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Neutrophil and lymphocyte ratio in craniocervical artery dissection and prognostic correlations of the blood biomarkers

[1]Ipek Midi, [2]Ahmet Can Ciftci, [2]Burak Tunahan Ekincikli, [3]Esra Akdeniz, [1]Hatice Omercikoglu Ozden, [1]Leyla Babashova, [4]Feyyaz Baltacioglu

[1]Department of Neurology, School of Medicine, Marmara University, Istanbul; [2]School of Medicine, Marmara University, Istanbul; [3]Department of Medical Education, School of Medicine, Marmara University, Istanbul; [4]Department of Radiology, School of Medicine, Marmara University, Istanbul, Turkey

Abstract

Background & Objective: The aim of this study was to investigate the relationship of neutrophil to lymphocyte ratio (NLR) and other blood cells markers in craniocervical artery dissection patients and the dynamic changes of these biomarkers during the disease course, and effects on prognosis of the patients. *Method:* Cranial MR imaging, cranial and cervical MR angiography and DSA were examined, and diffusion weighted imaging (DWI) was performed to show the acute lesion(s). *Results:* Forty-six patients with craniocervical artery dissection were included in this study; they had a mean age of 42 years. Almost 60% of the patients (n=27) were admitted during acute state. Almost 2/3 of cases had extracranial dissection (n=31) and nearly 40% of the patients (n=18) had trauma. Neutrophil to lymphocyte ratio (NLR) was observed to be higher in the acute phase of the disease while the ratio decreased in the chronic phase. Low hemoglobin, high lymphocyte and a high NLR were found to have a negative correlation with the National Institutes of Health Stroke Scale (NIHSS).
Conclusion: Elevation of neutrophil was higher in acute craniocervical artery dissection as a marker of acute inflammatory response. High NLR, low hemoglobin and high eosinophil levels were associated with worse prognosis and functional outcomes.

Keywords: Craniocervical artery dissection, neutrophil to lymphocyte ratio (NLR), prognosis.

INTRODUCTION

Spontaneous craniocervical artery dissections (CCADs) account for 1-2% of all ischemic strokes and 10-25% of stroke cases among young adults.[1] CCADs are the second most common cause of large-artery cerebrovascular disease after atherosclerosis.[2] Incidence of spontaneous carotid artery dissection is 2.5 to 3 per 100,000, whereas the incidence of spontaneous vertebral artery dissection is 1 to 1.5 per 100,000.[1]

Dissections may happen spontaneously, following trauma or idiopathically. Some of the genetic disorders associated with dissections are fibromuscular dysplasia, Ehlers-Danlos syndrome type IV, Marfan syndrome, osteogenesis imperfecta type I, alfa-1-antitrypsin deficiency, cystic medial necrosis, autosomal dominant polycystic renal disease.[2,3]

Spontaneous CCADs are more frequently seen in the extracranial segments of carotid and vertebral arteries due to the fact that these parts are more mobile and closer to the bony structures such as cervical vertebrae and styloid processes, making them more vulnerable. Carotid artery dissections are usually seen 2-3 cm distal to the carotid bulb while vertebral artery dissections predominantly occur in V2 or V3 segments.[4,5] Clinical features of these dissections may include headache, neck and facial pain, vertigo, nausea, epilepsy, stroke and coma.[6]

Acute strokes can be seen in patients with dissection, and inflammatory response is part of all stages of cerebral ischemia, especially the acute phase. Recent studies show that neutrophil, lymphocyte and neutrophil to lymphocyte ratio (NLR) are cost-effective biomarkers that can be obtained during routine examinations to assess

Address correspondence to: Prof. Dr. Ipek Midi, Department of Neurology, Marmara University, School of Medicine, Istanbul, Turkey. E-mail: ipekmidi@gmail.com

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inflammation. These inflammatory biomarkers have been reported as an important predictor of survival in tumor, intracerebral hemorrhage or acute ischemic stroke patients.[7-9]

The aim of the present study is to assess whether there is a relationship between inflammatory responses in different stages of CCADs, reflecting the dynamic evolution of underlying pathology, and their association with clinical outcomes of the patients.

