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ORIGINAL ARTICLE

Relation Between Neutrophil Lymphocyte Ratio, Brain Imaging and Carotid Duplex Findings in Acute Ischemic Stroke.

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ABSTRACT

Background: Neutrophil lymphocyte ratio (NLR) reflects the balance between neutrophils and lymphocytes. It may represents a prognostic predictor for the acute ischemic stroke severity**. Objective:** This study aimed to assess the relationship of NLR with the brain imaging (Computed Tomography (CT) and or Magnetic Resonance Imaging (MRI)) and carotid duplex findings in acute ischemic stroke patients. **Methods:** This study was conducted on sixty acute ischemic stroke patients (26 males, 34 females), their ages ranged from 45 to 95 years. Patients were subjected to detailed medical, neurology history taking, laboratory assessment including white blood cells (WBCs) count, absolute neutrophil count (ANC), and absolute lymphocyte count (ALC). NLR was calculated by dividing ANL by ALC, imaging investigation including CT and or MRI and carotid duplex ultrasonography. **Results:** There was a statistical significant association between NLR and the size of infarction among the studied patients, however there was no statistic al significant association between NLR and findings of carotid duplex in our study. **Conclusion:** The higher the neutrophil lymphocyte ratio, the larger the size of infarction is expected.

Keywords: Ischemic Stroke, Neutrophil lymphocyte ratio, Carotid duplex, Computed Tomography.

INTRODUCTION

Acute ischemic stroke (AIS) is one of the world's leading causes of death, and due to the high mortality and morbidity rates associated with stroke, it is becoming a significant public health concern worldwide since the third of these cases are fatal and survivors typically have severe or permanent disabilities [(1)].

Early high white blood cell and neutrophil levels were found to be associated with greater infarct volumes and increased stroke severity in patients with acute ischemic stroke [(2)] .

Neutrophils can play a role in indirect cerebral injury by occluding cerebral microvessels, causing the infarct to spread further, or by releasing neurotoxic substances and inflammatory mediators into the penumbra and focal ischemic brain [(3)].

Neutrophil lymphocyte ratio is a simple marker that can be easily calculated from the differential white blood cells count, It reflects the balance between neutrophils and lymphocytes [(4)]. It is a prognostic indicator of inflammation severity and patient outcome following AIS [(5)].

In the early stages of atherosclerosis, the development of carotid intima-media thickness (CIMT) is a marker of early vascular wall injury. It's recently been discovered to be a successful indicator of possible vascular incidents like ischemic stroke [(6)].

AIM OF WORK

This study was to determine the relation between NLR, the findings of brain imaging and carotid duplex in AIS patients.

PATIENTS AND METHODS

This is a prospective cohort study included 60 patients presented with AIS; 26 males and 34 females, ages ranged from 45 to 95 years. This research was conducted in Intensive Care and Stroke Units, Department of Neurology, Zagazig University Hospitals, during the period between February 2019 to February 2020. All patients or their relatives signed written informed consents. The Study ethics was extensively followed up by the Institutional Review Board (IRB) of Zagazig Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria

Patients with AIS clinically diagnosed and confirmed by brain imaging (Computed Tomography and/or Magnetic Resonance Imaging for brain stem lesions) within the first two days of stroke onset [(7)].

Exclusion criteria

Hemorrhagic stroke, cerebral venous sinus thrombosis, head trauma, respiratory, liver failure, chronic kidney diseases and chest or urinary tract infection.

Patients with history of steroid or immunosuppressant drugs usage, cancer, autoimmune diseases, myeloproliferative, hematological disorders were excluded.

All participants were subjected to detailed neurological history taking (with stressing on the vascular, cardiac risk factors), full general and neurological examination. Glasgow coma scale (GCS) was used to detect the depth of coma [8]. Stroke severity was assessed using the national institutes of health stroke scale (NIHSS) [9] and modified Rankin Scale (mRS) [10] .GCS, NIHSS and mRS are important scales used to assess their level of consciousness, stroke severity, follow up and short-term outcome of stroke.

Within 48 hours of stroke onset, routine laboratory tests including complete blood image {total and differential count of WBCs, ANC, ALC, NLR}, liver, kidney function tests, C-reactive protein (CRP), sedimentation rate of erythrocytes, coagulation profile and lipid profile were performed. After the calculation of NLR with dividing ANC by ALC [11], and our patients were divided into three groups according to NLR value [2]:

- ..Group one: NLR <2 (favorable outcome).
- ..Group two: NLR 2-3.
- ..Group three: NLR >3 (unfavorable outcome).

