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# Can disease activity be detected with serum biomarkers in ankylosing spondylitis?

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## ABSTRACT

**Aims:** The inflammation in ankylosing spondylitis (AS) patients is crucial regarding disease activity and progression. This study aims to evaluate the diagnostic significance of inflammatory markers in assessing disease activity in AS.

**Methods:** Seventy-six patients meeting the criteria were retrospectively evaluated between January 2024 and June 2024. Inflammatory markers such as neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio, platelet-to-lymphocyte ratio, Systemic Inflammatory Index (SII), and uric acid-to-HDL cholesterol ratio (UHR) were analyzed. Patients were divided into two groups as active and inactive AS according to the Bath Ankylosing Spondylitis Disease Activity Index score. Receiver operating characteristic (ROC) analysis was performed to investigate the diagnostic role of UHR and SII in indicating active disease.

**Results:** In the active disease group, parameters indicating inflammation, such as NLR (p=0.003), SII (p=0.001), and UHR (p=0.008), were found to be significantly elevated statistically. Positive statistically significant correlations were observed in correlation analysis between disease activity score and SII (r=0.36, p=0.006) and UHR (r=0.46, p=0.0001). ROC analysis revealed that UHR and SII have a high diagnostic role in indicating active disease.

**Conclusion:** NLR, SII, and UHR are considered to have a diagnostic role in indicating inflammation and active disease in AS patients.

**Keywords:** Ankylosing spondylitis, inflammation, uric acid-to-HDL cholesterol ratio

## INTRODUCTION

Axial spondyloarthritis is a chromatic disease that primarily affects the axial spine and can be associated with peripheral symptoms such as arthritis, enthesitis, dactylitis, and various systemic diseases.[1] Ankylosing spondylitis (AS) is at the forefront of this group of diseases. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are nonspecific inflammatory markers that monitor these diseases.[2] However, alternative markers for indicating inflammation have been increasingly utilized due to their low sensitivity and specificity. Complete blood count (CBC) is a simple, cost-effective, and non-time-consuming laboratory test frequently used to monitor rheumatic diseases. Blood cells are often affected during inflammatory states, allowing inflammatory activity to be assessed using circulating blood cells.[3] Platelet, lymphocyte, neutrophil, neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and Systemic Immune-Inflammatory Index (SII) have been found valuable in indicating disease activity in AS in previous studies.[2,4-6] Additionally, the uric acid/high-density lipoprotein (HDL) cholesterol ratio (UHR) is a biochemical marker associated with chronic inflammatory conditions such as thyroiditis, metabolic syndrome, type 2 diabetes mellitus, sacroiliitis, cardiovascular diseases, and chronic kidney failure.[7-11]

The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) is the most commonly used scale for determining disease activity in AS, but its reliance on patient-reported outcomes limits the attainment of highly objective results. This index consists of 6 questions assessing fatigue, spinal pain, peripheral joint pain, sensitivity to touch or pressure, duration, and severity of morning stiffness. Each question is scored from 0 to 10, and a score of 4 or higher indicates active disease.[12] The non-objective results on this scale have led to the search for new markers that can be used to show disease activity in AS, in patient follow-up, and treatment decisions.

This study aimed to explore the relationship between disease activity and blood parameters obtained from CBC and biochemical tests, which are commonly used to diagnose and monitor chronic inflammatory conditions.

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## METHODS

The study was carried out with the permission of the Sivas Cumhuriyet University Non-interventional Clinical Researches Ethics Committee (Date: 21.03.2024, Decision No: 2024-03/42). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

76 AS patients meeting the ASAS criteria were retrospectively enrolled in the rheumatology outpatient clinic between January 2024 and June 2024.[13] Sacroiliac MRI images of the patients were evaluated according to ASAS criteria (**Figure 1**). Exclusion criteria included metabolic, endocrine, hematologic pathologies, and infectious diseases.