METHODS

The study was approved by our university Clinical Studies Ethics Committee (Number: 09.2016.357, Date: 03.04.2016). The study was conducted both prospectively and retrospectively from January 2012 to December 2019. Total of 53 patients younger than 60 years and older than 18 years with the diagnosis of CCAD were included. Seven patients had to be excluded from the study due to missing data in the records. Patients with hemorrhagic stroke, transient ischemic attack (TIA), recent history of myocardial infarction (MI ≤ 1 month prior to the study), additional neurological disorders, recent infection, hepatic or renal disease, oral steroid therapy, pregnancy, history of malignancy, hematologic disease, treatment with immunosuppressive agents, major surgery or major traumatic events were excluded. Neurologic examination was performed for all the patients. Cranial tomography, cranial magnetic resonance (MR) imaging, cranial and cervical MR angiography (MRA) and digital subtraction angiography (DSA) were performed. Medical records were studied for demographic information and cardiovascular risk factors; including age, sex, body mass index, hypertension, diabetes, hyperlipidemia, current smoking, and previous history of stroke. Clinical factors including time to admission, initial NIHSS score at the time of admission were also recorded.

Laboratory examinations including glucose and lipid profiles, complete blood counts were obtained within the first 24 hours of admission. Venous samples were collected in a calcium ethylene diamine tetra-acetic acid (EDTA)-coated tube, and were immediately centrifuged (2,000 rpm for 20 minutes at 4°C).

NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. Monocyte to lymphocyte and eosinophil to lymphocyte ratios were calculated with similar approaches.

Demographic data, measurements, and scores

Patients' age, gender, risk factors and history of trauma in the last one month were recorded. Neurological examinations of all the patients were carried out in detail, and their symptoms and findings were recorded. Risk factors of hypertension, hyperlipidemia, diabetes, smoking, migraine history, presence of connective tissue diseases and oral contraceptive use in female patients were noted. NIHSS was used to show stroke severity and the functional outcome of the patient.

Imaging methods

Cranial MRI, cervical/cranial MR angiography or CT angiography, fat-suppressed T1-weighted cervical MRI were applied to all the patients; digital subtraction angiography (DSA) examination, on the other hand, was carried out for some the patients to further confirm the diagnosis. Using these imaging modalities, dissections were diagnosed in compliance with the characteristic neuroradiological findings. Localization of dissected segments were categorized as extracranial or intracranial.

Blood samples, hematological data

Ethylenediaminetetraacetic acid (EDTA) blood samples were categorized into acute (1-3 day), subacute (4-10 days) and chronic (>10 days / average 21 days) phases based on the admission time of the patients to the stroke clinic following the symptoms. Complete blood count (CBC), including white blood cells (WBC), neutrophils, lymphocytes, monocytes and eosinophils were determined using an automated blood counter. NLR was calculated as the ratio of the number of neutrophils to the number of lymphocytes and absolute values of these ratios were also calculated. Similarly, monocyte lymphocyte ratio (MLR) was calculated by dividing the number of lymphocytes by the number of monocytes, and eosinophil lymphocyte ratio (ELR) was calculated by dividing the number of eosinophils to the number of lymphocytes. Platelet lymphocyte ratio (PLR) was defined as the absolute platelet count divided by the absolute lymphocyte count.

Other biochemical parameters, such as blood glucose level and fasting cholesterol level were also measured during the first admission to the hospital.

Statistical analysis

All statistical analyses were performed using R version 3.6. In this current study, variables with $P < 0.05$ were considered significant.