Electrocardiography, Echocardiography were made for each participant at Cardiology Department at Zagazig University Hospitals.

Brain imaging was performed to confirm the diagnosis and detect the location, size, and homogenecity of brain infarctions via Philips CT brain (Tomoscan 350 with 4.8 scanning time and 512 x 512 matrix size, axial scans were obtained with the patients supine, the slice thickness was nine mm), MRI brain (using 1.5 tesla MRI machine (Philips) with section thickness was 5 mm with a gap of 1 mm) which were done at Radiology Department at Zagazig University Hospitals.

Proper assessment of infarction volume according to the rules used by **Tu et al.[12]:**

..Volume = 0.5 x a x b x c

(a and b are the largest perpendicular diameters measured on CT and c is the number of 10-mm slices containing infarct).

Then according to **Alemam et al.[13]** ischemic stroke lesion volume classified into:

- ..Small; when volume was less than 1.5 cm^3.
- ..Moderate; when volume was ranging from 1.5 cm^3 to 3 cm^3.
- ..Large; when volume was more than 3 cm^3.

Brain edema, was graded as follow according to **Dhar et al. [14]:**

..Slight: when only there is sulcal effacement or compression of the ventricle.

..Moderate: When there is partial ventricular shift across the midline.

..Severe: when there is total ventricular shift across the midline.

Ultrasonography of the Carotid Doppler was also done at Radiology Department, which detect degree of stenosis and was classified into:

..No stenosis

..Mild (<40%).

..Moderate (40 - 70%).

..Severe (≥70%).

Ischemic stroke was classified according to The Trial of Org 10172 in Acute Stroke Treatment (TOAST) [15] into Large artery atherosclerosis, Cardio embolism, Lacunar(small vessel disease), other determined etiology (diagnosed non-atherosclerotic vasculopathy, hypercoagulable state, or hematologic disorder etiology) and undetermined etiology (inability to classify after extensive evaluation and evidence of ≥two stroke subtypes).

Statistical analysis

All data were collected, tabulated, and statistically analyzed using version 25 [16] of the Social Science Statistical Package (SPSS) program. P-value of ≤ 0.05 was accepted as statistically significant [16]. Quantitative data as mean, interquartile, and median range were given. As frequencies and proportions it produced qualitative data. The Kolmogorov-Smirnov and Levene tests were used to determine the distribution characteristics and homogeneity of variables. Pearson's chi square ($\chi 2$) test and the exact fisher's test were used as needed to evaluate qualitative results.

RESULTS

Patients with AIS who met the inclusion criteria in the current research were sixty. Twenty six patients (43.3%) were males and thirty four pateints (56.7%) were females between 45 and 95 years old of age with mean 64.8 ± 10.2 years.

The most frequent site of lesion was lobar (60.0%) followed by subcortical (50.0%). Left sided lesions were encountered in 51.7% of the studied patients, 16.7% had surrounding edema and 35.0% had medium sized infarction (Table 1).

Regarding to carotid duplex findings, 18.3% of the studied patients had plaques and 6.7% had stenosis (Table 2).

There was a statistical significant association between NLR and the size of infarction among the studied patients (Table 3).

There was no statistical significant association between NLR and the findings of the carotid duplex among the studied patients (Table 4)

Table (1) Findings of brain imaging (CT&MRI) among the studied patients:

Variables	Studied patients (n=60)	
	No.	*%*
Site of lesion:		
Cortical	14	23.3
Subcortical	30	50.0
Lobar	36	60.0
Brainstem	11	18.3
Cerebellar	3	5.0
Side of lesion:		
Right	29	48.3
Left	31	51.7
Surrounding edema	10	16.7
Size of infarction:		
Small (<1.5 cm^3)	20	33.3
*Medium(*1.5 cm^3 to 3 cm^3)	21	35.0
Large (>3 cm^3)	19	31.7

CT: Computed Tomography, MRI: Magnetic Resonance Imaging.

