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Correlations among quality of life, spinal mobility, and disease activity in early-treated axial spondyloarthritis: a single-center crosssectional study

Tinh Khampaen^{1*}, Thanuchporn Kafaksom¹, Nichapa Dechapaphapitak¹, Nattakirana Tongdee¹ and Parawee Chevaisrakul¹

Abstract

Background Axial spondyloarthritis (axSpA) significantly impacts patients' lives. The ASAS-OMERACT guideline was formulated for the multidimensional evaluation of axSpA patients, employing a specific set of tools. Given the pivotal role of patient perception, comprehensive correlation among these tools, especially concerning quality of life, may provide a clinically relevant perspective and enhance treatment efficacy in the early stages of the disease. This study aims to investigate the correlation among disease activity, functional ability, and quality of life in early-treated axSpA patients. In addition, the association between high disease activity and clinical characteristics was explored.

Methods This cross-sectional study was conducted in a tertiary hospital in Thailand. Patients diagnosed with axSpA according to ASAS classification criteria and receiving treatment from rheumatologists within three years of onset of symptoms were included. Clinical and laboratory data were retrieved from a hospital database. Disease activity was assessed using the Ankylosing Spondylitis Disease Activity Score with ESR or CRP (ASDAS-ESR/CRP) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). Spinal mobility was measured using the Bath Ankylosing Spondylitis Metrology Index (BASMI), while quality of life and function were evaluated using the ASAS Health Index (ASAS-HI) and Bath Ankylosing Spondylitis Functional Index (BASFI), respectively. The correlation between these measurements was analyzed using the Pearson correlation coefficient (r). Additionally, factors associated with high disease activity (ASDAS/CRP > 2.1) were explored using multivariate regression analysis.

Results Sixty-six patients (41 males; mean age 49.3 ± 13.3 years) were enrolled between April to December 2022. Disease activity (ASDAS-CRP) was significantly inversely correlated with spinal mobility (BASMI), function (BASFI), and quality of life (ASAS-HI). High disease activity was associated with obesity (BMI \ge 30 kg/m²) and a longer duration of symptoms before treatment (\ge 2 years).

Conclusion In early-treated axSpA patients, ASDAS-CRP showed significant correlations with functional ability, quality of life, and spinal mobility. High disease activity was associated with obesity and a longer pre-treatment

*Correspondence: Tinh Khampaen tinhxin052@gmail.com

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symptom duration in our study. Early treatment may enhance patients' function, mobility, and quality of life, with weight reduction being possibly beneficial for obese axSpA patients.

Clinical trial number Not applicable.

Keywords Axial spondyloarthritis, Early-treated, Disease activity, Quality of life, Functional ability, Spinal mobility

Introduction

Axial spondyloarthritis (axSpA) classically includes ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA). However, psoriatic arthritis (PsA) is typically categorized as peripheral spondyloarthritis, which may present axial components and also fulfill criteria of axSpA (some may represent as axPsA) [1, 2]. The Ankylosing Spondylitis Disease Activity Score with CRP (ASDAS-CRP) has emerged as a preferred tool for disease assessment in current practice recommendations due to its longitudinal correlation with syndesmophyte formation, which influences spinal mobility [3–7].

Given the pivotal role of patient perception, the ASAS Health Index (ASAS-HI) is designed to gauge the quality of life (QoL) across various domains like pain, emotional well-being, sleep, and mobility [8]. However, the practical application of ASAS-HI in routine clinical practice faces challenges with its complexity and the wide-ranging aspects it encompasses [8]. Understanding the intricate relationships between disease activity, functional ability, and quality of life, particularly regarding ASAS-HI, may provide a clinically relevant perspective and enhance treatment efficacy [9–13].

Many modifiable factors might attenuate the efficacy of treatment in axSpA patients. For example, the correlations between spinal mobility and disease activity emphasize the role of treatment in the early stage of axSpA to prevent structural damage to the spine, influencing spinal mobility [14]. Obese axSpA patients exhibit higher disease activity, more functional impairment and are refractory to treatment [15]. Sleep disturbance is also reported as a predictor of poor functional outcomes in axSpA patients, emphasizing the need for comprehensive evaluation and intervention [16, 17].

This study endeavors to bridge knowledge gaps by investigating the connection among disease activity, functional ability and quality of life in early-treated axSpA patients. The results may offer practical insights for clinicians managing these patients, especially those at risk of unfavorable outcomes, to optimize holistic care.

