

THE RELATION OF NEUTROPHIL/LYMPHOCYTE RATIO, PLATELET/LYMPHOCYTE RATIO AND MEAN PLATELET VOLUME WITH IDIOPATHIC ACUTE ANTERIOR UVEITIS

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Abstract

ABSTRACT Purpose: In this study, leukocyte, lymphocyte, neutrophil, platelet count, mean platelet volume (MPV), neutrophil/lymphocyte (NLR) ratio and platelet/lymphocyte ratio (PLR) were retrospectively evaluated in patients with idiopathic acute anterior uveitis. **Methods:** Medical records were retrospectively reviewed from March 2016 to February 2020. 50 patients, 25 men and 25 women, and 50 healthy volunteers, 25 males and 25 females, as the control group were included in the study. Blood samples of the patients were taken before starting treatment. A complete ophthalmological examination including corrected visual acuity, tonometry, slit lamp and fundus examination was performed in all patients. Gender, age, leukocyte, neutrophil, lymphocyte, platelet, MPV, PLR, NLR values of the patients were recorded. **Results:** In this study, a statistically significant difference was found in the values of leukocyte ($p<0.001$), neutrophil ($p<0.001$), platelet ($p<0.001$), NLR ($p<0.001$) and PLR ($p<0.001$). There was no significant difference between the two groups in terms of the number of lymphocyte ($p=0.063$) and value of MPV ($p=0.051$). Leukocyte, neutrophil, platelet count, NLR, PLR values were found to be higher in the uveitis group compared to the control group. **Conclusions:** In this retrospective study, it is thought that leukocyte, neutrophil, platelet count, PLR, NLR, levels are significant in patients with idiopathic acute anterior uveitis and can be used in early diagnosis.

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Methods: Medical records were retrospectively reviewed from March 2016 to February 2020. 50 patients, 25 men and 25 women, and 50 healthy volunteers, 25 males and 25 females, as the control group were included in the study. Blood samples of the patients were taken before starting treatment. A complete ophthalmological examination including corrected visual acuity, tonometry, slit lamp and fundus examination was performed in all patients. Gender, age, leukocyte, neutrophil, lymphocyte, platelet, MPV, PLR, NLR values of the patients were recorded.

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KEYWORDS: Platelet/lymphocyte ratio, neutrophil/lymphocyte ratio, inflammation, uveitis, blood parameters.

INTRODUCTION

Uveitis is the inflammation of the middle vascular layer of the eye, the uvea. It is an important cause of blindness and low vision. It can be seen at any age, most often between the ages of 20-59. Its incidence in the community is 17-52 / 100,000 per year (1, 2).

Uveitis is divided into groups according to its localization; anterior uveitis (involves iris and ciliary body), intermediate uveitis (vitreous, pars plana of the ciliary body and peripheral retina), posterior uveitis (choroid and retina), panuveitis (general inflammation of the entire uvea). Anterior uveitis constitutes 50-92% of all uveitis cases (3, 4, 5). In most cases, the causes of anterior uveitis cannot be found. Uveitis in this group defined as idiopathic anterior uveitis constitutes 38-88% of all anterior uveitis. It is the most common form of uveitis in the community. (5, 6).

The underlying mechanisms that cause acute anterior uveitis are unknown. It has been reported that immune complex and cell-mediated autoimmune processes may be responsible (7). With the development of laboratory techniques used in the diagnosis of uveitis since the middle of the last century, the etiology of uveitis has become more pronounced (8).

Association of systemic diseases with uveitis is known. The frequency of systemic disease underlying uveitis is %19-46 (3, 4). In recent studies, it has been reported that white blood cells, neutrophils, neutrophil / lymphocyte ratio, platelet / lymphocyte ratio can be easily counted in whole blood count and can be used as an inflammation biomarker in subclinical systemic inflammation. The underlying mechanisms that cause acute anterior uveitis are unknown. Akut ön üveite neden olan altta yatan mekanizmalar bilinmemektedir. Its importance in predicting prognosis in cancers, diabetes mellitus, hypertension and cardiovascular diseases has been stated. According to his clinic; Kliniğine göre; According to clinical; It has been reported that it may be biomarker in eye diseases such as idiopathic acute anterior uveitis, retinal vein occlusion, age-related macular degeneration, keratoconus and pseudoexfoliation syndrome, and neovascular glaucoma (9, 10).