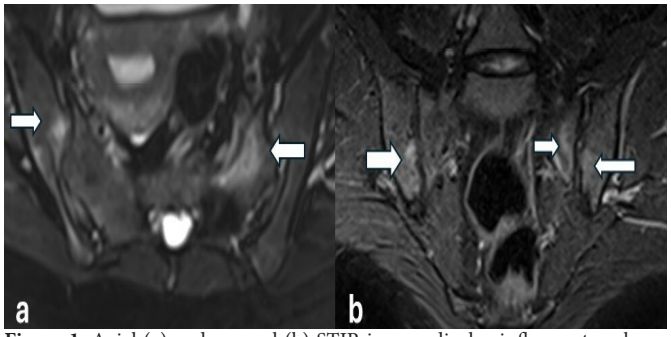


**Figure 1.** Axial (a) and coronal (b) STIR images display inflammatory bone marrow lesions (arrows) bilaterally

The laboratory parameters of the study group were accessed from the hospital's electronic database. Age, gender, ESR, CRP, neutrophil, lymphocyte, monocyte, platelet, uric acid, and HDL cholesterol levels of the patients in the study group were recorded. Disease duration, HLA-B27 genetic test results, and medications were also queried. BASDAI was used to assess disease activity, with scores of 4 and above indicative of active disease. NLR, MLR, PLR, UHR, and the SII, calculated using the formula platelet count X neutrophil count/lymphocyte count, were also calculated and recorded.

### Statistical Analysis

Data analyses were conducted using SPSS version 22.0. Continuous variables were expressed as mean±standard deviation, while categorical variables were reported as percentages. The Kolmogorov-Smirnov test assessed data normality. Qualitative data analysis employed the chi-square ($X^2$) test. Either the T test or the Mann-Whitney U test was applied to continuous data based on normality. Pearson's correlation test evaluated the relationships between variables. Receiver operating characteristic (ROC) analysis was used for diagnostic accuracy. The level of significance was less than 0.05 in all analyses.

## RESULTS

Clinical and demographic data of the patients in the study group are given in **Table 1**.

There was no significant difference in age and gender between the two groups with and without active disease (p>0.05). NLR, SII, and UHR were found to be elevated in the active disease group and statistically significant (p<0.05) (**Table 2**).

Correlation analysis between BASDAI score and SII revealed a statistically significant positive correlation (r=0.36, p=0.006). Similarly, a statistically significant strong positive correlation was found between BASDAI score and UHR (r=0.46, p=0.0001).

**Table 1. Clinical and demographic data of AS patients**

| | AS patients (n=76) |
|---|---|
| **Age, years, mean (±SD)** | 42.98±10.72 |
| **Gender, female, n (%)** | 44 (58%) |
| **Disease time, years, median(min-max)** | 8 (1-40) |
| **HLA-B27 positivity, n (%)** | 57 (75%) |
| **Treatment, n (%)** | |
| NSAIDs | 7 (9%) |
| DMARDs | 11 (15%) |
| Biologic drug | 58 (76%) |
| **BASDAI, mean (±SD)** | 5.20±2.21 |

AS: Ankylosing spondylitis, SD: Standard deviation, NSAIDs: Non-steroidal anti-inflammatory drugs, DMARDs: Disease-modifying antirheumatic drugs, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index

**Table 2. Comparison of demographic and laboratory data according to AS disease activity**

| | | Active AS | Inactive AS | p |
|---|---|---|---|---|
| Gender | Female (n, %) | 29 (38.1%) | 15 (19.7%) | 0.37[1] |
| | Male (n, %) | 18 (23.7%) | 14 (18.5%) | |
| Age (years) | | 43.97±9.28 | 41.05±13.15 | 0.33[2] |
| CRP (mg/L) | | 4.54 (0.56-20.50) | 1.87 (0.37-31.00) | 0.68[3] |
| ESR (mm/h) | | 11 (3-33) | 8 (2-29) | 0.02[3]* |
| Neutrophil count ($10^9$/L) | | 5.49±1.62 | 3.83±1.30 | 0.0001[2]* |
| Lymphocyte count ($10^9$/L) | | 2.38 (1.49-4.98) | 2.27 (1.48-4.56) | 0.64[3] |
| Monocyte count ($10^9$/L) | | 0.44 (0.16-0.96) | 0.44 (0.29-0.74) | 0.85[3] |
| Platelet count ($10^9$/L) | | 277 (188-478) | 270 (165-348) | 0.44[3] |
| Uric acid (mg/dl) | | 4.86±1.15 | 3.90±0.55 | 0.001[2]* |
| HDL cholesterol (mg/dl) | | 47.21±18.38 | 57.36±13.49 | 0.007[2]* |
| NLR | | 2.31±0.75 | 1.70±0.66 | 0.003[2]* |
| MLR | | 0.18 (0.10-0.40) | 0.19 (0.12-0.40) | 0.44[3] |
| PLR | | 106.76 (46.56-230.92 | 116.58 (57.09-179.73) | 0.78[3] |
| SII | | 643.75±255.17 | 434.15±179.87 | 0.001[2]* |
| UHR (%) | | 9.7 (4-31) | 6.7 (4-29) | 0.008[3]* |

