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ARAŞTIRMA MAKALESİ / RESEARCH ARTICLE

# Increased Neutrophil Count As a Marker of Systemic Inflammation in Patients with Seborrheic Dermatitis: A Retrospective Controlled Study

## Seboreik Dermatitli Hastalarda Sistemik Inflamasyonun Bir Belirteci Olarak Artmış Nötrofil Sayısı: Retrospektif Kontrollü Bir Çalışma

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**ÖZET**

**Amaç:** Bu çalışmanın amacı, seboreik dermatit (SD) tanılı hastalarda ve sağlıklı bireylerden oluşan bir kontrol grubunda inflamatuar parametreleri araştırarak hastalığın şiddetiyle olası ilişkileri değerlendirmektir.

**Gereçler ve Yöntemler:** Şubat ve Ağustos 2023 tarihleri arasında SD tanısına sahip 107 hastanın elektronik tıbbi kayıtları taranmıştır. Hasta grubu ile yaş ve cinsiyet açısından uyumlu 73 sağlıklı birey kontrol grubunu oluşturmuştur. Hastalar ve kontroller tam kan sayımından elde edilen nötrofil sayısı (NEU), lenfosit sayısı (LYM), beyaz kan hücresi sayısı (WBC), trombosit sayısı (PLT), trombosit-lenfosit oranı (PLR) ve trombosit-krit (PCT) ile ortalama trombosit hacmi (MPV)nden oluşan trombosit indeksleri açısından karşılaştırıldı. Her hasta için Seboreik Dermatit Alan ve Şiddet İndeksi (SDAŞİ) skoru ve her hastanın inflamatuar belirteçlerinin yaş ve SDAŞİ skoru ile korelasyonu hesaplanmıştır.

**Bulgular:** Ortalama NEU hasta grubunda sağlıklı kontrol bireylerine kıyasla anlamlı derecede yüksekti, ( 4.51 ± 1.489 x10$^3$/mm$^3$'e karşı 4.09 ± 1.096 x10$^3$/mm$^3$, p=0.038). Tek değişkenli analiz sonuçlarına göre, SD tanısı konan hastalarda NEU, kontrol grubuna kıyasla anlamlı derecede farklıydı (odds oranı, 1.274; %95 güven aralığı, 1.010-1.607, p=0.041). SD'li bireylerin ortalama MPV, NLR, PLR, WBC, NEU, LYM, PLT, ve SII değerleri kontrollere kıyasla daha yüksek olmasına rağmen, bu farklılıklar istatistiksel olarak anlamlı değildi. Hastaların MPV, NLR, PLR, SII, WBC, NEU, LYM, veya PCT değerleri ile yaş veya SDAŞİ skorları arasında anlamlı bir korelasyon bulunmamıştır. Bununla birlikte, PLT ile yaş arasında istatistiksel olarak anlamlı negatif korelasyon saptanmıştır (p=0.008). SDAŞİ skorları yaşla birlikte anlamlı olarak artış göstermiştir (p=0.025).

**Sonuç:** NEU, SD'de inflamatuvar bir belirteç olarak kullanılabilir. Yaş ve PLT arasındaki negatif korelasyon, SD'deki inflamasyon seviyesinin yaşla birlikte azaldığını gösterebilir.

**Anahtar Kelimeler:** İmmunoloji, İnflamatuar parametreler, Nötrofiller, Seboreik dermatit.

**ABSTRACT**

**Objective:** This study aimed to investigate inflammatory parameters in individuals affected by seborrheic dermatitis (SD) and in a control group of healthy subjects to assess potential associations with the severity of the disease.

**Material and Methods:** The electronic health data of 107 patients with SD enrolled between February and August 2023 were scanned. We employed a control group comprising 73 age-and- sex-matched healthy subjects. The patients and controls were compared for neutrophil count (NEU), lymphocyte count (LYM), white blood cell count (WBC), platelet count (PLT) counts, platelet-lymphocyte ratio (PLR) along with thrombocyte indices including platelet-crit (PCT) and mean platelet volume (MPV) measured from CBC. The Seborrheic Dermatitis Area and Severity Index (SDASI) of each patient was determined, and the correlations between each patient's age and SDASI score, and inflammatory markers were calculated.

