed-up for the next three months. During the course of their stay in the hospital, patients were assessed daily using the National Institutes of Health Stroke Scale (NIHSS).

Results: The mean age of the study population was 67.48±11.29 years, with 37 (59.68%) males and 25 (40.32%) females. The mean NLR on day 1 and day 5 were 5.42±2.85 and 3.51±1.97, respectively. There was a positive correlation between NLR and length of hospital stay (r=0.9661; p<0.0001). Patients having NLR >8, were observed to have complications such as aspiration pneumonia 3 (33%), seizures 2 (22%), and urinary tract infection 1 (11%).

Conclusion: NLR is useful marker in detecting length of stay, complications in the hospital and three months outcome of a patient admitted with AIS.

INTRODUCTION

Inflammation plays a crucial role in the pathophysiology of acute ischaemic stroke. Among such inflammatory markers, the NLR is identified as a critical indicator of systemic inflammation [1]. Decreasing the leukocyte adherence, via targeting of multiple adhesion molecules, prevents leukocytes from entering ischaemic brain, and resulting in decreased neurologic damage [2]. NLR has been extensively explored as a predictive factor because it is inexpensive and the investigations are routinely done [2-4].

Numerous meta-analyses have established that an elevated NLR level is a poor prognostic predictor in patients with AIS and spontaneous intracerebral haemorrhage [5-8]. Brooks SD et al., conducted a retrospective cohort research in 2014 and discovered that NLR 5.9 was associated with a poor outcome and mortality at 90 days [9]. However, another multicentre study conducted by Duan Z et al., demonstrated that NLR 7.0 was independently related with poor functional outcome and that there was no significant correlation between NLR level and three month death [10].

This study aimed to bridge the gap in literature and to provide an overview about the role of NLR in ischaemic stroke, its correlation with duration of in-hospital stays, complications, and three month outcome of the patient. This can help clinicians use this novel biomarker in their everyday practice and impact early diagnosis in such cases.

MATERIALS AND METHODS

This was a prospective cohort clinical study that was conducted in the Department of General Medicine, Mahatma Gandhi Medical College and Research Institute, a tertiary care hospital, Pillaiyarkuppam, Puducherry. Total of 62 patients were enrolled between December 2019-May 2021. The study was started after obtaining the approval of Institutional Human Ethical Committee (MGMCRI/Res/01/2019/35/IHEC/111) on 09.03.2020.

Inclusion criteria: AIS patients above 18 years presenting to the institution, within less than three days of onset of symptoms were included in the study.

Exclusion criteria: Pregnant and lactating females, patients with acute or chronic infections, deranged liver and renal parameters, major trauma and surgery, cancer, haematologic disease or use of any immunosuppressants were excluded from the study.

Study Procedure

Patients who fell under the selection criteria and voluntarily agreed to be involved in the study were enrolled. Informed consent was obtained from each patient recruited for this study after explaining the nature of the study and the possible investigations involved. A complete history of the patient was obtained regarding the onset of stroke, with associated co-morbidities. Then physical examination was carried out including general examination and vitals. All routine blood investigations such as complete blood count, blood urea, serum creatinine, serum electrolytes, random blood sugar, fasting blood sugar, postprandial and HbA1c etc. NLR was calculated on the day of admission and on day five. Then every patient was followed-up for the next three months through regular telephonic conversations and outpatient visits. During the course of the stay in the hospital, patients were assessed daily using the NIHSS [11].

The patients were categorised based on NLR values as

- 'good' (>3 to 5.9),
- 'fair' (6 to 8.9), and
- 'poor' (>9) [12],

then were compared with the length of hospital stay to identify the precise NLR values.

They were treated with anticoagulants, antiplatelets, and statins along with regular physiotherapy. If the patients had any co-morbidities such

as diabetes, hypertension was controlled by Oral Hypoglycaemic Agents (OHA)/Insulin and antihypertensives, respectively.

STATISTICAL ANALYSIS

The data was entered in an excel sheet. Data was exported to Medcalc version 19.0 for further processing. All categorical variables were expressed as percentages and the continuous variables were expressed as mean±standard deviation. The statistical significance of mean differences was compared in three groups using a one-way ANOVA analysis. The Pearson's correlation analysis was also done. A p-value <0.05 was considered to be significant.

RESULTS

The mean age of the study population was 67.48±11.29 years, with 37 (59.68%) males and 25 (40.32%) females. Smoking habits was observed in 40.32% of the patients, and 37.09 % patients had a history of alcohol consumption. Diabetes mellitus was observed in 40.32%, and 71% patients were hypertensive [Table/Fig-1].

Variables	Yes n (%)	No n (%)
Smoking	25 (40.32)	37 (59.68)
Alcohol	23 (37.09)	39 (62.90)
Hypertension	44 (70.96)	18 (29.03)
Diabetes mellitus	25 (40.32)	37 (59.68)
[Table/Fig-1]: Risk factor stratification.		

