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Neutrophil-to-Lymphocyte Ratio, Neutrophil-to-Monocyte Ratio, Platelet-to-Lymphocyte Ratio, and Systemic Immune-Inflammation Index in Psoriasis Patients: Response To Treatment With Biological Drugs

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Keywords: psoriasis; neutrophil/lymphocyte ratio; platelet/lymphocyte ratio; neutrophil/monocyte ratio; systemic immune-inflammation index

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Neutrophil-to-Lymphocyte Ratio, Neutrophil-to-Monocyte Ratio, Platelet-to-Lymphocyte Ratio, and Systemic Immune-Inflammation Index in Psoriasis Patients: Response To Treatment With Biological Drugs

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Abstract: Background: Psoriasis is a chronic immune-mediated skin disease in which systemic inflammation plays an important role in the pathogenesis. In recent years, neutrophil-to-lymphocyte ratio (NLR), neutrophil-to-monocyte ratio (NMR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) have been shown to be important indicators of inflammation. In this study, our aim is to investigate NLR, NMR, PLR, and SII levels in psoriasis patients treated with biologic agents. **Method:** Clinical and biochemical data of 209 patients who received systemic therapy for psoriasis were obtained by retrospectively reviewing their medical records. NLR, NMR, PLR, and SII values were calculated from the hemogram values of the patients. **Results:** In the third month of follow-up, the mean CRP, NLR, NMR, PLR, and SII values were significantly decreased compared to the baseline values. SII values showed strong positive correlations with NLR, NMR and PLR. Adalimumab, etanercept, and infliximab, which are TNF-α blockers, were observed to be more effective on PLR and NLR and especially NMR. **Conclusion:** NLR, NMR, PLR, and SII, which are data obtained from routine blood tests, can be used in the monitoring of treatment of psoriasis, especially with TNF- α blockers.

Keywords: psoriasis; neutrophil/lymphocyte ratio; platelet/lymphocyte ratio; neutrophil/monocyte ratio; systemic immune-inflammation index

Introduction

Psoriasis is a chronic systemic inflammatory disease that can affect the skin and/or joints, affecting 2-3% of the world's population [1]. As in many inflammatory diseases, it is important to determine the severity of the disease for safe and effective treatment. As there is no single tool that can fully assess the severity of psoriasis, the assessment of the disease becomes more complex [2]. The psoriasis area severity index (PASI), which evaluates the degree of induration, erythema, and desquamation in the affected body parts, is one of the most commonly used scales since 1978 [3]. In cases where PASI cannot be performed, body surface area (BSA) distribution percentage is another simple scale used. In addition, parameters used in routine blood tests such as CRP, cytokines, and adhesion molecules in psoriasis patients were also used to evaluate disease activity [4-6]. However, new parameters are required due to the lack of objective evaluation criteria, insufficient evaluation of chronic inflammation causing disease, and differences among clinicians.

Due to the role of inflammation in the pathogenesis of psoriasis and the increase in our knowledge about cytokines, interleukins, and serum autoantibodies over time, better markers for the diagnosis and severity of psoriasis are available. Therefore, identification of widely used and low-cost biomarkers of systemic inflammation that play a role in the pathogenesis of psoriasis, in addition to the clinical data of the patients, may be useful for the evaluation of psoriasis patients. Recently, many indexes related to systemic inflammation from routine complete blood count (CBC) tests have been used because of their ability to predict outcomes in pathological conditions [7]. Platelet-to-lymphocyte ratio (PLR), Neutrophil-to-lymphocyte ratio (NLR), and Neutrophil-to-monocyte ratio

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(NMR), which can be easily measured as a part of routine CBC, are widely used in chronic inflammatory diseases as simple markers of systemic inflammatory response [5,8]. Studies have investigated the use of PLR, NLR, and NMR as markers of systemic inflammation in rheumatoid arthritis, ulcerative colitis, acute coronary syndrome, diabetes mellitus, end-stage renal disease, tuberculosis, familial Mediterranean fever, and cirrhosis [8-13]. In addition, there are studies using PLR and NLR to determine prognosis in cancer patients [14]. There are studies suggesting that PLR and NLR are increased in psoriasis patients compared to controls, and therefore they can be easy and inexpensive markers for psoriasis patients [15-17]. Similar to PLR and NLR, there are studies showing that systemic immune inflammation index (SII), another marker obtained from routine CBC, can be used as an effective prognostic factor in diseases where chronic inflammation is causative [18].

The immune axis of tumor necrosis factor (TNF)-α/interleukin (IL)-23/IL-17 is involved in the pathogenesis of psoriasis. Therefore, biologics targeting these cytokines have been used in the treatment of psoriasis in recent years [19]. Although TNF-α inhibitors show high efficacy against rash, their effects on PLR, NMR, NLR and SII, which are the markers of the inflammatory reaction, have not been adequately studied. In other words, the answer to whether PLR, NLR, NMR, and SII can be biomarkers for the efficacy of TNF-α inhibitors has not been fully elucidated. Therefore, our aim in this retrospective study is to investigate the effects of the TNF- α blockers adalimumab, etanercept, and infliximab, and the IL-17A antagonist ustekinumab, secukinumab, and ixekizumab as well as acitretin and methotrexate, which are used in the treatment of psoriasis, on PLR, NLR, NMR, and SII in psoriasis patients, and to seek answers to the question of whether these parameters can be biomarkers of treatment efficacy for these drugs.

Material methods

This retrospective study was carried out on patients who were followed up and treated with the diagnosis of psoriasis between 2015-2021 in the Dermatology outpatient clinic of Namık Kemal University Faculty of Medicine. The study protocol was approved by the Namık Kemal University Ethical commity (identifiers: Clinical Ethical Approval No: 2021.39.02.02). Patients aged 18 years and older with a diagnosis of psoriasis and who had received systemic treatment for psoriasis were included in the study. Patients under 18 years of age, with malignant tumor, active infection or any systemic inflammatory disease, and patients whose hematological data could not be obtained were excluded from the study.

Using hospital information, age, gender, disease duration, PASI values, treatments applied to the patients, and hematological values were recorded. In hemogram tests, erythrocytes, hemoglobin, hematocrit, mean erythrocyte volume (MCV), mean erythrocyte hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red blood cell distribution width (RDW), white blood cell (WBC) counts, neutrophil counts, lymphocyte counts, eosinophil counts, basophil counts, monocytes counts, platelets counts, mean platelet volume (MPV), platelet distribution width (PDW), CRP, and erythrocyte sedimentation rate (ESR) were recorded. NLR was obtained by dividing the neutrophil count by the lymphocyte count, the NMR by dividing neutrophil count by the monocyte count, and the PLR was obtained by dividing the platelet count by the lymphocyte count. SII was calculated with the formula of neutrophil (N) x platelet (P)/lymphocyte (L) (SII=N x P/L ratio) and recorded.

In addition, the systemic treatments (methotrexate, adalimumab, acitretin, ustekinumab, etanercept, secukinumab, ixekizumab, and infliximab) taken by the patients were recorded and hematological values were compared according to the treatment groups.

Statistical analysis was performed using SPSS 20 statistical software. Shapiro-Wilk test was used to evaluate the suitability of the measured data to the normal distribution. The mean, standard deviation, median, minimum, and maximum values of continuous variables, and n and percentage values of categorical variables were given. One way ANOVA test was used for the analysis of normally distributed data in the comparison between groups, and the Kruskal-Wallis test was used for data that did not show normal distribution. Friedman test was used to compare repeated measurements. If there was a difference between the measurements, Wilcoxon test was used for pairwise comparison. Spearman's test was performed for the correlation of hematological parameters. For all statistics, $p < 0.05$ was determined to be significant

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Results

The demographic characteristics of all participants included in the study are shown in Table 1. The mean age of the participants was 42.40±13.01 years, the mean PASI value was 11.76±6.42, and the mean time post-onset was 13.73±10.27 years. Of the 209 participants, 129 were male and 80 were female. 64 patients were using methotrexate, 43 patients were using acitretin, 40 patients were using ustekinumab, and 26 patients were using adalimumab.

The change in hematological values of the participants over time with treatment is shown in Table 2. In the 3rd month of follow-up, mean RBC, neutrophil, platelet, CRP, ESR, NLR, NMR, PLR, and SII values decreased significantly compared to baseline values, while mean MCV, RDW, lymphocyte, monocyte, MPW, and PDW values increased significantly compared to baseline values. In the sixth month of follow-up, the mean RBC, HCT, neutrophil, NLR, and PLR values increased significantly compared to the third month. However, although NMR and PLR increased, they were still significantly lower than baseline. While the mean MCH, WBC, monocyte, PDW, CRP, ESR and NMR values decreased significantly at the sixth month of the follow-up compared to the third month, the mean MCH, CRP, ESR and NMR values at the sixth month were still significantly different from the baseline values.