**Results:** The mean NEU was significantly elevated in the patient group compared with that of the healthy controls, (4.51 ± 1.489 x10$^3$/mm$^3$ versus 4.09 ± 1.096 x10$^3$/mm$^3$, p=0.038). Based on the univariate analysis results, NEU in patients diagnosed with SD was significantly different compared to the control group (odds ratio, 1.274; 95% confidence interval, 1.010-1.607, p=0.041). Although individuals with SD had higher mean MPV, NLR, PLR, WBC, NEU, LYM, PLT, and SII values in comparison to the controls, these differences were not statistically significant. There was no significant correlation between age or SDASI scores in the MPV, NLR, PLR, SII, WBC, NEU, LYM, or PCT of the patients. However, PLT and age had a significant negative correlation (p=0.008). SDASI scores increased significantly with age (p=0.025).

**Conclusion:** NEU can serve as an inflammatory marker in SD. The negative correlation between age and PLT may indicate that the level of inflammation in SD decreases with age.

**Keywords:** Immunology, Inflammatory parameters, Neutrophils, Seborrheic dermatitis.

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## INTRODUCTION

Seborrheic dermatitis (SD) is a chronic disease accompanied by erythematous scaly lesions. Although documented in individuals of all ages, SD is most commonly observed among infants and young adults (1). SD's multifactorial etiopathogenesis includes Malassezia colonization, immunological factors, keratinocyte proliferation and differentiation, and deterioration of the cutaneous barrier. Individuals with this condition show elevated levels of many inflammatory cytokines, including IL-1, IL-2, IL-4, IL-6, IL-10, IL-12, TNF-α, and interferon-γ (2).

A complete blood count (CBC) is an easy-to-access test used to measure a range of inflammatory markers. Neutrophil count (NEU), lymphocyte count (LYM), white blood cell count (WBC), platelet count (PLT) counts, platelet-lymphocyte ratio (PLR) along with thrombocyte indices including platelet-crit (PCT) and mean platelet volume (MPV) measured from CBC, and neutrophil-lymphocyte ratio (NLR) have been documented as inflammatory markers in various chronic inflammatory diseases, including cardiovascular disease, diabetes, psoriasis, and atopic dermatitis (3-5). The Systemic Immune-Inflammation Index (SII) has been useful in determining prognoses in various malignancies, including melanoma, gastrointestinal, and urinary cancers, and Behçet's disease (6,7). Specifically, the SII has recently been found to increase in individuals affected by psoriasis (8). In the current study, we sought to evaluate changes in inflammatory markers and their various correlations with disease severity in individuals affected by SD compared with healthy controls.

## MATERIALS AND METHODS

This retrospective controlled study received approval from the Karatay University Clinical Research Ethical Board (Date: 26.09.2023; Decision no: 2023/004). To determine the number of participants of the groups, a power analysis was conducted. Based on the results, to test the statistical significance at 80%, a 5% (α:0.05) margin of error level, the minimum sample size was determined as n = 73 people in each group. The effect size (d) of the PLR difference between the groups was 0.467, and the standard deviation was 40.7. The sample size was determined utilizing the G*Power 3.0.10 software package (Franz Faul, Universität Kiel, Kiel, Germany).

The electronic health data of 107 patients with SD enrolled between February and August 2023 were scanned. SD cases documented as acute exacerbations in patient records were included in the study. We employed a control group comprising 73 age-and- sex-matched healthy subjects. Smokers and those with a history of chronic inflammation, drug, or alcohol abuse, or both were eliminated from the study. The following characteristics were examined in both the patients and the controls: age, sex, platelet indices (MPV and PCT); and SII from CBC, NLR, PLR, PLT, WBC, NEU, and LYM. NLR was obtained by dividing NEU by LYM (NLR = NEU / LYM), while PLR was obtained by dividing PLT by LYM (PLR = PLT / LYM). The same formula (platelets × neutrophils / lymphocytes) was utilized to create SII values. Finally, each patient's Seborrheic Dermatitis Area and Severity Index (SDASI) score was determined, and the correlations between each patient's age and SDASI score, and inflammatory markers were calculated.

### *Statistical analysis*

SPSS 22.0 statistical software was employed for the statistical analysis (SPSS Inc., Chicago, IL, USA) (9). When comparing the qualitative data for both patients and controls, Pearson's chi-square test was employed. The compatibility of the parameters with normal distribution was analyzed based on the Kolmogorov-Smirnov test. Intergroup comparisons were performed using Student's t-test for normally distributed parameters and the Mann-Whitney U test for non-normally distributed parameters. Spearman's or Pearson's rank correlation coefficients were employed to determine the correlations between the variables. An analysis of univariate logistic regression was employed. Level of significance was determined as $p < 0.05$.

