Original Article

Cukurova Anestezi ve Cerrahi Bilimler Dergisi

Effects of Anti-IL-17 Therapy on Serum Red Cell Distribution Width and Mean Platelet Volume in Ankylosing Spondylitis: A Retrospective Cohort Study

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Abstract

Objective: To investigate the effects of anti-IL-17 therapy on serum red cell distribution width (RDW) and mean platelet volume (MPV) in patients with ankylosing spondylitis (AS) and to evaluate their relationship with disease activity markers. **Methods:** This retrospective cohort study included 130 AS patients (86 males, 44 females; mean age 35.7 ± 8.9 years) receiving anti-IL-17 inhibitors (secukinumab or ixekizumab). Pre-treatment and post-treatment (mean 21.4 ± 19.0 months) RDW, MPV, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were recorded. Paired t-tests with Bonferroni correction, Pearson correlation analyses, and multiple linear regression analyses were performed. **Results:** Anti-IL-17 therapy resulted in significant reductions in RDW (15.43 ± 0.79 vs. 14.60 ± 0.83%, $p < 0.001$; Cohen's $d = 2.94$), MPV (10.46 ± 0.71 vs. 10.16 ± 0.74 fL, $p < 0.001$; Cohen's $d = 1.48$), BASDAI (6.53 ± 1.27 vs. 3.30 ± 1.51, $p < 0.001$; Cohen's $d = 4.28$), ESR (27.19 ± 12.27 vs. 15.29 ± 12.23 mm/h, $p < 0.001$), and CRP (17.42 ± 9.26 vs. 9.21 ± 8.72 mg/L, $p < 0.001$). Good clinical response (≥50% BASDAI reduction) was achieved in 48.5% of patients. Pre-treatment RDW correlated significantly with BASDAI ($r = 0.33$, $p < 0.001$), ESR ($r = 0.45$, $p < 0.001$), and CRP ($r = 0.42$, $p < 0.001$).**Conclusion:** Anti-IL-17 therapy effectively suppresses disease activity and systemic inflammation in AS patients. The significant reductions in RDW and MPV alongside clinical and inflammatory markers suggest that these readily available hematologic parameters might serve as adjunctive, hypothesis-generating biomarkers for monitoring treatment response and systemic inflammation in AS.

Keywords: Ankylosing spondylitis; Anti-IL-17; RDW; MPV; Disease activity; Biomarkers; Secukinumab; Ixekizumab; Systemic inflammation; Hematologic parameters

Received: 05.02.2026
Accepted: 09.06.2026
Published: 30.06.2026

1. Introduction

Ankylosing spondylitis (AS) is a chronic, progressive, and systemic inflammatory disease primarily affecting the sacroiliac joints and spine, characterized by pain, stiffness, and progressive functional limitation[1]. The pathogenesis of AS involves complex interactions between genetic factors and environmental triggers, with the IL-23/IL-17 axis emerging as a central mechanism in disease development and progression[3,15].

Interleukin-17 (IL-17), primarily produced by Th17 cells and other innate lymphoid cells, plays a pivotal role in the pathogenesis of AS. The recognition of IL-17's central role has led to the development of anti-IL-17 monoclonal antibodies, including secukinumab and ixekizumab, which have demonstrated superior efficacy compared to TNF inhibitors in clinical trials and are now recommended as first-line biologic DMARDs for AS[5,17].

Red cell distribution width (RDW) reflects the heterogeneity in erythrocyte size, while mean platelet volume (MPV) represents the average size of circulating platelets. These simple, inexpensive hematologic parameters have been investigated as markers of systemic inflammation in various chronic inflammatory diseases[20,27]. In AS specifically, elevated RDW and MPV have been associated with disease activity, and their normalization with effective treatment may reflect resolution of systemic inflammation[7,20]. A recent meta-analysis of AS patients receiving TNF inhibitors demonstrated that RDW and MPV decreased with effective disease suppression[7].

