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ORIGINAL ARTICLE

The Relation Between Neutrophil-Lymphocyte Ratio and Etiologic Subtypes in Acute Ischaemic Stroke

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Abstract

Introduction: The role of leukocytes in tissue damage in acute ischaemic stroke is well-known. There are some studies examining the relationship between etiologic subtypes of acute ischaemic stroke and neutrophil/lymphocyte ratio (NLR). In this study, we planned to investigate the relationship between NLR and etiologic subtypes of acute ischaemic stroke.

Methods: In this study, acute ischaemic stroke patients who were admitted to our hospital in the first 24 hours were included. Etiologic classification of patients was done by TOAST classification system. Patients who had history of acute coronary syndrome and pulmonary emboli were excluded.

Results: We included 467 acute ischemic stroke patients and 162 control patients. Of the patients, 239 were females (51%) and 228 were males (49%). Of the control group, 77 (47%) were females and 85 (53%) were males. Mean ages in patient and control groups were 69.41±14.4 and 67.35±19.41, respectively. NLR's in acute stroke and control groups were 3.38±3.43 and 2.12±1.11, respectively, and this difference was found to be statistically significant (p=0.001). NLR'S in atherothrombotic and cardioembolic groups were 3.26±2.35 and 4.46±5.6, respectively, and this was found to be statistically significant (p=0.03).

Discussion and Conclusion: High NLR was found to be related with cardioembolic etiology in acute ischaemic stroke. We think that more detailed investigation for cardioembolic sources may be necessary in patients with high NLR at first admission.

Keywords: Cardioembolism; ischaemic stroke; Neutrophil/Lymphocyte ratio.

Stroke affects more than 20 million people all over the world per year and it is the cause of death for approximately one quarter of them[1]. It is well known that inflammation plays an important role in atherosclerotic disorders[2,3]. Recently, there have been some evidence that leukocytes have a similar role in ischaemic events[4,5]. Inflammation following acute ischaemic stroke (AIS) is a well known pathological process in damaged brain tissue[4,5]. The inflammatory process in AIS gives rise to excretion of cytokines and chemokines from ischaemic tissues, promoting the accumulation of leukocytes to the ischaemic tissues[5,6]. Among circulating leukocytes, neutrophils have been regarded as crucial mediators of ischaemic injury[6,7]. Accumulated neutrophils release free oxygen radicals, various inflammatory cytokines, and neurotoxic substances, all of which cause cellular necrosis and apoptosis in ischaemic tissues[8]. Lymphocytes are also known to be involved in inflammatory responses to AIS[9]. Low lymphocyte counts increase sympathetic activity and baseline cortisol levels, which can cause an increase in the production of inflammatory cytokines that aggravate ischaemic injury[9]. Theoretically, anti-inflammatory therapy may be beneficial in stroke management and has been proven to be effective in some experimental models[10,11]. However, anti-neutro-

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phil therapy has not been shown to be effective in clinical studies of AIS[12,13]. An increase in the neutrophil/lymphocyte ratio (NLR) has been shown to increase mortality and morbidity in patients with acute coronary syndrome[14]. However, the effects of the NLR on short-term functional outcome in AIS are still uncertain[15]. In this study, we assessed the significance of the NLR in AIS patients and the sensitivity as a predictor of etiologic subtypes according to TOAST classification in patients with AIS.

Materials and Methods

The patients who applied to the neurology department of our hospital with ischaemic stroke within the first 24 hours were included in the study. Patients were classified according to TOAST classification system. On admission, patients with infection, acute coronary syndrome,and pulmonary embolism were excluded from the study. Venous blood samples were collected from the medial cubital vein. NLRs were calculated from complete blood counts obtained at admission. The study was a retrospective data analaysis, so we did not admit to hospital ethic committee.