Adalimumab, acitretin, etanercept, and infliximab significantly decreased NMR at the third month of treatment compared to baseline values, while all biologics used in the treatment significantly decreased NMR at the sixth month of treatment compared to baseline values. Adalimumab, acitretin, etanercept, and infliximab significantly decreased PLR at the third month of treatment compared to baseline values, while infliximab, ustekinumab, and adalimumab significantly decreased PLR at the sixth month of treatment compared to baseline values. Adalimumab and infliximab significantly decreased NLR at the third month of treatment compared to baseline values, while only adalimumab significantly decreased NLR at the sixth month of treatment compared to baseline values. Adalimumab treatment alone decreased the SII values at both the third and sixth months of treatment compared to the baseline values.

There was no difference between the treatment agents in terms of NLR-NLR3, NLR-NLR6, NMR-NMR3, NMR-NMR6, PLR-PLR3 and PLR-PLR6 changes (Table 4).

Correlations of NLR, NMR, and PLR with other parameters are given in Table 5. NLR had a weak positive correlation with PASI and CRP and a strong positive correlation with NMR and PLR. SII showed a weak positive correlation with PASI and CRP, and a strong positive correlation with PLR, NMR, and NLR. No significant correlations were observed in terms of other parameters.

Table 1. Demographic and clinical data of the participants.

		Psoriasis vulgaris
Gender	Male	129 (%61.7)
	Female	80 (%38.3)
Nail Psoriasis	No	10 (%18.5)
	Yes	44 (%81.5)
Joint involvement	No	8 (%20)
	Yes	32 (%80)
Biological agent	Metotrexate	64 (%30.6)
	Adalimumab	26 (%12.4)
	Asitretin	43 (%20.6)
	Ustekinumab	40 (%19.1)
	Etanercept	13 (%6.2)
	Secukinumab	9 (%4.3)
	Ixekizumab	6 (%2.9)
	Infliximab	8 (%3.8)
Age (Year)		42.40±13.01, 42 (18-69)
Time post-onset (Year)		13.73±10.27, 11.5 (1-52)
PASI		11.76±6.42, 10 (3.2-36)

Table 2. Comparison of the changes in hematological values of the participants over time.

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	Pre-treatment	After treatment (3rd month)	After treatment (6th month)
RBC	4.75±0.47 4.73 (3.7-6.5)	4.68±0.63[a] 4.65 (1-7)	4.81±1.04[b] 4.70 (3-15)
HGB	14.26±1.53 14.234(9.00-18.87)	14.24±1.68 14.40 (10-20)	14.21±1.45 14.20 (10-17)
HCT	42.67±4.23 42.80 (30.50-56.50)	42.49±4.77 42.60 (31-60)	43.14±5.67[b] 42.70 (33-88)
MCV	90.09±6.48 91.00 (60.0-106.0)	90.64±7.03 92.00 (59-106)	90.46±8.63 91.00 (30.104)
MCH	23.30±12.80 29.80 (0.00-34.20)	30.37±2.52[a] 30.82 (19.00-35.00)	30.19±2.52[a, b] 30.52 (20-35)
MCHC	33.45±1.10 33.45 (29.0-35.83)	33.52±1.05 33.54 (30.00-36.00)	33.05±1.92[a, b] 33.10 (16-36)
RDW	13.87±1.53 13.55 (11.0-19.30)	14.23±2.48[a] 13.60 (12.00-32.00)	13.84±1.95 13.60 (4-21)
WBC	7.75±2.02 7.55 (393-15.31.)	8.18±4.70 4.50 (2.00-59.00)	7.72±1.92[b] 7.60 (4-13)
Neutrophil	4.95±4.63 4.38 (2.00-60.40)	4.44±1.53[a] 4.16 (1.00-9.00)	4.96±3.63[b] 4.38 (2-31)
Lymphocyte	2.37±1.10 2.27 (0.96-13.70)	2.44±0.70[a] 2.30 (1.00-5.00)	2.42±1.17[a] 2.30 (1-13)
Monocyte	0.57±0.18 0.55 (0.20-1.32)	0.61±0.20[a] 0.58 (0.00-1.00)	0.59±0.24[b] 0.56 (0-2)
Eosinophil	0.20±0.12 0.17 (0.04-0.85)	0.20±0.10 0.19 (0.00-1.00)	0.21±0.11 0.17 (0-1)
Basophil	0.03±0.02 0.03 (0.00-0.11)	0.03±0.02 0.03 (0.00-0.12)	0.03±0.02 0.03 (0-0.1)
Platelet	265.80±62.84 259.50 (114.0-408.0)	254.86±69.48[a] 246.00 (71.00-442.00)	254.07±66.63[a] 250.00 (8-417)
MPV	8.79±0.78 8.80 (7.0-11.0)	8.93±.093[a] 8.80 (6.90-14.50)	8.89±0.84[a] 8.80 (6-12)
PDW	14.86±2.55 15.00 (0.0-22.50)	15.24±2.58[a] 15.00 (2.00-22.00)	15.01±2.61[b] 14.80 (0-22)
CRP	5.34±9.21 2.65 (0.0-75.0)	4.96±6.45[a] 2.24 (0.40-29.70)	4.88±7.82[a, b] 2.49 (0-48)
ESR	17.52±18.02 12.0 (1.0-107.0)	13.28±12.44[a] 9.00 (1.00-60.00)	13.50±12.06[a. b] 9.70 (1-51)
NLR	2.21±1.54 1.88 (0.44-17.46)	1.91±0.73[a] 1.85 (0.72-4.55)	2.26±1.79[b] 1.88 (0.44-14.25)
NMR	8.83±5.60 8.01 (2.98-64.26)	7.56±2.42[a] 7.34 (2.46-14.93)	2.42±1.17[a.b] 2.30 (0.59-13.40)
PLR	121.78±40.25 117.17 (23.43-276.24)	111.60±42.81[a] 103.33 (46.86-323.46)	114.57±42.56[a.b] 110.31 (12.88-253.10)
SII	594.76±445.61 500.15 (94.28-4992.60)	504.06±281.31[a] 427.42 (111.26-1644.34)	576.96±455.22[a] 469.96 (26.92-3316.60)

[a] indicates that it is significant when compared with the baseline value.[b] indicates that it is significant when compared with the 3rd month value.

Table 3. Comparison of clinical parameters according to the biologics used in the treatment.

	Pre-treatment	After treatment (3rd month)	After treatment (6th month)

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RBC	Metotrexate	4.78±0.38 4.75 (3.7-6.2)	4.57±0.34 [a] 4.68 (3.8-5.6)	4.69±0.34 [a,b] 4.81 (3.9-5.8)
	Adalimumab	4.69±0.40 4.75 (4.0-5.6)	4.79±0.59 4.68 (3.9-6.7)	4.76±0.48 4.81 (3.8-6.4)
	Asitretin	4.78±0.40 4.75 (3.8-5.9)	4.80±0.37 4.68 (4.2-6.0)	5.05±1.53 4.81 (4.3-14.7)
	Ustekinumab	4.64±0.35 4.75 (3.8-5.5)	4.68±0.38 4.68 (4.2-5.6)	4.81±0.32 [a,b] 4.81 (4.0-5.4)
	Etanercept	4.74±0.34 4.75 (4.1-5.6)	4.43±1.02 [a] 4.68 (1.0-5.1)	4.83±0.28 4.81 (4.3-5.6)
	Secukinumab	4.97±0.65 4.75 (4.4-6.6)	4.91±0.71 4.68 (4.1-6.5)	4.87±0.55 4.81 (4.2-6.2)
	Ixekizumab	4.88±0.40 4.77 (4.3-5.5)	4.78±0.44 4.77 (4.2-5.4)	4.63±0.25 4.77 (4.2-4.8)
	Infliximab	4.76±0.26 4.75 (4.3-5.3)	4.55±0.42 [a] 4.68 (3.6-5.1)	4.65±0.62 4.81 (3.2-5.4)
HGB	Metotrexate	14.34±1.35 14.26 (10.82-18.87)	14.11±1.23 14.24 (10.6-17.7)	14.13±1.15 [a] 14.20 (10.5-17.2)
	Adalimumab	14.01±1.29 14.22 (11.21-16.90)	14.33±1.57 14.24 (11.1-19.87)	14.14±1.18 14.20 (11.4-16.7)
	Asitretin	14.38±1.56 14.35 (9.0-16.52)	14.55±1.09 14.24 (12.2-17.2)	14.37±0.84 14.20 (12.4-17.2)
	Ustekinumab	14.23±1.04 14.26 (11.54-16.60)	14.32±1.53 14.24 (10.-17)	14.46±1.32 14.20 (10.6-16.7)
	Etanercept	14.19±1.18 14.26 (11.85-16.58)	13.99±1.28 14.24 (11.9-16.4)	14.04±0.81 14.20 (11.9-15.3)
	Secukinumab	13.80±1.95 14.10 (10.17-16.68)	13.50±2.12 14.22 (9.8-15.9)	13.74±1.54 14.20 (11.6-15.7)
	Ixekizumab	14.76±1.90 14.59 (11.56-16.75)	14.65±1.72 14.61 (12.6-16.7)	13.81±0.45 13.92 (13.1-14.2)
	Infliximab	14.21±0.59 14.26 (12.90-15.0)	13.75±1.24 [a] 14.24 (10.7-14.4)	13.86±1.15 14.20 (11.2-15.1)
HCT	Metotrexate	43.00±3.75 42.67 (32.90-56.50)	42.07±3.45 [a] 42.48 (33.1-53.0)	42.78±3.10 43.14 (33.2-50.6)
	Adalimumab	42.00±3.85 41.80 (34.40-51.60)	43.03±5.00 42.48 (34.0-59.8)	42.86±3.48 43.14 (35.2-52.5)
	Asitretin	43.13±4.10 43.40 (30.50-50.60)	43.25±3.39 42.48 (34.7-51.9)	44.54±7.18 43.14 (38-88)
	Ustekinumab	42.29±2.83 42.67 (35.40-48.40)	42.78±4.09 42.48 (31.9-49.8)	43.76±3.57 [a,b] 43.14 (33.3-51.4)
	Etanercept	42.52±3.52 42.67 (36.80-50.10)	41.80±3.12 42.48 (35.8-46.4)	41.98±2.90 43.14 (34.9-45.2)
	Secukinumab	41.17±4.96 42.10 (31.60-47.30)	40.51±5.14 42.30 (3.05-46.8)	41.09±3.91 42.5 (35.0-45.6)
	Ixekizumab	43.48±5.01 43.40 (35.70-49.80)	43.44±4.65 43.19 (38.3-49.0)	41.73±1.57 41.97 (39.8-43.1)
	Infliximab	42.50±1.68 42.67 (38.70-44.60)	40.91±3.83 [a] 42.48 (31.5-42.5)	42.12±3.66 [b] 43.14 (33.2-45.0)
MCV	Metotrexate	90.82±5.22 90.09 (73-103)	92.17±5.08 [a] 91.00 (78.0-103.0)	91.98±4.83 [a] 90.45 (78-104)
	Adalimumab	90.40±6.15 90.09 (80-101)	90.72±7.03 90.63 (76-106)	91.50±6.15 90.45 (81-103)