The mechanistic link between IL-17 and hematologic parameters involves several pathways. IL-17 directly inhibits erythropoietin (EPO) production and impairs iron absorption, leading to elevated RDW in chronic inflammatory conditions[10,16,24]. IL-17 also directly stimulates megakaryopoiesis and promotes platelet activation, potentially increasing MPV[25,26].

While RDW and MPV have been studied in AS patients receiving TNF inhibitors, their specific response to anti-IL-17 therapy has not been systematically investigated, representing a significant knowledge gap. This study aimed to investigate the effects of anti-IL-17 therapy on RDW and MPV levels and their relationship with disease activity in a cohort of AS patients.

2. Methods

2.1. Study Design and Patient Population

This retrospective cohort study was conducted at Adana City Training and Research Hospital, Department of Rheumatology. We reviewed medical records of 130 consecutive AS patients who received anti-IL-17 inhibitor therapy (secukinumab or ixekizumab) between January 2020 and December 2023. All patients met the 1984 Modified New York criteria for AS diagnosis. The study was approved by the Clinical Research Ethics Committee (Date: 27.01.2022, Decision No: 1761), and informed consent was obtained from all participants.

2.2. Inclusion and Exclusion Criteria

Inclusion criteria: (1) Diagnosis of AS according to the 1984 Modified New York criteria; (2) Age ≥18 years; (3) Received anti-IL-17 inhibitor therapy for at least 3 months; (4) Complete laboratory data available at baseline and follow-up. Exclusion criteria: (1) Active infection or malignancy; (2) Pregnancy or lactation; (3) Severe hepatic or renal impairment; (4) Incomplete laboratory data; (5) Concurrent use of other biologic DMARDs.

2.3. Data Collection

Demographic data, disease duration, treatment duration, treatment adherence, and baseline comorbidities were extracted from medical records. Laboratory measurements including RDW, MPV, ESR, and CRP were obtained at baseline (pre-treatment) and at the last follow-up visit (post-treatment, mean 21.4 ± 19.0 months). BASDAI scores were calculated from patient questionnaires at both time points. Information regarding primary treatment failure, secondary treatment failure, and development of inflammatory bowel disease (IBD) was recorded.

2.4. Treatment Response Classification

Patients were classified into two groups based on post-treatment BASDAI response: (1) Good Response: ≥50% reduction in BASDAI score; (2) Partial Response: <50% reduction in BASDAI score. Subgroup analyses were performed stratified by sex, age groups, disease duration, treatment duration, and treatment adherence.

2.5. Statistical Analysis

Continuous variables were expressed as mean ± SD. Paired t-tests were used to compare pre- and post-treatment values. Independent t-tests were used to compare variables between treatment response groups. Multiple comparisons correction (Bonferroni correction) was applied. Pearson correlation coefficients were calculated to assess relationships between variables. Effect sizes were calculated using Cohen's d. Multiple linear regression analyses were performed to evaluate the independent effect of anti-IL-17 therapy on RDW and MPV changes, adjusting for potential confounders including age, disease duration, comorbidities, and concurrent medications. Statistical significance was defined as $p < 0.05$.

3. Results

3.1. Demographic and Clinical Characteristics

The study cohort consisted of 130 AS patients with a mean age of 35.7 ± 8.9 years. The male-to-female ratio was 86:44. Mean disease duration was 4.5 ± 3.2 years, and mean anti-IL-17 treatment duration was 21.4 ± 19.0 months. HLA-B27 positivity was documented in 118 patients (90.8%). Treatment failure was documented in 19 patients: primary treatment failure in 9 (6.9%), secondary treatment failure in 10 (7.7%), and development of IBD in 4 (3.1%).

