IL-41: A novel serum marker correlates with disease activity in patients with ankylosing spondylitis

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ABSTRACT

Introduction: Interleukin (IL)-41, a type of cytokine also known as Metrnl, is involved in the pathogenesis of various inflammatory and immune-related diseases. However, its role in Ankylosing Spondylitis (AS), a field yet to be explored, remains a mystery. This study therefore assesses the diagnostic utility of IL-41 in patients with AS and examines the correlations among IL-41 levels, disease activity, and patients' demographic and clinical data. Such novel insights could have significant implications for the diagnosis and management of AS.

Materials and methods: Eighty-eight patients diagnosed with AS were enrolled from the Rheumatology Unit at Baghdad Teaching Hospital. Participants were categorized into two groups based on disease status: inactive (n = 44) and active (n = 44). Additionally, 44 matched healthy individuals were included as controls. Comprehensive medical histories were obtained, including disease duration, body mass index, sex, and age. Laboratory parameters related to the disease—such as C-reactive protein, human leukocyte antigen (HLA-B27), and rheumatoid factor—were also measured. Serum IL-41 levels were quantified using an enzyme-linked immunosorbent assay.

Results: The study revealed a significant difference in levels of IL-41 in patients with AS (17.721±0.705 ng/L) compared to controls (8.495±0.984 ng/L; P = 0.009). The mean serum IL-41 concentration was highest in the active group (23.037±5.268 ng/L), followed by the inactive group (12.411±1.672 ng/L; p = 0.001) and controls (8.495±0.984 ng/L). Serum IL-41 levels demonstrated strong validity for diagnosing AS, with a cut-off value of ≥ 9.35 ng/mL and an area under the curve of 0.991. The sensitivity, specificity, and accuracy were 97.7%, 79.5%, and 92.38%, respectively (p = 0.002).

Conclusions: IL-41 is a potential new diagnostic biomarker for AS and associated with patient's disease activity. These insights could potentially transform the way we diagnose and manage AS, offering new avenues for improved patient care and outcomes.

KEYWORDS:
Ankylosing Spondylitis, Interleukin-41, Autoimmune disease, HLA-B27, Disease activity

INTRODUCTION

Ankylosing Spondylitis (AS) is a common inflammatory autoimmune disease primarily targeting spine joints that leads to severe and chronic pain, and in severe cases, vertebrae fusion.[1-3] Diagnosis of AS can be challenging due to the wide range of non-specific, musculoskeletal and extra-articular symptoms associated with the disease. The development of more effective and specific diagnostic tools has been limited, partly due to the limited knowledge of AS pathogenesis.[1]

While pathogenesis remains unclear, AS has been associated with aberrant immune cell function. Consequently, the biochemical markers responsible for mediating immune interactions and cell communications have been investigated.[3] The biochemical parameters for AS diagnosis published by NICE (National Institute for Health and Care Excellence) include human leukocyte antigen (HLA)-B27 levels.[4] In addition, elevated levels of pro-inflammatory cytokines and anti-inflammatory cytokine activity have been associated with vital inflammatory processes in AS.[1,5-6] However, little is known about the association between AS and interleukin (IL)-41, which is the focus of this study.

Interleukins, a type of cytokine, are frequently used as biomarkers to track disease progression and various conditions. Specific interleukins have shown potential in diagnosing and monitoring various diseases. For instance, IL-37 is a potential diagnostic biomarker for juvenile idiopathic arthritis, and IL-39 and IL-40 have been linked to rheumatoid arthritis, autoimmune thyroid disease, and systemic lupus erythematosus.[7-12] IL-6 is involved in rheumatoid arthritis and systemic lupus erythematosus.[13-15] IL-41—also known as meteorin-like (Metrnl) protein—is a cytokine involved in various biological processes, including immune response modulation and tissue repair. Also referred to as IL-41 du e to its cytokine-like functions and, it is encoded by the METRNL gene, located on human chromosome 17 (17q25.3).[16] Although the specific cells responsible for producing IL-41, its target cells, and the signalling pathways involved in its activation are still under investigation, research indicates that many tissues express this cytokine, particularly the barrier tissues of the skin, intestines, and respiratory tract. Additionally, IL-41 has been associated with innate and adaptive immunity, as it is expressed in alternatively activated and M2-like macrophages.[17]