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	Asitretin	89.89±4.78 90.09 (73.0-100.0)	89.72±3.33 90.63 (78-98)	88.84±9.72 90.45 (29.9-99.0)
	Ustekinumab	91.42±5.25 90.09 (80.0-106.0)	90.95±5.29 90.63 (73-101)	90.52±5.54 90.45 (73-102)
	Etanercept	89.96±3.68 9.09 (82.0-99.0)	90.52±2.73 90.63 (85-96)	88.59±3.65 [b] 90.45 (81.0-93.0)
	Secukinumab	83.34±11.18 87.00 (60-95)	82.55±12.00 75.00 (59-95)	84.87±10.05 90.00 (63.0-93.0)
	Ixekizumab	89.00±8.17 90.50 (74-97)	90.93±6.60 91.50 (79-99)	90.39±3.18 90.45 (85.0-95.0)
	Infliximab	89.68±2.39 90.09 (84-92)	89.89±4.40 90.63 (81-97)	91.91±5.84 90.45 (83.0-103.0)
MCH	Metotrexate	24.02±12.35 29.92 (0.0-33.7)	30.91±1.76 [a] 30.89 (25.8-34.2)	30.49±1.66 [a,b] 30.19 (25.2-33.7)
	Adalimumab	24.40±12.34 29.79 (0.0-34.10)	30.24±2.42 30.37 (24.6-34.2)	30.33±2.29 30.19 (26.2-35.2)
	Asitretin	25.74±10.67 30.14 (0.0-32.94)	30.19±1.12 30.37 (26.4-32.6)	30.13±1.33 30.19 (25.7-33.9)
	Ustekinumab	21.72±14.49 30.21 (0.0-34.20)	30.44±2.11 [a] 30.37 (22.8-34.8)	30.04±2.14 [b] 30.19 (23.2-34.7)
	Etanercept	16.12±15.60 26.40 (0.0-32.86)	30.26±1.48 [a] 30.37 (26.9-33.9)	29.83±1.65 [a] 30.19 (25.3-31.8)
	Secukinumab	24.59±10.14 28.24 (0.0-33.74)	27.56±4.47 29.04 (19.2-32.4)	28.44±3.88 30.19 (20.3-31.9)
	Ixekizumab	30.27±3.36 30.77 (23.88-33.88)	30.61±2.62 30.76 (25.9-33.7)	30.18±1.42 30.19 (27.8-32.2)
	Infliximab	11.14±15.39 0.00 (0.0-30.60)	30.22±0.87 [a] 30.37 (28.3-31.5)	30.50±1.89 [a] 30.19 (27.8-34.7)
MCHC	Metotrexate	33.38±0.83 33.45 (31-35.14)	33.55±0.84 33.51 (30.0-35.9)	33.04±0.99 [b] 33.04 (30.8-35.6)
	Adalimumab	33.43±1.04 33.45 (30.58-35.16)	33.31±0.87 33.51 (31.0-35.0)	33.04±1.12 33.04 (30.5-35.1)
	Asitretin	33.39±1.31 33.45 (29-35.83)	33.65±0.72 33.51 (32.0-36.1)	32.75±2.70 [a,b] 33.04 (15.-35.2)
	Ustekinumab	33.66±0.84 33.53 (31.86-35.51)	33.47±1.00 33.51 (31.2-36.0)	33.04±0.89 [a] 33.04 (30.9-34.8)
	Etanercept	33.39±0.50 33.45 (32.20-34.17)	33.48±0.73 33.51 (31.8-35.3)	33.53±1.05 33.04 (31.0-34.9)
	Secukinumab	33.45±1.03 33.45 (32.22-35.33)	33.24±1.40 32.76 (31.3-35.2)	33.43±0.82 33.27 (32.3-34.5)
	Ixekizumab	33.92±1.32 34.27 (32.35-35.15)	33.68±0.43 33.70 (33.0-34.1)	33.18±0.47 33.04 (32.5-33.9)
	Infliximab	33.40±0.17 33.45 (33.00-33.60)	33.64±0.64 33.51 (32.6-34.9)	33.06±0.50 [b] 33.04 (32.0-33.7)
RDW	Metotrexate	13.74±1.32 13.78 (11.4-18.8)	14.52±1.58 [a] 14.22 (11.8-20.5)	13.93±1.17 [b] 13.83 (11.8-18.0)
	Adalimumab	14.56±1.61 14.15 (11.90-18.30)	14.31±1.53 14.22 (11.9-19.8)	14.09±1.53 13.83 (11.7-18-9)
	Asitretin	13.43±1.21 13.5 (11-17)	14.20±1.97 [a] 14.22 (12.5-25.7)	13.60±1.18 13.83 (7.4-16.1)
	Ustekinumab	13.77±1.04 13.87 (11.50-17.10)	13.78±1.50 13.70 (11.8-20.9)	13.76±2.33 13.83 (4.4-20.6)

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	Etanercept	13.92±0.86 13.87 (12.40-15.70)	13.93±1.12 14.22 (12.1-16.6)	13.50±1.02 13.83 (11.6-15.9)
	Secukinumab	14.50±1.40 14.90 (11.80-17.00)	14.43±1.88 14.60 (11.9-18.3)	14.14±1.99 13.83 (12.7-19.3)
	Ixekizumab	13.91±2.79 13.30 (11.0-19.3)	14.20±2.90 13.25 (11.8-19.9)	13.85±0.85 13.83 (12.5-15.2)
	Infliximab	14.19±0.51 13.87 (13.87-15.00)	13.87±0.90 14.22 (11.7-14.5)	14.19±1.27 13.83 (12.4-16.7)
WBC	Metotrexate	7.67±1.73 7.73 (4.5-14.7)	7.76±1.68 8.17 (3.9-13.4)	7.44±1.17 7.71 (4.2-10.7)
	Adalimumab	8.14±2.25 7.75 (4.24-13.70)	8.35±20.6 8.17 (5.3-14.3)	7.89±1.63 7.71 (4.0-11.8)
	Asitretin	7.30±2.07 6.87 (3.93-15.31)	7.90±1.39 [a] 8.17 (4.8-12.1)	7.59±1.49 7.71 (4.2-12.7)
	Ustekinumab	7.90±1.55 7.25 (4.80-12.60)	8.01±1.80 8.17 (2.2-11.4)	8.09±1.91 7.71 (5.0-12.8)
	Etanercept	7.72±0.92 7.75 (5.40-9.49)	7.68±1.30 8.17 (5.3-10.8)	7.43±1.14 7.71 (6.1-10.7)
	Secukinumab	7.38±1.44 7.75 (5.50-9.50)	13.21±17.04 8.11 (4.3-58.5)	8.09±1.62 8.54 (4.4-9.9)
	Ixekizumab	9.44±1.37 9.37 (7.75-11.55)	8.18±1.24 8.43 (6.3-9.7)	7.67±1.24 7.71 (6.2-9.9)
	Infliximab	7.87±0.67 7.75 (7.10-9.45)	7.67±1.09 8.17 (5.0-8.2)	8.26±0.93 7.71 (7.7-10.0)
Neutrophil	Metotrexate	4.58±1.37 4.64 (2.48-10.80)	4.46±1.23 4.43 (2.2-8.6)	5.01±3.45 4.96 (2.4-31.2)
	Adalimumab	5.10±2.01 4.95 (2.0-10.0)	4.58±1.39 4.43 (2.4-8.3)	4.59±1.27 4.84 (2.4-7.8)
	Asitretin	4.32±1.39 4.25 (2.06-8.54)	4.38±1.03 4.43 (0.9-8.5)	4.66±1.34 4.96 (2.1-10.9)
	Ustekinumab	6.14±8.86 4.95 (2.54-60.40)	4.54±1.53 [a] 4.43 (0.9-8.5)	5.57±4.41 [b] 4.96 (1.8-30.9)
	Etanercept	4.70±0.86 4.95 (2.80-6.40)	4.30±1.10 4.43 (2.5-7.4)	4.94±1.27 4.96 (3.0-7.8)
	Secukinumab	4.53±1.04 4.95 (2.77-6.05)	4.12±1.48 4.28 (1.8-7.0)	5.08±1.11 [b] 4.96 (2.8-6.7)
	Ixekizumab	6.05±1.80 6.06 (4.12-8.90)	4.59±1.21 4.32 (3.5-6.8)	4.97±0.78 4.96 (3.9-6.3)
	Infliximab	5.12±0.77 4.95 (3.94-6.68)	4.22±0.70 [a] 4.43 (2.8-5.2)	5.07±0.17 [b] 4.96 (5.0-5.5)
Lymphocyte	Metotrexate	2.53±1.50 2.37 (1.22-13.70)	2.33±0.55 2.44 (1.1-3.8)	2.27±0.46 2.42 (0.8-3.4)
	Adalimumab	2.24±0.56 2.34 (0.96-3.27)	2.76±0.69 [a] 2.73 (1.4-4.3)	2.54±0.55 [a] 2.42 (1.1-3.6)
	Asitretin	2.22±0.68 2.17 (1.35-5.39)	2.42±0.46 [a] 2.44 (1.5-4.5)	2.34±0.60 2.42 (0.6-4.4)
	Ustekinumab	2.39±0.51 2.37 (1.15-4.13)	2.48±0.54 2.44 (0.9-4.0)	2.78±1.77 2.42 (1.7-13.4)
	Etanercept	2.39±0.31 2.37 (1.72-3.10)	2.35±0.26 2.44 (1.8-2.8)	2.37±0.25 2.42 (1.9-2.8)
	Secukinumab	2.10±0.61 2.24(0.99-3.13)	2.13±0.83 2.22 (0.8-3.4)	2.24±0.53 2.42 (1.0-2.7)