AS: Ankylosing spondylitis, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, HDL: High-density lipoproteins, NLR: Neutrophil/lymphocyte ratio, MLR: Monocyte/lymphocyte ratio, PLR: platelet/ lymphocyte ratio, SII: Systemic Inflammatory Index, UHR: Uric acid/HDL cholesterol ratio, Chi-square analysis, Independent-sample T test, Mann-Whitney U test, *p<0.05: Statistically significant

The diagnostic role of UHR and SII in determining active disease was investigated using ROC analysis. UHR values above 7.3% showed 67.6% sensitivity and 73.7% specificity (AUC: 0.71, p=0.008, 95% CI: 0.58-0.85). Likewise, SII values above 523.92 demonstrated 70.3% sensitivity and 73.7% specificity (AUC: 0.74, p=0.003, 95% CI: 0.60-0.87) (**Figure 2**).

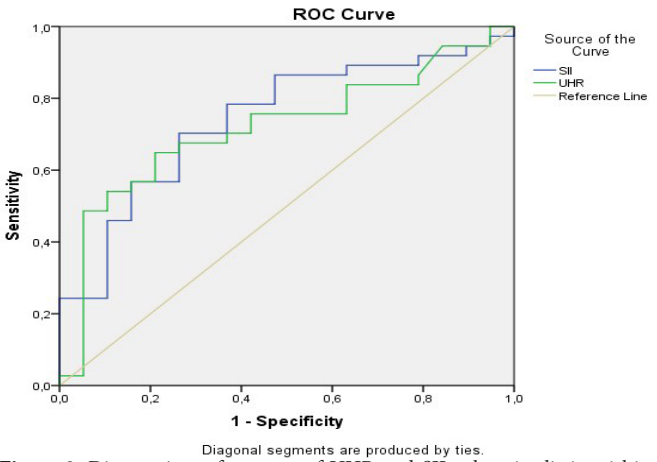


**Figure 2.** Diagnostic performance of UHR and SII values in distinguishing active disease from inactive disease by ROC curve analysis

UHR: Uric acid-to-HDL cholesterol ratio, SII: Systemic Inflammatory Index, ROC: Receiver operating characteristic

## DISCUSSION

In this study, inflammatory markers such as NLR, SII, and UHR were found to be elevated in active AS patients. Additionally, it was concluded that SII and UHR have diagnostic importance in identifying active disease.

NLR is a biomarker widely used in various inflammatory conditions, and numerous studies have investigated its relationship with disease activity and utility in rheumatic diseases.[14-17] In a study assessing the predictability of NLR and PLR in determining disease activity in AS patients, these markers were elevated in the group identified as having active disease based on BASDAI.[18] A meta-analysis examining the role of NLR in twelve studies related to AS concluded that high NLR serves as a robust indicator of underlying inflammation in AS.[19] Consistently, this study also concludes that elevated NLR in AS patients is associated with disease activity and is a useful predictor in forecasting disease activity, aligning with findings from other research.

SII is noted for its ease of use and cost-effectiveness for patients and clinicians.[2] Initially identified as a prognostic marker in liver cancers, SII has since been studied in various cancer types, including cardiovascular, endocrine, and rheumatologic diseases.[20-24] In a study involving 136 AS patients and 63 healthy volunteers, SII was found to be higher in AS patients compared to healthy individuals, and among the patient group, it was higher in those with active disease compared to those with inactive disease. Thus, SII was concluded to be a marker that can indicate disease activity in AS.[2] In another study by Wu et al.,[2] which used BASDAI to calculate disease activity, SII was also found to be valuable in determining disease activity. Sara et al.,[3] in their study on the importance of complete blood count in determining activity in rheumatologic diseases, similarly concluded that SII was elevated in AS patients and correlated with disease activity. This study also arrived at similar conclusions, highlighting SII as an important biomarker for indicating disease activity in AS. Unlike Sara et al.'s study, which used ASDAS instead of BASDAI to indicate disease activity, the current study also emphasizes the role of SII in assessing disease activity in AS.