3.2. Effects of Anti-IL-17 Therapy on Laboratory and Clinical Parameters

Anti-IL-17 therapy resulted in statistically significant reductions across all measured parameters. RDW decreased from 15.43 ± 0.79% to 14.60 ± 0.83% ($p < 0.001$, Cohen's $d = 2.94$). MPV decreased from 10.46 ± 0.71 fL to 10.16 ± 0.74 fL ($p < 0.001$, Cohen's $d = 1.48$). BASDAI decreased from 6.53 ± 1.27 to 3.30 ± 1.51 ($p < 0.001$, Cohen's $d = 4.28$). ESR decreased from 27.19 ± 12.27 to 15.29 ± 12.23 mm/h ($p < 0.001$, Cohen's $d = 1.80$), and CRP decreased from 17.42 ± 9.26 to 9.21 ± 8.72 mg/L ($p < 0.001$, Cohen's $d = 1.40$). These results are summarized in Table 1.

Table 1. Pre- and Post-treatment Laboratory and Clinical Parameters

Parameter	Pre-treatment (Mean±SD)	Post-treatment (Mean±SD)	p-value	Cohen's d
RDW (%)	15.43 ± 0.79	14.60 ± 0.83	<0.001	2.94
MPV (fL)	10.46 ± 0.71	10.16 ± 0.74	<0.001	1.48
BASDAI	6.53 ± 1.27	3.30 ± 1.51	<0.001	4.28
ESR (mm/h)	27.19 ± 12.27	15.29 ± 12.23	<0.001	1.80
CRP (mg/L)	17.42 ± 9.26	9.21 ± 8.72	<0.001	1.40

Abbreviations: RDW, red cell distribution width; MPV, mean platelet volume; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; SD, standard deviation. Statistical method: paired t-test with Bonferroni correction.

3.3. Treatment Response Analysis

Good clinical response (≥50% BASDAI reduction) was achieved in 63 patients (48.5%), while 67 patients (51.5%) demonstrated partial response. No significant differences were observed in RDW change or MPV change between good and partial responders.

Table 2. Comparison of Hematologic Changes Between Treatment Response Groups

Parameter	Good Response (n=63)	95% CI	Partial Response (n=67)	95% CI	p-value	Cohen's d
RDW Change (%)	0.84 ± 0.31	0.77-0.92	0.82 ± 0.26	0.76-0.88	0.649	0.080
MPV Change (fL)	0.27 ± 0.18	0.23-0.31	0.32 ± 0.22	0.28-0.36	0.220	-0.413
Treatment Adherence (%)	84.5 ± 9.3	82.2-86.8	86.0 ± 8.7	84.0-88.0	0.337	-0.173

Note: *CI, confidence interval; Cohen's d values indicate effect sizes between groups.*