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	Ixekizumab	2.45±0.81 2.34 (1.56-3.92)	2.61±0.66 2.52 (1.9-3.8)	2.12±0.47 2.42 (1.5-2.5)
	Infliximab	2.14±0.50 2.37 (1.01-2.46)	2.31±0.68 2.44 (1.3-3.5)	2.42±0.35 [a] 2.42 (1.9-3.2)
Monocytes	Metotrexate	0.57±0.16 0.57 (0.27-1.32)	0.59±0.19 0.61 (0.2-1.3)	0.57±0.16 0.59 (0.2-1.3)
	Adalimumab	0.58±0.17 0.57 (0.20-1.07)	0.65±0.18 [a] 0.61 (0.4-1.3)	0.63±0.17 0.59 (0.3-1.0)
	Asitretin	0.53±0.09 0.53 (0.21-1.12)	0.61±0.11 [a] 0.61 (0.3-0.9)	0.56±0.13 [b] 0.59 (0.1-1.0)
	Ustekinumab	0.59±0.14 0.57 (0.30-0.95)	0.61±0.16 0.61 (0.2-1.1)	0.59±0.16 0.59 (0.3-1.1)
	Etanercept	0.57±0.09 0.57 (0.40-0.82)	0.60±0.09 0.61 (0.4-0.7)	0.57±0.08 0.59 (0.4-0.8)
	Secukinumab	0.54±0.18 0.48 (0.39-0.98)	0.51±0.11 0.57 (0.4-0.7)	0.57±0.11 0.57 (0.4-0.8)
	Ixekizumab	0.69±0.08 0.69 (0.6-0.84)	0.61±0.09 0.61 (0.5-0.8)	0.55±0.08 0.59 (0.4-0.6)
	Infliximab	0.60±0.07 0.57 (0.57-0.80)	0.61±0.01 0.61 (0.6-0.6)	0.80±0.55 0.59 (0.6-2.2)
Eosinophil	Metotrexate	0.21±0.10 0.20 (0.06-0.71)	0.19±0.07 0.20 (0.0-0.5)	0.19±0.06 0.20 (0.1-0.4)
	Adalimumab	0.19±0.10 0.19 (0.04-0.47)	0.20±0.09 0.20 (0.0-0.5)	0.20±0.11 0.20 (0.0-0.5)
	Asitretin	0.22±0.16 0.20 (0.06-0.85)	0.21±0.09 0.20 (0.1-0.7)	0.21±0.08 0.20 (0.0-0.5)
	Ustekinumab	0.19±0.08 0.20 (0.07-0.58)	0.19±0.08 0.20 (0.1-0.6)	0.20±0.08 0.020 (0.1-0.5)
	Etanercept	0.17±0.04 0.20 (0.09-0.21)	0.18±0.04 0.20 (0.1-0.2)	0.19±0.05 0.20 (0.1-0.3)
	Secukinumab	0.18±0.07 0.20 (0.09-0.35)	0.22±0.17 0.17 (0.0-0.6)	0.27±0.20 0.20 (0.1-0.8)
	Ixekizumab	0.20±0.05 0.18 (0.17-0.32)	0.23±0.07 0.23 (0.1-0.4)	0.21±0.09 0.20 (0.1-0.4)
	Infliximab	0.21±0.06 0.20 (0.11-0.32)	0.19±0.05 [a] 0.20 (0.01-0.03)	0.23±0.07 [b] 0.20 (0.2-0.4)
Basophil	Metotrexate	0.03±0.01 0.03 (0.01-0.08)	0.03±0.01 0.03 (0.0-0.1)	0.03±0.01 0.03 (0.0-0.1)
	Adalimumab	0.03±0.02 0.03 (0.0-0.09)	0.03±0.01 0.3 (0.0-0.1)	0.03±0.01 0.03 (0.0-0.1)
	Asitretin	0.03±0.01 0.03 (0.0-0.08)	0.03±0.01 0.03 (0.0-0.1)	0.03±0.01 0.03 (0.0-0.1)
	Ustekinumab	0.3±0.1 0.3 (0.0-0.07)	0.03±0.01 0.03 (0.0-0.1)	0.03±0.02 0.03 (0.0-0.1)
	Etanercept	0.03±0.01 0.03 (0.01-0.08)	0.02±0.01 0.03 (0.0-0.1)	0.03±0.01 0.03 (0.0-0.1)
	Secukinumab	0.02±0.01 0.02 (0.01-0.07)	0.3±0.1 0.3 (0.0-0.1)	0.03±0.08 0.03 (0.0-0.1)
	Ixekizumab	0.04±0.01 0.04 (0.02-0.07)	0.03±0.01 0.03 (0.0-0.1)	0.04±0.03 0.03 (0.0-0.1)
	Infliximab	0.02±0.01 0.03 (0.01-0.04)	0.02±0.01 0.03 (0.0-0.0)	0.03±0.01 [a,b] 0.03 (0.1-0.3)