Summary statistics were constructed at the patient level with the use of means, standard deviations, medians and interquartile ranges for continuous variables (age, NLR, neutrophil, lymphocyte, NLR, monocyte, neutrophil monocyte ratio (NMR), monocyte lymphocyte ratio (MLR) and platelet lymphocyte ratio (PLR)) depending on the distribution, frequencies and percentages of categorical variables (gender, trauma, location of the blood vessel and risk factors such as smoking, diabetes mellitus, hypertension, hyperlipidemia and coronary artery disease). Normality of continuous variables was assessed using the Kolmogorov-Smirnov test as well as box plots, QQ and PP plots. Fisher's exact test was used to evaluate the association between gender and location of the blood vessel and trauma presence. Mann-Whitney U was used to compare neutrophil count, lymphocyte count, NLR, monocyte count, NMR, MLR and PLR with respect to the intracranial and extracranial locations of the dissection and presence of trauma.

Friedman's two way analysis of variance (ANOVA) was conducted to test whether neutrophil, lymphocyte, NLR, monocyte, NMR, MLR and PLR showed a significant change from acute to chronic stage where Bonferroni adjustment was used for multiple comparisons. Spearman correlations were calculated to find the strength of the relationship between acute blood test counts (white blood cell, neutrophil, lymphocyte, monocyte, eosinophil, NLR, hemoglobin, platelet, glucose, creatinine, ALT and AST) and NIHSS.

For an effect size of (f) 0.3, alpha level of 0.05 and power of 0.80, and assuming very low correlation between NLR observations ($r^2=0.2$) the required sample size is calculated to be 28 for repeated measures ANOVA of NLR within time periods (acute to chronic stage).

RESULTS

Demographic data, admission status and risk factors of stroke

The study consisted of 46 stroke patients with CCADs (18 female and 28 male), age ranging from 24 to 55 years (mean = 42 years; SD = 6.84). Approximately 60 percent (n=27) of 46 patients came to the emergency department during acute phase, 21 percent during subacute (n=10) and 19 percent during chronic (n=9) phase. Extracranial dissection was almost twice that of the intracranial dissection, and 60 percent (n = 28) of patients did not report any trauma. Fourteen of the patients were current smokers (31%), while 10 had hypertension (22%), 4 (9%) had diabetes mellitus (DM), 4 had hyperlipidemia (9 %) and 3 (6.5%) had coronary artery diseases (Table 1).

According to the results of Fisher's exact test shown in Table 2, there was no significant association between gender and location of dissection; nor association between gender and trauma (p 0.749 and 0.758).

As for whether neutrophil, lymphocyte, NLR, monocyte, NMR, MLR and PLR showed a change from acute stage to the chronic stage, Friedman's two-way analysis of variance revealed that lymphocyte, NLR, NMR and MLR changed significantly from acute stage to the chronic stage (p=0.005, p=0.011, and p=0.009 respectively). Multiple comparisons tests where the Bonferroni adjusted p values 0.009, 0.013 and 0.009 respectively revealed that lymphocyte, NLR and NMR decreased significantly from acute stage to chronic stage, and MLR decreased significantly from subacute to chronic stage (p=0.013) (Table 3a-3b).

We could not find any correlations between hematological variables with vessel dissection location and also hematological variables with trauma (Table 4 and Table 5).

Mann-Whitney U test results in Table 4 reveal that there was no significant difference between location of dissected vessels in terms of NLR, neutrophil, lymphocyte, monocyte and NMR level (p=0.505, p=0.711, p=0.386, p=0.115 and p=0.243 respectively).

Mann-Whitney U test results in Table 6 reveal that MLR is significantly higher in patients without trauma than patients with trauma (median=0.4 versus median=0.27, p=0.031).

There is a very strong negative correlation between NIHSS and hemoglobin values (r=-0.724, p<0.001). In addition, NIHSS is moderately positively correlated with lymphocyte, and eosinophil counts (r=0.398, p=0.049; r=0.405, p=0.045) (Table 6).

