# **Journal of Surgery and Medicine**

e-ISSN: 2602-2079

# Association of fear assessment in inflammatory rheumatic diseases (FAIR) questionnaire with ankylosing spondylitis quality of life and disease activity in patients with ankylosing spondylitis

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#### **Ethics Committee Approval**

Ethics Committee approval was taken from the Dışkapı Yıldırım Beyazıt Research and Training Hospital, Number:1115/10, Date:12.07.2021. All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

#### **Conflict of Interest**

No conflict of interest was declared by the authors.

#### Financial Disclosure

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

# Published

2022 July 10

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Published by JOSAM

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#### Abstract

Background/Aim: Fear against disease course, treatment, and limitations in family, work, and social life are commonly seen but mostly overlooked by physicians of patients with chronic inflammatory rheumatic diseases. Ankylosing spondylitis (AS) is a chronic inflammatory disease in young adults characterized by limitations in spinal mobility. The Fear Assessment (FAIR) Questionnaire was designed especially for patients with rheumatoid arthritis and spondyloarthritis to assess the level of fear from the patient's perspective. Here we evaluate the FAIR score in AS patients and its association with disease activity, AS quality of life (ASQoL), depression, anxiety, and fatigue levels.

Methods: This cross-sectional study included 79 patients with AS, and disease activity was assessed by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), AS-Disease Activity Score-C reactive protein, and functional status was assessed by Bath Ankylosing Spondylitis Functional Index (BASFI). Patient global assessment of disease and pain were scored on 0-10 cm visual analog scores. All patients completed FAIR and ASQoL questionnaires. The depression and anxiety were evaluated by Hospital Anxiety and Depression Scale (HADS), and fatigue was assessed by Fatigue Severity Scale (FSS).

Results: The mean age of AS patients (62% male) was 41.7 (11.3) years. Most of the patients were on biological disease-modifying anti-rheumatic drugs (bDMARDs). The patients' median BASDAI, ASDAS-CRP, and BASFI were 5.4 (range, 3.8–7.4), 3.83 (1.4), and 4.0 (range, 2.3–6.2), respectively. The overall FAIR, ASQoL, FSS, HADS-depression, and HADS-anxiety scores were 75 (range, 52-91), 9.6 (5.2), 5.4 (range, 4.1-7), 7.7 (4.4) and 9.6 (5.2), respectively. There were statistically significant correlations between disease activity indices and FAIR, ASQoL, FSS, and HADS scores. The FAIR scores significantly correlated with ASQoL, FSS, and HADS scores. The patients with active disease (BASDAI ≥ 4) had significantly higher levels of FAIR, ASQoL, FSS, and HADS. The best cut-off value for the FAIR score of AS patients with moderate to severe disease activity was 50 (AUC: 0.734, 95% CI [0.599-0.870], P = 0.002), with a sensitivity of 89.8%, specificity of 55%, positive likelihood ratio of 1.99, and Youden index of 0.45.

Conclusion: This study shows that AS patients face a high level of fear which is associated with higher disease activity, higher risk of mood disorders, and lower quality of life. Physicians should not only focus on the physical improvement of the patient but also handle the fear of patients against their diseases and their treatment. This holistic approach will improve the dialogue between the physician and the patient, which will result in increased compliance with treatment and will raise the quality of care.

Keywords: Ankylosing spondylitis, Fear, Quality of life, Pain

How to cite: Kelesoğlu Dincer AB, Sezer S. Association of fear assessment in inflammatory rheumatic diseases (FAIR) questionnaire with ankylosing spondylitis quality of life and disease activity in patients with ankylosing spondylitis. J Surg Med. 2022;6(7):679-683

# Introduction

Ankylosing spondylitis (AS) is a young-onset chronic inflammatory rheumatic disease (CIRD) that mainly affects the axial skeleton and is characterized by a progressive bony fusion of the vertebral column and hence, limitation of spinal mobility [1, 2]. It is a complex and debilitating disease that leads to chronic pain, stiffness, and disability [3]. These factors cause physical challenges and difficulties in participating in family, work, and overall social life [4]. Furthermore, the chronicity of the disease, unpredictable disease course, concerns about selfimage, and long-term treatment are common in patients with CIRDs like AS [4]. Therefore, almost one-third of patients with a CIRD develop psychiatric disorders, most commonly depression and anxiety [4]. The relative risk of developing depression and anxiety was found in AS patients as 1.51 and 1.85 [2]. Due to decreased energy and reduced muscle capacity, fatigue is also very common in CIRDs [5]. Fatigue is defined as the sensation of generalized tiredness and exhaustion [6]. Physiological, psychological, social, and personal factors affect fatigue development, and more than half of the AS patients report fatigue.