In this study, leukocyte, lymphocyte, neutrophil, platelet count, neutrophil / lymphocyte ratio (NLR), platelet / lymphocyte ratio (PLR) and mean platelet volume (MPV) were retrospectively evaluated in patients with idiopathic acute anterior uveitis.

MATERIALS AND METHODS

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MALZEMELER VE YÖNTEMLER

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In the study, patients diagnosed with acute idiopathic anterior uveitis at İnönü University Faculty of Medicine, Department of Eye Diseases between March 2016 and February 2020, Malatya, Turkey were retrospectively investigated. All patients' notes were retrospectively reviewed and their clinical results were reported. Helsinki declaration was followed in the study. Written informed consent is obtained routinely in our hospital from all patients and healthy volunteers before the initiation of any procedure after thorough explanation. This research study was conducted retrospectively from data obtained for clinical purposes, and the protocol was approved by the institutional review board (IRB number: 25.10.2022 / 17). 50 patients, 25 men and 25 women, and as the control group, 50 people, 25 males and 25 females, consisting of healthy volunteers, were included in the study. Blood samples of the patients were taken into ethylenediaminetetraacetic acid (EDTA) tubes before starting treatment. A complete ophthalmological examination including corrected visual acuity, tonometry, slit lamp and fundus examination was performed in all patients. Gender, age, leukocyte, neutrophil, lymphocyte, platelet count, MPV, PLR, NLR values of the patients were recorded. The NLR was calculated by dividing the absolute number of neutrophils in the blood by the absolute number of lymphocytes. PLR was calculated by dividing the absolute number of platelets in the blood by the absolute number of lymphocytes. Each parameter belonging to the uveitis and control groups were compared with each other. Blood parameters were measured using an automated blood cell counter (Beckman Coulter LH 780 Hematology Analyzer, Miami, Florida, USA). The following reference values were determined for leukocyte: $4.3-10.3 \times 10^3 / \text{mL}$, neutrophil: $2.0-6.9 \times 10^3 / \text{mL}$, lymphocyte: $0.6-3.4 \times 10^3 / \text{mL}$, platelet: $150-400 \times 10^3 / \text{mL}$, MPV: $6.8 - 10.8 \text{ fL}$.

Those with chronic diseases (diabetes mellitus, hypertension, cancer, hematological diseases, rheumatologic diseases, infectious diseases, autoimmune diseases, pulmonary diseases and endocrine disorders), patients with ocular disease and drug treatment, smokers were not included in the study. The control group consisted of healthy volunteers with no evidence of intraocular inflammation and history of ocular and systemic disease except refractive error.

Statistical Analysis

The statistical analyses were conducted by using the Statistical Package for Social Science v25.0 software (SPSS, Chicago, IL, USA). Demographic, clinical and biochemical variables were classified as categorical

variables or continuous variables. A Kolmogorov-Smirnov test for normality was performed. Student's t-test or Mann-Whitney U test were used to compare the groups as appropriate. P-values less than 0.05 were considered to be statistically significant. Receiver operating characteristic (ROC) analysis was also performed to identify the cut-off threshold and quantify the accuracy of N/L and P/L. Sensitivity, specificity and the area under the ROC curve were used for an overall estimation of the accuracy of the classifier.

RESULTS

50 patients, 25 men and 25 women, in the uveitis group and 50 people, 25 males and 25 females, as the control group were included in the study. The mean age of the patients in the uveitis group was 38.14 ± 9.58 years; the mean age of the control group was found to be 38.38 ± 8.60 years. In this study, no significant difference was found between uveitis and control groups in terms of age ($p > 0.05$). When variables were compared according to genders, the difference was found to be statistically significant in platelet values ($p = 0.005$). No gender differences were found between the other mean and median values ($p > 0.05$ for each) (Table 2).

The mean values of whole blood parameters and derivatives of the uveitis and control groups are shown in Table 1. In this study, a statistically significant difference was found in the values of leukocyte ($p < 0.001$), neutrophil ($p < 0.001$), platelet ($p < 0.001$), NLR ($p < 0.001$) (Figure 1A), PLR ($p < 0.001$) (Figure 1B). There was no significant difference between the two groups in terms of the number of lymphocyte ($p = 0.063$) and value of MPV ($p = 0.051$). Leukocyte, neutrophil, platelet count, NLR, PLR values were found to be higher in the uveitis group compared to the control group.