Methods

Study design

This cross-sectional study was conducted from April to December 2022, took place at the Division of Allergy, Immunology, and Rheumatology, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University. Written informed consent was obtained from all participants and the study received approval from the Human Research Ethics Committee, Faculty of Medicine Ramathibodi Hospital, Mahidol University (MURA2022/252) according to the Declaration of Helsinki, the Belmont Report. An institutional Review Board (IRB) reviewed the data safety in accordance with the personal data protection act (PDPA), study conduction, and scientific validity throughout the research to maintain its integrity.

Participants

Eligible patients were ≥ 18 years of age and diagnosed with axial spondyloarthritis (axSpA) according to Assessment of Spondyloarthritis International Society (ASAS) classification criteria [18]. Patients must have been receiving treatment from rheumatologists at the Ramathibodi Hospital Rheumatology Clinic within three years of the onset of symptoms. Patients who were ineligible to obtain BASDAI, BASMI, BASFI, ASAS-HI, and ASDAS or those who lost follow-up of more than one year were excluded.

Procedures

After obtaining written informed consent, demographic data comprising gender, age, disease duration, disease features, comorbidities, treatment, and laboratory tests were collected. The same investigator reviewed and examined all participants throughout the study period. Demographic data and laboratory results were retrieved from a hospital database. A set of questionnaires was used to collect disease activity (ASDAS-ESR/ CRP, BASDAI), function, and quality of life (BASFI, and ASAS-HI) [3, 8, 19, 20]. To assess spinal mobility using BASMI which measures range of motion through the tragus-to-wall test, cervical rotation test, modified lumbar Schober's test, lumbar side flexion test, and intermalleolar distance were recorded and reported as a 2-point definition and 10-step definition composite index, BASMI2 and BASMI10, respectively [21]. These questionnaires have been validated in the Thai version [22].

Statistical analysis

To evaluate the influence of modifiable factors such as obesity, sleep disturbance, and mood disorder on disease activity in axSpA patients, stratified by disease activity, ASDAS-CRP \geq .

2.1, we collected data of body mass index (BMI), Mood disorder was defined using Hospital Anxiety and Depression Scale (Thai HADS) [23], while sleep disturbance was determined by the answer of question number 16 in the ASAS-HI questionnaire (yes or no).

Demographic data were analyzed using descriptive statistics. Pearson correlation coefficients (r) were employed to assess the relationships between disease activity, spinal mobility, function, and quality of life. Multivariate regression analysis was conducted to identify factors associated with disease activity. For comparisons between groups, p-values were obtained using independent samples t-tests or Mann-Whitney U tests for continuous variables, and Chi-square tests or Fisher's exact tests for categorical variables. For comparisons involving more than two groups, ANOVA tests were used. All statistical analyses were performed using Stata, with a significance level set at a two-tailed p-value < 0.05.

The sample size was calculated based on the correlation coefficient between disease activity and quality of life measures, using a p-value of 0.05 and a power of 0.80. This resulted in a required sample size of 29 patients to detect a moderate correlation (r=0.5) among disease activity, function, quality of life, and spinal mobility measures.

Results

The study included 66 patients identified as having earlytreated axSpA. The majority of these patients were male (61.2%). Among the participants, 48 (72.3%) were classified as having radiographic axSpA according to the Modified New York criteria for ankylosing spondylitis [24]. Psoriasis was present in 18.2% of the patients. The HLA-B27 antigen was detected in 60% of the participants, with a higher prevalence in those with ankylosing spondylitis (90%) and radiographic axSpA (81.2%). Peripheral joint involvement was present in 37.9% of the patients. 9 (13.6%) patients were diagnosed with psoriatic arthritis (PsA) with axial radiographic changes in this study group before enrollment. Detailed clinical and laboratory data are presented in Table 1.

The correlation between disease activity, spinal mobility and quality of life/function

Multiple assessment tools provide a multi-dimensional perspective on the disease. However, routine clinical practice may face challenges due to the complexity of these tools, especially in evaluating the quality of life.

Given the pivotal role of patient perception, a comprehensive correlation between disease activity (ASDAS-ESR/CRP), mobility (BASMI), and, particularly, quality of life and function (ASAS-HI, BASFI) was performed to offer a clinically relevant perspective and enhance the efficacy of treatment in the early stage of the disease (refer to Table 2).