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IL-41 is a novel immunomodulatory cytokine associated with inflammatory conditions such as psoriatic arthritis and is also an anti-inflammatory agent in other conditions.[18-20] Its potential role in spinal inflammation, particularly in AS, has yet to be fully understood. However, early studies suggest that IL-41 may modulate inflammatory responses in tissue repair and immune response, which are central to AS pathogenesis. Further research is required to establish a clearer link between IL-41 and spinal inflammation in AS patients, but the cytokine's dual role in inflammation may indicate its relevance in disease mechanisms. Furthermore, given the promising results of inhibiting some interleukins in inflammatory conditions, including AS, in-depth investigations into pro- and anti-inflammatory cytokines are of utmost importance.[6,21] Thus, evaluating IL-41's role in AS may not only contribute to understanding its pathogenesis but also pave the way for the development of practical diagnostic tools and potentially more effective treatments, underscoring the significance of our research.

One limitation of current biomarkers for AS is their need for more specificity and sensitivity in tracking disease progression. While human leukocyte antigen (HLA-B27) is helpful for diagnosis, it does not correlate with disease severity or treatment response. Additionally, general inflammatory markers like C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are nonspecific and cannot accurately reflect the dynamic inflammatory processes characteristic of AS.

The present study therefore evaluates the novel potential of IL-41 as a biomarker for AS by measuring its levels in patients' serum. Additionally, the correlation between IL-41 levels and AS activity was assessed, and other patient characteristics were evaluated. To the best of our knowledge, this is the first study to investigate the role of IL-41 in AS, offering a fresh perspective and potential breakthrough in our understanding of this complex disease.

MATERIALS AND METHODS

This study enrolled 88 patients over the age of 18 diagnosed with AS based on the Assessment of Spondylarthritis International Society for Spondylarthritis (ASAS) classification criteria.[22] The patients were divided into two subgroups: inactive (n=44) and active (n=44). Additionally, 44 healthy individuals who matched the age and sex of the patients were included as a control group. The participants were recruited from the Rheumatology Unit at the Baghdad Teaching Hospital between November 2023 and January 2024. Exclusion criteria included: patients with overlapping inflammatory disorders, such as rheumatoid arthritis, psoriasis or inflammatory bowel disease; pregnant women; patients with comorbidities, such as malignancies; and refusal to participate. The study was approved by the Committee of Scientific Ethics from the College of Medicine, University of Baghdad (approval number: 0231).

For each patient, recorded baseline data included disease duration, body mass index (BMI), sex, age and ESR. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Bath Ankylosing Spondylitis Functional Index (BASFI) were used to evaluate disease activity and functional impairment, respectively. In both cases, patients were categorised into two groups, with < 4.0 considered inactive and ≥ 4.0 considered active.[23-24] The full patient information page data and consent forms were completed under the direction of a rheumatologist. Disease-related laboratory parameters included CRP, HLA-B27 and rheumatoid factor (RF). Blood samples (5 mL) were collected from the patients and healthy controls using disposable plastic syringes. Each blood sample was collected in a gel separation tube and then subjected to centrifugation at 3000 rpm for 15 minutes. After centrifugation, the serum samples were frozen at -20°C. The enzyme-linked immunosorbent assay technique (ELISA) was used to measure serum IL-41 (Cloud-clone Corp Company (USA) with product code SER740Hu), CRP levels (Cloud-clone Corp Company (USA) with product code EH0099), HLA-B27 (Elabscience Company (USA) with product code E-EL-H0157) and RF (FineTest Company (USA) with product code EH4269). All manufacturers' instructions were strictly followed during the testing process. All samples were run in duplicate. A plate reader was used to measure the absorbance at 450 nm. The immunological testing was conducted at the International Centre for Research and Development.