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Platelets	Metotrexate	269.64±53.94 265.80 (151-408)	254.56±53.22 [a] 254.86 (96-401)	253.85±48.15 254.07 (101-386)
	Adalimumab	277.38±61.40 270.50 (140-397)	266.19±73.69 257.43 (71-442)	260.52±49.43 254.07 (148-372)
	Asitretin	249.92±61.37 251 (136-404)	239.37±35.61 254.86 (152-353)	239-84±47.61 254.07 (7.6-352.0)
	Ustekinumab	265.84±47.30 265.80 (114-373)	254.86±62.71 254.86 (104-427)	262.19±59.68 254.07 (133-417)
	Etanercept	279.52±45.63 265.80 (242-389)	263.62±48.67 [a] 254.86 (193-355)	270.03±49.45 254.07 (209-386)
	Secukinumab	283.75±64.40 267.0 (186-396)	270.22±82.04 255.00 (148-405)	250.12±78.67 [a] 254.07 (130-365)
	Ixekizumab	255.83±74.10 242.50 (162-365)	247.81±80.86 245.43 (158-346)	253.70±39.20 254.07 (186-308)
	Infliximab	263.25±10.03 265.80 (246-279)	251.78±40.87 254.86 (195-334)	252.17±24.16 [a] 254.07 (199-286)
MPV	Metotrexate	8.75±0.62 8.79 (7.4-10.5)	8.78±0.65 8.93 (6.9-10.4)	8.86±0.51 8.89 (7.6-10.1)
	Adalimumab	8.76±0.75 8.79 (6.9-10.2)	8.89±0.63 8.93 (7.7-10.1)	8.80±0.75 8.89 (6.4-10.0)
	Asitretin	8.88±0.75 8.79 (7.3-10.8)	9.05±0.64 8.93 (8.2-11.5)	8.97±0.78 8.89 (7.6-11.8)
	Ustekinumab	8.70±0.71 8.79 (7.2-11.3)	8.74±0.66 8.75 (7.3-10.1)	8.91±0.66 8.89 (7.4-10.5)
	Etanercept	8.87±0.47 8.79 (8.2-10.1)	8.93±0.36 8.93 (8.2-9.9)	8.83±0.43 8.89 (7.7-9.6)
	Secukinumab	8.73±0.87 8.79 (7.6-10.1)	9.36±2.15 8.40 (7.4-14.5)	8.87±1.06 8.70 (7.6-10.6)
	Ixekizumab	8.75±0.49 8.90 (7.8-9.1)	9.13±0.54 8.96 (8.6-10.0)	8.62±0.34 8.79 (8.1-8.9)
	Infliximab	8.78±0.63 8.79 (7.4-9.6)	8.80±0.67 8.93 (7.2-9.5)	8.94±0.33 8.89 (8.4-9.6)
PDW	Metotrexate	14.72±2.05 14.86 (6.40-19.30)	15.14±1.86 15.23 (9.5-21.0)	15.00±1.64 15.00 (11.0-21.5)
	Adalimumab	14.96±1.94 14.86 (9.8-19.3)	15.17±1.86 15.23 (9.8-18.3)	14.90±2.06 15.00 (9.3-18.5)
	Asitretin	15.15±2.25 14.86 (10.5-20.0)	15.76±1.96 15.23 (12.8-22.3)	15.19±1.51 15.00 (12.0-21.0)
	Ustekinumab	14.72±1.95 14.86 (11.30-22.50)	14.93±1.85 15.11 (11.5-20.5)	15.11±2.01 15.00 (11.8-20.8)
	Etanercept	15.00±0.98 14.86 (13.0-16.80)	15.20±1.24 15.23 (12.8-17.5)	14.71±1.38 15.00 (11.8-17.3)
	Secukinumab	13.19±5.39 14.0 (0.0-18.0)	13.70±4.86 13.80 (2.4-20.3)	14.02±5.78 15.00 (0.0-19.8)
	Ixekizumab	15.35±2.12 15.25 (12.0-18.50)	15.77±2.43 15.51 (13.0-19.3)	14.68±1.55 15.00 (12.3-17.0)
	Infliximab	14.98±1.42 14.86 (12.30-17.50)	15.24±1.69 15.23 (11.8-18.0)	14.91±1.04 15.00 (13.5-17.0)
CRP	Metotrexate	5.27±3.20 5.34 (0.8-26.7)	5.10±3.54 [a] 4.96 (0.7-29.2)	5.42±5.08 [b] 4.87 (0.9-44.8)
	Adalimumab	9.55±15.78 5.34 (1.0-75.0)	5.04±5.54 4.00 (0.4-21.9)	4.36±4.01 [a] 3.61 (4.0-22.0)

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	Asitretin	5.15±0.86 5.34 (0.7-5.9)	4.96±0.00 [a] 4.96 (5.0-5.0)	4.68±0.87 [a,b] 4.87 (0.7-4.9)
	Ustekinumab	4.23±4.23 2.85 (0.4-23.0)	4.83±5.15 4.22 (0.7-29.7)	4.07±3.73 4.27 (0.6-20.6)
	Etanercept	3.52±2.60 3.40 (1.0-8.0)	3.51±2.73 2.60 (0.8-11.0)	6.65±12.77 1.80 (0.4-47.7)
	Secukinumab	4.95±1.34 5.34 (2.1-5.3)	7.93±7.56 4.96 (1.4-25.9)	4.52±2.71 4.87 (1.1-10.0)
	Ixekizumab	3.77±1.39 3.65 (2.1-5.3)	3.09±1.66 3.09 (1.2-5.0)	5.00±3.55 4.87 (1.6-11.6)
	Infliximab	4.33±3.55 3.20 (1.1-10.4)	5.38±6.73 3.90 (1.2-21.7)	4.90±2.75 4.87 (1.6-10.3)
ESR	Metotrexate	16.63±5.84 17.51 (1.0-34.0)	13.93±5.99 [a] 13.27 (3.0-45.0)	13.51±2.46 [a,b] 13.50 (4.0-25.0)
	Adalimumab	20.58±13.41 17.51 (2.0-67.0)	13.44±9.11 [a] 13.27 (1.0-33.0)	15.23±11.39 13.50 (2.0-51.0)
	Asitretin	19.46±10.63 17.51 (12-83)	13.27±0.00 [a] 13.27 (13.3-13.3)	12.79±3.09 [a,b] 13.50 (1.0-20.0)
	Ustekinumab	17.11±19.58 14.75 (1.0-107.0)	14.49±12.40 13.27 (2.0-60.0)	12.56±8.07 13.50 (1.0-39.0)
	Etanercept	10.91±5.86 11.00 (1.0-19.0)	8.72±4.04 10.0 (1.0-13.3)	10.82±7.93 9.70 (3.0-34.0)
	Secukinumab	23.00±18.12 19.0 (5.0-59.0)	13.75±12.91 13.27 (2.0-6.0)	13.72±13.44 11.00 (3.0-48.0)
	Ixekizumab	12.33±5.74 13.00 (2.0-17.5)	9.63±5.16 12.63 (3.0-13.3)	18.00±10.30 [b] 13.50 (1.5-39.0)
	Infliximab	17.75±14.41 16.25 (2.0-49.0)	12.81±8.03 13.27 (2.0-24.0)	18.31±12.56 13.50 (6.0-45.0)
NLR	Metotrexate	1.98±0.63 2.05 (0.44-3.86)	2.01±0.61 1.91 (0.72-4.55)	2.40±1.69 [a,b] 2.26 (0.87-14.25)
	Adalimumab	2.49±1.44 2.24 (0.79-8.19)	1.72±0.43 [a] 1.88 (0.78-2.51)	1.93±0.58 [a] 2.11 (0.78-3.00)
	Asitretin	2.01±0.62 1.95 (1.1-4.33)	1.89±0.46 1.91 (0.94-3.47)	2.34±1.81 [b] 2.26 (0.97-13.63)
	Ustekinumab	2.48±2.48 2.21 (1.28-14.46)	1.91±0.74 1.91 (0.97-4.27)	2.19±1.34 2.26 (0.44-9.14)
	Etanercept	2.05±0.49 2.21 (1.35-3.02)	1.87±0.42 1.91 (1.19-2.87)	2.04±0.78 2.26 (1.26-4.22)
	Secukinumab	2.35±0.99 2.00 (1.44-4.29)	2.09±0.78 2.17 (1.04-3.83)	2.37±0.41 2.26 (1.75-2.91)
	Ixekizumab	2.84±1.60 2.82 (1.05-5.71)	1.88±0.76 1.89 (1.12-3.26)	2.50±0.34 2.40 (2.26-3.14)
	Infliximab	2.73±1.27 2.21 (1.60-5.54)	2.03±0.68 [a] 1.91 (1.02-3.51)	2.25±0.26 2.26 (1.72-2.68)
NMR	Metotrexate	8.36±2.58 8.46 (2.98-19.85)	8.05±2.21 7.56 (2.76-14-93)	2.27±0.46 [a,b] 2.42 (0.84-3.37)
	Adalimumab	9.64±6.56 8.83 (4.27-39.30)	7.17±1.94 [a] 7.40 (4.28-13.08)	2.54±0.55 [a,b] 2.42 (1.12-3.64)
	Asitretin	8.43±2.17 8.48 (3.96-14.71)	7.37±1.68 [a] 7.56 (4.22-13.41)	2.34±0.60 [a,b] 2.42 (0.59-4.38)
	Ustekinumab	9.72±9.04 8.78 (5.27-64.26)	7.45±1.71 7.56 (3.19-11.79)	2.79±1.78 [a,b] 2.42 (1.66-13.40)

