Association of neutrophil / lymphocyte ratio, platelet / lymphocyte ratio and brachial retinal vein occlusion

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Abstract
Aim: In this study, we aimed to measure neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) levels in brachial retinal vein occlusion (BRVO) patients and to determine whether there it could be used as a marker for BRVO. Brachial retinal vein occlusion is a serious disease that causes vision loss and is associated with inflammation.

Material and Methods: This retrospective study included 77 patients with BRVO and 69 healthy controls. BRVO was diagnosed with ophthalmic examination. Blood samples were obtained from venous blood and serum neutrophil, lymphocyte, and platelet data of all patients were recorded also, NLR-PLR values were calculated.

Results: Significant difference were not found between the BRVO group and control group with the level of white blood cells (WBC) and platelets (p>0.05). Neutrophil count was significantly increased in BRVOs compared to the controls (4.79±1.89 vs 4.02±1.47, p=0.007). Lymphocyte count was significantly decreased in BRVOs compared to the controls. (2.17±0.76 vs 2.52±1.03, p=0.022) NLR was significantly increased in BRVOs compared to the controls. (2.60±2.05 vs 1.74±0.70, p=0.001) Also, PLR was significantly increased in BRVOs compared to the controls. (129.70±68.77 vs 107.96±40.65, p=0.023)

Conclusion: In our study we found that NLR and PLR were significantly increased in BRVOs than in controls.

Keywords: Neutrophil/lymphocyte ratio; platelet/lymphocyte ratio; brachial retinal vein occlusion, retinal vessels.

INTRODUCTION
Diabetic retinopathy is the most common cause of retinal vasculopathy and retinal vein occlusion (RVO) is the second reason (1). According to a prevalence study by Rogers et al, approximately 16.4 million people are affected by RVO. 13.9 million of these people affected by brachial retinal vein occlusion (BRVO) and 2.5 million affected by central retinal vein occlusion (CRVO) and. Also, in all ethnic populations prevalence of BRVO was higher than CRVO (2). RVO usually affects the middle-aged and elderly patient population (3). Several studies have shown that RVO is associated with glaucoma, hypercoagulable conditions and systemic diseases (such as hypertension, diabetes, systemic vascular disease) (4-5). In the pathogenesis of BRVOs, it is known that compression of veins at arteriovenous crossings is the main reason (6). Systemic and local inflammations are thought to have a serious effect in the etiology of RVO (7). A study of Ross showed that atherosclerosis is a chronic, low-grade inflammatory condition and RVO patients are independently associated with atherosclerosis (8).

Neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR), calculated from hemogram are systemic inflammatory responses. Many different studies published before have shown that NLR and PLR are indicative of systemic inflammation (9-11). Mean platelet volume (MPV) is a parameter that indicates the status of platelets, and MPV is associated with inflammation (12). In this study, we aimed to measure NLR and PLR in BRVOs and to determine whether there it could be used as a marker for BRVO.
MATERIAL and METHODS

This study was performed retrospectively in the Sakarya University Third Affiliated Training and Research Hospital Department of Ophthalmology. Data were excluded from the file records of patients who diagnosed with BRVO between January 2016 and August 2018. All subjects underwent complete ophthalmic evaluation of both the eyes, including the best corrected visual acuity, slit-lamp inspection of the anterior segment, applanation tonometry and slit-lamp examination of fundus with 90D Volk lens. Color fundus photographs and fundus fluorescein angiography were performed to the patients and the diagnosis of BRVO was defined accordingly (13).

The study consisted 77 BRVOs and 69 controls. Healthy control patients consisted of patients with presbyopia in ophthalmology outpatient clinic. Age and sex matched in the groups. Also, patients with hypertension (HT) was matched.

Criteria for exclusion were; systemic diseases (such as cardiovascular diseases and diabetes), history of stroke, blood disorders, anemia, renal failure, hepatic disorders, malignancies, and vasculitis. Also, patients with glaucoma and with a history of eye surgery were excluded from the study.

Hemogram parameters of all cases were measured by Cell-DYN 3700 (Cell-DYN 3700, Abbott Diagnostics, Abbott Park, IL, USA) automated hematology analyzer. According to the results of hemogram; neutrophil, lymphocyte and platelet data of all cases were recorded and NLR-PLR values were calculated.

The study was carried out under the ethical principles of the Helsinki Declaration and approved by the Sakarya University Medical School Ethics Committee.

Statistical Analysis

Data analyzed due to the SPSS (17.0, SPSS Inc., Chicago, IL, USA) software program. Numerical data were presented as mean and standard deviation. Comparison of the independent groups was done by parametric Student t test. Cut-off point between BRVO group and control group determined regarding receiver operating characteristic (ROC) curve analysis. According to the cut-off value, sensitivity and specificity values were calculated. The results were evaluated according to 95% confidence interval (CI) and P<0.05 level.