Statistical analysis

Statistical analyses were performed using the SPSS Statistical package (Version 26; SPSS, IBM) and Microsoft Office Excel (2010) for drawing the figures, except for the receiver operating characteristic (ROC) curve. Normally distributed data are expressed as (Mean ± SD) (randomised sampling). Independent samples of students (t-tests), analyses of variation (ANOVA) tests and least significant difference (LSD) tests were performed to allow for comparisons of quantitative variables between studied groups (e.g., age, BMI, serum 41 ng/mL). Pearson and chi-square tests were used for comparisons of qualitative variables among the groups (i.e., age, BMI and smoking). Pearson's correlation tests were used to identify relationships among serum 41 ng/mL, age, BMI, duration of AS disease, ESR, CRP, HLA–B27, BASDI and BASFI disease activity. The validity of these tests was estimated with an ROC curve, cut-off value, area under curve (AUC), sensitivity (%), specificity (%), positive predictive value % (PPV), negative predictive value % (NPV) and accuracy. The statistical significance threshold (P–value) was set at P>0.05 for non-significant differences (NS), P<0.05 for significant difference (S) and P<0.01 for highly significant difference (HS).

RESULTS

Table I shows 88 patients with AS, between 18 and 59 years of age, were divided into two groups according to AS disease severity (44 inactive and 44 active). In addition, 44 healthy individuals whose ages ranged from 18 to 57 years old were used as control subjects. Non-significance was set at P>0.05. The greatest number of subjects was within the age range of 31–40 years for the controls (20, 45.5%) and AS patients (31, 35.2%). This was followed by the age range of 18–30 years, with 36.39% (16) controls and 29.5% (26) AS patients in this group. Next was the 41–50-year age range, with 11.4% (5) in controls and 28.46% (25) in AS patients (P = 0.174). The mean ages of the two studied groups were similar, with controls at 33.21 ± 9.113 years and AS patients at 36.47 ± 9.151 years (P = 0.038).

Table I: Demographics and other parameters: distributions within AS patient groups and controls

Parameters	Activity of AS disease			P-value	
	Control	Inactive	Active		
Age group					
18–30	16 (36.4%)	18 (40.9%)	8 (18.2%)	P = 0.107	
31–40	20 (45.5%)	12 (27.3%)	19 (43.2%)		
41–50	5 (11.4%)	11 (25%)	14 (31.8%)		
51–60	3 (6.8%)	3 (6.8%)	3 (6.8%)		
Sex Male	30 (68.2%)	37 (84.1%)	24 (54.5%)	P = 0.011	
Female	14 (31.8%)	7 (15.9%)	20 (45.5%)		
BMI group					
Normal weight	24 (54.5%)	4 (9.1%)	11 (25%)	P = 0.005	
Overweight	15 (34.1%)	15 (34.1%)	16 (36.4%)		
Obese	5 (11.4%)	25 (56.8%)	17 (38.6%)		
Smoking					
Smokers	17 (38.6%)	20 (45.5%)	13 (29.5%)	P = 0.811	
Non-smokers	27 (61.4%)	24 (54.5%)	31 (70.5%)		
Age					
Mean	33.21	34.49	38.11	A	P =0.249
Std. Deviation	9.113	10.317	7.973	B	P =0.004
Std. Error	1.35	1.562	1.195	C	P =0.072
ANOVA test (P-value):	**P = 0.017**				
BMI					
Mean	25.740	27.212	29.066	A	P =0.191
Std. Deviation	4.3702	5.534	5.573	B	P =0.003
Std. Error	0.650	0.833	0.840	C	P =0.102
ANOVA test (P-value):	**P = 0.021**				

Note: P>0.05 = non-significant difference, P<0.01 = highly significant difference.
A = control vs. inactive; B = control vs. active; C = inactive vs. active.