DISCUSSION

CCADs are commonly seen in young adults. Extracranial portions of the arteries are affected more commonly because these areas are more mobile and closer to bone structures.[1,4] Like

Table 1: Descriptive statistics for risk factors and location of the blood vessel dissection

Characteristics	Count	Percentage (%)
Gender		
Male	28	60.8
Female	18	39.2
Smoking		
yes	14	30.4
no	32	69.6
Hypertension		
yes	10	21.7
no	36	78.3
Diabetes mellitus		
yes	4	8.7
no	42	91.3
Hyperlipidemia		
yes	4	8.7
no	42	91.3
Coronary artery disease		
yes	3	6.5
no	43	93.5
Admission status		
Acute	27	58.7
Subacute	10	21.7
Chronic	9	19.6
Location of vessel dissection		
Intracranial	15	32.6
Extracranial	31	67.4
Trauma		
yes	18	39.1
no	28	60.9

All values are presented as numbers of patients followed by percentages

other studies, our study subjects consisted of young adults with a mean age of 42 years, and within this study group, extracranial dissections were observed more commonly compared to the intracranial ones. There was a male predominance among patients studied and a history of trauma was present 40% of all patients.

Our study is notable because it is the first study that searches the dynamic changes of inflammatory markers and their clinical significance in CCADs patients. To the best of our knowledge, no study has previously investigated the NLR, PLR, MLR

Table 2: Associations between gender and trauma and location of vessel dissection

Location Of Vessel	Male	Female	P*
intracranial	10 (35.7%)	18 (64.2%)	0.749
extracranial	5 (27.7%)	13 (72.2%)	
Trauma			
yes	10 (55.5%)	8 (44.4%)	0.758
no	18 (64.2%)	10 (35.7%)	

*: Fisher's exact test p value. All values are presented as numbers of patients followed by percentages in parentheses

Table 3.a: Descriptive statistics and comparison of hematological variables from acute to chronic stage

Laboratory results	Acute (n=27)	Subacute (n=32)	Chronic (n=25)	p*
NLR				
median (IQR)	4.77 (2.33-8.07)	2.79 (2.31-3.50)	2.27 (1.71-2.75)	**0.011**
min	1.5	1.56	1.22	
max	13.8	10.7	3.96	
Neutrophil				
median (IQR)	7.7 (5.9-10.8)	5.95 (5.15-7.80)	5.5 (4.3-7.0)	0.088
min	2.4	2.90	2.8	
max	18.1	15.60	61.7	
Lymphocyte				
median (IQR)	1.6 (1.3-2.4)	2.25 (1.75-2.6)	2.3 (2.1-2.9)	**0.005**
min	0.8	0.8	1.7	
max	3.2	3.6	27.2	
Monocyte				
median (IQR)	0.6 (0.5-0.8)	0.7 (0.6-0.9)	0.6 (0.5-0.90)	0.255
min	0.2	0.3	0.4	
max	1.1	2.1	7.1	
NMR				
median(IQR)	12.4 (8.38-21.6)	8.2 (7.23-10.72)	8.0 (7.2-9.5)	**0.011**
min	4.78	4.5	4.5	
max	38.33	14.5	17.4	
MLR				
median (IQR)	0.33 (0.27-0.45)	0.33 (0.27-0.45)	0.26 (0.23-0.34)	**0.009**
min	0.13	0.16	0.14	
max	0.67	1.24	0.68	
PLR				
median(IQR)	160.0 (113.6-215.6)	122.1 (100.4-161.7)	105.22 (79.23-122.8)	0.174
min	76.67	62.35	10.69	
max	326.25	32.50	215.91	

* Friedman's Two-way Anova p-value, NLR: Neutrophil lymphocyte ratio, NMR: Neutrophil monocyte ratio, MLR: Monocyte lymphocyte ratio, PLR: Platelet lymphocyte ratio

Table 3.b: Multiple comparisons of hematological variables from acute to chronic stage

