

Neutrophil/lymphocyte ratio and mean platelet volume in Behçet's disease

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Abstract. – OBJECTIVE: With this retrospective study, we researched the effects of mean platelet volume (MPV) and neutrophil/lymphocyte ratio (NLR) on the activity of Behçet's disease and susceptibility to thrombosis.

PATIENTS AND METHODS: One hundred eighty-six patients with Behçet's disease, who met the inclusion criteria, were separated into two groups: 120 patients had active Behçet's disease (Group I) and 66 patients with inactive Behçet's disease (Group II). 79 healthy subjects as controls were included in the study.

RESULTS: MPV was similar between all three groups. CRP (C reactive protein) was statistically higher in the active BD group when compared to the inactive BD group and the control group. CRP of the inactive BD and the healthy control group were similar. In addition, erythrocyte sedimentation rate (ESR) was found higher than the control group in both active and inactive BD groups, whereas ESR of the active BD group was higher than the inactive BD group. N/L ratio was found statistically higher in the active BD group when compared to inactive BD and healthy control groups, while the N/L ratio of inactive BD and healthy control groups were found similar to each other. While MPV, CRP, and NLR didn't statistically differ between active BD subgroups with and without thrombosis, ESR was statistically and significantly higher in the active BD group with thrombosis when compared to the active BD group without thrombosis.

CONCLUSIONS: The data obtained from the present study showed that the patients with BD are exposed to chronic inflammation. And the N/L ratio may be a simple, inexpensive, and convenient diagnostic marker of active BD.

Key Words:

Behçet's disease, N/L ratio, Mean platelet volume.

Introduction

Behçet's disease (BD) is a chronic multisystem inflammatory disease characterized by recurrent oral aphthous ulcers, genital ulcers, uveitis, and skin lesions¹. While the exact pathogenesis of Behçet's disease is not known, neutrophil hyperfunction, vasculitis, and an autoimmune response seems to be responsible for the disease.

Behçet's disease does not have specific laboratory findings or a pathological physical examination sign. There are many suggested markers for inflammation in BD. Studies on this issue have shown that IL-6, IL-1 β , TNF- α , thrombomodulin, E-selectin, VEGF, total homocysteine, α -1 antitrypsin, α -2 macroglobulin are the considered markers -associated with BD²⁻⁵. Recently, reports have concluded that the neutrophil/lymphocyte ratio (NLR) and mean platelet volume (MPV) are indicators of systemic inflammation⁵⁻⁹.

The mean size of the thrombocytes have been reported on the blood count as mean platelet volume (MPV). MPV is indirectly associated with the activity of platelets. Large platelets are more active than small ones by means of metabolic and enzymatic function. In addition, they also have a higher potential of thrombogenicity¹⁰⁻¹⁵. Neutrophil lymphocyte ratio is an easy-to-calculate indicator that can be calculated by leukocyte subgroup of complete blood count. Also, it has been reported that N/L ratio might have prognostic importance for some diseases¹⁶⁻²⁰. To the best of our knowledge, there is no research in the literature that evaluates both MPV and N/L ratio for patients with Behçet's disease. With this retrospective study, we investigated the effects of MPV and NLR on the activity of Behçet's disease and susceptibility to thrombosis.

Patients and Methods

A total of 186 patients (110 male, 76 female) with Behçet's disease, who met inclusion criteria, were included in this retrospective study by scanning hospital records of the patients. The diagnosis of BD was made according to the criteria of International Study Group. A control group of 79 healthy individuals (46 male, 33 female) matching the study group by means of age and sex were also included in the study.

Inclusion criteria were:

- Not having comorbidities accompanying Behçet's disease;
- Absence of smoking and alcohol consumption (currently or in the past);
- Not using steroids and/or immunosuppressive drugs during the period of blood analysis (complete blood count, erythrocyte sedimentation rate, C-reactive protein) for this study;
- Absence of infection during the period for blood analysis (complete blood count, erythrocyte sedimentation rate, C-reactive protein) of this study.