In early-treated axSpA, the study revealed a robust correlation between tools evaluating disease activity, specifically ASDAS-CRP and BASDAI (rho=0.7260, p<0.0001). Notably, moderate correlations emerged among tools assessing disease activity (ASDAS-CRP), function (BASFI), and quality of life (ASAS-HI) (rho=0.5443 and 0.5434, p<0.0001 for both). Nonetheless, the correlation between disease activity (ASDAS-CRP) and spinal mobility (BASMI) was low (rho=0.3338, p=0.0062). Additionally, a strong correlation was found between tools determining mobility (BASMI 2-point and BASMI 10-point systems) (rho=0.8838, p<0.0001). Unfortunately, ASDAS-ESR showed moderate to low correlations with other tools.

When comparing tool performance to assess disease activity defined by using a cut-off ASDAS-CRP>2.1 (balancing between sensitivity and specificity) among tools evaluating disease activity, mobility, and quality of life, we used ROC curve analysis (refer to Fig. 1). As expected, ASDAS-ESR exhibited the highest performance (AUC 0.8295), followed by BASFI, ASAS-HI, and BASMI10. BASMI2 had the lowest performance in predicting high disease activity (AUC 0.6459).

Factors predicting high disease activity in earlytreated axSpA

To optimize holistic care in the early stages of disease, it is crucial to identify individuals at risk of unfavorable outcomes. Although the sample size of this study was not specifically estimated for this purpose, it is worthwhile to analyze whether there is an association between modifiable factors and high disease activity (ASDAS>2.1).

We categorized patients into groups of high and low disease activity based on ASDAS-CRP scores at a threshold of 2.1 and observed that both groups exhibited similar age ranges and gender distributions. No significant differences were noted in HLA-B27 status, radiographic damage, smoking habits, peripheral joint involvement, enthesitis, and previous uveitis (Table 1). There is no difference in the use of conventional DMARDs between the two groups. Notably, only 24.2% of patients had received biologics, and there were no significant differences in disease activity between biologics users and non-users. However, we observed a trend towards a higher proportion of biologics users achieving low disease activity.

In contrast, several notable differences were observed between the groups. The high disease activity group had a higher mean body mass index (BMI) of 27.5 compared to 24.7 in the low disease activity group, as well as a significantly greater prevalence of obesity (31.3% vs. 8.1%). Longer disease duration appeared to correlate with higher disease activity, as the high disease activity group

Table 1 Demographic data

	Total (n=66)	ASDAS- CRP< 2.1	ASDAS- CRP ≥ 2.1	P- value
		(n=37)	(n = 29)	
Age, years, mean (SD)	49.3 (13.5)	49.08 (14.01)	49.65 (13.13)	0.868
Male sex, n (%)	41 (62.1)	22 (59.46)	19 (65.52)	0.615
BMI, mean (SD)	25.9 (6.2)	24.7 (3.57)	27.5 (8.21)	0.060
- BMI < 30, n (%) *	54 (81.8)	34 (91.9)	20 (66.7)	0.017
- BMI ≥ 30, n (%)	12 (18.2)	3 (8.1)	9 (31.3)	
HLA-B27 positivity, n (%)	44	23 (62.16)	21 (72.41)	0.381
Radiographic change, n (%)	48	25 (67.57)	23 (79.31)	0.288
Smoking, n (%)	10	4 (10.8)	6 (20.69)	0.315
Previous duration of diagnosis before enroll- ment, years, median (IQR)	8 (4–12)	8 (3–10)	9 (4–15)	0.164
Duration of symptoms	1.2 (1.2)	0.9 (1.1)	1.6 (1.3)	0.034
prior to treatment, years,	43 (65.2)	29 (78.4)	14 (48.3)	0.011
mean (SD)* - ≤ 2 years, n (%) - > 2 years, n (%)	23 (34.8)	8 (21.6)	15 (51.7)	
Peripheral joint involve-	25 (37.9)	12 (32.4)	13 (44.8)	0.303
ment, n (%)	0.4 (1.8)	0.1 (0.3)	0.8 (2.7)	0.020
- TJC-28, mean (SD) - SJC-28, mean (SD)	0.3 (1.6)	0	0.7 (2.5)	0.009
Enthesitis, n (%)	36 (54.5)	19 (51.4)	17 (58.6)	0.556
Previous uveitis, n (%)	25 (37.9)	13 (35.1)	12 (41.4)	0.604
Syndesmophyte pres- ence, n (%)*	30 (45.5)	11 (29.7)	19 (65.5)	0.004
The highest grade of sacroiliitis, median (IQR)	3 (2–4)	3 (2–3)	3 (2–4)	0.155
Psoriasis, n (%)	12 (18.2)	8 (21.6)	4 (13.8)	0.413
Nail abnormalities, n (%)	11 (16.7)	7 (19.0)	4 (13.8)	0.743
Inflammatory bowel disease (%)	1 (1.5)	0	1 (3.45)	0.439
WBC (x 10^3 cumm), mean (SD)*	7.0 (2.1)	6.1 (1.6)	8.2 (2.1)	< 0.001
Lymphocyte count (x 10^3 cumm), mean	2.0 (0.8)	2.0 (0.9)	2.1 (0.9)	0.661
(SD)				
Hemoglobin (g/dL), mean (SD)	12.7 (1.9)	12.9 (1.8)	12.4 (2.0)	0.274
Platelet count (x 10^3 cumm), mean (SD)	280 (73)	268 (75)	294 (70)	0.164
ESR (mm/Hg), median (IQR)*	28 (15–49)	23 (7–38)	41 (24–67)	0.002
CRP (mg/dL), median (IQR)*	2.5 (0-14.1)	1.5 (0-2.4)	16.2 (7.2–28.9)	< 0.001
Concurrent Medication	44 (66.7)	20 (54.1)	22 (75.9)	0.068
usage, n (%)	34 (51.5)	15 (40.5)	19 (65.5)	0.044
- NSAIDS	56 (84.8)	30 (81.1)	26 (84.9)	0.493
- MTX*	16 (24.2)	6 (16.2)	10 (34.5)	0.086
- SSZ	7 (10.6)	1 (2.7)	6 (20.7)	0.038
- LEF - Glucocorticoid*	16 (24.2) 11 (16.7)	12 (32.4) 9 (24.3)	4 (13.79) 2 (6.9)	0.079 0.095
Biologic usage, n (%) - Anti TNF	5 (7.6)	9 (24.3) 3 (8.1)	2 (6.9) 2 (6.9)	1.000
-Secukinumab *P-value<0.05				