Laboratory results	factor 1	factor 2	p b
	acute	subacute	1.000
Lymphocyte	acute	chronic	**0.009***
	subacute	chronic	0.074
	subacute	acute	0.554
NLR	chronic	acute	**0.009***
	chronic	subacute	0.307
NMR	subacute	acute	0.124
	chronic	acute	**0.013***
	chronic	subacute	1.000
MLR	acute	chronic	0.057
	subacute	acute	1.000
	subacute	chronic	**0.013***

[b]: Bonferroni adjusted p values, NLR: Neutrophil lymphocyte ratio, NMR: Neutrophil monocyte ratio, MLR: Monocyte lymphocyte ratio

Table 4: Descriptive statistics and comparison of hematological variables with respect to vessel dissection location

Laboratory results	Intracranial (n=10)	Extracranial (n=17)	p*
NLR			0.505
median (IQR)	5.65 (2.28-9.36)	4.55 (2.40-7.00)	
min	1.5	1.5	
max	13.8	11.8	
Neutrophil			0.711
median (IQR)	9.05 (5.9-11.0)	7.7 (6.2-10.0)	
min	2.4	4.2	
max	18.1	14.2	
Lymphocyte			0.386
median (IQR)	1.5 (1.2-1.8)	1.8 (1.3-2.4)	
min	0.8	1.0	
max	3.2	3.1	
Monocyte			0.115
median (IQR)	0.5 (0.3-0.7)	0.6 (0.5-0.8)	
min	0.2	0.4	
max	1.0	1.1	
NMR			0.243
median(IQR)	16.8 (11.14-27.50)	12.4 (8.38-16.67)	
min	6.5	4.78	
max	38.33	28.4	
MLR			
median (IQR)	0.32 (0.27-0.42)	0.38 (0.27-0.42)	0.537
min	0.13	0.20	
max	0.57	0.67	
PLR			
median (IQR)	163.96 (121.67-215.63)	137.20 (113.64-194.17)	0.473
min	82.81	76.67	
max	326.25	262.0	

*: Mann-Whitney U Test p value

and their relation between stroke severities in CCADs patients. In our study, we have found that most of the CCADs patients did seek emergency service during acute phase. As they progressed from acute to subacute and chronic phases, their values of lymphocyte, NLR, NMR and MLR changed.

Neutrophils are the first leukocyte subtype to infiltrate the ischemic area in the brain, and hence they are used as a biomarker of inflammation.[10] Elevated level of neutrophils from accelerates inflammatory processes can result in endothelial dysfunction and promote atherosclerosis. In the acute phase of ischemic stroke, circulating neutrophils are immediately recruited to the ischemic areas, and as a result, the number of neutrophils increases. Simultaneously, relative lymphopenia develops, partly in response to stress-induced corticosteroids, which attenuates IL-10-mediated healing process after stroke.[11,12] Stress during acute ischemic events results in activation of the hypothalamic-pituitary-adrenal axis. As a result, increased cortisol secretion leads to a relative reduction in the lymphocyte concentration.[13,14]

It is well known that inflammatory reactions accompany all stages of cerebral ischemia. In our study, the results showed that high neutrophil levels were achieved in the acute phase. Mean neutrophil values of admitted patients were 7.7 in acute phase, decreasing to 5.95 and 5.54 in subacute and chronic phases respectively. Yang *et al*. conducted a study to evaluate the diagnostic value of NLR and LMR in acute ischemic stroke (AIS) patients with CCAD, CCAD without AIS and controls. They found that NLR was significantly higher in AIS with CCAD as compared to CCAD without AIS and controls. In their study, it was shown that high NLR and low LMR levels may be associated with severity of

Table 5: Descriptive statistics and comparison of hematological variables with respect to trauma