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	Etanercept	8.39±1.80 8.83 (5.32-11.43)	7.31±1.45 [a] 7.56 (5.18-10.01)	2.37±0.25 [a,b] 2.42 (1.85-2.80)
	Secukinumab	8.90±2.96 8.94 (4.01-12.60)	8.03±2.67 7.74 (4.29-2.67)	2.24±0.53 [a,b] 2.42 (1.03-2.70)
	Ixekizumab	8.55±1.59 8.71 (6.70-10.60)	7.68±2.73 7.56 (4.55-8.13)	2.42±0.47 [a,b] 2.42 (1.52-2.45)
	Infliximab	8.58±1.17 8.83 (6.91-10.60)	7.03±1.22 [a] 7.56 (4.55-8.13)	2.42±0.35 [a,b] 2.42 (1.92-3.17)
PLR	Metotrexate	118.46±31.01 121.78 (23.43-194.17)	116.16±34.47 111.60 (52.75-219.64)	120.87±35.23 114.57 (66.38-253.10)
	Adalimumab	132.89±41.45 127.02 (47.14-262.10)	100.67±28.96 [a] 97.91 (46.88-176.53)	110.79±31.16 [a] 114.57 (40.66-183.93)
	Asitretin	118.82±32.11 121.78 (61.01-210.37)	104.15±17.74 [a] 111.60 (64.04-149.40)	111.82±35.79 [b] 114.57 (12.88-249.12)
	Ustekinumab	117.70±28.81 121.78 (60.29-206.08)	110.15±29.14 111.60 (52.24-192.96)	107.16±35.79 [a] 114.50 (18.66-202.05)
	Etanercept	124.39±34.85 121.78 (81.94-226.16)	117.74±30.52 [a] 111.60 (83.39-181.46)	119.90±28.34 114.57 (87.52-208.65)
	Secukinumab	145.11±47.99 121.78 (95.65-245.96)	146.96±80.17 111.35 (80.0-323.46)	115.98±28.02 115.02 (50.0-152.72)
	Ixekizumab	112.71±43.84 115.13 (61.83-163.87)	101.07±42.50 97.68 (54.30-166.35)	129.54±36.07 114.57 (108.57-202.63)
	Infliximab	140.44±55.60 121.78 (102.44-276.24)	126.03±57.49 [a] 111.60 (59.60-258.91)	111.29±13.77 [a] 114.57 (82.65-131.19)
SII	Metotrexate	519.05±226.73 463.40 (140.12-1257.43)	534.24±286.90 464.17 (157.15-1644.34)	617.37±471.16 503.24 (169.94-2963.29)
	Adalimumab	708.39±375.70 624.17 (94.28-1588.00)	451.88±21.390 [a] 401.79 (116.25-909.96)	486.55±220.39 [a] 445.10 (115.47-1040.63)
	Asitretin	495.31±221.02 467.57 (162.80-1228.56)	414.34±154.92 378.90 (206.70-790.31)	495.28±458.59 396.39 (26.92-2329.88)
	Ustekinumab	693.68±859.26 542.42 (166.41-4992.60)	527.02±338.68 417.20 (111.26-1638.27)	627.52±611.77 437-25 (110.63-3316.60)
	Etanercept	590.98±340.29 445.81 (333.79-1173.78)	523.75±276.16 403.54 (262.31-996.62)	562.72±474.24 402.08 (262.57-1627.46)
	Secukinumab	667.87±349.36 548.35 (454.92-1488.07)	585.35±389.16 449.00 (312.00-1549.18)	594.19±244.07 629.69 (290.00-1015.59)
	Ixekizumab	719.24±388.04 779.01 (265.26-1198.08)	505.14±389.46 301.57 (187.86-1127.83)	709.80±248.27 687.25 (473.57-968.58)

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	Infliximab	952.81±572.98 907.88 (403.61-1546.93)	543.68±284.87 685.13 (215.77-730.14)	553.65±114.28 532.73 (451.27-676.95)

[a] indicates that it is significant when compared with the baseline value.[b] indicates that it is significant when compared with the 3rd month value.

Table 4. Comparison of the changes in NLR, NMR and PLR after the treatment.

	Metotrexate	Adalimumab	Asitretin	Ustekinumab	Etanercept	Secukinumab	Ixekizumab	Infliximab
NLR-NLR3	-0.02±0.76 0.11 (-3.16-1.59)	0.77±1.28 0.34 (-0.51-5.68)	0.12±0.58 0.03 (-0.99-2.41)	0.56±2.56 0.30 (-2.04-15.56)	0.17±0.46 0.30 (-0.74-1.13)	0.26±0.89 0.003 (-0.74-1.94)	0.95±1.52 0.68 (-0.48-3.82)	0.70±1.07 0.30 (0.18-3.36)
NLR-NLR6	-0.41±1.82 -0.20 (-12.73-1.96)	0.56±1.44 0.13 (-0.86-5.93)	-0.33±1.95 -0.08 (-12.06-2.06)	0.28±2.82 -0.45 (-7.57-15.20)	0.008±0.73 -0.04 (-2.0-1.28)	-0.18±0.88 -0.26 (-0.96-1.59)	0.33±1.64 -0.03 (-1.21-3.44)	0.48±1.15 -0.45 (-0.12-3.18)
NMR-NMR3	0.30±3.04 0.28 (-7.0-14.34)	2.46±6.57 1.49 (-3.17-32.22)	1.05±2.40 1.02 (-4.58-7.15)	2.26±9.29 0.74 (-5.44-56.71)	1.07±0.88 1.26 (-0.66-3.15)	0.87±2.20 0.93 (-2.64-3.57)	0.86±2.45 1.35 (-3.43-3.80)	1.55±0.56 1.26 (1.17-2.48)
NMR-NMR6	5.96±2.96 6.16 (-6.02-17.72)	7.71±6.46 6.57 (2.93-37.04)	6.08±2.78 6.38 (-5.29-12.45)	7.52±9.21 6.19 (-1.96-61.99)	6.35±1.81 6.57 (4.07-10.04)	6.53±2.82 6.74 (1.75-10.35)	6.04±1.51 5.84 (4.44-8.33)	6.32±1.00 6.57 (4.63-7.93)
PLR-PLR3	2.32±37.91 6.47 (-196.21-72.71)	32.21±42.35 23.02 (-54.74-150.49)	14.66±29.83 10.18 (-43.91-103.08)	7.55±31.11 10.18 (-53.20-93.97)	6.65±25.89 10.18 (-67.45-47.77)	-1.85±66.60 19.17 (-158.6-55.74)	11.63±26.84 6.16 (-15.96-52.85)	14.40±12.01 10.18 (4.15-42.83)
PLR-PLR6	-2.37±42.37 4.20 (-229.67-62.30)	22.10±34.09 7.51 (-33.86-90.96)	6.99±42.50 4.56 (-99.49-108.91)	10.54±31.16 7.21 (-54.29-93.37)	4.48±42.26 7.21 (-86.86-111.59)	29.12±35.43 14.72 (-13.16-93.24)	-16.83±44.61 -36.84 (-52.74-55.30)	29.14±47.71 7.21 (7.21-145.04)

Table 5. Correlation of hematological values with each other.

	PASI		CRP		Time post-onset		PLR		NMR		NLR	
	rho	*p*	*rho*	*p*	*rho*	*p*	*rho*	*p*	*rho*	*p*		
SII	**0.201**	**0.033**	**0.303**	**0.013**	0.079	0.361	**0.612**	**<0.001**	**0.477**	**<0.001**	**0.848**	**<0.001**
NLR	**0.201**	**0.032**	**0.263**	**0.029**	0.133	0.124	**0.461**	**<0.001**	**0.500**	**<0.001**		
NMR	0.118	0.210	0.22	0.066	0.010	0.910	0.138	0.77				
PLR	0.129	0.170	0.031	0.803	0.096	0.265						

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Time post-onset	0.153	0.87	-0.089	0.413
CRP	0.69	0.578		

Discussion

In this study, we investigated the effects of treatments applied to patients with psoriasis on hematological parameters. In the third month of follow-up, the mean CRP, NLR, NMR, PLR, and SII values were significantly decreased compared to the baseline values. SII values showed strong positive correlation with PLR, NMR, and NLR. Adalimumab, etanercept, and infliximab, which are TNF-α blockers, were observed to be more effective on PLR, NLR, and especially NMR.

Unfortunately, there is no laboratory marker to evaluate disease activity in psoriasis. Therefore, there is a need to identify better markers for the assessment of psoriasis severity and treatment outcomes. In recent studies, NLR, MLR, and PLR, which can be easily calculated from neutrophil, monocyte, lymphocyte, and platelet counts, have been defined as markers of inflammation [20]. NLR, MLR, and PLR, which have been shown to be biomarkers in many diseases associated with systemic inflammation, have also been shown to be associated with psoriasis and the severity of the disease. In controlled studies, it was reported that NLR is significantly higher in psoriasis patients than in controls, and there is a correlation between NLR and PASI [3,15-17,21]. In a meta-analysis including 1067 psoriasis patients and 799 healthy controls, it was reported that NLR was higher in psoriasis patients than in healthy controls, and NLR values were higher in patients with PASI > 10 than in patients with PASI < 10. This meta-analysis also found no correlation between NLR values and PASI scores [7]. In the same meta-analysis, it was documented that NLR was correlated with the presence, not severity, of the disease in psoriasis patients. Wang et al., in their study on Chinese psoriasis patients, determined that NLR was significantly higher in psoriasis patients than in healthy controls. However, they observed that there was no correlation between NLR and PASI score [22]. The reason for the inconsistency in the results of the studies is due to the duration of the disease, the number of cases, and the different types of studies, and racial and ethnic differences.

In addition to NLR, platelets, which are an easily measurable parameter, have been found to increase during infectious and inflammatory diseases including psoriasis [23]. PLR, another data measurable with platelets, is another suggested indicator of systemic inflammation [24]. Studies have shown that PLR values in psoriasis patients are higher than in healthy controls [3,15]. According to a meta-analysis, PLR values in psoriasis patients were significantly higher than in healthy controls [7]. In another study evaluating psoriasis subtypes, it was reported that both peripheral blood platelet counts and PLR were significantly higher in all four subtypes of psoriasis compared to control subjects [22]. Yurtdaş and colleagues [17] documented that PLR is high in psoriasis patients and that PLR correlates with PASI. There are also studies evaluating MPV as another biomarker of platelet activation. There are studies reporting that MPV is higher in psoriatic patients than in healthy controls [25-28]. They also determined that MPV showed a positive correlation with PASI [25;26;28]. However, there are studies reporting that MPV does not show a significant change in psoriasis patients [29;30] and other studies showing that MPV is lower in patients with psoriasis[31].