Higher disease activity, pain, and functional disability are associated with a higher risk of mood disorders and fatigue [7]. Besides the mentioned concerns, patients with CIRDs face fear about dependence on others, limitations of daily life, and continuous need for treatment. The fear that the patients feel can trigger psychiatric disorders. Therefore, early recognition and handling of their fears give a chance to decrease the frequency of mood disorders and improve physician-patient communication [4]. The Fear Assessment in Inflammatory Rheumatic Diseases (FAIR) Questionnaire was developed in 2018 for patients with CIRD, such as rheumatoid arthritis (RA) and spondyloarthritis, with confirmed reliability and validity. This large cohort study revealed that almost 20% of patients had high fear scores [8]. Among all these psychiatric disorders, fatigue and fear result in poorer life quality in patients with AS. The AS quality of life (ASQoL) is an instrument to assess the disease severity, outcome and the impact of the disease from the patient's perspective [9].

This study aimed to evaluate the fear level of AS patients due to the disease itself and its treatment from the patient's perspective via a novel patient-reported measure of fear, namely the FAIR questionnaire, and to investigate its association with disease activity indices, ASQoL and, other psychological conditions.

# Materials and methods

#### Study population

This cross-sectional study included 79 patients ≥ 18 years old diagnosed with AS according to 1984 Modified New York Criteria and admitted to the rheumatology outpatient clinic between September 2021 and April 2022 [10]. Exclusion criteria included concomitant rheumatic diseases other than AS, current or past history of malignancy, current or past history of drug and/or alcohol abuse and psychiatric disorder, mental retardation, pregnancy, and breast-feeding. The patients were included in the study consecutively according to inclusion and exclusion criteria.

The study was conducted according to the recommendations of the Declaration of Helsinki and was approved by the Ethics Committee of Dışkapı Yıldırım Beyazıt Research and Training Hospital (Number:1115/10, Date:12.07.2021). Written informed consents were obtained from all subjects.

# Demographic characteristics and clinical assessment

The demographic characteristics, clinical, and treatment features were obtained during recruitment. Laboratory analysis included hepatic transaminases, serum creatinine, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and complete blood count (CBC) and was performed in the morning after 8 h of fasting.

# Assessment of disease activity

The disease activity of AS patients was assessed using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score-CRP (ASDAS-CRP), and Bath Ankylosing Spondylitis Functional Index (BASFI) [11-13]. The patient-reported global assessment of overall disease activity and pain severity were reported on a 0–10 cm Visual Analogue Scales (VAS). BASDAI  $\geq$  4 cm on a 0–10 scale was accepted as an "active disease". ASDAS-CRP levels below 2.1 show remission or low disease activity, whereas 2.1-3.5 high disease activity and levels above 3.5 indicate very high disease activity.

#### **Measurement tools**

The Hospital Anxiety and Depression Scale (HADS): HADS is an instrument for screening clinically significant anxiety and depression in patients at non-psychiatric outpatient clinics, which was first developed by Zigmond and his colleagues [14]. It consists of 14 items, of which seven items are related to anxiety, and the other seven items assess depression. Each item is scored on a 4-point scale (0–3) and ranges between 0 to 21 for each subscale. A score between 0 to 7 states a normal mental state, with 8–10 possibility of anxiety/depression, and a score above 11 points show definite anxiety or depression. The Turkish reliability and validity study was conducted [15].

The Fatigue Severity Scale (FSS): FSS is a nine-item instrument that measures the impact of fatigue on daily functioning, which is a simple and short self-assessment questionnaire [16]. Each item is scored between 1 (totally disagree) and 7 (totally agree), and a total score of  $\geq$ 4 indicates severe fatigue. Its validation and translation to Turkish patients were performed in many diseases [17,18].

Ankylosing Spondylitis Quality of Life (ASQoL): ASQoL comprises 18 dichotomous items which assess patient-reported symptoms, functioning, and disease-related concerns. In each item, yes is scored as one point, and no is scored as 0 with a total score of 18 [19]. Higher scores of ASQoL indicate poor quality of life. Duruöz et al. [20] conducted a validity and reliability study of ASQoL.

Fear Assessment in Inflammatory Rheumatic Diseases (FAIR): FAIR is a self-reported measure to assess fear in AS and RA patients that includes 10 questions that are scored on a 10-point numerical scale ranging from 0 (no fear) to 10 (strong fear) and the total score is calculated by the sum of 10 individual item scores (0–100) [8]. The higher scores indicate more fear. The

translation and validation to the Turkish language are performed by a total of 115 patients (58 AS, 57 RA) [4].

## Statistical analysis

IBM SPSS Statistics for Windows, version 25.0 (SPSS Inc, Chicago, IL, USA) was used for data analysis. Visual (histograms, probability plots) and analytical (Kolmogorov-Smirnov/Shapiro-Wilk's test) were used to determine the data distribution. The normally distributed continuous variables were presented as mean (standard deviation), and skewed data were expressed as median (IQR). Categorical variables were summarized as (%). Student's T-test and Mann-Whitney U test were used to compare normally distributed and skewed data, respectively. Chi-Square or Fisher tests were used for categorical variables when appropriate. The correlation analysis between scores was performed with Pearson correlation or Spearman rank correlation tests. We used receiver operating characteristics (ROC) analysis to determine the optimal cut-off score for FAIR patients with moderate to high disease activity. The Youden index was applied to select the best cut-off value. P < 0.05 was considered significant.