## RESULTS

The research sample consisted of 180 participants. Between 107 patients and 73 healthy controls, there was no statistically significant difference with respect to sex or age (p=0.240 and p=0.162 for sex and age, respectively) (Table 1).

The mean NEU was significantly elevated in the patient group compared with that of the healthy controls (Table 2). Individuals with SD had higher mean MPV, NLR, PLR, WBC, NEU, LYM, PLT, and SII in comparison to the controls, these differences were not statistically significant (Figure 1). The patients' mean SDASI score was 3.42 ± 1.37.

There was no significant correlation between age or SDASI scores in the MPV, NLR, PLR, SII, WBC, NEU, LYM, or PCT of the patients (Table 3). However, PLT and age had a significant negative correlation (p=0.008). Moreover, the SDASI scores increased significantly with age (p=0.025).

Based on the univariate analysis results, NEU in patients diagnosed with SD was significantly different compared

**Table 1.** Mean Ages and Sex of the Patients and Controls

| | | Patients (n = 107) | Controls (n = 73) | p | t/ $\chi^2$ |
|---|---|---|---|---|---|
| Age in years Mean±SD | | 39.04 ± 17.953 | 42.67 ± 15.632 | 0.162 | −1.404 |
| Sex n (%) | | | | | |
| | Female | 49 (45.8%) | 27 (37%) | 0.240 | 1.380 |
| | Male | 58 (54.2%) | 46 (63%) | | |

t: Student's t test, $\chi^2$: Pearson's chi-square test

**Table 2.** Between-Group Comparisons of Inflammatory Blood Parameters

| | Patients (n = 107) | Controls (n = 73) | p[b] | t/z |
|---|---|---|---|---|
| WBC (×10³/mm³) Mean±SD | 7.69 ± 1.626 | 7.24 ± 1.406 | 0.054 | 1.937 |
| MPV (fL) Mean±SD | 10.44 ± 0.881 | 10.37 ± 0.774 | 0.576 | 0.560 |
| PCT[a] (%) Median (IQR) | 0.26 (0) | 0.26 (0) | 0.729[a] | −0.346[a] |
| NEU (×10³/mm³) Mean±SD | 4.51 ± 1.489 | 4.09 ± 1.096 | 0.038 | 2.085 |
| LYM (×10³/mm³) Mean±SD | 2.39 ± 0.706 | 2.35 ± 0.560 | 0.676 | 0.418 |
| PLT[a] (×10³/mm³) Median (IQR) | 251 (75) | 260 (75) | 0.854[a] | −0.184[a] |
| NLR[a] Median (IQR) | 1.92 (1) | 1.65 (1) | 0.235[a] | −1.189[a] |
| PLR Mean±SD | 119.98 ± 43.502 | 118.12 ± 38.488 | 0.769 | 0.295 |
| SIIa Median (IQR) | 462.77 (394) | 441.32 (257) | 0.216[a] | −1.237[a] |
| SDASI score Mean±SD | 3.42 ± 1.37 | NA | NA | NA |

Note. Data are presented as M ± SD. LYM: lymphocyte count, MPV: mean platelet volume, NEU: neutrophil count, NLR: neutrophil-to-lymphocyte ratio, PCT: platelet-crit count, PLR: platelet-to-lymphocyte ratio, SDASI: Seborrheic Dermatitis Area and Severity Index, SII: Systemic Immune-Inflammation Index, WBC: white blood cell count.
[a] Mann–Whitney U test.
[b] p < 0.05 indicates statistical significance.

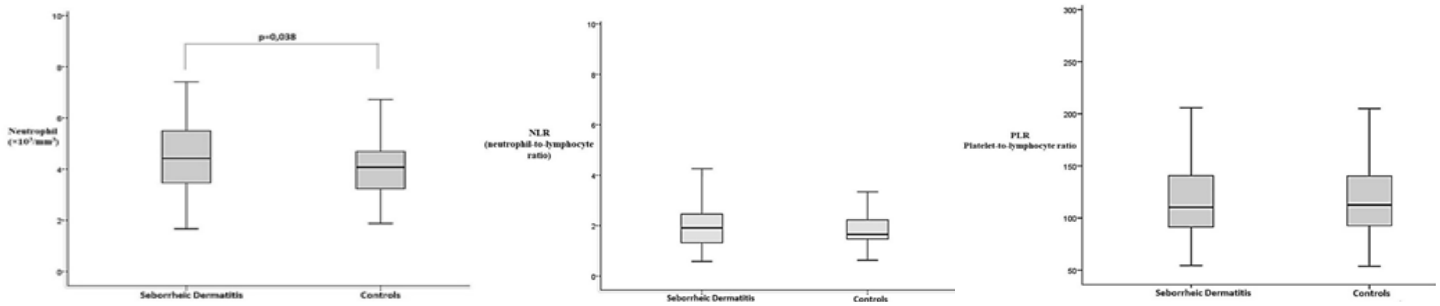


**Figure 1.** Comparison of NEU, NLR, and PLR measurements in patients with seborrheic dermatitis and the control group

**Table 3.** Correlation Coefficients between Age, SDASI Score, WBC, MPV, NEU, LYM, PLR, NLR, SII, PCT, and PLT in the Patient Group

