ÖZGÜN ARAŞTIRMA ORIGINAL RESEARCH

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EVALUATION OF NEUTROPHIL LYMPHOCYTE RATIO, PLATELET LYMPHOCYTE RATIO AND MEAN PLATELET VOLUME IN MAJOR DEPRESSIVE DISORDER

MAJÖR DEPRESİF BOZUKLUKTA NÖTROFİL LENFOSİT ORANI, TROMBOSİT LENFOSİT ORANI VE ORTALAMA TROMBOSİT HACMİ DEĞERLENDİRİLMESİ

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Öz

Amaç
Kronik inflamasyonun psikiyatrik bozukluklarla ilişkisi daha önce yapılan çalışmalarda gösterilmiştir. Nötrofil lenfosit oranı (NLO), platelet lenfosit oranı (PLO) ve ortalama trombosit hacmi (OTH) sistemik inflamatuar yanıtın değerlendirilmesinde yeni belirteçler olarak görülmektedir. Bu kapsamda, bu çalışmanın amacı, majör depresif bozukluk (MDB) hastalarında NLO, PLO ve OTH düzeylerinin kontrol grubu ile karşılaştırılarak değerlendirilmesi, MDB ile bu biyobelirteçler arasındaki ilişkinin araştırılmasıdır.

Gereç ve Yöntem
Kesitsel tarzda tasarlanan çalışma 15 Temmuz 2020-15 Mayıs 2021 tarihleri arasında Antalya Eğitim ve Araştırma Hastanesi Psikiyatri Polikliniğinde yapıldı. Çalışmaya katılmayı kabul eden 92 MDB hastası (DSM-5 tanı kriterlerine göre) ve 72 sağlıklı kontrol ile çalışma yürütüldü. Tüm katılımcılar ile yüzyüze görüşüldü ve sosyodemografik veri formu dolduruldu. Ayrıca MDB hastalarına hastalığın şiddetini belirlemek için Hamilton Depresyon Ölçeği uygulandı.

Bulgular
Gruplar arasında yaş ortalaması ve cinsiyet dağılımı açısından anlamlı fark yoktu (p>0.05). MDB'li hastalar ve sağlıklı kontroller NLO, PLO ve OTH puan ortalamaları açısından karşılaştırıldı ve gruplar arasında anlamlı farklılık bulunmadı (p>0.05). Ayrıca hasta grubunda depresyon şiddetine göre (hafif, orta, ciddi) NLO, PLO ve OTH puan ortalamaları karşılaştırıldı, istatistiksel olarak anlamlı bir farklılık bulunmadı (p>0.05).

Sonuç
Bu çalışma, MDB hastalarında NLO, PLO ve OTH biyobelirteçlerini sağlıklı kontrollerle karşılaştırarak aynı anda değerlendiren ilk çalışmadır. Çalışmada NLO, PLO ve OTH düzeyleri ile MDB arasında anlamlı bir ilişki olmadığı bulunmuştur. Ayrıca depresyon şiddeti ile bu belirteçler arasında da anlamlı bir ilişki olmadığı belirlenmiştir. Bunları ve başka biyobelirteçleri konu alan daha kapsamlı ve daha ileri çalışmalar, MDB'deki inflamatuar süreç hakkında daha fazla bilgi sağlayacaktır.

Anahtar Kelimeler: Majör depresif bozukluk, Nötrofil lenfosit oranı, Ortalama trombosit hacmi, Platelet lenfosit oranı

Abstract

Objective
The relationship between chronic inflammation and psychiatric disorders has been evaluated in previous studies. Neutrophil-lymphocyte ratio (NLR), platelet-

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lymphocyte ratio (PLR), and mean platelet volume (MPV) appear to be new markers for the evaluation of systemic inflammatory response. In this study, it was aimed to evaluate the levels of NLR, PLR and MPV biomarkers in patients with major depressive disorder (MDD) by comparing them with healthy controls, and also investigate the relationship between biomarkers and MDD.

Material and Method
This cross-sectional study was carried out from July 15, 2020 to May 15, 2021. The study was conducted with 92 patients with diagnosed MDD and 72 healthy controls who agreed to participate. The sociodemographic data form and SCID-5/CV form were filled out for each participant through face-to-face interviews with all participants. Additionally, Hamilton Depression Scale was applied to the patient group to determine the severity of MDB.

Results
Patients with MDD and healthy controls were compared in terms of the mean scores of NLR, PLR and MPV, and no statistically significant difference was found between the groups (p>0.05). Additionally, in the patient group, there was no statistically significant difference between the levels of depression severity (mild, moderate, severe) in terms of the mean scores of NLR, PLR, and MPV (p>0.05).

Conclusion
This is the first study to evaluate NLR, PLR and MPV biomarkers simultaneously in MDD patients by comparing them with healthy controls. In this study, it was found that there was no significant relationship between NLR, PLR and MPV levels and MDD. Additionally, it was determined that there was no relationship between the severity of depression and the aforementioned markers. Further studies investigating these and another biomarkers with prospective and larger studies will provide more insight into the inflammatory process in MDD.

