



The effect of systemic therapies on hemogram parameters and C-reactive protein in patients with psoriatic arthritis

Psoriatik artritli hastalarda sistemik tedavilerin hemogram parametreleri ve C-reaktif protein üzerine etkisi

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Abstract

Background and Design: Although some inflammatory markers were elevated in patients with psoriatic arthritis (PsA) compared to healthy controls, are few studies evaluated the effects of systemic treatments for PsA on these markers. The aim of this study is to investigate the changes in hemogram parameters and C-reactive protein (CRP) in PsA patients receiving systemic therapies.

Materials and Methods: In this retrospective study, hemogram parameters, CRP and systemic inflammation indices [neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio, systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI)] of 50 PsA patients were analyzed before and in the third month of the treatments.

Results: While mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and hemoglobin (Hb) were higher in the third month of all treatments compared to the baseline ($p=0.009$, 0.003 , and 0.036 , respectively), platelet, CRP and SII were lower ($p=0.001$, 0.000 , and 0.000 , respectively). In the biological therapy group ($n=21$), platelet, SIRI, and SII were lower, while MCHC was higher in the third month than baseline ($p=0.023$, 0.033 , 0.000 , and 0.003 , respectively). CRP and SII were lower in the third month of the non-biologic treatment group ($n=29$) compared to the baseline, and MCH and mean corpuscular volume (MCV) were higher ($p=0.001$, 0.000 , 0.027 , and 0.044 , respectively). No statistically different changes were recorded in NLR, PLR, and other parameters.

Conclusion: Hb, MCH, and MCHC increased, and platelet, CRP, and SII decreased in the third month of all systemic therapies. MCV was higher in the non-biologic treatment group, and SIRI was lower in the biological treatment group in the third month than baseline. Therefore, these parameters may be useful for monitoring the effects of treatments in PsA.

Keywords: Systemic treatments, biologics, psoriatic arthritis, hemogram parameters, C-reactive protein

Öz

Amaç: Psoriatik artritli (PsA) hastalarda sağlıklı kontrollere göre bazı enflamatuvar belirteçlerde yükseklik olduğu tespit edilmekle beraber PsA'da kullanılan sistemik tedavilerin bu belirteçler üzerine etkisini değerlendiren az sayıda çalışma bulunmaktadır. Bu çalışmanın amacı sistemik tedavi almakta olan PsA hastalarında bu tedavilerin hemogram parametreleri ve C-reaktif protein (CRP) üzerine etkisini incelemektir.

Gereç ve Yöntem: Bu retrospektif çalışmada 50 PsA hastasının tedavi öncesi ve tedavilerinin 3. ayında olmak üzere hemogram parametreleri, CRP ve sistemik enflamasyon indeksleri [nötrofil-lenfosit oranı (NLR), trombosit-lenfosit oranı, sistemik immünoenflamasyon indeksi (SII) ve sistemik enflamasyon yanıt indeksi (SIRI)] analiz edildi.

Bulgular: Ortalama eritrosit hemoglobini (MCH), ortalama eritrosit hemoglobin konsantrasyonu (MCHC) ve hemoglobin (Hb) tüm tedavilerin üçüncü ayında başlangıca göre daha yüksekken (sırasıyla; $p=0,009$, $0,003$ ve $0,036$) trombosit sayısı, CRP ve SII ise daha düşüktü (sırasıyla; $p=0,001$, $0,000$ ve $0,000$). Biyolojik tedavi grubunda ($n=21$) trombosit, SIRI ve SII 3. ayda başlangıca göre daha düşük, MCHC daha yüksekti (sırasıyla; $p=0,023$, $0,033$, $0,000$ ve $0,003$). Biyolojik olmayan tedavi grubunda ise ($n=29$) 3. ayda başlangıca göre CRP ve SII daha düşük, MCH

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ve ortalama eritrosit hacmi (MCV) daha yüksekti (sırasıyla; $p=0,001$, $0,000$, $0,027$ ve $0,044$). NLR, PLR ve diğer parametrelerde istatistiksel olarak anlamlı bir değişiklik izlenmedi.