Table II: Mean distributions of parameters within AS patient groups

Parameter	Activity of AS	N	Mean	Std. Deviation	Std. Error	P-value	
Duration							
	Inactive	44	7.61	4.602	0.717	P = 0.838	
	Active	44	7.38	4.911	0.742		
	Total	88					
Disease activity							
BASDI	Inactive	44	2.413	1.083	0.163	P = 0.004	
	Active	44	5.112	0.973	0.147		
	Total	88					
BASFI	Inactive	44	2.523	1.222	0.185	P = 0.002	
	Active	44	5.267	1.283	0.194		
	Total	88					
ESR	Control	44	6.123	3.662	0.546	A	P = 0.002
	Inactive	44	15.104	10.507	1.583	B	P = 0.004
	Active	44	22.595	13.799	2.081	C	P = 0.006
	Total	132	ANOVA test (P–Value): P = 0.005				
CRP (mg/l)	Control	44	2.57	0.334	0.052	A	P = 0.003
	Inactive	44	2.38	0.375	0.057	B	P = 0.007
	Active	44	1.95	0.298	0.054	C	P = 0.001
	Total	132	ANOVA test (P–Value): P = 0.005				
RRF (IU/mL)	Control	44	27.99	5.315	0.811	A	P = 0.097
	Inactive	44	25.71	5.753	0.873	B	P = 0.236
	Active	44	26.12	7.216	1.101	C	P = 0.801
	Total	132	ANOVA test (P-Value): P = 0.471				
HLA-B27 ng/mL)	Control	44	4.604	1.060	0.162	A	P = 0.005
	Inactive	44	6.247	1.032	0.167	B	P = 0.002
	Active	44	9.545	2.358	0.354	C	P = 0.007
	Total	132	ANOVA test (P–Value): P = 0.003				

Note: P>0.05 = non-significant difference, P<0.01 = highly significant difference.
A = control vs. inactive, B = control vs. active; C = inactive vs. active.

Table III: Mean distributions of IL-41 levels within AS patient groups and controls

		IL-41 (ng/mL)				
Activity of AS	**N**	**Mean**	**Std. Deviation**	**Std. Error**	**P-value**	
Control	44	8.495	0.985	0.150	A	P = 0.002
Inactive	44	12.411	1.672	0.252	B	P = 0.004
Active	44	23.037	5.268	0.795	C	P = 0.001
Total	132	ANOVA test (P-Value):		P = 0.003		

Note: P>0.05 = non-significant difference, P<0.01 = highly significant difference.
A = control vs. inactive; B = control vs. active; C = inactive vs. active.

Table IV: Treatment intake distributions within AS patient groups

Type of Medication		**Activity**				**P-value**
		Inactive		**Active**		
		Intake	**NON**	**Intake**	**NON**	
Sulfasalazine	N	0	44	4	40	P = 0.041
	%	0%	100%	9.1%	90.9%	
Methotrexate	N	0	44	1	43	P = 0.315
	%	0%	100%	2.3%	97.7%	
Adalimumab (Humera)	N	0	44	1	43	P = 0.315
	%	0%	100%	2.3%	97.7%	
Etanercept (Enbrel)	N	31	13	30	14	P = 0.817
	%	70.5%	29.5%	68.2%	31.8%	
Adalimumab (Amgevita)	N	7	37	6	38	P = 0.764
	%	15.9%	84.1%	13.6%	86.4%	
Infliximab (ixifi)	N	3	41	0	44	P = 0.078
	%	6.8%	93.2%	0%	100%	
Infliximab (Remsima)	N	3	41	2	42	P = 0.645
	%	6.8%	93.2%	4.5%	95.5%	

Table V: Correlation study between IL-41 and HLA-B27 levels and other AS disease parameters