It has been demonstrated in previous studies that NLR, PLR, and MLR are increased in psoriasis patients compared to controls and that they can be a biomarker that can be easily used in psoriasis patients. Moreover, there are studies investigating how NLR, MLR, and PLR are affected due to treatments in psoriasis patients. In the study by Asahina et al. [31], it was determined that NLR decreased in psoriasis patients after twelve months of treatment with ustekinumab, infliximab, and adalimumab, and there was no difference in terms of the treatments applied. Moreover, they suggested that NLR could be used to examine the efficacy of treatment in psoriasis patients. In the study by An et al. [32], it was reported that NLR decreased after six months of treatment, regardless of the biological agent applied. Aktas Karabay and colleagues [21]observed that PASI scores and NLR values decreased after treatment with narrowband methotrexate, acitretin, ultraviolet B, cyclosporine, ustekinumab, adalimumab, and etanercept in psoriasis patients. Moreover, the reduction in PASI and NLR showed a positive correlation. In the study of Hagino et al. [33], it was documented that PASI, NLR, MLR, PLR, and CRP values at 12 and 52 weeks of treatment with

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infliximab, adalimumab, and certolizumab pegol decreased significantly compared to baseline. Moreover, it was observed that NLR, MLR, PLR, and CRP values were mostly correlated with each other before and after treatment with TNF-α inhibitors. In the study by Nobari et al. [34], it was determined that NLR and PLR decreased significantly after one year of treatment with TNF-α inhibitors.

In our study, the mean neutrophil, platelet, CRP, ESR, NLR, NMR, and PLR values were significantly decreased compared to baseline values in the third month of treatment, regardless of the type of biological agent applied. Although the values increased again at the sixth month of treatment, the NMR and PLR values were still significantly different from the baseline values. We think that the change in parameter values in the sixth month of treatment is because the patients do not use their medications regularly. Among the biological agents used in the treatment, especially the TNF-α blockers adalimumab, etanercept and infliximab were found to be more effective on NLR, NMR, and PLR. In the sixth month of treatment, the efficacy of all biological agents, especially on NMR, was more pronounced. No difference was observed in terms of changes in NLR, PLR, and NMR caused by biological agents. The results of our study especially confirm the results of previous studies that demonstrated the effectiveness of TNF-α blockers. Again, when the correlation of NLR, PLR, and NMR with other parameters was examined in our study, we determined that NLR was positively correlated with PASI, CRP, NMR, and PLR, in line with previous studies.

SII, a novel inflammation-based biomarker derived from neutrophils, platelets, and lymphocytes, has recently been identified. It has been suggested that SII, like the other hematological inflammatory indices NLR, PLR, and NMR, could be a simple and inexpensive tool to predict the progression of many diseases [35;38]. In a study conducted with psoriasis patients, it was reported that SII was significantly higher than controls [39]. Moreover, it was determined that SII values increased with the increase in the severity of psoriasis. In the same study, it was also observed that there was a positive correlation between SII and PASI [39]. In our study, we determined that SII decreased after treatment. While numerical decrease was observed in other biological agents in SII after treatment, a significant decrease was determined in adalimumab. In addition, SII exhibited weak positive correlation with PASI and CRP, and strong positive correlation with NLR, PLR, and NMR.

Our study has revealed a link between the SII levels of psoriasis patients and the treatment they received. This is the strength of our study. The small number of patients examined and the retrospective analysis are the limitations of our study. Therefore, prospective studies with larger numbers of patients are needed.

In conclusion, in this retrospective study, we aimed to determine a new biomarker from routine blood values for the effectiveness of the treatment applied in psoriasis patients. In our study, a decrease was observed in NMR, NLR, and PLR as a result of treatment, which is consistent with previous studies. In particular, NLR correlated with other markers. We determined that SII, a recently identified biomarker, also decreased as a result of treatment and correlated with other markers. We think that SII can be evaluated in addition to other blood values in the severity of psoriasis and the effectiveness of treatment.

References

1. Langley R. G, Krueger G. G , Griffiths C. E. Psoriasis: epidemiology, clinical features, and quality of life. *Ann Rheum Dis* **2005**; 64 Suppl 2: ii18-23; discussion ii24-15 PMID: 15708928 PMCID: PMC1766861 DOI: 10.1136/ard.2004.033217
2. Paul, C., Gourraud, P. A., Bronsard, V., Prey, S., Puzenat, E., Aractingi, S., Aubin, F., Bagot, M., Cribier, B., Joly, P., Jullien, D., Le Maitre, M., Richard-Lallemand, M. A., & Ortonne, J. P.. Evidence-based recommendations to assess psoriasis severity: systematic literature review and expert opinion of a panel of dermatologists. *J Eur Acad Dermatol Venereol* **2010**; 24 Suppl 2: 2-9. PMID: 20443994 DOI: 10.1111/j.1468-3083.2009.03561.x
3. Polat M, Bugdayci G, Kaya H , Oguzman H. Evaluation of neutrophil-tolymphocyte ratio and platelet-to-lymphocyte ratio in Turkish patients with chronic plaque psoriasis. . *Acta Dermatovenerol Alp Pannonica Adria*t **2017**; 26: 97-100. PMID: 29264899 DOI: 10.15570/actaapa.2017.28
4. Dowlatshahi E. A, van der Voort E A, Arends L R, Nijsten T. Mark ers of systemic inflammation in psoriasis: a systematic review and meta-analysis. *Br J Dermatol* **2013**; 169: 266-282. PMID: 23550658 DOI: 10.1111/bjd.12355
5. Leithead J A, Rajoriya N, Gunson B K, Ferguson J. W. Neutrophil-to-lymphocyte ratio predicts mortality in patients listed for liver transplantation. *Liver Int* **2015**; 35: 502-509. PMID: 25234369 DOI: 10.1111/liv.12688