Sonuç: Tüm sistemik tedavilerle 3. ayda Hb sayısı, MCH ve MCHC artarken trombosit sayısı, CRP ve SII azalmıştır. Ek olarak biyolojik olmayan tedavi grubunda bazale göre tedavilerin 3. ayında MCV daha yüksek iken, biyolojik tedavi grubunda ise SIRI daha düşük bulunmuştur. Bu parametreler tedavilerin PsA'daki etkilerini izlemek için yararlı olabilir.

Anahtar Kelimeler: Sistemik tedaviler, biyolojikler, psoriatik artrit, hemogram parametreleri, C-reaktif protein

Introduction

Psoriasis is a multisystemic chronic inflammatory disease associated with psoriatic arthritis (PsA) at approximately 25%, and its prevalence varies between 0.51 and 11.43 % in the adult population¹. PsA is a heterogeneous disease in the spondylarthritides group that can affect both peripheral and axial joints. PsA has the potential to cause erosive articular involvement and loss of function; therefore, early diagnosis and treatment play an important role^{2,3}.

In recent years, some parameters based on hemogram, including neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), mean platelet volume (MPV), and C-reactive protein (CRP), have been shown as important systemic inflammation indicators and prognostic markers^{4,6}. In addition, systemic immune inflammation index (SII) and systemic inflammation response index (SIRI) are relatively new parameters. They have been used in terms of systemic inflammation and prognosis in various conditions, such as cardiovascular diseases, malignancies, and rheumatologic diseases^{7,9}. Both parameters include three important components of complete blood count (neutrophil, platelet and lymphocyte for SII and neutrophil, monocyte and lymphocyte for SIRI) and seem easily calculable parameters that may provide more information on both systemic inflammation and evaluation of treatment response. Studies have shown that CRP, NLR, PLR, MPV, and SII are higher than healthy controls in PsA^{5,9,10}. It has also been stated that particularly NLR, PLR, and CRP were parameters that can be used to evaluate the effectiveness of various systemic treatments in PsA^{3,11}. To the best of our knowledge, there is no study evaluating the effect of systemic therapies on the change of SII and SIRI in patients with PsA.

This study aims to evaluate the hemogram parameters, NLR, PLR, SII, SIRI, and CRP before and in the third month of the different systemic treatments in patients with PsA.

Materials and Methods

Patients and Study Design

Adult patients diagnosed with PsA according to the Classification Criteria for PsA criteria and followed up in dermatology and rheumatology outpatient clinics for at least six months between January 2021 and July 2022 were included in this cross-sectional retrospectively designed study.

Patients older than 18 years and who had not been receiving any systemic treatment for at least three months were included in the study. Age, sex, duration of disease, presence of psoriasis, hemogram parameters including count of white blood cell (WBC), neutrophil, lymphocyte, monocyte, eosinophil, basophil, platelet, hemoglobin, hematocrit, and value of mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), MPV, CRP,

NLR, PLR, SIRI, and SII values of the patients were obtained from electronic medical records. The data of the patients' laboratory parameters before and in the third month of systemic therapy were analyzed. Patients with another dermatological disease, pregnancy, and lactation were excluded from the study.

The NLR value was calculated by dividing the number of neutrophils by the number of lymphocytes, and the PLR value by dividing the number of platelets by the number of lymphocytes. The SIRI was calculated by multiplying the neutrophil count by the monocyte count divided by the lymphocyte count, and the SII was calculated by multiplying the neutrophil count by the platelet count divided by the lymphocyte count.

The approval of the Uşak University Non-invasive Research Ethics Committee was received [IRB approval status (approval number: 38-38-13, date: 05.01.2023)].

Statistical Analysis

Statistical analysis was carried out using IBM SPSS Statistics 28.0. Continuous data were given as mean \pm standard deviation and median \pm interquartile range (IR). Categorical data were given as a percentage. The paired samples t-test was used to compare the means of two measurements of variables with normal distribution, and the Wilcoxon signed-rank test was used for variables without normal distribution. To test the normal distribution, the Kolmogorov-Smirnov test was used. For statistical significance; $p<0.05$ was accepted as the criterion.

The approval of the Institutional Review Board was received [IRB approval status (approval date and number: 05.01.2023/38-38-13)].