The complete blood count, NLR and NIHSS are illustrated in [Table/Fig-2]. The mean NLR on day 1 and day 5 were 5.42±2.85 and 3.51±1.97, respectively, which showed a significantly decreasing trend.

Parameters	Day 1	Day 5	p-value
Total count	9559.46±3797.69	10722.22±3712.07	0.7321
Neutrophil	70.64±10.92	72.51±8.97	0.4369
Lymphocytes	19.81±9.47	18.05±7.88	0.4739
Platelet	247348±96278.3	244944.44±73918.853	0.6623
NLR	5.42±2.85	3.51±1.97	0.0011
NIHSS	10.59±5.45	7.47±4.75	<0.001
[Table/Fig-2]: Routine blood indices, NLR, and NIHSS. NIHSS: National institutes of health stroke scale; NLR: Neutrophil lymphocyte ratio; A p-value <0.05 was consisedred to be significant			

The NLR values of admission day were categorised into three groups as ->3 to 5.9, 6 to 8.9, and >9. Each group was compared with the length of hospital stay. It was observed that when NLR values increased at the day of admission, the length of hospital stay also increased [Table/Fig-3].

NLR	NLR	Length of hospital stay (days)	Pearson's correlation coefficient (r)	p-value	Complication	NIHSS at 90th day	Outcome at 3rd month
>3-5.9 (n=34)	3.3±0.77	2.82±1.2	0.8254	<0.0001	None	5.1±3.01	Good
6-8.9 (n=19)	6.46±0.93	5.95±1.13	0.8844	<0.0001	None	5.74±0.73	Fair
>9 (n=9)	10.12±1.34	8.67±1.58	0.9661	<0.0001	Yes	8.67±1.41	Poor
[Table/Fig-3]: Comparison of NLR with length of hospital stay, complication, NIHSS at day 90, and outcome at 3 months. A p-value <0.05 was consisedred to be significant							

Complications were analysed among the three groups based on NLR. The first two groups (>3-5.9 and 6-8.9) did not have any complications [Table/Fig-3]. Whereas, in the third group (NLR >9), there were complications such as aspiration pneumonia, seizures, urinary tract infection, deep vein thrombosis, and haemorrhagic transformation. There were total nine patients in third group out of which one patient passed away due to aspiration pneumonia which signifies that NLR value >9 increases duration of hospital stay and also have high risk of complications including mortality.

The outcome of the study patients was analysed using NIHSS score. The patients were grouped based on NLR values and each group was compared with the length of hospital stay to identify the precise NLR values.The mean NLR values positively correlated with increased length of hospital stay in NLR group >9 (r=0.9661; p<0.0001), with a poorer three month outcome [Table/Fig-3].

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, duration of the stay, complications and three month outcome with relation to admission NLR. The NLR values of day one came down significantly on day five. 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]. But different studies used varying cut-off values for NLR, so in this study the patients were grouped based on NLR values between 3-5.9, 6-8.9, and >9. Each group was compared with the length of hospital stay to identify the precise NLR values. The summary of the observations revealed that, when NLR values are high at the day of admission, the length of hospital stay was prolonged. Similarly, 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 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 [19]. Although, in the present study, the patients were admitted for observation despite no complications that might have reflected on the duration of hospital stay.

In the group with NLR >9, out of nine patients, eight had complications. He L et al., determined that patients with NLR >5.79 had more poststroke infections but in the present study, there were no complications in this particular range [20]. Goyal N et al., studied NLR values at the time of admission in AIS patients with large vessel occlusion and reported that NLR >8.5 had intracranial haemorrhage, NLR >5.79 had increased 3 month mortality and NLR >4.4 had poor functional outcome at three months [21]. This was probably due to the procedure of mechanical thrombectomy that the patients had undergone.

In this study, the mean NLR values positively correlated with a good three month outcome in NLR >3-5.9 group. The higher the NLR, (>5.9) the worse was the three month outcome. Overall, if the NLR values were high at the day of admission, the overall three month outcome was poor. Similarly, Celikbilek et al., also concluded that a

cut-off value of 4.1 for 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±4.5 had a poor prognosis [22]. Brooks SD et al., also found a significant relationship between NLR ≥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.

Limitation(s)

The sample size was limited. All patients were classified under moderate stroke (NIHSS- 4 to 24), mild (NIHSS <4), and severe (NIHSS >21) form of stroke was not included in the study.

CONCLUSION(S)

The NLR level is an ensuring marker of stroke prognosis. This study showed a significant correlation between raised NLR values with increased length of hospital stay, complications and three month outcome of the patient. Early inflammatory response of neutrophils and lymphocytes can predict clinical outcome of stroke patients. NLR is inexpensive and easily calculated from complete haemogram which helps clinicians stratify risk and initiate early treatment, thus preventing complications.

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