The receiver-operating characteristic (ROC) analysis of the studied variables are shown in Figure 2. According to ROC analysis the area under the ROC (AUROC) value of the N/L to distinguish controls and patients was found to be 0.805. The best cut-off value was 2.49. Sensitivity was 56.0% and specificity was 98.0% (Figure 2). The AUROC value of the P/L to distinguish controls and patients was 0.657 with the cut-of value 11.17. Sensitivity was 52.0% and specificity was 98.0% (Figure 2).

According to its localization; **DISCUSSION** Acute anterior uveitis forms the basic mechanisms are unknown. Akut ön üveitin temel mekanizmaları bilinmemektedir.

Acute anterior uveitis is usually self-limiting, but there is no evidence for how long and how often, in which patients it will regress spontaneously. Complications are posterior synechiae, glaucoma, cataracts, cystoid macular edema and chronic uveitis (11). In this study, it is thought that PLR and NLR, as inflammation markers can guide the diagnosis of the disease, its severity, development of complications and prediction of prognosis.

All over the world, the etiology of uveitis includes infections, cancers, systemic diseases, immunological diseases, traumas, and drugs (8). History, physical examination, various laboratory tests and imaging techniques are used to determine the etiology of the patient presenting with acute uveitis attack. One of these tests is a whole blood count test. Its application is simple and it is widely used in diagnosis (12). Leukocyte, neutrophil, lymphocyte, platelet count, NLR, PLR, MPV levels were examined in the study.

Leukocytes (White blood cells) make up less than 1% of the total blood volume. There are several types of leukocytes in different size, function and structure (neutrophil, lymphocyte, monocyte, eosinophil, basophil). They constitute the body's main defense mechanism against diseases by protecting them from the damage caused by pathogens and eliminating damaged cells, waste products and toxins (13).

Neutrophils (polymorph nuclear leukocytes) are the most abundant leukocytes in human blood. Neutrophils make up 50-70% of circulating leukocytes. It is produced in the bone marrow and is released at a constant rate under homeostatic conditions. Neutrophils provide defense against bacteria, fungi, viruses and parasites. They are short-lived, but their lifespan is prolonged in inflammatory and infectious conditions (14, 15). Neutrophils migrate for phagocytosis of various particles found in inflamed areas in the acute inflammatory state. They induce an immune response by releasing cytokines, eicosanoids, platelet activating factor and cationic proteins (7). In their study, Zhang et al., found that mean levels of neutrophils were significantly

higher in patients with neovascular glaucoma secondary to retinal vein occlusion (10). In this study, the neutrophil count was found to be significantly higher in the uveitis group compared to the control group.

Lymphocytes make up 20-30% of the white blood cells in the circulation. They are responsible for the specific defense known as immunity against infections. There are three types of T cells, B cells and natural killer cells (13). In their study, Şimşek et al., found that lymphocyte count increased and NLR level decreased in patients with Fuchs uveitis syndrome compared to the control group (16). In this study, there was no significant difference in the lymphocyte count between the two groups.

Platelets are specialized blood cells that play a central role in hemostasis, thrombosis, inflammation and wound healing. It is the smallest in size of blood cells. They are released from megakaryocytes in the bone marrow (17). Leukocytes and platelets are markers of inflammation (9, 10, 18). In the study, the platelet counts were found to be significantly higher in the uveitis group compared to the control group.

MPV is a parameter of whole blood count. It is associated with platelet function and activation (19). In inflammation, cytokines have been shown to suppress the size of the platelets by affecting the megakaryopoiesis and cause the release and decrease of smaller platelets into the bloodstream. In some other studies, it has been stated that larger platelets resulting from increased turnover as a result of platelet activation are released into the bloodstream. MPV is an indicator of inflammation and disease activity in various inflammatory diseases (20, 21). In the study of Kısacık et al., MPV was found to be significantly lower in patients with ankylosing spondylitis and patients with active rheumatoid arthritis compared to the control group (19). Türkçü et al., reported that the MPV in patients with active uveitis was lower than in controls (22). In this study, there was no significant difference between the two groups in the value of MPV level.