Pearson Correlation (patients with AS)		**IL-41 (ng/mL)**	**HLA-B27 (ng/mL)**
HLA-B27	r	0.702	
(ng/mL)	P-value	0.0001	
	Sign.	HS	
Age	r	0.146	0.239
	P-value	0.174	0.025
	Sign.	NS	Significant
BMI (kg/m2)	r	0.028	0.158
	P-value	0.794	0.141
	Sign.	NS	NS
Duration	r	0.163	0.002
	P-value	0.130	0.989
	Sign.	NS	NS
BASDI	r	0.633	0.545
(disease activity)	P-value	0.0004	0.0006
	Sign.	HS	HS
BASFI	r	0.591	0.578
(disease activity)	P-value	0.0001	0.0009
	Sign.	HS	HS
ESR mm/h	r	0.170	0.114
	P-value	0.112	0.291
	Sign.	NS	NS
CRP (ng/mL)	r	-.382	-.304
	P-value	0.0007	.004
	Sign.	HS	HS
RF (IU/mL)	r	.104	.140
	P-value	0.333	0.195
	Sign.	NS	NS

Note: P>0.05 = non-significant difference (NS), P<0.01 = highly significant difference (HS).

Male patients predominated, accounting for 64.8% (57) of patients with AS and 65.91% (29) of the control group (P = 0.896).

Regarding BMI, obesity was most common among AS patients, at 47.8% (42), followed by normal weight (35.2%, 31) and overweight (28.4%, 25). In contrast, in the controls, normal weight was at 50% (22), followed by overweight at 36.4% (16) and obese 13.6% (6) (P = 0.004).

Patients with AS were more likely to be non-smokers (65.9%, 58) than smokers (34.1%, 30), while the distribution was even in the control group, at 50% (22) for both smokers and non-smokers (P = 0.976).

The mean BMI in patients with AS was 28.1109 ± 5.58991, which was significantly higher than that of the control group, at 25.7402 ± 4.37015, (P = 0.019).

The 31–40-year age group was the largest among patients with active AS, at 43.2% (19), and controls, at 45.5% (20), whereas those with inactive AS were most likely to be in the 18–30-year age range (40.9%, 18) (P = 0.107).

Among patients with inactive AS, 84.1% (37) were males, and among controls, 30 (68.2%) were males. In contrast, among those with active AS, only 54.5% (24) were males and 45.5% (20) were females (P = 0.011 at P<0.05).

For BMI, obesity rates were elevated among patients with inactive AS (56.8%, 25) and among those with active AS (38.6%, 17); this was followed by overweight (active at 36.4% [16] and inactive at 34.1% [15]). Normal weight was the most common in the control group at 54.5% (24) (P = 0.005).

Regarding smoking, non-smokers made up the largest group both among patients with active AS 31 (70.5%) and among those with inactive AS 24 (54.5%), and their healthy control was highly frequent, while smokers made up 38.6% (17) of the control group, 45.5% (20) of the inactive AS group and 29.5% (13) of the active AS group (P = 0.811).

The mean age was similar in all three groups, with the control group at 33.21 ± 9.113, inactive patients with AS at 34.49 ± 10.317 and active AS patients at 38.11 ± 7.973, with all differences non-significant at P>0.05, except for the difference between controls and patients with active AS, with P = 0.0004.

Mean BMI was also similar among controls (25.740 ± 4.3702), patients with inactive AS (27.212 ± 5.534) and those with active AS (29.066 ± 5. 573), with a non-significant difference at P>0.05 – except for between controls and patients with active AS, where P = 0.003.

Table II shows a highly significant difference at P<0.01 for most parameters when comparing patients with different disease severity. The exceptions are RF IU/mL and duration, which show a non-significant difference at P>0.05 and similar mean ± standard deviations.

The mean for disease activity level was lower in patients with inactive AS (BASDI [2.413 ± 1.083] and BASFI [2.523 ± 1.222]) than in those with active AS (BASDI [5.112 ± 0.973] and BASFI [5.267 ± 1.283]).

The mean ESR mm/h result was higher in patients with active AS (22.595 ± 13.799) than in patients with inactive AS (15.104 ± 10.507) and even lower in the controls (6.123 ± 3.662).

The mean CRP in sera was highest in the controls (2.57 ± 0.334), followed by inactive AS (2.38 ± 0.375) and then active AS (1.95 ± 0.298).

The mean HLA–B27 (ng/mL) was lower in the controls (4.604 ± 1.060) than in the patients with active (9.545 ± 2.358) and inactive AS (6.247 ± 1.032).