Results

A total of 50 patients, 36 females (72%) and 14 males (28%), were included in the study. The mean age of patients was 48.9 ± 10.56 years. The median disease duration of PsA was four years (IR 7.3). 80% of patients ($n=40$) also had a diagnosis of psoriasis. The non-biological systemic treatments used by the patients were as follows: methotrexate (50%, $n=25$), non-steroidal anti-inflammatory drugs (NSAIDs) (42%, $n=21$), systemic steroid (30%, $n=15$), leflunomide (18%, $n=9$), sulphasalazine (8%, $n=4$), hydroxychloroquine (6%, $n=3$), and colchicine (6%, $n=3$). 42% of patients ($n=21$) were receiving a biologic agent treatment. The biologic agents were adalimumab (20%, $n=10$), secukinumab (10%, $n=5$), ixekizumab (6%, $n=3$), ustekinumab (2%, $n=1$), certolizumab pegol (2%, $n=1$), and infliximab (2%, $n=1$). There were patients in both groups who used various combinations. These combinations were NSAID + systemic steroid ($n=1$), NSAID + sulphasalazine ($n=1$), methotrexate + systemic steroid ($n=7$), methotrexate + NSAID ($n=4$), methotrexate + leflunomide ($n=1$), methotrexate + NSAID + hydroxychloroquine ($n=1$), methotrexate + NSAID + leflunomide ($n=1$), NSAID + sulphasalazine + leflunomide ($n=1$), NSAID + leflunomide + systemic steroid ($n=2$), methotrexate + NSAID + hydroxychloroquine + colchicine ($n=1$), methotrexate + sulphasalazine + hydroxychloroquine

Table 1. Laboratory parameters of patients at baseline and in the third month of their therapies

| Parameter | Baseline* mean ± SD or median (IR) | In the third month** mean ± SD or median (IR) | p value |
|-----------------------------------|---------------------------------------|--|--------------|
| WBC (x10 ³ /μL) | 8.44 (IR 2.97) | 8.07 (IR 2.79) | 0.330 |
| Neutrophil (x10 ³ /μL) | 5.20±2.49 | 5.28±2.49 | 0.881 |
| Lymphocyte (x10 ³ /μL) | 2.47 (IR 1.40) | 2.37 (IR 1.49) | 0.647 |
| Platelet (x10 ³ /μL) | 309 (IR 94) | 285.59±67.47 | 0.001 |
| Monocyte (x10 ³ /μL) | 0.51 (IR 0.28) | 0.48 (IR 0.17) | 0.312 |
| Eosinophil (x10 ³ /μL) | 0.20 (IR 0.17) | 0.20±0.12 | 0.842 |
| Basophil (x10 ³ /μL) | 0.04 (IR 0.03) | 0.04 (IR 0.03) | 0.596 |
| RBC (x10 ⁶ /μL) | 5.79±6.25 | 4.83±0.37 | 0.316 |
| Hemoglobin (g/dL) | 13.61±1.51 | 13.84±1.39 | 0.036 |
| Hematocrit (%) | 42.10 (IR 4.3) | 42.10 (IR 4.3) | 0.220 |
| MCV (fL) | 86.48±5.25 | 86.56±4.76 | 0.098 |
| MCH (pg) | 28.30 (IR 3.1) | 28.64±2.05 | 0.009 |
| MCHC (g/dL) | 32.72±0.90 | 33.07±1.08 | 0.003 |
| RDW (%) | 13.60 (IR 1.8) | 14.10 (IR 2.1) | 0.095 |
| MPV (fL) | 9.32±1.06 | 9.45±1.11 | 0.210 |
| CRP (mg/dL) | 8.50 (IR 15.6) | 2.5 (IR 6.2) | 0.000 |
| NLR | 1.91 (IR 0.67) | 1.98 (IR 1.07) | 0.838 |
| PLR | 129.91 (IR 62.9) | 119.65 (IR 69) | 0.194 |
| SIRI | 1.02 (IR 0.80) | 0.84 (IR 0.71) | 0.581 |
| SII | 7580.26 (IR 5590.47) | 538.66 (IR 398) | 0.000 |