Keywords: Major depressive disorder, Mean platelet volume, Neutrophil lymphocyte ratio, Platelet lymphocyte ratio

Introduction

Immune ability in major depressive disorder (MDD) has been assumed to only change in a decreasing direction for a long time. However, it has recently been found that stress and MDD cause inflammatory activation in addition to suppressing immunity. Serum concentrations of lymphocytes, B cells and T cells decrease in MDD. There may be an increase in autoantibodies. Lymphocyte proliferation and T natural killer activity decrease or disrupt (e.g. there is not enough lymphocyte production against viruses) (1). The role of inflammation on MDD etiopathogenesis is evaluated in previous studies (2-4). White blood cells have an important role in inflammatory processes. Neutrophil lymphocyte ratio (NLR) and Platelet lymphocyte ratio (PLR) are considered as new determinants in the evaluation of inflammatory response (5). Previous studies indicated that NLR is higher among patients with MDD, schizophrenia and Alzheimer's disease (6-8). Additionally, it has been reported in a meta-analysis study that NLR and PLR values were increased in mood disorders (MDD and bipolar disorder) (9). Peripheral platelet models are commonly used as the indicators of central serotonin (5-HT) metabolism since they reflect central serotonergic function (10). Mean platelet volume (MPV) is a potential indicator of platelet activity (11), and a significant relationship has been reported between MPV and MDD (12).
In summary, chronic inflammation is associated with MDD. PLR, NLR, and MPV have been considered as new biomarkers for the inflammatory response. In this context, we aimed to evaluate the levels of MPV, PLR, and NLR biomarkers in MDD patients by comparing them with healthy controls, and also investigate the relationship between biomarkers and MDD. In addition, the relationship between these biomarkers and depression severity will be evaluated.

Material and Method

The patient group included 92 participants who applied to Antalya Training and Research Hospital Psychiatry Outpatient Clinic from July 15, 2020 to May 15, 2021 and who were diagnosed with MDD based on the DSM-V criteria (13). Patients who have not a comorbid psychiatric disorder and have not a history of psychiatric treatment in the last 1 month were included in the study. The control group consisted of 72 healthy volunteers who had not a history of any psychiatric disorders. Hemogram samples were obtained from each participant and complete blood parameters were studied in the Biochemistry Laboratory of Antalya Training and Research Hospital. Participants who agreed to participate were interviewed face to face, sociodemographic data form and SCID-5/CV form were filled out for each

participant and also Hamilton Depression Scale (HDS) was applied to patients diagnosed with MDD. The participants were informed about the study and written informed consent was obtained from each participant. This study conducted in accordance with the principles stated in the Declaration of Helsinki, and ethical approval was obtained from the Ethical Committee of Antalya Training and Research Hospital (decision dated 04.06.2020, and numbered 8/19).

The exclusion criteria for the all participants were as following; a) having inflammatory or autoimmune diseases, severe neuropsychiatric diseases that may cause mental cognition problems, (epilepsy, dementia, mental retardation, cerebrovascular disease, etc.), chronic systemic diseases, (diabetes mellitus, hypertension, cardiovascular disease, renal failure, etc.), blood cell diseases (hematopoietic disease, malignancy, acute infection, etc.) and using medication (chemotherapy, glucocorticoid treatment within the last three months), b) pregnancy or being in the breastfeeding period, c) history of alcohol/ substance abuse or addiction, d) being under 18 years old.

Assessment Tools

Structured Clinical Interview for DSM-5 Clinical Version (SCID5/CV): SCID-5/CV is an interview guide developed to establish major DSM-5 diagnoses (14). It is administered by a mental health professional with clinical experience. The Turkish validity and reliability study of the scale was performed by Elbir et al. (15).

Hamilton Depression Scale (HDS): HDS scale developed by Hamilton to evaluate depression severity and depression subtypes in patients (16). HDS is administered by the clinician. The scale consists of 17 items and the highest score to be obtained from the test is 53. In the evaluation, 0-7 points are considered as normal, 8-15 points as mild depression, 16-28 points as moderate depression, and 29 and above points as severe depression. The Turkish validity and reliability study of the scale was performed by Akdemir et al. (17). The Cronbach's alpha of the HDS is 0.86 in this study.

Statistical Analysis

In statistical analysis, Kruskal-Wallis test, t-test and Mann-Whitney U test were used to determine differences between groups in independent samples. Chi-square ($\chi 2$) test was used to determine group differences of categorical variables. ANOVA test was used to compare between groups. The statistical significance level was determined as $p<0.05$. Statistical analyzes were performed with SPSS Windows version 21.0.