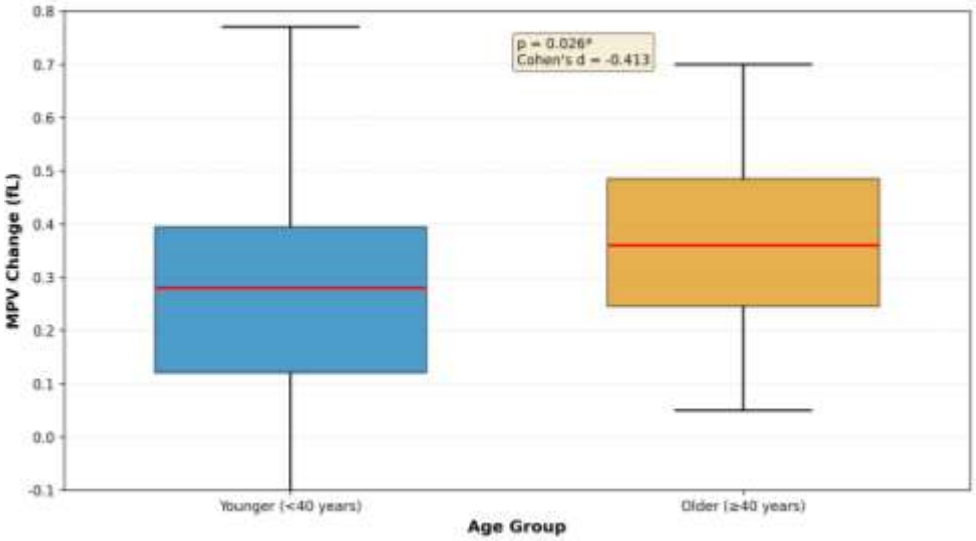

Figure 1. Mean Platelet Volume Changes by Age Group

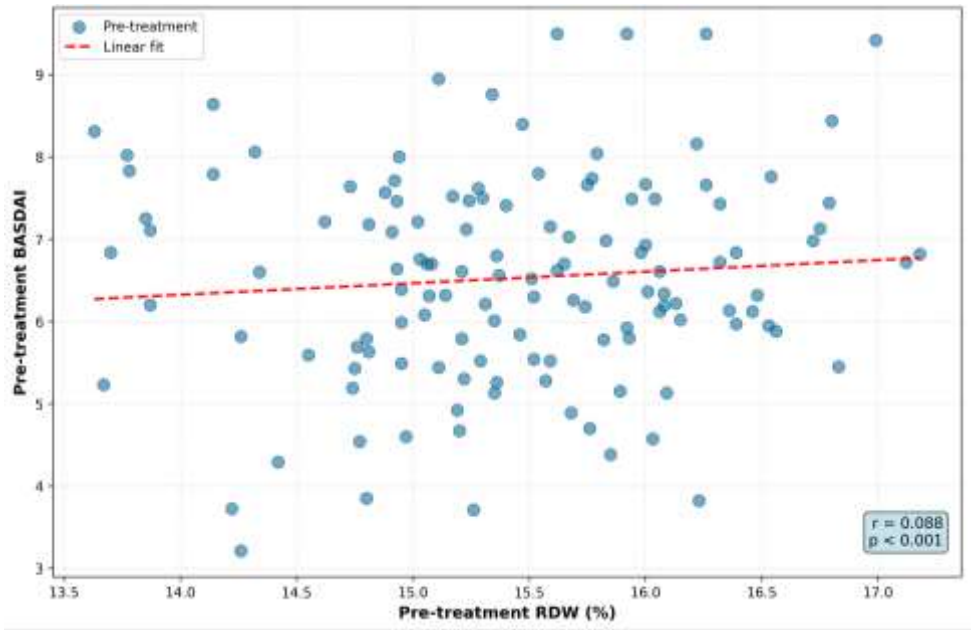

Figure 2. Correlation between RDW and BASDAI at baseline

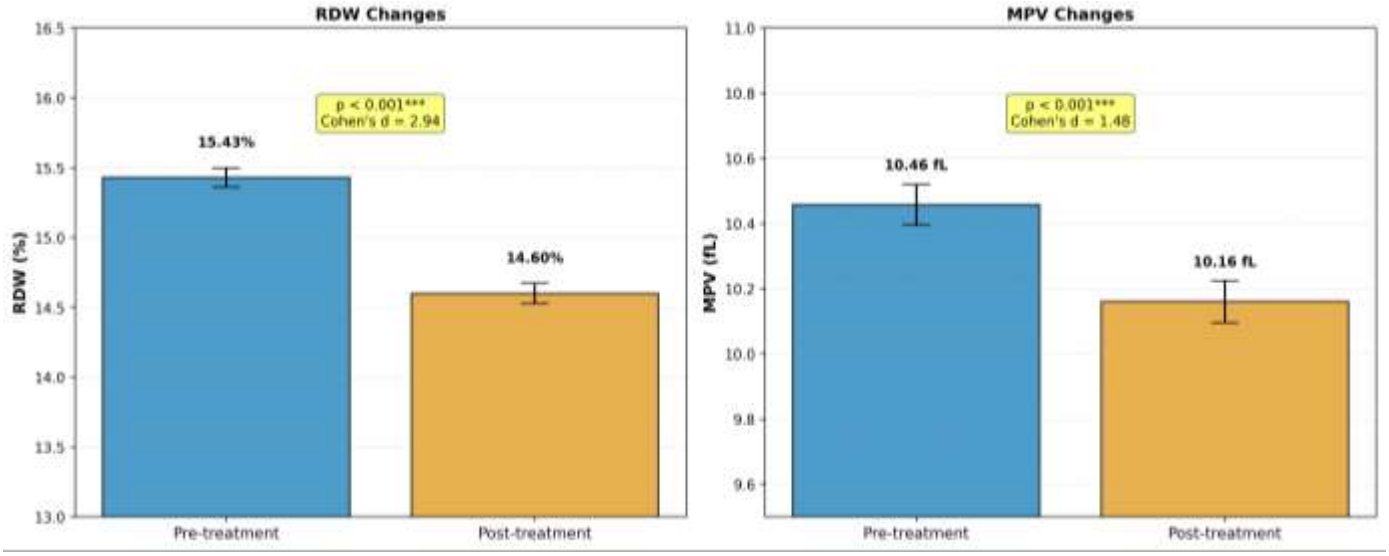

Figure 3. Pre and post Treatment Hematologic parameters

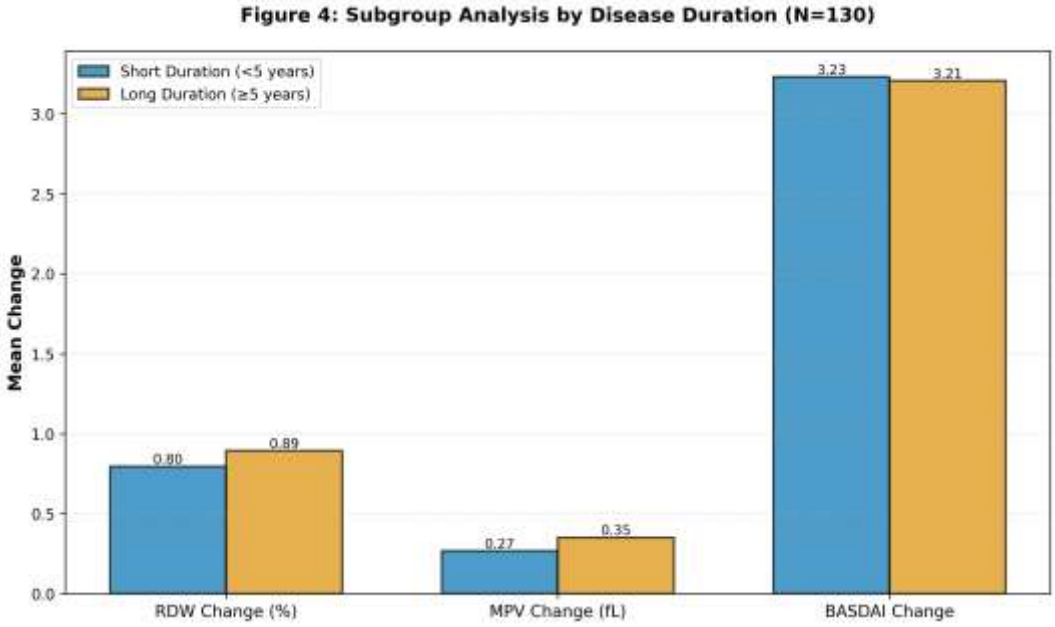

Figure 4. Subgroup Analysis by Disease Duration

3.4. Subgroup and Regression Analyses

Age-stratified analysis showed that older patients (≥40 years) demonstrated greater MPV reduction (0.35 ± 0.20 fL) compared to younger patients (<40 years, 0.27 ± 0.19 fL, $p = 0.026$). Disease duration-stratified analysis revealed that patients with longer disease duration (≥5 years) showed greater MPV reduction (0.35 ± 0.20 fL) compared to those with shorter duration (0.27 ± 0.20 fL, $p = 0.020$). Multiple linear regression analysis confirmed that the reductions in RDW and MPV remained statistically significant after adjusting for potential confounders.