RESULTS

Our study consisted of a total of 146 patients, including 77 patients with BRVO and 69 healthy controls. The BRVO group consisted of 34 male and 43 female patients, and the control group included 31 male and 38 female patients. The mean age of the BRVO group was 59.22±11.98 years and the control group was 56.97±10.78 years. There was no significant difference between BRVO group and control group in terms of gender and age. (p>0.05) (Table 1). In addition, there was no significant difference between the control group (69 to 18) and BRVO (77 to 26) in terms of the presence of HT. (p=0.316)

No statistically significant difference was found between the BRVO group and the control group in terms of white blood cells and platelet levels (p>0.05). Significantly increased neutrophil count was seemed in BRVOs compared to the controls (4.79±1.89 vs 4.02±1.47, p=0.007). Significantly decreased lymphocyte count was seemed in BRVOs compared to the controls (2.17±0.76 vs 2.52±1.03, p=0.022).

NLR was significantly increased in BRVOs compared to the controls (2.60±2.05 vs 1.74±0.70, p=0.001). Also, PLR was significantly increased in BRVOs compared to the controls (129.70±68.77 vs 107.96±40.65, p=0.023) (Table 1).

In logistic regression analysis, we found that NLR was an independent indicator of BRVO[odds ratio (OR) = 1.709; 95% CI= 1.146-2.549; p=0.009]. But PLR was not an independent indicator of BRVO. (OR= 1.006; 95% CI= 0.999-1.012; p=0.116).

According to the ROC analysis, the area under curve (AUC) for NLR was 0.645, the cut-off value was 1.775, the sensitivity was 60%, and the specificity was 58%. (95% CI: 0.555-0.734). The AUC for PLR was 0.564, the cut-off value was 109.950, the sensitivity was 55%, and the specificity was 55%. (95% CI: 0.468-0.660) (Figure 1).

Figure 1: ROC curve analysis of NLR and PLR in BRVO patients. NLR was determined to be more sensitive and had a higher rate as a predictor of inflammation compared to PLR. AUC for NLR: 0.645, cut-off value: 1.775, sensitivity: 60%, specificity: 58%. (95% CI: 0.555-0.734). AUC for PLR: 0.564, cut-off value: 109.950, sensitivity: 55%, specificity: 55%. (95% CI: 0.468-0.660)
ROC: receiver operating characteristic; BRVO: brachial retinal vein occlusion; NLR: neutrophil/lymphocyte ratio; PLR: platelet/lymphocyte ratio; AUC: area under curve.

**DISCUSSION**

In this study we found that NLR and PLR were significantly increased in BRVOs and NLR can be used an independent marker for BRVO. According to studies in the literature, this is the first study to investigate the relationship between NLR, PLR and BRVO.

Both systemic and local inflammations are thought to have a serious effect in the etiology of RVO (7). The mechanism of RVO development in systemic inflammation is due to systemic hypercoagulation triggering. In systemic inflammation, levels of many inflammatory chemokines/cytokines (such as interleukin-1 beta and interleukin-6) are increases and it activates the coagulation. At the same time, these chemokines / cytokines activate pathways that inhibit fibrinolysis (14-16. Noma et al. have shown that local inflammation in the eye can cause RVO formation. He also reported that, patients with RVO had elevated levels of high proinflammatory cytokines/chemokines (such as interleukin-1, interleukin-6 and interleukin-8) in the vitreous fluid (17).

NLR is calculated by dividing the number of neutrophils by the lymphocyte count and is considered a cheap indicator of systemic inflammation. Systemic inflammation typically involves lymphopenia and neutrophilia (18). Gokhan et al showed that NLR was found to be an independent variable for symptomatic carotid artery disease. Also, NLR was higher in symptomatic patients than asymptomatic patients with stroke and transient ischemic attack (19). (p = < 0.001) A meta-analysis by Bhat et al. showed that NLR may play a serious role in the diagnosis and prognosis of peripheral vascular diseases (20). In another study performed by Dursun et al. showed that NLR was significantly increased in RVOs compared to the controls (21). (p <0.001) In our study, NLR was significantly increased in BRVOs than the controls, which may contribute to the pathogenesis of BRVO. Logistic regression analysis showed that NLR is an independent indicator of BRVO.

The PLR is calculated by dividing the number of platelets to lymphocyte count and it is cheap, and giving some information about condition of platelets and white cells. Thrombocytes have a significant role in coronary artery disease and cardiovascular disease(22). Azab et al. reported a relationship between increased PLR and long-term mortality in patients with myocardial infarction (23). In a different study, Ferroni et al. reported a relationship between increased PLR and risk of symptomatic venous thromboembolism (24). This study showed that PLR was significantly increased in BRVOs than the controls. However, logistic regression analysis showed that PLR was not an independent indicator of BRVO.

The limitations of the study are the small number of patients, the lack of body mass index and retrospective design of the study. New studies including more patients are needed to investigate the possible role of serum NLR and PLR levels in BRVO. However, further prospective studies are needed.

**CONCLUSION**

In conclusion, in this study we found that NLR and PLR were significantly increased in BRVOs than the controls. NLR may be used to estimate the risk of BRVO from haemogram parameters. Larger studies are needed to enable NLR to be used to estimate BRVO risk.

**Competing interests: The Authors declares that there is no conflict of interest**

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