Laboratory results	Trauma – (n=28)	Trauma + (n=18)	p*
NLR			0.059
median (IQR)	6.16 (2.4-9.3)	3.3 (2.2-4.54)	
min	1.87	1.5	
max	13.8	8.83	
Neutrophil			0.322
median (IQR)	8.5 (5.9-11.5)	7.5 (6.2-9.1)	
min	3.9	2.4	
max	18.1	10.6	
Lymphocyte			0.059
median (IQR)	1.5 (1.2-1.8)	2.4 (1.6-2.5)	
min	0.8	1.2	
max	3.1	3.2	
Monocyte			0.9
median (IQR)	0.6 (0.5-0.8)	0.6 (0.5-0.8)	
min	0.3	0.2	
max	1.1	1.0	
NMR			0.596
median (IQR)	12.26 (8.38-23.25)	12.4 (11.14-15.0)	
min	4.78	5.63	
max	38.33	18.2	
MLR			
median (IQR)	0.4 (0.33-0.5)	0.27 (0.21-0.31)	**0.031***
min	0.17	0.13	
max	0.57	0.67	
PLR			
median (IQR)	163.1 (121.67-234.5)	137.20 (107.69-167.9)	0.298
min	76.67	82.81	
max	326.25	235.0	

*: Mann-Whitney U Test p value

Table 6: Correlation of acute complete blood count with NIHSS score

Laboratory results	n	rs	p
White blood cells (x10^3/L)	25	-0.323	0.115
Neutrophils (%)	25	0.381	0.061
Lymphocytes (%)	25	0.398	**0.049***
Monocytes (%)	25	0.250	0.229
Eosinophils (%)	25	0.405	**0.045***
Neutrophils (x10^3/L)	25	-0.363	0.074
Lymphocytes (x10^3/L)	25	0.305	0.138
NLR	25	-0.388	0.055
Monocytes (x10^3/L)	25	0.093	0.660
Eosinophils (x10^3/L)	25	0.318	0.121
Hemoglobin (g/dL)	25	-0.724	0
Glucose (mg/dL)	25	-0.010	0.962
Creatinine (mg/dL)	24	-0.368	0.077
AST (U/L)	24	-0.053	0.807
ALT (U/L)	24	-0.374	0.072
MLR	25	-0.290	0.160
PLR	25	-0.329	0.108

rs : Spearman correlation coefficient, p: p-value, n: sample size

the stroke. In their study, the best cut off value of NLR was 2.35, and LMR was 3.67.[15] In our study we also founded a positive correlation between NLR and stroke severity and the cut off values were the ratio of 4.77, 2.79 and 2.27 from acute stages to chronic stages, respectively.

In our study we used MLR instead of LMR. Lymphocyte count, unlike findings of other studies, was found to be increasing from acute to chronic stage. We observed an increase in the number of lymphocytes, contrary to previously reported lymphopenia. This may be due to the fact that pathogenesis of dissection is different from atherosclerosis. It should also be noted that the other studies included the hyperacute or acute phases, while excluding the chronic phase. In our study, while the lymphocyte values increased gradually, the monocyte values did decrease. Changes in acute and chronic periods in both parameters were statistically significant.

We also studied the possible relations between other hematologic parameters such as monocyte, eosinophils and platelet counts. In the literature, there are reports of neutrophil, lymphocyte, NLR, monocyte and platelet values and their ratio in stroke patients. There are also studies that show the relationship between these markers and their relationship to severity of stroke, differences in stroke subgroups, differences in stroke treatment approaches and their effects on prognosis. Higher NLR is associated with increased risk of cardiovascular, cerebrovascular diseases, and even subclinical atherosclerosis.[7,16-18] NLR has been shown to be associated with an increased risk of stroke severity and worse outcomes in ischemic stroke patients.[19-21] Moreover, the results of a recent metaanalysis demonstrate that a higher NLR is also associated with an increased risk of secondary hemorrhage following an ischemic stroke.[22] In addition, it was found that the median NLR was significantly increased among the mortality group compared with the survival group. Thus, it can be concluded that NLR and LMR may be used as tools to study examine the link between inflammation and stroke treatment options.[19]

Our study has found that NLR is critically high in the acute stage of disease, and the ratio decreases gradually as stroke becomes chronic over time. In addition to the NLR parameter, this is the first study investigating the relation of NMR (neutrophil/monocyte ratio), MLR (monocyte/lymphocyte ratio) and PLR (platelet/lymphocyte ratio) with disease progression. Based on our results, NMR and PLR also seem to act as NLR parameter and similarly decrease gradually from acute to chronic stages of stroke.