3.5. Correlation Analyses

Pre-treatment RDW values demonstrated significant positive correlations with disease activity markers: BASDAI ($r = 0.33$, $p < 0.001$), ESR ($r = 0.45$, $p < 0.001$), and CRP ($r = 0.42$, $p < 0.001$). Changes in RDW and MPV did not significantly correlate with changes in BASDAI.

Table 3. Subgroup Analyses of Hematologic Parameter Changes

Subgroup	n	RDW Change (Mean ± SD)	MPV Change (Mean ± SD)	BASDAI Change (Mean ± SD)
Gender				
Male	86	0.84 ± 0.29	0.31 ± 0.18	3.26 ± 0.72
Female	44	0.81 ± 0.27	0.28 ± 0.23	3.15 ± 0.82
p-value		0.631	0.411	0.468
Age				
<40 years	83	0.80 ± 0.28	0.27 ± 0.19*	3.23 ± 0.75
≥40 years	47	0.88 ± 0.29	0.35 ± 0.20*	3.21 ± 0.76
p-value		0.160	0.026*	0.861
Disease Duration				
<5 years	83	0.80 ± 0.28	0.27 ± 0.20*	3.23 ± 0.79
≥5 years	47	0.89 ± 0.27	0.35 ± 0.20*	3.21 ± 0.68
p-value		0.059	0.020*	0.857
Treatment Duration				
<18 months	65	0.81 ± 0.28	0.29 ± 0.20	3.21 ± 0.75
≥18 months	65	0.86 ± 0.29	0.32 ± 0.19	3.25 ± 0.77
p-value		0.291	0.389	0.721
Treatment Adherence				
≥85%	70	0.83 ± 0.28	0.31 ± 0.19	3.19 ± 0.76
<85%	60	0.83 ± 0.29	0.29 ± 0.21	3.26 ± 0.76
p-value		0.990	0.599	0.589

Note: ***Significant difference after Bonferroni correction (corrected alpha = 0.0033). SD, standard deviation.**

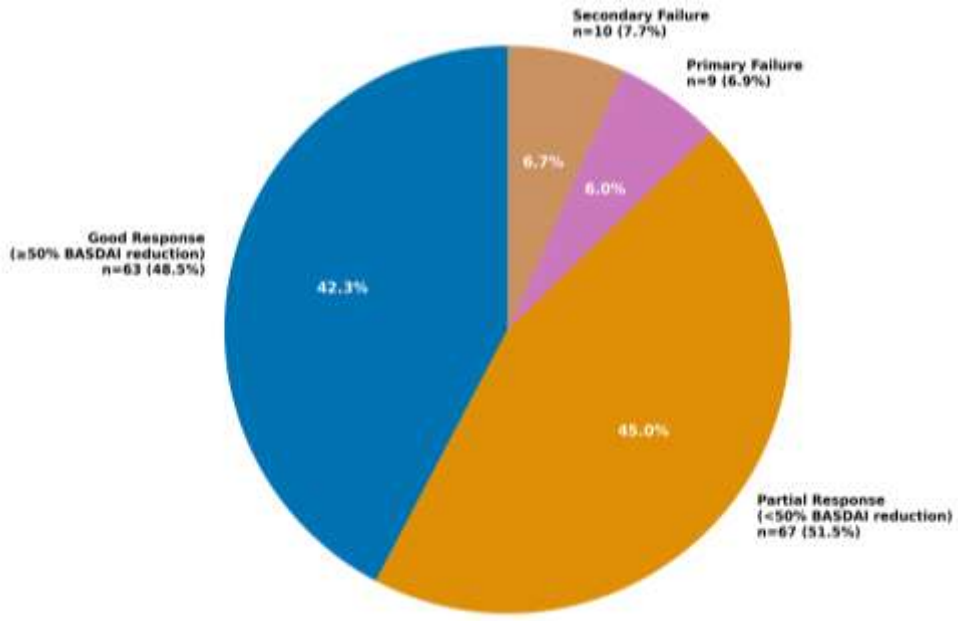

Figure 5. Treatment Response Distribution

4. Discussion

This retrospective study demonstrates that anti-IL-17 therapy effectively suppresses disease activity and systemic inflammation in AS patients, with significant reductions in clinical and laboratory disease activity markers. The 48.5% good clinical response rate aligns with published efficacy data for anti-IL-17 therapy in AS[22].