*The number of patients was 50 for CRP, 48 for eosinophil, basophil and RDW and 49 for all other parameters.
**The number of patients was 50 for CRP, 46 for eosinophil and basophil and 49 for all other parameters.
SD: Standard deviation, IR: Interquartile range, WBC: White blood cell, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW: Red cell distribution width, MPV: Mean platelet volume, CRP: C-reactive protein, NLR: Neutrophil lymphocyte ratio, PLR: Platelet lymphocyte ratio, SIRI: Systemic inflammation response index, SII: Systemic immune-inflammation index

+ systemic steroid (n=1), methotrexate + sulphasalazine + NSAID + systemic steroid (n=1), infliximab + leflunomide + methotrexate (n=1), ustekinumab + methotrexate (n=1), adalimumab + NSAID + systemic steroid (n=1), adalimumab + NSAID + methotrexate (n=1), adalimumab + methotrexate (n=1), adalimumab + NSAID (n=1), golimumab + leflunomide (n=1), secukinumab + leflunomide (n=1), secukinumab + NSAID + systemic steroid (n=1) and ixekizumab + NSAID + systemic steroid (n=1).

Fifty-two percent of the patients had at least one comorbid disease, including hypertension (n=11), diabetes mellitus (n=7), coronary artery disease (n=2), hyperlipidemia (n=2), hypothyroidism (n=4), anxiety disorder (n=3), asthma (n=2), Sjögren's syndrome (n=2), systemic sclerosis (n=1), Familial Mediterranean Fever (n=1), Crohn's disease (n=1), ulcerative colitis (n=1), osteoporosis (n=1), polycystic ovary syndrome (n=1), benign prostate hyperplasia (n=1), parathyroid adenoma (n=1), adrenal adenoma (n=1), and nephrolithiasis (n=1).

While MCH, MCHC, and hemoglobin values were higher in the third month of the treatments compared to the baseline, platelet count, CRP, and SII values were found to be lower. The difference between these parameters was statistically significant. The mean or median values of hemogram parameters, including counts of WBC, neutrophil, lymphocyte, monocyte, eosinophil, basophil, platelet, RBC, hemoglobin, hematocrit, and values of MCV, MCH, MCHC, RDW, MPV and CRP, NLR, PLR, SIRI, and SII at baseline and the third month of the systemic therapies, are shown in Table 1.

Forty-two percent of patients (n=21) were under biologic treatments. Platelet counts, SIRI, and SII values were lower, while MCHC value was higher in the third month of the biologic treatments compared to the baseline. The difference between these parameters was statistically significant. The comparison of laboratory parameters at baseline and the third month of treatment in those receiving biologic treatment is shown in Table 2. The results of the same parameters of the patients, who only received conventional systemic therapy, are shown in Table 3. In these patients, platelet counts, CRP, and SII values were lower, while MCH and MCV values were higher in the third month of the conventional systemic treatments compared to the baseline. The difference between these parameters also was statistically significant.

Discussion

Evaluation of inflammation status in inflammatory diseases is important in determining the severity of the disease, predicting the prognosis, and evaluating the treatment response. Therefore, studies are being carried out to identify the biomarkers that can be used safely in the clinic. For example, CRP, a well-known non-specific acute phase reactant, is a widely used biomarker shown to be higher in various inflammatory conditions. Also, in recent years, due to their availability and low cost, hemogram components, including neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, mean platelet volume, and red cell distribution width, have been used to evaluate the status of systemic

Table 2. Laboratory parameters of patients at baseline and the third month of biologic agent therapies