Table (2) Findings of the carotid duplex in the studied patients:

Variables	Studied patients (n=60)	
	No.	*%*
Plaques		
Yes	11	18.3
No	49	81.7
Degree of stenosis		
No stenosis	56	93.3
Mild (<40%)	0	0.0
Moderate (40 - <70%)	1	1.7
Severe (≥70%)	3	5.0

Table (3) Association between neutrophil lymphocyte ratio and findings of brain imaging (CT&MRI) among the studied patients:

Findings of brain imaging	Neutrophil / Lymphocyte Ratio						χ^2	P value
	<2 (n=13)		**2-3 (n=8)**		**>3 (n=39)**			
	No.	%	No.	%	No.	%		
Site of lesion:								
Cortical	2	15.4	1	12.5	11	28.2	1.2	0.4
Subcortical	5	38.5	4	50.0	21	53.8	0.9	0.6
Lobar	7	53.8	6	75.0	23	59.0	0.9	0.6
Brainstem	2	15.4	1	12.5	8	20.5	0.4	0.8
Cerebellar	0	0.0	1	12.5	2	5.1	1.6	0.4
Side of lesion:								
Right	7	53.8	3	37.5	19	48.7	0.5	0.7
Left	6	46.2	5	62.5	20	51.3		
Surrounding edema	1	7.7	2	25.0	7	17.9	1.2	0.5
Size of infarction:								
Small	7	53.8	5	62.5	8	20.5	10.9	**0.02***
Medium	5	38.5	2	25.0	14	35.9		
Large	1	7.7	1	12.5	17	43.6		

**: significant, CT: Computed Tomography, MRI: Magnetic Resonance Imaging, χ2: Chi square test.*

Table (4) Association between neutrophil lymphocyte ratio and the findings of the carotid duplex among the studied patients:

Findings of carotid duplex	Neutrophil Lymphocyte Ratio						χ^2	P value
	<2 (n=13)		2-3 (n=8)		>3 (n=39)			
	No.	%	No.	%	No.	%		
Carotid Plaques:								
Yes	2	15.4	3	37.5	6	15.4	2.3	0.3
No	11	84.6	5	62.5	33	84.6		
Degree of stenosis								
No stenosis	12	92.3	8	100	36	92.3	1.2	0.8
Moderate (40 - <70%)	0	0.0	0	0.0	1	2.6		
Severe (≥70%)	1	7.7	0	0.0	2	5.1		

χ2: Chi square test

DISCUSSION

The discovery of a connection between inflammatory biomarkers like Neutrophil lymphocyte ratio (NLR) and the findings of brain imaging and carotid duplex in AIS patients could help to support the idea that anti-inflammatory therapy could be a viable treatment option for acute ischemic stroke [(2)].

The early elevation of neutrophil count was linked to a greater amount of early ischemic tissue, so it's worth seeing if suppressing neutrophil responses will help slow the spread of ischemic damage [(17)].

In our work, the most frequent site of brain infarction (as revealed by brain imaging studies including CT or MRI) was lobar (60.0%) followed by subcortical (50.0%). This was consistent with the results of **Rangarajan et al.** [(18)]. **Eapen et al.** [(19)] and **Behera et al.** [(20)] showed that the most common site of infarct was parietal (18.51%), followed by periventricular (10.87%), occipital lobe (7.98%). This was explained by larger sample size (300 patients) and wider range of age from 25 to 95 years in their study.

Our study showed that there was statistical significant association between NLR and the size of infarction (p value =0.02). This matched with the findings of **Buck et al.** [(17)], On the contrary, **Tokgoz et al.** [(21)] found no association between NLR and the size of infarction in AIS patients.

Studying of carotid arteries by duplex was shown that 18.3% of the studied patients had carotid plaques and 6.7% had stenosis. This matched with the results of **Sahoo et al.** [(22)], but disagreed with **Al Najim.** [(23)] who found that 63% of stroke patients had carotid plaques, our findings did not reveal statistical significant association between the NLR and the carotid duplex findings. This might be due to small number of patients in our study.

It was found that there was no statistical association between NLR and carotid stenosis (P value=0.8). This matched with results of **Min et al.** [(24)] who found that there was no statistical association between neutrophil lymphocyte ratio values and carotid artery stenosis (p value =0.31).

On the contrary of our findings, **Hyun et al.** [(25)] showed that NLR had a significant positive association with carotid stenosis ($P < 0.001$), **Köklü et al.** [(26)] showed that NLR values increased in symptomatic intermediate carotid artery stenosis, so it was an independent variable for symptomatic carotid artery plaques.

CONCLUSION

The higher NLR, the larger the size of infarction in AIS patients is expected.

RECOMMENDATIONS

We recommend using the values of NLR in predicting the size of infarction in AIS patients. Also, further studies should be done with larger sample size and for longer duration.

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