One hundred eighty-six patients with Behçet's disease, who met the inclusion criteria, were separated into two groups as following: (Group I) patients with active Behçet's disease and (Group II) patients with inactive Behçet's disease. The Group of patients with active BD was divided into subgroups according to the presence of thrombosis. Inactive BD was defined as the absence of any sign or symptom, including oral aphthae. Active BD was defined as involvement of at least two of the following features such as oral ulcers, genital ulcers, involvement of eyes, skin lesions, arthritis and thrombosis-thrombophlebitis. Definitive diagnosis of thrombosis has been made with imaging techniques such as ultrasound and angiography accompanied by physical examination findings of the patients. Demographic data and medical records of all patients and control group were recorded on a form developed by our researchers. MPV, N/L ratio, erythrocyte sedimen-

tation rate (ESR), C-reactive protein (CRP) of participants were noted on that form. Cell Dyn 3700 with capabilities of laser and impedance methods was used for complete blood count (hemogram). Architect CI 4100 with the capability of the immunoturbidimetric assay was used for CRP and Biomedical Systems, which is compatible with the automatic Westergren method used for ESR.

Statistical Analysis

Definitive data was presented as mean, standard deviation, frequency, and percentage values. Student *t*-test or Mann-Whitney U test were used to analyze any difference in between numerical values of study groups. Kruskal-Wallis test was used to analyze differences in numerical values of three different groups. When there was any statistically significant difference, binary correlations were made by Mann-Whitney U test with Bonferroni correction ($\alpha=0.017$). In order to assess the association between numerical values, Spearman's rank correlation coefficient was used. SPSS version 21.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. A *p*-value less than 0.05 was considered as statistically significant ($p < 0.05$).

Results

Mean age of the active Behçet's disease (Group 1), inactive Behçet's disease (Group 2), and control group were 37.83 ± 11.86 , 37.96 ± 12.02 , and 37.63 ± 10.82 years old, respectively. All three groups were similar by means of age and gender (Table I).

MPV was similar between all three groups. CRP was statistically higher in the active BD group when compared to the inactive BD group and the control group. CRP of the inactive BD and the healthy control group were similar. In addition, ESR was found higher than the control group in both active and inactive BD groups,

Table I. Baseline characteristics in study groups.

Baseline characteristics	Group I (n=120)	Group II (n=66)	Control (n=79)	<i>p</i>
Age, y	37.83±11.86	37.96±12.02	37.63±10.82	0.98
Male, n (%)	72 (60)	38 (58)	46 (58)	0.94

Group I: Active BD; Group II: Inactive BD

Table II. Study parameters in all groups.

	Group I (n=120)	Group II (n=66)	Control (n=79)	<i>p</i>
MPV (f/L)	8.16 ± 1.09	8.39 ± 0.86	8.47 ± 0.87	0.66
CRP (mg/L)	0.51 (0.23-0.89)	0.19 (0.04-0.36)	0.13 (0.08-0.18)	<0.001 [†]
ESR (mm/h)	19.5 (12-20)	13.0 (11-16)	11.0 (9-13)	<0.001 [‡]
NLR	4.41 (2.77-6.20)	1.82 (1.47-1.99)	1.72 (1.32-2.04)	<0.001 [†]

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate MPV, mean platelet volume; NLR, neutrophil lymphocyte ratio; [†]There was a statistically significant difference between group I with group II and group I with control but no statistically significant difference between group II and control.

[‡]There was a statistically significant difference in all groups.

whereas ESR of the active BD group was higher than the inactive BD group. N/L ratio was found statistically higher in the active BD group when compared to inactive BD and healthy control groups, while the N/L ratio of inactive BD and healthy control groups were found similar to each other (Table II).

While there was no significant difference in MPV, CRP, and NLR between active BD subgroups with and without thrombosis, ESR was significantly higher in the active BD group with thrombosis when compared to the active BD group without thrombosis (Table III).

Discussion

This study revealed that NLR was higher in active Behçet's disease than in inactive Behçet's disease and the healthy control group. However, MPV did not differ between study groups. This study is the first to evaluate both the MPV and NLR values in patients with BD.

Etiopathogenesis of Behçet's disease remains unknown. The widely accepted hypothesis is that abnormal inflammatory response is triggered by a stimulus in individuals with genetic predisposition^{21,22}. The main pathophysiological changes in

BD are neutrophil hyperfunction, vasculitis, and autoimmune response. Cytokines are important mediators of immune inflammatory response, and endothelial dysfunction can developed as a result of the immune-mediated inflammatory response. Skin lesions in the patients with Behçet's disease developed upon vasculitis, which occurred due to perivascular inflammation. Major active cells of perivascular inflammation are lymphocytes, monocytes, and neutrophils. CRP, ESR, and white blood cell count are commonly used as inflammatory markers. Of note, the N/L ratio has been used to determine the severity of the inflammation in various inflammatory diseases²³⁻²⁵. To date, the N/L ratio is considered as a cost effective and valid marker for systemic inflammation²⁶.