| Parameter | Baseline * mean ± SD or median (IR) | In the third month ** mean ± SD or median (IR) | p value |
|-----------------------------------|--|---|--------------|
| WBC (x10 ³ /μL) | 8.98±2.52 | 9.48±2.59 | 0.120 |
| Neutrophil (x10 ³ /μL) | 5.19±1.55 | 4.85±2.34 | 0.157 |
| Lymphocyte(x10 ³ /μL) | 2.93±1.12 | 2.84±0.98 | 0.891 |
| Platelet(x10 ³ /μL) | 315±113.29 | 281.33±76.26 | 0.023 |
| Monocyte (x10 ³ /μL) | 0.57±0.17 | 0.50±0.11 | 0.453 |
| Eosinophil (x10 ³ /μL) | 0.24±0.11 | 0.24±0.12 | 0.733 |
| Basophil (x10 ³ /μL) | 0.04±0.02 | 0.03±0.01 | 0.543 |
| RBC (x10 ⁶ /μL) | 4.87±0.43 | 4.95±0.35 | 0.614 |
| Hemoglobin (g/dL) | 13.91±1.28 | 14.25±1.29 | 0.081 |
| Hematocrit (%) | 42.37±3.36 | 42.86±3.00 | 0.405 |
| MCV (fL) | 86.12±4.46 | 86.58±4.06 | 0.776 |
| MCH (pg) | 28.58±1.90 | 29.75±1.83 | 0.137 |
| MCHC (g/dL) | 32.79±0.87 | 33.20±1.03 | 0.003 |
| RDW (%) | 14.00 (IR 1.8) | 13.85 (IR 2.1) | 0.546 |
| MPV (fL) | 9.49±1.13 | 9.63± 1.20 | 0.740 |
| CRP (mg/dL) | 4.70 (IR 11.8) | 2.10 (IR 4.4) | 0.065 |
| NLR | 1.72 (IR 0.61) | 1.53 (IR 0.89) | 0.170 |
| PLR | 118.84±54.83 | 110.26±41.63 | 0.172 |
| SIRI | 1.08 (IR 0.68) | 0.76 (IR 0.51) | 0.033 |
| SII | 6274.27 (IR 4711.15) | 434.47 (IR 334.03) | 0.000 |

*The number of patients was 21 for all parameters.
 **The number of patients was 19 for eosinophil and basophil and 21 for all other parameters.
 SD: Standard deviation, IR: Interquartile range, WBC: White blood cell, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MHCH: Mean corpuscular hemoglobin concentration, RDW: Red cell distribution width, MPV: Mean platelet volume, CRP: C-reactive protein, NLR: Neutrophil lymphocyte ratio, PLR: Platelet lymphocyte ratio, SIRI: Systemic inflammation response index, SII: Systemic immune-inflammation index

inflammation in different medical conditions, such as malignancies, infectious diseases, cardiovascular diseases, and rheumatologic diseases^{5,12-14}.

PsA is a progressive and systemic inflammatory disease characterized by peripheral arthritis, axial involvement, enthesitis, and dactylitis due to the infiltration of synovial membranes by immune cells responsible for releasing various pro-inflammatory cytokines. Pro-inflammatory cytokines are responsible for the recruitment and activation of neutrophils and are associated with lymphocyte apoptosis that causes lymphopenia^{9,15}. Platelets are other important cells that play a role in inflammatory responses because they are rich in pro-inflammatory molecules. Mean platelet volume is a parameter that reflects platelet activation^{5,16}. Various studies have shown that NLR, PLR, and MPV are higher in patients with PsA than in controls^{5,9,10,17}. However, only a few studies evaluated the effect of systemic treatments on these parameters in patients with PsA.

In a study with 50 PsA patients treated with infliximab, adalimumab, and ustekinumab, CRP, NLR, platelet, PLR, and MPV values decreased after three months of therapy to be statistically different and at follow-up up to 12 months. These results remained consistent regardless of the treatment used¹¹. Similarly, in a study including psoriasis patients in which PsA was present in approximately 15% of the cases (n=11), CRP, NLR, platelet, PLR, and MPV were found to be significantly lower than baseline in the third and sixth months of etanercept, adalimumab, infliximab, and ustekinumab treatments, regardless of the treatment