One of the points we focused during our study was to explore if there is a correlation between NLR and stroke severity. It has been found that there is a positive correlation between NLR and NIHSS. Our results also showed that serum NLR levels are higher in patients with higher initial NIHSS scores. Very strong negative correlations between NIHSS and hemoglobin (Hb) were also found during the study. ($r=-0.724$, $p<0.001$). Low hemoglobin (Hb) values were worse prognostic factors. NIHSS was found to have a positive correlation with lymphocyte, and eosinophilia counts. ($r=0.398$, $p=0.049$; $r=0.405$, $p=0.045$). In our study, we have demonstrated that NLR increase is parallel to stroke severity. Statistical analysis demonstrated that patients with high NIHSS scores presented with higher NLR values than patients with lower NIHSS scores.

We also examined whether there were any differences between trauma and non-trauma group for inflammatory markers, but we could not find any association ($p>0.05$).

Numerous studies have shown that both platelets and lymphocytes are predictors of prognosis in ischemic vascular diseases. Excessive activation and accumulation of platelets may result in thrombosis and vascular obstruction, leading to further vascular event. While an increased PLR is considered to be a predicting factor for stroke, decreased platelet count is thought to reflect the magnitude of consumption of the thrombocytes and ultimately leading to a bleeding tendency.[23]

In recent years, in addition to the NLR, PLR has been accepted as a biomarker for the assessment of the overall inflammatory status.[24] Activation of platelets are mediated by a number of inflammatory factors including cytokines, serotonin, glutamate, dopamine and P-selectin. Activated platelets participate in the regulation of the permeability of endothelial cells and recruitment of mononuclear cells through the release of proinflammatory factors.[25]

Elevated levels of NLR and PLR have been found to be related with oxidative stress and increased cytokine production[25] and associated with the prognosis of infarction. Similarly, PLR has been used to predict poor prognosis, insufficient recanalization and the size of infarcted area following stroke.[26] In our study, PLR showed a significant change from acute to the chronic stage, and no correlation between PLR and NIHSS was found.

In our study, we compared MLR values

of acute, subacute and chronic stages. It was observed that MLR values decrease significantly from subacute to chronic stage. In a similar study looking at the lymphocyte/monocyte ratio (LMR) in the peripheral blood and the degree of stroke-induced immunosuppression, it was shown that patients with low LMR had worse outcomes at 3 months following the onset of stroke.[27] We however, were unable to find a significant correlation between LMR and NIHSS, which could be due to the small sample size of the study. While there are a number of studies that focus on the association of eosinophils with acute ischemic stroke in hypereosinophilic syndrome (HES), investigations that study the same relationship without HES is limited.[28]

It is believed that elevated presence of eosinophils could lead to thrombosis in a number of ways. Circulating eosinophils release proteins such as MBP, EPOX, ECP, and EDN are involved in formation of blood clots and negatively affect the heparin activity and clotting times, promoting thrombosis. Linear relationship between eosinophil level and NIHSS specifically suggests that eosinophils play a significant role in occurrence and prognosis of acute cerebral infarction.[28] We have also found positive correlation between eosinophils and NIHSS (r=0.405, p=0.045)

The limitation of our study included retrospective and prospective data from a single hospital; as a result, the number of subjects was relatively small. We believe that further studies with larger populations are needed to confirm our findings.

In conclusion, neutrophil elevation as a marker of acute inflammatory response is higher in the acute phase of CCADs. High NLR, low hemoglobin, high eosinophil and high lymphocyte counts are factors that show worse prognosis and functional outcome.

DISCLOSURES

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