The role of platelets (PLTs) and their roles in hemostasis have been reported for many years. In addition, vascular permeability can be increased in inflammation, and PLTs can facilitate the secretion of some inflammatory cytokines during this process²⁷. When PLTs are activated, they undergo changes in their shape and size. Interestingly, PLT function and size are associated most likely due to the larger PLTs that contain more granules that are metabolically and enzymatically more active²⁸. MPV, which is a machine-

Table III. Study parameters in patients with Behçet's disease

	Tromboz (+) (n=15)	Tromboz (-) (n=105)	<i>p</i>
MPV (f/L)	7.81 ± 1.00	8.28 ± 1.01	0.10
CRP (mg/L)	0.44 (0.17-1.04)	0.37 (0.09-0.55)	0.41
ESR (mm/h)	24 (13-42)	16 (11-22)	0.04
NLR	3.52 (1.68-5.55)	2.72 (1.79-5.26)	0.88

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate MPV, mean platelet volume; NLR, neutrophil lymphocyte ratio.

calculated measurement of the average size of platelets, is useful to determine platelet activation. Increased MPV levels have been associated with many inflammatory-associated diseases, including Crohn's disease, rheumatoid arthritis, familial Mediterranean fever, ulcerative colitis, acute pancreatitis, acute ischemic stroke, diabetes mellitus, and myocardial infarction^{6-9,15,29,30}.

Açıkgöz et al³¹ found that MPV was statistically and significantly higher in patients with BD compared to the control group, and was associated with an increased tendency to develop thrombosis. However in our study, we did not notice any statistically significant difference in MPV values of patients with BD. MPV was similar between patients with active and inactive BD. MPV was also found similar when subgroups of active BD with or without thrombosis compared.

Lee et al³² and Türkçü et al³³ reported that MPV of patients with BD was lower than the healthy control group. Acıkgöz et al³¹ reported statistically and significantly higher MPV in patients with BD, when compared to healthy control group. While MPV of patients with active and inactive BD were similar, the same study reported that patients with BD who had thrombosis had higher MPV levels. Ricart et al³⁴ reported that patients with BD, who had posterior uveitis or thrombosis, had similar MPV levels. In our study, we found that MPV of patients with both active and inactive BD was similar to the healthy control group. In a study of patients with rheumatoid arthritis and ankylosing spondylitis, the MPV of the patients was found to be statistically and significantly lower than healthy control group. This study also reported a minimal increase in the MPV of the patients with immunosuppressive treatment. These data suggest that immunosuppressive treatment can affect MPV. Thus, we didn't include patients receiving steroids and/or immunosuppressive treatment in our study. By doing this, we aimed to exclude the effects of systemic immunosuppressive treatment on MPV.

Neutrophil and lymphocyte count could be obtained from white blood count part of the complete blood count. The N/L ratio is considered to be an indicator of inflammation and thought to have prognostic importance in several systemic diseases^{5,16-20}. The N/L ratio is important because it provides information on two different pathways: 1) neutrophils responsible for ongoing inflammation and 2) lymphocytes on regulatory pathway. Öztürk et al⁴ found higher N/L ratio in

patients with BD compared to the control group. They also reported a positive correlation between carotid intima-media thickness (cIMT) and N/L ratio. According to the results of this study, Öztürk et al⁴ reported that the increased N/L ratio might be associated with endothelial dysfunction and reflect activity of BD without serious cardiovascular involvement. However, Öztürk et al⁴ did not compare the patients with inactive BD and the healthy control group. In our study, we found a statistical and significant increase in the N/L ratio of the patients with active BD compared to the patients with inactive BD and healthy control group. The N/L ratio was similar between the patients with inactive BD and healthy control group.

Conclusions

The N/L ratio may be a good indicator of platelet activation in patients with BD. Many cytokines and biomarkers have been investigated for their use as indicators of inflammation in patients with BD³⁵⁻³⁸. However, these parameters used in these studies are very expensive. The N/L ratio is a cost-effective and easily applicable parameter that can be measured in any laboratory. In conclusion, the data obtained in the present study showed that the patients with BD are exposed to chronic inflammation. However, further studies with larger sample sizes are needed to define the role of platelets in NLR and MPV as well as understand the pathophysiology of its clinical significance.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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