option¹⁸. In another study evaluating 100 psoriasis patients, 13% of whom had concomitant PsA, using one of the treatments such as acitretin, narrow-band ultraviolet B, cyclosporin, methotrexate, etanercept, adalimumab and ustekinumab, CRP and NLR values were found to be lower at three months of treatment. The presence of concomitant PsA did not affect these findings¹⁹. Similarly, in another study involving psoriasis patients with PsA, NLR and PLR values were found to be lower than baseline at the end of 1 year of tumor necrosis alpha inhibitor treatment (infliximab, adalimumab, etanercept), regardless of arthritis²⁰. In our study, similar to these studies, CRP and platelet values were found to be statistically significantly lower than baseline in the third month of treatment. However, there was no difference in NLR, PLR, and MPV values. When we grouped the treatments as biologics and non-biologics, we observed that platelets were significantly lower in both groups. CRP was also low in both groups, but this decrease was statistically significant only in the group that did not receive biologics. NLR, PLR, and MPV did not differ significantly in both groups. In a study evaluating the effects of secukinumab in psoriasis patients (number of PsA=8) in the fourth month in terms of these parameters, there was no difference in NLR, PLR, and MPV values similar to our study. Unlike our study, neutrophil counts decreased significantly compared to the baseline in this study, but there was no significant change in platelet count²¹. In another study in which PsA (n=6) patients receiving secukinumab were evaluated,

Table 3. Laboratory parameters of patients at baseline and in the third month of non-biologic treatments

| Parameter | Baseline * mean ± SD or median (IR) | In the third month ** mean ± SD or median (IR) | p value |
|-----------------------------------|--|---|--------------|
| WBC (x10 ³ /μL) | 8.44 (IR 3.64) | 8.42 (IR 3.35) | 1 |
| Neutrophil (x10 ³ /μL) | 5.42 (IR 2.37) | 5.44 (IR 2.61) | 0.539 |
| Lymphocyte (x10 ³ /μL) | 2.14 (IR 0.90) | 2.29 (IR 1.10) | 0.158 |
| Platelet (x10 ³ /μL) | 314.91±51.28 | 288.9±61.28 | 0.018 |
| Monocyte (x10 ³ /μL) | 0.51 (IR 0.28) | 0.45 (IR 0.16) | 0.846 |
| Eosinophil (x10 ³ /μL) | 0.17 (IR 0.10) | 0.17 (IR 0.13) | 0.657 |
| Basophil (x10 ³ /μL) | 0.03 (IR 0.03) | 0.04 (IR 0.02) | 0.982 |
| RBC (x10 ⁶ /μL) | 4.76 (IR 0.78) | 4.76 (IR 0.49) | 0.311 |
| Hemoglobin (g/dL) | 13.38±1.65 | 13.52±1.41 | 0.260 |
| Hematocrit (%) | 40.93±4.34 | 40.94±3.51 | 0.597 |
| MCV (fL) | 85.97±5.84 | 86.55±5.34 | 0.044 |
| MCH (pg) | 28.80 (IR 3.8) | 29.30 (IR 3.3) | 0.027 |
| MCHC (g/dL) | 32.67±0.94 | 32.97±1.13 | 0.208 |
| RDW (%) | 14.03±1.23 | 14.45±1.35 | 0.089 |
| MPV (fL) | 9.18±1.00 | 9.31±1.04 | 0.177 |
| CRP (mg/dL) | 11.70 (IR 17) | 2.60 (IR 11) | 0.001 |
| NLR | 2.06 (IR 1.54) | 2.29 (IR 1.12) | 0.179 |
| PLR | 141.34 (IR 37.21) | 121.42 (IR 90.15) | 0.964 |
| SIRI | 0.94 (IR 0.93) | 0.92 (IR 1.04) | 0.362 |
| SII | 8167.80 (IR 4907.08) | 578.6 (IR 351.83) | 0.000 |

*The number of patients was 29 for CRP, 27 for eosinophil and basophil and 28 for all other parameters.

**The number of patients was 29 for CRP, 27 for eosinophil and basophil and 28 for all other parameters.

SD: Standard deviation, IR: Interquartile range, WBC: White blood cell, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW: Red cell distribution width, MPV: Mean platelet volume, CRP: C-reactive protein, NLR: Neutrophil lymphocyte ratio, PLR: Platelet lymphocyte ratio, SIRI: Systemic inflammation response index, SII: Systemic immune-inflammation index

there was no significant change in CRP, NLR, PLR, and MPV in the sixth month of treatment, similar to our results. However, unlike our study, they did not observe any change in platelet counts³.