| | Age in years | | SDASI score | |
|---|---|---|---|---|
| | r | p[b] | r | p[b] |
| WBC (×10³/mm³) | −0.039 | 0.691 | −0.083 | 0.394 |
| MPV (fL) | 0.135 | 0.166 | 0.036 | 0.712 |
| NEU (×10³/mm³) | −0.058 | 0.551 | −0.043 | 0.663 |
| LYM (×10³/mm³) | −0.038 | 0.700 | 0.001 | 0.992 |
| PLR | −0.125 | 0.201 | 0.155 | 0.111 |
| NLR[a] | 0.001 | 0.991 | 0.010[a] | 0.921[a] |
| SII[a] | −0.080 | 0.413 | 0.046[a] | 0.635[a] |
| PCTa (%) | −0.176 | 0.069 | 0.157[a] | 0.106[a] |
| PLTa (×10³/mm³) | −0.255 | 0.008 | 0.134[a] | 0.168[a] |
| SDASI score | 0.216 | 0.025 | – | – |

Note. LYM: lymphocyte count, MPV: mean platelet volume, NEU: neutrophil count, NLR: neutrophil-to-lymphocyte ratio, PCT: platelet-crit count, PLR: platelet-to-lymphocyte ratio, PLT: platelet count, SDASI: Seborrheic Dermatitis Area and Severity Index, SII: Systemic Immune-Inflammation Index, WBC: white blood cell count.
Pearson's correlation. [a] Spearman's correlation test was performed for the number sequence test.
[b] p < 0.05 indicates statistical significance.

**Table 4.** Logistic Regression Analysis of NEU Showing Significant Effect on Diagnosis of Seborrheic Dermatitis

| | | 95% CI | | |
|---|---|---|---|---|
| | OR | Lower | Upper | p |
| NEU | 1.274 | 1.010 | 1.607 | 0.041 |
| Constant | 0.517 | | | 0.210 |

Note. CI: confidence interval, NEU: neutrophil count, OR: odds ratio.

**Table 5.** Inflammatory Blood Parameters in Seborrheic Dermatitis

| | Metin et al. (n = 47) | Tosun et al. (n = 100) | Our study (n = 107) |
|---|---|---|---|
| Study design | Prospective case–control study | Retrospective case–control study | |
| Mean age, in years | 35.7 | 35.2 | 39 |
| Male-to-female ratio | 23/24 | 56/44 | 58/49 |
| Blood parameters compared with controls | Elevated NMR | Elevated PLR, MPV, and CRP | Elevated NEU |
| Correlation with SDASI score | LYM and LMR | RDW | - |
| Correlation with age | BMI | CRP | PLT and SDASI |
| Correlation with smoking | NEU | No data on smokers | Smokers excluded |
| Correlation with BMI | WBC, NEU, LYM, ESR, and CRP | Not evaluated | Not evaluated |

Note. BMI: body mass index, CRP: C-reactive protein level, ESR: erythrocyte sedimentation rate, LMR: lymphocyte-to-monocyte ratio, LYM: lymphocyte count, MPV: mean platelet volume, NEU: neutrophil count, NMR: neutrophil-to-monocyte ratio, PLR: platelet-to-lymphocyte ratio, PLT: platelet count, RDW: red cell volume distribution width, SDASI: Seborrheic Dermatitis Area and Severity Index, WBC: white blood cell count.

to the control group. The results of the logistic regression analysis showed that the model was significant (p=0.036). The Nagelkerke R square value was 0.033, and the explanatory coefficient of the model was 55.6%. The effect of NEU on the model showed statistical significance (p=0.041). A one-unit increase in NEU increased the risk of seborrheic dermatitis by 1.274 times (Table 4).