PLR is a new biomarker that shows inflammation. It is indicative of poor prognosis in people with peripheral arterial occlusive disease due to its key role in atherosclerosis and atherothrombosis. In addition, it is a sensitive marker and prognostic factor in many malignancies (21, 23). Osami et al., reported that there was a significant difference in leukocyte, neutrophil, lymphocyte, platelet count, NLR and PLR levels in patients with ankylosing spondylitis when those with active disease and those with inactive disease were compared (24). Jiang et al., reported that the PLR level is significantly higher in active Behçet's disease than in inactive Behçet's disease (25). İcel et al., reported that NLR and PLR levels were significantly increased in patients with degenerative high axial myopia compared to patients with non-degenerative high axial myopia, and there was a connection between the development of myopia and increased inflammation (26). Kurtul et al., reported that the PLR level is high in patients with retinal vein occlusion (27). Özgönül et al., reported in their study that PLR and NLR levels were significantly higher in patients with idiopathic acute anterior uveitis compared to the control group (28). In this study, PLR was found to be significantly higher in the uveitis group compared to the control group.

The NLR can be easily calculated from whole blood results. It is an easily obtainable marker showing the inflammation status in the body. NLR is often used as an inflammation marker (21, 29, 30). NLR has been studied in inflammatory diseases, diabetes, hypertension, malignancy, age-related macular degeneration, diabetic retinopathy, keratoconus, retinal vein occlusion. In the study reported by Bozkurt et al., no significant difference was found in the NLR level when the keratoconus group was compared with the control group. PLR was found to be significantly higher in the keratoconus group compared to the control group (31). In the study reported by Jiang et al., in Behçet's patients, NLR and PLR were found to be significantly higher than the control group (25). High NLR and PLR are indicators of increased inflammation (23). Balci et al., stated that leukocyte, neutrophil, thrombocyte and NLR values are important in distinguishing systemic infectious and non-infectious etiology in patients presenting with a uveitis attack for the first time. In the study, they found that the leukocyte, neutrophil, platelet, and NLR levels were significantly higher in the systemic infectious group compared to the systemic non-infectious group. There was no significant difference in PLR between the groups. Lymphocyte level was found to be lower in the systemic infectious group compared to the non-infectious group (12). Qin et al., found that PLR, NLR and MPV levels were increased in patients with systemic lupus erythematosus in their study. They reported that increased NLR and PLR levels correlated with the activity of the disease (21). In this study, NLR was found to be significantly higher

in the uveitis group compared to the control group.

Laboratory scans to diagnose the underlying disease causing uveitis are expensive and time consuming. Whole blood parameters frequently used in the clinic are easily applicable and inexpensive. In this retrospective study, it is thought that leukocyte, neutrophil, platelet counts, PLR, NLR, levels are significant in patients with idiopathic acute anterior uveitis and can be used in early diagnosis. However, since this study was retrospective, only spot blood values of the patients were studied. Since the blood values in the follow-up of the patients could not be checked, evaluation could not be made in terms of prognosis. Studies on this subject in patients with idiopathic anterior uveitis are very few. It will be used as a diagnostic marker with more studies in the future and will be useful in early diagnosis and predicting the prognosis of the disease.

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The data that support the findings of this study are available from the corresponding author, [UD], upon reasonable request.

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Inonu University Faculty of Medicine Department of Ophthalmology between March 2016- February 2020 study 'moment of acute idiopathic anterior uveitis patients were studied retrospectively.

İnönü Üniversitesi Tıp Fakültesi Göz Hastalıkları Anabilim Dalı Mart 2016-Şubat 2020 tarihleri arasında 'akut idiyopatik anterior üveit hastalarının anı' retrospektif olarak incelendi.

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ön üveit (iris ve siliyer cisim), ara üveit (vitreus, siliyer cismin pars planası ve periferik retina), arka üveit (koroid ve retina), panüveit (tüm uvee'nin genel iltihabı).

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ön üveit (iris siliyer cisim), ara üveit (vitroz, periferik retina ve siliyer cisim pars plana), arka üveit (koroid ve retina), panüveit (üveanın tüm genel iltihabı).

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