*P-value<0.05

 Table 2
 Correlation matrix (Spearman's rho) of the ASDAS-ESR/

 CRP versus other disease activity score without laboratory tests
 (BASDAI), function (BASFI), quality of life (ASAS-HI), and spinal mobility measurements (BASMI)

	BASDAI	BASFI	ASAS-HI	BASMI 2-point system	BASMI 10-point system
ASDAS-CRP	0.7260	0.5443	0.5434	0.1918	0.3338
ASDAS-CRP	< 0.0001	<0.0001 <	<0.0001	0.1918	0.3338
ASDAS-ESR	0.7040 <0.0001	0.4968 <0.0001	0.5640 <0.0001	0.1360 <0.0001	0.2254 0.0689
BASDAI		0.5776 <0.0001	0.6558 <0.0001	-0.0896 0.4744	0.0261 0.8355
BASFI			0.7435 <0.0001	-0.0551 0.6602	0.2693 0.0288
ASAS-HI				-0.0551 0.6602	0.0698 0.5774
BASMI					0.8838
2-point system					<0.0001

had a slightly longer median disease duration (9 years vs. 8 years) and a greater percentage of patients with disease onset exceeding 10 years (41.5% vs. 16.5%) (see Table 1). More specifically, the high disease activity group had a longer duration before starting treatment (1.6 years vs. 0.9 years).

We stratified patients into three groups based on the duration of time before treatment: less than 1 year, 1-2 years, and 2-3 years. There was no significant difference in the proportion of patients exhibiting high disease activity among the groups (27.3%, 41.7%, and 68.1%, respectively; p=0.206). However, we did observe a trend indicating that shorter time to treatment was associated with lower disease activity. When further stratifying patients based on disease duration prior to treatment using a cutoff of 2 years, we found that a higher percentage of patients with a longer time to treatment exhibited high disease activity (51.7% vs. 21.6%, p=0.011). Similarly, when using a cutoff of 1 year, we also noted that a greater percentage of patients with a longer time to treatment exhibited high disease activity (60.6% vs. 27.3%, p = 0.021).

Moreover, patients experiencing high disease activity also demonstrated elevated levels of sleep disturbance (62% vs. 35%, p=0.030) and higher Hospital Anxiety and Depression Scale–Depression (HADS-D) scores, indicating increased symptoms of depression (p=0.026). Additional data can be found in Supplementary Appendix Table 1. In multivariate analysis, it was found that obesity (OR 6.24, P-value 0.027) and longer disease duration before treatment (OR 7.33, P-value 0.003) were significantly associated with high disease activity (Table 3).