The results show that the mean IL–41 ng/mL in the sera of patients with AS (17.721 ± 6.609) is more elevated than in the control group (8.495 ± 0.984), with a highly statistically significant difference (P = 0.009 at P<0.01). Additionally, as shown in Table III, all statistical tests found that the IL–41 ng/mL in the sera of patients with active AS (23.037 ± 5.268) was higher than in patients with inactive AS (12.411 ± 1.672) and controls (8.495 ± 0.984).

Clearly, Etanercept (enbrel) was predominant in patients with inactive AS, at 70.5% (31), and in patients with active AS, at 68.2% (30). This was followed by Adalimumab (Amgevita), at 15.9% (7) in inactive AS and 13.6% (6) in active AS, showing no significant difference (P = 0.158). In most comparisons of medication intake in patients with inactive and active AS, except for sulfasalazine, there was a significant difference at P<0.05. Table IV shows the frequencies for each.

There were no significant differences in IL–41 ng/mL and HLA-B27 among AS patients and those on different medications. Levels of serum IL–41 and other parameters had highly significant inverse (negative) relationships (P<0.01) with CRP (r = -0.382, P = 0.0007). There were highly significant positive relationships (P<0.01) with HLA-B27 (r = 0.702, P = 0.0001), BASDI disease activity (r = 0.633, P = 0.0004) and BASFI disease activity (r = 0.591, P = 0.0001). All other correlations were identified as weakly positive and were not significant (P>0.05). However, HLA-B27 levels and other parameters were significantly positively correlated (P<0.05) with age (r = 0.239, P = 0.025). In addition, there was a significant positive relationship (P<0.01) between BASDI disease activity (r = 0.545, P = 0.0006) and BASFI disease activity (r = 0.578, P = 0.0009). All other correlations were weakly positive and classified as non-significant (P>0.05).

Validity of tests

The results demonstrated that serum IL-41 can be used for diagnosing patients with AS at a cut-off value of 9.35 ng/mL and an AUC of 0.991. Moreover, the tests showed that sensitivity increased greatly (97.7%), with very good specificity (79.5%) and positive predictive (90.5%) and negative predictive (94.6%) values. The accuracy of the tests was also high (92.38%), with a highly statistically significant

difference (P<0.001). Moreover, serum HLA–B27 was shown to have high validity, with a cut-off value of 5.2 ng/mL, an AUC of 0.953, a sensitivity of 95.5%, good specificity (70.5%), and positive predictive and negative predictive values of 86.6% and 88.6%, respectively. In addition, its accuracy was 67.12%, and it had a highly statistically significant difference at P < 0.007.

DISCUSSION

IL-41 is gaining recognition within the immunological community for its roles in autoimmune pathophysiology. Its effects on both the pro-inflammatory[25] and anti-inflammatory pathways[26-27] suggest its utility as a biomarker for various inflammatory conditions. AS, a chronic condition affecting the axial skeleton, poses diagnostic challenges due to its complex symptoms and similarity to other rheumatologic diseases.[28] Here, we critically assess the findings of this study in light of the existing literature to explore IL-41's capability to refine diagnostic criteria and enhance AS-treatment strategies.

The results showed that IL-41 serum levels are significantly higher in patients with active AS, highlighting its potential as a biomarker for assessing disease activity. This correlation is particularly compelling because it dovetails with emerging research which suggests that cytokines play a central role in the pathogenesis and monitoring of inflammatory diseases.[29] In the context of AS, the activity of the disease is often evaluated through clinical assessments and inflammatory markers such as CRP and ESR. However, levels of these markers do not always correlate directly with symptoms or long-term outcomes, which complicates disease management.[30] The use of IL-41 as a biomarker may offer a more direct and reliable measurement of the underlying inflammation specific to AS pathophysiology. IL-41 levels may serve as a potential biomarker for disease activity in AS, but further multicentre studies with larger sample sizes are required to confirm its role and explore its potential clinical applications. Furthermore, studies on other rheumatologic diseases have shown that cytokines such as IL-6 and IL-23 are valuable for both diagnosis and therapeutic targets.[31] The hypothesis that IL-41 could serve a dual role in both diagnostic and therapeutic frameworks is supported by our finding that high IL-41 levels are directly correlated with disease severity in patients with AS.