RDW and MPV Reduction

The normalization of RDW following anti-IL-17 therapy suggests that IL-17 inhibition effectively reduces systemic inflammation and restores normal erythropoiesis and iron metabolism. Similarly, the reduction in MPV suggests a decrease in both platelet consumption and compensatory production upon IL-17 inhibition. The observation that older patients and those with longer disease duration showed significantly greater MPV reduction suggests that chronic inflammation may lead to more pronounced platelet consumption and turnover, which is more dramatically reversed upon effective anti-IL-17 therapy. The regression analysis further strengthened these findings by showing that the changes in RDW and MPV are independent of age, disease duration, and comorbidities.

Discordance Between Hematologic and Clinical Responses

The absence of significant correlation between changes in RDW/MPV and changes in BASDAI is a critical finding. BASDAI is a patient-reported outcome measure heavily influenced by subjective symptoms such as pain and fatigue. In ankylosing spondylitis, chronic pain memory, central sensitization, and central pain mechanisms play a significant role[12,23]. Therefore, even when peripheral systemic inflammation is effectively suppressed (as evidenced by reductions in objective markers like RDW, MPV, CRP, and ESR), patients may still report high BASDAI scores due to these central pain mechanisms. This discordance highlights that RDW and MPV reflect fundamental systemic hematologic responses to inflammation, while BASDAI may capture a combination of residual inflammation and chronic pain sensitization.

Clinical Implications and Proposed Cut-off Values

The significant reductions in RDW and MPV in parallel with clinical and inflammatory markers suggest that they might serve as potential adjunctive biomarkers for monitoring treatment response. Based on our preliminary findings, we propose the following exploratory observations: (1) RDW reduction of ≥0.80% and (2) MPV reduction of ≥0.27 fL. However, it is crucial to emphasize that these proposed thresholds represent strictly exploratory, hypothesis-generating findings from this single-center retrospective study. They are not supported by predictive analyses such as ROC curves and require robust validation in prospective, multi-center studies before any clinical implementation.

Limitations

This study has several limitations. First, the retrospective design limits the ability to establish causality. Second, the absence of a control group (untreated AS patients or TNF inhibitor-treated patients) means that conclusions regarding RDW and MPV as monitoring biomarkers should be interpreted cautiously. Third, while we adjusted for some confounders via regression analysis, factors like specific concurrent NSAID or corticosteroid doses and detailed lifestyle factors were not fully controlled.

5. Conclusion

Anti-IL-17 therapy effectively suppresses disease activity and systemic inflammation in AS patients. The significant reductions in RDW and MPV alongside clinical and inflammatory markers suggest that these readily available hematologic parameters may be considered as potential adjunctive, hypothesis-generating biomarkers for monitoring treatment response and systemic inflammation in AS. Due to the retrospective nature of the

study and the lack of a control group, these findings should be interpreted cautiously. Future prospective, multi-center studies with larger cohorts, longer follow-up periods, and predictive modeling are needed to validate the clinical utility of RDW and MPV as biomarkers in AS.

Author Contributions: Emrah Koç: Conceptualization, data curation, formal analysis, investigation, methodology, writing – original draft, writing – review & editing. Suade Özlem Badak: Conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, supervision, validation, visualization, writing – original draft, writing – review & editing. Both authors reviewed and approved the final manuscript.

Acknowledgments: We thank the patients who participated in this study and the nursing staff at the Department of Rheumatology for their assistance in data collection.

Ethical Approval: This study was approved by the Clinical Research Ethics Committee of Adana City Training and Research Hospital (Date: 27.01.2022, Decision No: 1761). Informed consent was obtained from all participants.

Conflict of Interest: The authors declare no competing interests.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data Availability: The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

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