Uric acid is formed as a result of purine metabolism. Elevated uric acid levels have been shown to correlate with inflammatory markers such as interleukin 1β (IL-1β), IL-6, and CRP.[25,26] HDL cholesterol is a protective factor that reduces cardiovascular risk, with roles including anti-thrombotic, anti-inflammatory, and antioxidant functions.[27] UHR has been studied in various conditions from endocrine disorders to sacroiliitis, where it is important in diagnosis, detecting complications, and determining prognosis.[8,9,28,29] In a study investigating the diagnostic role of UHR in patients with sacroiliitis, UHR levels were found to be higher compared to the control group, and positive correlations with other inflammatory markers were identified, suggesting its usefulness in detecting sacroiliitis.[9] Another study on Hashimoto's thyroiditis, a common autoimmune endocrine disorder, concluded that UHR is easily accessible and correlates with other diagnostic tools.[7] In a study exploring the impact of metabolic parameters on inflammation in RA and SLE patients, it was found that uric acid levels were elevated in these patients, and high uric acid levels were indicative of abnormal lipid profiles.[30] It will be the first study in the literature to evaluate the relationship between UHR and disease activity in AS. Significant differences were found in uric acid elevation, HDL cholesterol decrease, and UHR increase in active AS patients compared to inactive ones. A positive correlation was found between the BASDAI score and UHR. According to ROC analysis results, UHR was found to have high diagnostic value in determining disease activity in AS. Based on these findings, we believe that UHR can also be used to assess disease activity in AS.

### Limitations

The retrospective design and relatively low sample size are limitations of this study. Previously, UHR has never been used to demonstrate inflammation in AS patients. The contribution of this study to the literature lies in the utilization of UHR and its correlation with disease activity.

## CONCLUSION

Inflammatory markers such as NLR, SII, and UHR have been found to increase in active disease in patients with AS. We believe that these markers can be used in the evaluation of disease activity in AS.

## ETHICAL DECLARATIONS

### Ethics Committee Approval

The study was carried out with the permission of the Sivas Cumhuriyet University Non-interventional Clinical Researches Ethics Committee (Date: 21.03.2024, Decision No: 2024-03/42).

### Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

### Referee Evaluation Process

Externally peer-reviewed.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

The authors declared that this study has received no financial support.

### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

## REFERENCES

1. Ramiro S, Nikiphorou E, Sepriano A, et al. ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. *Ann Rheum Dis*. 2023;82(1):19-34. doi:10.1136/ard-2022-223296
2. Wu J, Yan L, Chai K. Systemic Immune-inflammation Index is associated with disease activity in patients with ankylosing spondylitis. *J Clin Lab Anal*. 2021;35(9):e23964. doi:10.1002/jcla.23964
3. Taha SI, Samaan SF, Ibrahim RA, Moustafa NM, El-Sehsah EM, Youssef MK. Can complete blood count picture tell us more about the activity of rheumatological diseases? *Clin Med Insights Arthritis Musculoskelet Disord*. 2022;15:11795441221089182. doi:10.1177/11795441221089182
4. Deng J, Xu S, Gao X, Xu S, Shuai Z, Pan F. Red cell distribution width and mean platelet volume in patients with ankylosing spondylitis: a systematic review and meta-analysis. *J Clin Rheumatol*. 2021;27(7):292-297. doi:10.1097/RHU.0000000000001174
5. Gökmen F, Akbal A, Reşorlu H, et al. Neutrophil-lymphocyte ratio connected to treatment options and inflammation markers of ankylosing spondylitis. *J Clin Lab Anal*. 2015;29(4):294-298. doi:10.1002/jcla.21768