The analysis of IL-41 levels in relation to demographic and clinical characteristics in patients with AS yields additional insights into the disease's heterogeneity and its biomarkers. This study delineated how factors such as age, sex, BMI, and specific clinical markers (e.g., HLA-B27 and CRP) correlate with variations in IL-41 serum levels. Sex and age are critical demographic factors that often influence disease expression and prognosis in autoimmune diseases.[32-33] While we did not assess changes in IL-41 levels with treatment, the study suggests that IL-41 levels are associated with disease activity in AS and may serve as a potential biomarker. However, its robustness across various clinical variables, including treatment, warrants further investigation in larger, longitudinal studies. This implies broad applicability for IL-41 in clinical settings, irrespective of patient age or sex. Conversely, there was a notable association between IL-41 levels and BMI, with higher BMI correlating with increased cytokine levels. This finding is consistent with the literature, suggesting that adipose tissue can influence systemic inflammation and cytokine production.[34] The finding also raises the possibility that IL-41 could be used to evaluate metabolic aspects of inflammation in AS, which are increasingly recognised as important in the disease's pathology.[35] Moreover, the findings regarding clinical characteristics such as HLA-B27—a genetic marker strongly associated with AS—reveal that higher IL-41 levels correlate significantly with the presence of HLA-B27.[36] This result underscores IL-41's potential to serve not only as a marker of disease activity but also as an indicator of underlying genetic predispositions that exacerbate the disease.

The correlation between IL-41 and CRP, a well-established marker of inflammation[37-38] and therapeutic target[39], was significant. This finding reinforces the use of IL-41 as a biomarker for inflammatory status in patients with AS. The integration of IL-41 with traditional markers like CRP could enhance the precision of disease monitoring and potentially guide therapeutic interventions more effectively. These demographic and clinical insights into IL-41 levels not only augment our understanding of its role in AS but also suggest a multifaceted utility in diagnosing and managing the disease.

The comparative analysis between patients with AS and healthy controls in the study provides crucial insights into the specificity and sensitivity of IL-41 as a biomarker. Significantly higher levels of IL-41 in patients with AS (particularly those with active disease) compared to healthy controls underscore its potential utility in distinguishing between diseased and non-diseased states. The control group's IL-41 levels were consistently lower across all demographic and clinical variables, which reinforces the biomarker's specificity for inflammatory processes specific to AS. This distinction is critical for clinical applications, particularly in differential diagnosis, where distinguishing AS from other inflammatory and non-inflammatory conditions can be challenging.

The higher levels of IL-41 in patients with AS suggest that it is not a generic marker of inflammation but rather IL-41 is closely linked to the pathophysiological processes underlying AS. Moreover, the study's use of a healthy control group established baseline levels of IL-41, an essential step for developing diagnostic criteria. Establishing such baselines is a step towards integrating IL-41 measurements into routine diagnostic protocols, potentially improving early detection and accurate diagnosis of AS. The marked difference in IL-41 levels between active and inactive disease states within patients with AS compared to controls indicates IL-41's potential role in disease monitoring and management. This evidence supports the proposition that IL-41 can be a valuable addition to the biomarker panel for AS, not only for diagnostic purposes but also for the stratification of disease severity and monitoring of treatment efficacy.

CONCLUSION

This study provides strong evidence that serum IL-41 is higher in patients with AS and correlates with disease activity. These findings suggest that IL-41 has significant potential as a

novel diagnostic biomarker for AS, offering a new avenue for more precise and effective management of this chronic inflammatory disease. To our knowledge, this study is the first to show the potential of IL-41 for AS diagnosis and monitoring.

CONFLICTS OF INTEREST

No conflicts of interest.

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