Results

This study was conducted with a sample of 92 MDD patients and 72 healthy volunteers. The mean ages of the patient group and the control group were 36.60±11.34 (min: 18, max: 67) years and 35.78±11.84 (min: 18, max: 65) years, respectively. No statistically significant difference was found between the groups in terms of mean age ($p>0.05$). The ratio of male/ female participants in the patient group was 46.1% / 53.9% (n=29/63), and was 46.9% / 53.1% (n=23/49) in the control group. The mean age and gender distribution between the groups is shown in Table 1. No statistically significant difference was found between the groups in terms of gender distribution ($p>0.05$). The mean scores of NLR, PLR and MPV of the patient and control groups are presented in Table 2. According to the findings, no statistically significant difference was found between the groups in terms of the mean scores of NLR, PLR, and MPV ($p>0.05$). The mean score of HDS in the patient group was found to be 22.28±4.29. Additionally, the rates of MDD severity levels according to HDS scores were found to be as normal, mild, moderate, and severe; 8.7% (n=8), 30.4% (n=28), 45.7% (n=42) and 15.2% (n=14),

Table 1 Comparison of the mean age and gender distribution between the groups

	Patient group (n= 92)	Control group (n= 72)	p
Age (m ± sd)	36.60±11.34	35.78±11.84	0.687*
Male Female	29 (46.1%) 63 (53.9%)	23 (46.9%) 49 (53.1%)	0.104**

*t test, **$\chi 2$ test, m: mean, sd: standard deviation

Table 2 Comparison of the mean scores of NLR, PLR and MPV between the groups

	Patient group (m ± sd)	Control group (m ± sd)	p
NLR	2.26±0.86	2.14±0.82	0.396*
PLR	136.3±52.3	129.5±51.9	0.225*
MPV	10.83±1.05	10.65±0.93	0.332**

*Mann-Whitney U test , **t test, m: mean, sd: standard deviation, NLR: neutrophil lymphocyte ratio, PLR: platelet lymphocyte ratio, MPV: mean platelet volume

Table 3 Comparison of the mean scores of NLR, PLR and MPV according to the levels of disease severity

	Mild (m ± sd)	Moderate (m ± sd)	Severe (m ± sd)	p
NLR	2.35±0.98	2.16±0.73	2.14±1.25	0.302*
PLR	138.26±55.81	127.99±46.41	120.65±46.01	0.525*
MPV	11.38±1.09	10.32±1.03	10.23±0.98	0.453**

* Kruskal-Wallis test, **ANOVA test, m: mean, sd: standard deviation, NLR: neutrophil lymphocyte ratio, PLR: platelet lymphocyte ratio, MPV: mean platelet volume

respectively. On the other hand, the comparison of the mean scores of NLR, PLR, and MPV values in terms of disease severity levels is presented in Table 3. No statistically significant difference was found between the levels of disease severity in terms of the mean scores of NLR, PLR, and MPV (p>0.05).

Discussion

White blood cell count and sub-parameters are some of the determinants of chronic inflammation. NLR and PLR and MPV, which can be obtained through a simple blood count such as a hemogram, are studied as newer determinants in the evaluation of inflammatory response. In the literature, it is seen that the number of studies on NLR more than others. In addition to neuropsychiatric studies (7, 8, 18), there have been studies in several systemic diseases (19, 20). On the other hand, although many studies have reported that NLR levels are higher in MDD patients (9, 21), results can be vary according to study design. In this study, it was found that there was no significant difference between MDD patients and healthy controls.

There have been studies which reported that PLR level is better in measuring the severity of inflammation than NLR (22, 23). It was determined that psychiatric studies on PLR were mostly in the field of mood disorders. In a meta-analysis study, while PLR levels were higher in bipolar disorder patients, no difference was found in MDD patients (9). Consistent with this, no significant difference was found between MDD patients and healthy controls, in this study.

There is a limited number of studies that reported a significant relationship between MDD and MVP value. According to findings in a study, it has been reported that the MPV value is higher in MDD patients (12). However, in this study, it was found that there was no significant difference between MDD patients and healthy controls in terms of mean score of MPV. Another remarkable finding of this study is that there was no relationship between the severity of depression (mild, moderate, severe) and the levels of NLR, PLR, and MPV. Consistent with this result, it was stated in a study that there was no significant relationship between the severity of depression and NLR, and PLR values (24).

This study has some limitations. The generalizability of the findings is limited due to the fact that the study was single-centered and the sample was comparatively

low. Due to the design of the study, the results obtained reflect a certain time interval and temporal variation could not be evaluated. Another limitation is that the efficacy of the treatment was not evaluated after follow-up with antidepressant treatment. Despite these limitations, the remarkable findings obtained in the present study will be useful for further studies.

Conclusion

To the author's best knowledge, this is the first study to evaluate the NLR, PLR and MPV biomarkers together in comparison with MDD patients and healthy controls. According to the findings, it was found that there was no significant relationship between NLR, PLR and MPV levels and MDD. Additionally, it was determined that there was no relationship between the depression severity and the aforementioned markers. Further studies investigating these and another biomarkers with prospective and larger studies will provide more insight into the inflammatory process in MDD.

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Conflict of Interest Statement
The authors have no conflicts of interest to declare.

Ethical Approval
The study was conducted in line with the principles of the Helsinki Declaration. Ethical approval was obtained from the Ethical Committee of Antalya Training and Research Hospital (decision dated 04.06.2020, and numbered 8/19).

Consent to Participate and Publish
Written informed consent to participate and publish was obtained from all individual participants included in the study.

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Availability of Data and Materials
The data presented in this study are available on request from the corresponding author.

Authors Contributions
SK: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Visualization; Writing-original draft.

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