6. Zeb A, Khurshid S, Bano S, et al. The role of the neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio as markers of disease activity in ankylosing spondylitis. *Cureus*. 2019;11(10):e6025. doi:10.7759/cureus.6025
7. Kurtkulagi O, Tel BMA, Kahveci G, et al. Hashimoto's thyroiditis is associated with elevated serum uric acid to high density lipoprotein-cholesterol ratio. *Rom J Intern Med*. 2021;59(4):403-408. doi:10.2478/rjim-2021-0023
8. Kocak MZ, Aktas G, Erkus E, Sincer I, Atak B, Duman T. Serum uric acid to HDL-cholesterol ratio is a strong predictor of metabolic syndrome in type 2 diabetes mellitus. *Rev Assoc Med Bras (1992)*. 2019;65(1):9-15. doi:10.1590/1806-9282.65.1.9
9. Kalfaoglu ME. Could serum uric acid to HDL cholesterol ratio predict sacroiliitis? *PLoS One*. 2023;18(10):e0289624. doi:10.1371/journal.pone.0289624
10. Park B, Jung DH, Lee YJ. Predictive value of serum uric acid to HDL cholesterol ratio for incident ischemic heart disease in non-diabetic Koreans. *Biomedicines*. 2022;10(6):1422. doi:10.3390/biomedicines10061422
11. Cheng Y, Zhang H, Zheng H, et al. Association between serum uric acid/HDL-cholesterol ratio and chronic kidney disease: a cross-sectional study based on a health check-up population. *BMJ Open*. 2022;12(12):e066243. doi:10.1136/bmjopen-2022-066243
12. Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol*. 1994;21(12):2286-2291.
13. Rudwaleit M, van der Heijde D, Landewé R, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis*. 2009;68(6):777-783. doi:10.1136/ard.2009.108233
14. Pekdiker M, Oğuzman H. The first involved joints and associated factors in patients with rheumatoid arthritis. *Arch Rheumatol*. 2024;39(2):274-284. doi:10.46497/ArchRheumatol.2024.10417
15. Cho J, Liang S, Lim SHH, Lateef A, Tay SH, Mak A. Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio reflect disease activity and flares in patients with systemic lupus erythematosus-a prospective study. *Joint Bone Spine*. 2022;89(4):105342. doi:10.1016/j.jbspin.2022.105342
16. Yıldız F, Gökmen O. Haematologic indices and Disease Activity Index in primary Sjogren's syndrome. *Int J Clin Pract*. 2021;75(3):e13992. doi:10.1111/ijcp.13992
17. Kim DS, Shin D, Lee MS, et al. Assessments of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in Korean patients with psoriasis vulgaris and psoriatic arthritis. *J Dermatol*. 2016;43(3):305-310. doi:10.1111/1346-8138.13061
18. Al-Osami MH, Awadh NI, Khalid KB, Awadh AI. Neutrophil/lymphocyte and platelet/lymphocyte ratios as potential markers of disease activity in patients with ankylosing spondylitis: a case-control study. *Adv Rheumatol*. 2020;60(1):13. doi:10.1186/s42358-020-0113-5
19. Khorrampazhouh N, Omranzadeh A, Fazeli B, et al. A Systematic review and meta-analysis of clinical studies on ankylosing spondylitis and neutrophil to lymphocyte ratio. *Curr Rheumatol Rev*. 2022;18(2):160-167. doi:10.2174/1573397117666210921114431
20. Hu B, Yang XR, Xu Y, et al. Systemic Immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. *Clin Cancer Res*. 2014;20(23):6212-6222. doi:10.1158/1078-0432.CCR-14-0442
21. Kelesoglu S, Yilmaz Y, Elcık D, Kalay N. Systemic immune inflammation index: a novel predictor for coronary collateral circulation. *Perfusion*. 2022;37(6):605-612. doi:10.1177/02676591211014822
22. Erinc O, Yesilyurt S, Senat A. A comprehensive evaluation of hemogram-derived inflammatory indices in hashımoto thyroiditis and non-immunogenic hypothyroidism. *Acta Endocrinol (Buchar)*. 2023;19(4):435-440. doi:10.4183/aeb.2023.435
23. Başaran PÖ, Dogan M. The relationship between disease activity with pan-immune-inflammatory value and Systemic Immune-inflammation Index in rheumatoid arthritis. *Medicine (Baltimore)*. 2024;103(9):e37230. doi:10.1097/MD.0000000000037230
24. Ozdemir A, Baran E, Kutu M, Celik S, Yılmaz M. Could systemic immune inflammation index be a new parameter for diagnosis and disease activity assessment in systemic lupus erythematosus? *Int Urol Nephrol*. 2023;55(1):211-216. doi:10.1007/s11255-022-03320-3
25. Zhen R, Wang S, Chen S. The relationship between UA/HDL and diabetic peripheral neuropathy: a cross-sectional analysis. *Diabetes Metab Syndr Obes*. 2024;17:969-980. doi:10.2147/DMSO.S447809
26. Xiong Q, Liu J, Xu Y. Effects of Uric Acid on Diabetes Mellitus and Its Chronic Complications. *Int J Endocrinol*. 2019;2019:9691345. doi:10.1155/2019/9691345
27. Kjeldsen EW, Nordestgaard LT, Frikke-Schmidt R. HDL cholesterol and non-cardiovascular disease: a narrative review. *Int J Mol Sci*. 2021;22(9):4547. doi:10.3390/ijms22094547
28. Aktas G, Yilmaz S, Kantarci DB, et al. Is serum uric acid-to-HDL cholesterol ratio elevation associated with diabetic kidney injury? *Postgrad Med*. 2023;135(5):519-523. doi:10.1080/00325481.2023.2214058
29. Zhao H, Qiu X, Li HZ, Cui JJ, Sun YY. Association between serum uric acid to HDL-cholesterol ratio and nonalcoholic fatty liver disease risk among Chinese adults. *Biomed Environ Sci*. 2023;36(1):1-9. doi:10.3967/bes2022.111
30. Chandrashekara S, Dhote SV, Anupama KR. The differential influence of immunological process of autoimmune disease on lipid metabolism: a study on RA and SLE. *Indian J Clin Biochem*. 2019;34(1):52-59. doi:10.1007/s12291-017-0715-9