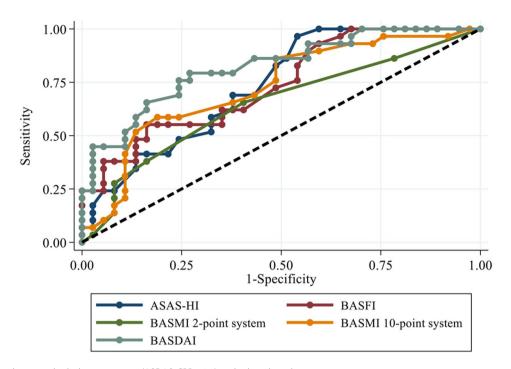


Fig. 1 ROC Curve between high disease activity (ASDAS-CRP ≥ 2.1) and other clinical assessment

Table 3 Univariate analysis and multivariate analysis for high disease activity (ASDAS-CRP ≥ 2.1)

Risk factor	Univariate analysis		Multivariate	Multivariate analysis	
	Odd ratios	P-value	Odd ratios	P-value	
BMI≥30	5.09	0.024	6.24	0.027	
	(1.23–21.07)		(1.23–31.63)		
HADS-D 8-10	3.67	0.090	3.55	0.149	
HADS-D ≥ 11	(0.82–16.43)	0.051	(0.63–19.86)	0.077	
	9.17		8.72		
	(0.99–84.61)		(0.79–95.73)		
Sleep	3.02	0.032	3.18	0.077	
disturbance	(1.10-8.28)		(0.88–11.51)		
Duration of	3.88	0.013	7.33	0.003	
symptoms	(1.33–11.31)		(1.93–27.91)		
prior to treat-					
ment > 2 years					
Syndesmoph-	4.49	0.003			
yte presence	(1.58–12.71)				
WBC count	1.000624	< 0.001			
	(1.000281-				
	1.000967)				

Discussion

Axial spondyloarthritis (axSpA) significantly impacts multiple dimensions of patient health, including disease activity, spinal mobility, and quality of life, with associated costs often underestimated. Establishing correlations among assessment tools—particularly those measuring quality of life—can enhance the efficacy of early treatment strategies.

In our study of early-treated axSpA patients, we found strong correlations among disease activity, spinal

mobility, and quality of life, aligning with previous studies on long-standing disease [9, 25]. In clinical practice, simpler assessment tools are often preferred due to time limitations. The Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP) well reflected for evaluating quality of life and function; however, the modest correlation observed between disease activity and spinal mobility indicates that insufficient treatment may not effectively prevent structural damage. Additionally, targeted therapies that have been shown to delay radiographic progression [26–29] were used by fewer than one-third of our participants during a time when biologics were not widely reimbursed nationally. This limitation restricts our ability to compare disease activity between biologic and non-biologic users due to the small sample size.

The context of our findings helps explain the high usage of conventional DMARDs, as many patients could not afford biologic treatments. Notably, our data revealed that a significant proportion of non-biologic users also achieved low disease activity. Previous studies have reported that a combination of sulfasalazine and methotrexate can reduce disease activity and the need for biologics [30]. Patients with axSpA may experience a partial response to conventional DMARDs, as indicated by the predominant drug use in our study, particularly in settings with limited resources. Nonetheless, we observed similar treatment responses when using either 1 year or 2 years as the cutoff for time to treatment. Our results illustrate the effects of time to treatment based on these cutoffs. We believe that the lack of significant differences when comparing the three groups (<1 year, 1–2 years, and 2–3 years) can be attributed to the minimal difference between the <1 year and 1–2 year groups. In contrast, those treated later than 2 years demonstrated a significant lower response. A prior study defined "2 years" as the threshold for early axSpA [31], which supports the relevance of this cutoff in our findings. These data may reinforce the concept of a "window of opportunity" for treatment in early axial spondyloarthritis.

Additionally, our multivariate regression analysis indicated that a longer disease duration before treatment is linked to an increased risk of unfavorable outcomes, confirming our earlier findings. We also found obesity to be associated with higher disease activity. Previous reports have identified depression and sleep disturbances as factors correlated with increased disease activity; however, these variables could not be adequately explored within the limited sample size of our study. This underscores the vital role of primary healthcare in the early detection of disease, particularly for individuals presenting with chronic inflammatory back pain. It also highlights the importance of a multidisciplinary approach in treating axSpA, especially in patients with obesity.