## DISCUSSION

In our study, compared to healthy controls, the mean NEU was significantly elevated in the patients with SD. Moreover, age was negatively correlated with PLT but positively correlated with SDASI scores in the patient group. Neutrophils, which determine immune response during chronic inflammation and can damage tissue, have an essential role in the pathogenesis of inflammatory diseases, including inflammatory bowel disease, atherosclerosis, diabetes, and systemic lupus erythematosus (SLE) (10). Neutrophils have a crucial role in the production of various inflammatory cytokines, including IL-1, IL-6, IL-12, and TNF-α, which are implicated in the development of SD (2,11). Considering that our study included cases of SD with acute exacerbations in which inflammatory activity increased, an elevated mean NEU was expected. Elevated NEU and other inflammatory markers have been documented in cases of inflammatory diseases, including psoriasis and cardiovascular disease. In a study with 2,041 patients, Pinto et al. (12) demonstrated that NEU and monocyte counts were significantly higher in individuals with cardiovascular disease than in controls. In another study (13), ESR, PLT, monocyte counts, and the levels of C-reactive protein (CRP) were also significantly elevated in rosacea cases compared to controls. In another study (14) involving 477 patients with psoriasis, WBC, NEU, PLT, NLR, and PLR were markedly elevated among the participants compared with the control population. Based on these results, the authors proposed that the NLR and PLR can be examined as systemic inflammation markers in psoriasis. However, the inflammatory markers examined in the study did not correlate with disease severity. Some studies suggest that SD may be associated with systemic inflammation and increased cardiometabolic risk (15-17). SD patients often have a higher prevalence of inflammatory markers (TNF-α, IL-6, CRP), dyslipidemia (low HDL, high triglycerides), and metabolic disorders such as insulin resistance and obesity. Additionally, Malassezia-induced inflammation and alterations in lipid metabolism may contribute to endothelial dysfunction, potentially increasing the risk of hypertension and cardiovascular risk. However, further research is needed to clarify these associations.

Only a few studies have investigated inflammatory markers in SD (see Table 5). In Metin et al.'s study (18), the NEU-to-monocyte ratio (NMR) was significantly elevated in SD patients compared to the controls, and both the LYM and lymphocyte-to-monocyte ratio were positively correlated with the SDASI score. The authors suggested that body mass index (BMI) and smoking may trigger SD by causing inflammation. Similarly, in our study, although we did not examine NMR, the significant increase in NEU among the patients compared with the controls indicates the role of chronic inflammation in SD. In Metin et al.'s study (18), patients with systemic disease or chronic medication use that might influence levels of chronic inflammatory markers were not excluded. However, in our study, we excluded patients with conditions that could affect the measurement of inflammatory blood parameters, and our patient sample was larger than in Metin et al.'s study (18) (n = 107 vs. n = 47).

In Tosun et al.'s study (19), PLR, MPV, and CRP were higher among patients with SD than controls, while red cell volume distribution width was positively correlated with SDASI score, and CRP was positively correlated with age. However, in Metin et al.'s study (18), CRP was not correlated with age. Although we did not examine CRP in our study, there was a negative correlation between PLT, a proinflammatory marker and age, which may indicate that the level of inflammation in SD decreases with age. With age, the activity of the sebaceous

glands decreases, which is the first step in SD pathogenesis and may reduce the formation of fatty acids and thus decrease inflammation (1,20). However, as far as we know, no previous research on SD has investigated changes in the inflammatory cytokine response in relation to age. In our study, the significant positive correlation between age and mean SDASI score may have been due to the relationship between age and Malassezia colonization. Previous research has shown that Malassezia colonization increases with age (21) and that Malassezia density and SD disease severity are directly correlated (22).

Platelet indices may vary over the course of chronic inflammatory diseases. For example, MPV increases in low-grade inflammatory diseases, such as psoriasis and Behçet's disease but decreases in high-grade inflammatory disorders, including RA and SLE (23). In our study, the finding that all inflammatory markers except PCT (i.e., NLR, PLR, SII, MPV, WBC, PLT, NEU, and LYM) were higher among patients than the controls, but not significantly so, may have been due to our small sample of patients.

Limitations of our study are as follows: This retrospective study included only patients with regular records in the patient registration system. Therefore, we could not analyze BMI or CRP. However, CRP is an essential indicator of systemic inflammation. In addition, the patients' BMIs may have affected their inflammatory blood parameters (24). The small number of patients was another limitation.

## CONCLUSION

As far as we know, the current study is the first report showing that NEU can serve as an inflammatory marker in SD. Although our sample of patients was small, the negative correlation found between age and PLT may suggest that the level of inflammation in SD decreases with age. Therefore, in future research, prospective trials of large samples are required to elucidate the importance of inflammatory markers in SD.

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