In this study, we found the Hb value was lower at baseline than in the third month of treatment. The relationship between Hb and PsA still needs to be well documented. Studies have reported conflicting results comparing patients with psoriasis with controls.^{6,10} In a study by Kim et al.⁶ Hb levels were significantly lower in PsA patients compared with psoriasis patients and controls. Increased burden of systemic inflammation and elevation of oxidative stress may be related to the low levels of Hb²². In a study conducted on patients with rheumatoid arthritis, ankylosing spondylitis, and PsA, compared with the control group, patients receiving golimumab treatment had significantly improved Hb levels similar to our study²³. In another study, although Hb values were found to be lower before secukinumab treatment, no significant change was detected in the sixth month of treatment³.

Our study determined that MCH and MCHC values increased significantly with treatment compared to baseline, and there was an additional increase in MCV values in those who did not receive biological agent treatment. It has been stated that the synergistic activity of hydroxychloroquine and methotrexate was accompanied by an increase in MCV in patients with rheumatoid arthritis and may be a biomarker that can be used to evaluate treatment response²⁴. In another study, it was mentioned that increased MCV by methotrexate might predict clinical response in psoriatic arthritis²⁵. Although clinical

response assessment was not performed in our study, the significant increase in MCV was similar in these studies, especially in the group that received non-biologic treatments. To the best of our knowledge, there is no study evaluating the effect of treatments on MCH change in patients with PsA. In a study evaluating the effect of secukinumab, there was no significant change in MCHC values³. A study that evaluated the changing of MCH and MCHC values after treatment in chronic generalized periodontitis patients reported an increase in these values, similar to our study²⁶. In addition, lower MCH and MCHC were associated with poor prognosis in patients with resected hepatocellular carcinoma and lung cancer and with disease severity in patients with hidradenitis suppurativa²⁷⁻²⁹. So, the lower values of these parameters may be related to chronic inflammation and be potential predictive markers to determine the inflammatory status and treatment response in other chronic inflammatory conditions, such as psoriasis and PsA.

SII and SIRI are relatively novel biomarkers based on complete blood cell counts, including neutrophil, platelet, and lymphocyte for SII and neutrophil, monocyte, and platelet for SIRI. Both indices are shown to be associated with survival and prognosis, especially in cancer patients^{30,31}. SII was also significantly higher than controls in patients with psoriasis and PsA, and significant positive correlations were shown between SII and disease activity of PsA^{9,32,33}. Nevertheless, to the best of our knowledge, no study evaluated the effects of treatments on the SII and SIRI in patients with psoriasis or PsA. In our study, SII was significantly lower than baseline regardless of treatment type. Also, it

was demonstrated that SIRI was lower in patients receiving biological treatment, and the difference was statistically significant. In a study where acne patients received systemic isotretinoin treatment, SII and SIRI were lower in the third month of the treatment, similar to our study³⁴. SII and SIRI have also been associated with an increased risk of developing cardiovascular disease. Therefore, the results obtained in our study supported that systemic treatments may have positive effects on reducing the development of cardiovascular disease in PsA patients, indirectly consistent with literature studies^{35,36}.

Study Limitations

The limitations of our study are retrospective design, lower number of patients, not excluding comorbidities that may be associated with systemic inflammation, not evaluating the effects of the treatments on laboratory parameters on follow-up period after three months, and not evaluating the disease severity clinically.

Conclusion

In this study, it was observed that Hb, MCH, and MCHC values increased and platelet count, CRP, and SII values decreased significantly in the third month of the treatments, including biologics and non-biologics in PsA patients. Additionally, MCV was found to be higher in patients who received non-biologic treatment, and SIRI was found to be lower in patients who received biologics. However, further studies are needed to confirm the clinical utility of these easily calculated and simple parameters.

Ethics

Ethics Committee Approval: The approval of the Uşak University Non-invasive Research Ethics Committee was received [IRB approval status (approval number: 38-38-13, date: 05.01.2023)].

Informed Consent: Retrospective study.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: S.K.Y., Design: S.K.Y., Data Collection or Processing: S.K.Y., A.Y., Analysis or Interpretation: S.K.Y., N.D.Ö., Literature Search: S.K.Y., Writing: S.K.Y., N.D.Ö., A.Y.

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