The results of the study were presented as mean±standard deviation. Univariate analyses were performed with chi-square test for categorical variables and with Student's T-test for continuous variables. In-group analyses were performed with Mann-Whitney U test for multiple groups when groups were non-normally distributed and sample sizes were unequal. Mean and standard deviation values were given for variables with normal distribution. Student's T-test was used for parametric variables with normal distribution. Chi-square test was used for non-parametric non-numeric data. P values less than 0.05 were considered statistically significant. Statistical analysis was performed using the 17 version of the Statistical Package for Social Sciences (SPSS).

Results

A total of 467 ischaemic stroke and 162 control patients were included in the study. There were 239 women (51%) and 228 men (49%) in the patient group. The control group consisted of 77 women (47%) and 85 men (53%). The mean age of the patients and controls were 69.41±14.4 and 67.35±19.41, respectively. The NLR were found to be 3.38±3.43 in the stroke group and 2.12±1.11 in the control group and there was a statistically significant difference between groups (p=0.001). The NLR was 3.26±2.35 in the atherothrombotic group, and 4.46±5.6 in the cardioembolic group, and the difference was statistically significant (p=0.03) (Tables 1, 2).

Table 1. Demographic variables

Variables	AIS patients n=467	Control group n=162	p
Gender Ratio (Female/Male) [n]	1.04 F: 239 M: 228	0.90 F: 77 M: 85	0.21
Age [yr]	69.41±14.4	67.35±19.41	0.12
N/L ratio	3.38±3.43	2.12±1.11	0.001

Table 2. N/L ratio according to the etiology

Variables	Atherotrombotic group n=254	Cardioembolic group n=213	p
Age [yr]	70.47±11.6	71.55±10.03	0.11
N/L ratio	3.26±2.35	4.46±5.6	0.03

Discussion

Inflammation plays an important role in AIS[16]. As inflammatory markers, different subtypes of WBC may have different roles in response to AIS. Previous studies have shown that neutrophil and lymphocyte counts attribute to the inflammatory response and to atherosclerotic processes[17-19]. These inflammatory cells may exacerbate damage in cerebral infarction by destroying the penumbra[20]. The initial response to an ischaemic brain zone is the migration of neutrophils into the damaged area[21]. In physiological conditions, the blood brain barrier controls the entry of immune cells into the brain. However, the entry of neutrophils is enhanced by a local blood brain barrier breakdown induced by ischemia[10,22]. Perivascular neutrophil migration into the intraparenchymal area occurs within 6 to 24 hours[22,23]. Lymphocytes are elevated 3-6 days after stroke in the ischaemic brain[24]. T cell lymphocytes may play an important role in repairing inflamed tissues[25,26]. Several studies have supported the hypothesis that the NLR can be accepted as a factor for predicting short-term mortality and functional prognosis in AIS[20,22,27]. Several studies have also attempted to determine the relationship between the NLR and stroke subtypes[21,28,29].

Vural et al.[30] studied with a group diagnosed with acute stroke including 418 patients, that had been classified according to the etiology including both ischaemic and hemorhhagic stroke subtypes. In this study the NLR ratio was similar between the atherosclerotic and cardioembolic groups, and significantly higher than that found both in the lacunar and transient ischaemic attack groups[30]. In a

study in which the stroke subtypes were also identified, the NLR was found to be significantly higher in atherosclerotic stroke patients when compared to both cardioembolic and lacunar stroke patients[31] and this finding is thougt to be attributed to more severe inflammation in atherotrombotic processes by authors. In the present study, we found a higher NLR in the patient group compared to the control group, which is correlative to results reported in other studies[26-31]. We also found NLR was higher in the cardioembolic group than the atherothrombotic group in contrast with some of these studies[30,31].

Conclusion

These findings in our study together with the literature, revealed the idea that the NLR may be an effective etiologic predictor of AIS. In our study, high NLR was found to be related with cardioembolic etiology in AIS, so we think that more detailed investigation for cardioembolic sources may be necessary in patients with high NLR at first admission. Further research is required in large prospective cohorts to better understand the predictive value of the NLR.

Ethical Committee Approval: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: M.Ü.; Design: F.D.; Data Collection or Processing: M.D.; Analysis or Interpretation: M.Ü.; Literature Search: R.K.; Writing: F.D.

Conflict of Interest: None declared.

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