6. 6 Uysal S, Yilmaz F M, Karatoprak K, Artuz F, Cumbul N. U. The levels of serum pentraxin3, CRP, fetuin-A, and insulin in patients with psoriasis. *Eur Rev Med Pharmacol Sci* **2014**; 18: 3453-3458. PMID: 25491620
7. Paliogiannis, P., Satta, R., Deligia, G., Farina, G., Bassu, S., Mangoni, A. A., Carru, C., & Zinellu, Associations between the neutrophil-to-lymphocyte and the platelet-to-lymphocyte ratios and the presence and severity of psoriasis: a systematic review and meta-analysis. *Clin Exp Med* **2019**; 19: 37-45. PMID: 30478648 DOI: 10.1007/s10238-018-0538-x
8. Huang, W., Huang, J., Liu, Q., Lin, F., He, Z., Zeng, Z., & He, L. Neutrophil-lymphocyte ratio is a reliable predictive marker for early-stage diabetic nephropathy. *Clin Endocrinol* (Oxf) **2015**; 82: 229-233. PMID: 25088518 DOI: 10.1111/cen.12576
9. Duzenli T, Koseoglu H, Akyol T. NLR and PLR as Novel Prognostic Biomarkers of Mucosal Healing in Ulcerative Colitis Patients Treated with Anti-TNF. *Inflamm Bowel Dis* **2020**; 26: e103. PMID: 32514550 DOI: 10.1093/ibd/izaa153
10. Fu, H., Qin, B., Hu, Z., Ma, N., Yang, M., Wei, T., Tang, Q., Huang, Y., Huang, F., Liang, Y., Yang, Z., & Zhong, R. Neutrophil- and platelet-to-lymphocyte ratios are correlated with disease activity in rheumatoid arthritis. *Clin Lab* **2015**; 61: 269-273. PMID: 25974992 DOI: 10.7754/clin.lab.2014.140927
11. Liu H, Li Y, Yi J, Zhou W, Zhao S, Yin G. Neutrophil-lymphocyte ratio as a potential marker for differential diagnosis between spinal tuberculosis and pyogenic spinal infection. *J Orthop Surg Res* **2022;** 17: 357. PMID: 35864551 PMCID: PMC9301616 DOI: 10.1186/s13018-022-03250-x
12. Metawea M.I , Moteleub H. Diagnostic role of simple indices in HCV-related liver cirrhosis outcomes: a prospective cross-sectional study. *Clin Exp Hepatol* **2022**; 8: 29-35. PMID: 35415262 PMCID: PMC8984797 DOI: 10.5114/ceh.2022.114169
13. Özer, S., Yılmaz, R., Sönmezgöz, E., Karaaslan, E., Taşkın, S., Bütün, İ., & Demir. Simple markers for subclinical inflammation in patients with Familial Mediterranean Fever. *Med Sci Monit* **2015**; 21: 298-303. PMID: 25615955 PMCID: PMC4315639 DOI: 10.12659/MSM.892289
14. Spolverato, G., Maqsood, H., Kim, Y., Margonis, G., Luo, T., Ejaz, A., & Pawlik, T. M.Spolverato G, Maqsood H, Kim Y. et al. Neutrophil-lymphocyte and platelet-lymphocyte ratio in patients after resection for hepato-pancreatico-biliary malignancies. *J Surg Oncol* **2015**; 111: 868-874. PMID: 25865111 DOI: 10.1002/jso.23900
15. Ataseven A, Bilgin A.U, Kurtipek G S. The importance of neutrophil lymphocyte ratio in patients with psoriasis. Mater Sociomed 2014; 26: 231-233. PMID: 25395882 PMCID: PMC4214808 DOI: 10.5455/msm.2014.231-233
16. Kim, D. S., Shin, D., Lee, M. S., Kim, H. J., Kim, D. Y., Kim, S. M., & Lee, M. G.. Assessments of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in Korean patients with psoriasis vulgaris and psoriatic arthritis. *J Dermatol* **2016**; 43: 305-310. PMID: 26381893 DOI: 10.1111/1346-8138.13061
17. Yurtdas M, Yaylali Y T, Kaya Y, Ozdemir M, Ozkan I ,Aladag N. Neutrophil-to-lymphocyte ratio may predict subclinical atherosclerosis in patients with psoriasis. *Echocardiography* **2014**; 31: 1095-1104. PMID: 24447343 DOI: 10.1111/echo.12511
18. Feng J F, Chen S, Yang X. Systemic immune-inflammation index (SII) is a useful prognostic indicator for patients with squamous cell carcinoma of the esophagus. *Medicine* (Baltimore) **2017;** 96: e5886. PMID: 28121932 PMCID: PMC5287956 DOI: 10.1097/MD.0000000000005886
19. Dapavo, P., Siliquini, N., Mastorino, L., Avallone, G., Merli, M., Agostini, A., Cariti, C., Viola, R., Stroppiana, E., Verrone, A., Ortoncelli, M., Quaglino, P., & Ribero, S. Efficacy, safety, and drug survival of IL-23, IL-17, and TNF-alpha inhibitors for psoriasis treatment: a retrospective study. *J Dermatolog Treat* **2022;** 33: 2352-2357. PMID: 34315331 DOI: 10.1080/09546634.2021.1961998
20. Fan W, Zhang Y, Wang Y, Yao X, J. Yang J , Li J . Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios as predictors of survival and metastasis for recurrent hepatocellular carcinoma after transarterial chemoembolization. *PLoS One* **2015**; 10: e0119312. PMID: 25742141 PMCID: PMC4351002 DOI: 10.1371/journal.pone.0119312
21. Aktas Karabay E, Demir D, Aksu A, Cerman. Evaluation of monocyte to high-density lipoprotein ratio, lymphocytes, monocytes, and platelets in psoriasis. *An Bras Dermatol* **2020;** 95: 40-45. PMID: 31889591 PMCID: PMC7058861 DOI: 10.1016/j.abd.2019.05.002
22. 22 Wang W M, Wu C, Gao Y M , Li F, Yu X L ,Jin H Z. Neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, and other hematological parameters in psoriasis patients. *BMC Immunol* **2021;** 22: 64. PMID: 34565327 PMCID: PMC8474773 DOI: 10.1186/s12865-021-00454-4
23. 23 Zareifar S, Farahmand Far M R, Golfeshan F, Cohan N. Changes in platelet count and mean platelet volume during infectious and inflammatory disease and their correlation with ESR and CRP. *J Clin Lab Anal* **2014**; 28: 245-248. PMID: 24478177 PMCID: PMC6807431 DOI: 10.1002/jcla.21673
24. 24. Uslu, A. U., Küçük, A., Şahin, A., Ugan, Y., Yılmaz, R., Güngör, T., Bağcacı, S., & Küçükşen, S. Two new inflammatory markers associated with Disease Activity Score-28 in patients with rheumatoid arthritis: neutrophil-lymphocyte ratio and platelet-lymphocyte ratio. *Int J Rheum Dis* **2015**; 18: 731-735. PMID: 25900081 DOI: 10.1111/1756-185X.12582 PMID: 25900081 DOI: 10.1111/1756-185X.12582

25. Canpolat F, Akpinar H, Eskioglu F. Mean platelet volume in psoriasis and psoriatic arthritis. *Clin Rheumatol* **2010**; 29: 325-328. PMID: 20012663 DOI: 10.1007/s10067-009-1323-8 PMID: 20012663 DOI: 10.1007/s10067-009-1323-8
26. 26. Chandrashekar, L., Rajappa, M., Revathy, G., Sundar, I., Munisamy, M., Ananthanarayanan, P. H., Thappa, D. M., & Basu, D.. Is enhanced platelet activation the missing link leading to increased cardiovascular risk in psoriasis? *Clin Chim Acta* **2015**; 446: 181-185. PMID: 25920693 DOI: 10.1016/j.cca.2015.04.023
27. Karabudak O, Ulusoy R.E, Erikci A.A, Solmazgul E, Dogan B, Harmanyeri Y. Inflammation and hypercoagulable state in adult psoriatic men. *Acta Derm Venereol* **2008**; 88: 337-340. PMID: 18709301 DOI: 10.2340/00015555-0456
28. Kim D.S, Lee J, Kim S.H, Kim S.M, Lee M.G. Mean platelet volume is elevated in patients with psoriasis vulgaris. *Yonsei Med J* **2015**; 56: 712-718. PMID: 25837177 PMCID: PMC4397441 DOI: 10.3349/ymj.2015.56.3.712
29. Erek Toprak A, Ozlu E, Uzuncakmak T.K, Yalcinkaya E, Sogut S, Karadag A.S. Neutrophil/Lymphocyte Ratio, Serum Endocan, and Nesfatin-1 Levels in Patients with Psoriasis Vulgaris Undergoing *Phototherapy Treatment. Med Sci Monit* **2016**; 22: 1232-1237. PMID: 27070789 PMCID: PMC4831300 DOI: 10.12659/msm.898240
30. Saleh H.M, Attia E.A, Onsy A.M, Saad A.A, Abd Ellah M.M. Platelet activation: a link between psoriasis per se and subclinical atherosclerosis--a case-control study. *Br J Dermatol* **2013**; 169: 68-75. PMID: 23448140 DOI: 10.1111/bjd.12285
31. Asahina A, Kubo N, Umezawa Y, Honda H,Yanaba K, Nakagawa H. Neutrophil-lymphocyte ratio, platelet-lymphocyte ratio and mean platelet volume in Japanese patients with psoriasis and psoriatic arthritis: Response to therapy with biologics. *J Dermatol* **2017;** 44: 1112-1121. PMID: 28493493 DOI: 10.1111/1346-8138.13875
32. An I, Ucmak D, Ozturk M. The effect of biological agent treatment on neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, mean platelet volume, and C-reactive protein in psoriasis patients. *Postepy Dermatol Alergol* **2020**; 37: 202-206. PMID: 32489355 PMCID: PMC7262800 DOI: 10.5114/ada.2020.94838
33. Hagino T, Saeki H, Kanda N. Biomarkers and Predictive Factors for Treatment Response to Tumor Necrosis Factor-alpha Inhibitors in Patients with Psoriasis. *J Clin Med* **2023**; 12. PMID: 36769622 PMCID: PMC9918195 DOI: 10.3390/jcm12030974
34. Najar Nobari N, Shahidi Dadras M, Nasiri S, Abdollahimajd F, Gheisari M. Neutrophil/platelet to lymphocyte ratio in monitoring of response to TNF-alpha inhibitors in psoriatic patients. *Dermatol Ther* **2020**; 33: e13457. PMID: 32319132 DOI: 10.1111/dth.13457
35. Chen, L. Kong X, Wang Z, Wang X, Fang Y, Wang J. Pre-treatment systemic immune-inflammation index is a useful prognostic indicator in patients with breast cancer undergoing neoadjuvant chemotherapy. *J Cell Mol Med* **2020**; 24: 2993-3021. PMID: 31989747 PMCID: PMC7077539 DOI: 10.1111/jcmm.14934
36. Ji Y, Wang H. Prognostic prediction of systemic immune-inflammation index for patients with gynecological and breast cancers: a meta-analysis. *World J Surg Oncol* **2020**; 18: 197. PMID: 32767977 PMCID: PMC7414550 DOI: 10.1186/s12957-020-01974-w
37. Kim J.W., Jung J.Y, Suh C.H., Kim H. A. Systemic immune-inflammation index combined with ferritin can serve as a reliable assessment score for adult-onset Still's disease. *Clin Rheumatol* **2021**; 40: 661-668. PMID: 32623648 DOI: 10.1007/s10067-020-05266-2
38. Liu, J., Li, S., Zhang, S., Liu, Y., Ma, L., Zhu, J., Xin, Y., Wang, Y., Yang, C., & Cheng, YSystemic immune-inflammation index, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio can predict clinical outcomes in patients with metastatic non-small-cell lung cancer treated with nivolumab. *J Clin Lab Anal* **2019**; 33: e22964. PMID: 31282096 PMCID: PMC6805305 DOI: 10.1002/jcla.22964
39. Yorulmaz A, Hayran Y, Akpinar U, Yalcin B. Systemic Immune-Inflammation Index (SII) Predicts Increased Severity in Psoriasis and Psoriatic Arthritis. *Curr Health Sci J* **2020**; 46: 352-357. PMID: 33717509 PMCID: PMC7948012 DOI: 10.12865/CHSJ.46.04.05