Notably, 18.2% of our participants had psoriasis, but only 13% were previously diagnosed with psoriatic arthritis (PsA) before being enrolled in our study. We classified individuals based on clinical back pain, enrolling those who met the Assessment of Spondyloarthritis International Society (ASAS) classification criteria. This group includes both ankylosing spondylitis (AS/axSpA) associated with psoriasis and axial psoriatic arthritis (axPsA). Given the clinical overlap we assumed between these entities, we chose not to differentiate between them. Our primary focus remained on disease activity and the patient assessment of "axial symptoms." However, a limitation of our study is the potential existence of distinct clinical features between these two entities, even though we currently apply the same treatment algorithm for both axSpA and axPsA.

Our study underscores the significance of syndesmophytes as a poor prognostic indicator in early-treated axSpA patients [32, 33]. The presence of syndesmophytes despite early treatment suggests worse outcomes, necessitating closer monitoring. Additionally, we found a high white blood cell count indicative of heightened disease activity [34], though no significant associations were detected with platelet or lymphocyte counts, likely due to our limited participant pool.

Our study's strengths lie in the focused inclusion of early-treated axSpA patients, a critical treatment period often overlooked. The comprehensive range of measures provides a nuanced understanding of the disease's impact, with the analysis of factors associated with higher disease activity offering valuable insights. Future research endeavors should consider these findings, addressing the highlighted limitation and further exploring the unique characteristics of early-treated axSpA patients for a more comprehensive understanding of their outcomes.

Nevertheless, the study had limitations beyond the sample size, including participant enrollment in a single tertiary hospital setting, potentially influencing selection bias and the generalizability of the results. Additionally, the study did not investigate the impact of certain comorbidities on the disease outcome, such as degenerative spine diseases and fibromyalgia [35].

Conclusion

ASDAS-CRP, a currently recommended disease activity measure for axSpA, demonstrated significantly inverse correlation with poorer spinal mobility and quality of life, in early-treated axSpA patients. Our study found associations between obesity, long disease duration before treatment and disease activity. Consequently, early treatment and a multidisciplinary team, including primary healthcare, may enhance treatment outcomes.

Abbreviations

ASDAS-ESR/CRP	Ankylosing Spondylitis Disease Activity Score with ESR or CRP
axSpA	axial spondyloarthritis
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BASFI	Bath Ankylosing Spondylitis Functional Index
BASMI	Bath Ankylosing Spondylitis Metrology Index
CASPAR	Classification for Psoriatic Arthritis
CRP	C-reactive protein
DMARDs	Disease-Modifying Anti-Rheumatic Drugs
HADS	Hospital Anxiety and Depression Scale
HLA	Human Leucocyte Antigen
NSAIDs	Nonsteroidal Anti-inflammatory Drugs
PsA	psoriatic arthritis
ROC	Receiver Operating Characteristic
SD	standard deviation
SJC-28	Swollen Joint Count of 28 joints
TJC-28	Tender Joint Count of 28 joints
TNF	Tumor Necrosis Factor
WBC	White Blood Cell

Supplementary Information

The online version contains supplementary material available at https://doi. org/10.1186/s41927-024-00426-2.

Supplementary Material 1

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Author contributions

The authors confirm their contributions to the paper as follows: study conception and design - T. Khampaen, P. Chevaisrakul; data collection - T. Khampaen, T. Kafaksom, N. Dechapaphapitak, N. Tongdee; access and verify the data, data analysis and interpretation - T. Khampaen, P. Chevaisrakul; study conclusion - T. Khampaen, P. Chevaisrakul; draft manuscript preparation - T. Khampaen (with valuable suggestions from P. Chevaisrakul). All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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Data availability

The datasets generated and/or analysed during the current study are available in the figshare repository, https://doi.org/10.6084/m9.figshare.25440484[36].

Declarations

Ethics approval and consent to participate

The study received approval from the Human Research Ethics Committee, Faculty of Medicine Ramathibodi Hospital, Mahidol University (MURA2022/252) according to the Declaration of Helsinki, the Belmont Report. Written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

¹Division of Allergy, Immunology, and Rheumatology, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, 270 Rama VI Road, Thung Phayathai Subdistrict, Ratchathewi, Bangkok 10400, Thailand

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