#### Results

In this study, 79 AS patients were included (62% male). The demographic and clinical characteristics of AS patients are shown in Table 1. More than half of the patients (50.6%) were on biological disease-modifying anti-rheumatic drugs (bDMARDs), which were adalimumab (42.5%), etanercept (22.5%), golimumab (20%), secukinumab (10%), and certolizumab pegol (5%), respectively. The majority of patients (74.7%) involved in the study had severe disease activity with a BASDAI of 5.4 (3.8–7.4) and ASDAS-CRP of 3.83 (1.4). The overall fatigue severity score was 5.4 (4.1–7), which indicates severe fatigue; while the majority of patients had higher anxiety scores (44.7%), most of the patients (50%) were within normal limits in terms of depression. The psychological status of AS patients are summarized in Table 1. The overall FAIR score was calculated as 75 (range, 52–91).

When the ROC analysis was used to determine the best cut-off value for a FAIR score of AS patients with moderate to severe disease activity, the optimal cut-off value was 50 (AUC: 0.734, 95% CI [0.599-0.870], P=0.002) with a sensitivity 89.8%, specificity 55%, the positive likelihood ratio of 1.99, and Youden index of 0.45.

There were statistically significant positive correlations between AS disease activity scores and FAIR, ASQoL, HADS-D, and HADS-A scores, as summarized in Table 2. Additionally, FAIR scores correlated significantly with ASQoL, FSS, HADS-D, and HADS-A scores (Table 3).

Table 1: The demographic, clinical and laboratory characteristics of AS patients (n = 79).

Parameter	Value
Age (years)*	41.7 (11.3)
Male Gender <sup>+</sup>	49 (62)
Disease Duration (months) ¥	36 (12-96)
HLA-B27 status+ (known for 27 patients)	16 (59.3)
Treatment features+	
Concomitant NSAIDs	37 (46.8)
Concomitant c-DMARDs	23 (29.1)
b-DMARDs	40 (50.6)
Disease Activity Status	
VAS Pain <sup>¥</sup> (0-10)	7.5 (5-9)
$Pt-VAS^{\Psi}$ (0-10)	6 (5-8)
BASDAI <sup>¥</sup>	5.4 (3.8-7.4)
BASFI <sup>¥</sup>	4 (2.3-6.2)
ASDAS-CRP*	3.83 (1.4)
Laboratory Features	
ESR <sup>¥</sup> (mm/h)	8 (3-18)
$CRP^{\Psi}$ (mg/L)	5 (1.2-12.9)
Psychological Status	
Overall Fatigue Severity Score¥	5.4 (4.1-7)
$< 4^{+}$	16 (20.5)
$\geq 4^+$	62 (79.5)
ASQOL*	9.6 (5.2)
Overall FAIR score <sup>¥</sup>	75 (52-91)
< 50 <sup>+</sup>	17 (21.5)
$\geq 50^{+}$	62 (78.5)
HADS-Depression Score*	7.7 (4.4)
0-7+	38 (50)
8-10 <sup>+</sup>	18 (23.7)
≥ 11+	20 (26.3)
HADS-Anxiety Score*	9.8 (4.9)
0-7+	22 (28.9)
8-10+	20 (26.3)
≥ 11+	34 (44.7)

NSAID: Non-steroidal anti-inflammatory drug, cDMARD: conventional disease modifying anti-rheumatic drug, bDMARD: biological disease modifying anti-rheumatic drug, VAS: Visual analogue score, ESR: Erythrocyte-sedimentation rate, CRP:C-reactive protein, Pt-VAS: Patient Visual analogue score, ASQoL: Ankylosing Spondylitis Quality of Life, FAIR: Fear Assessment in Inflammatory Rheumatic Diseases Questionnaire, HADS: Hospital Anxiety and Depression Scale, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, ASDAS: Ankylosing Spondylitis Disease Activity Score, \*mean (SD), \*n (%), \*median (Q1–Q3)

Table 2: The correlation between psychological status measurements and AS disease activity indices

	BASDAI		BASFI		Pt-VAS		Pain-VAS	
	r <sub>s</sub> /r	P-value	$r_s/r$	P-value	$r_s/r$	P-value	$r_s/r$	P-value
FAIR	0.357	0.001a	0.407	<0.001a	0.333	0.003a	0.367	0.001a
FSS	0.602	$<0.001^a$	0.488	$<0.001^a$	0.721	$<0.001^a$	0.462	$<0.001^a$
ASQoL	0.640	$<0.001^{b}$	0.655	$<0.001^{b}$	0.571	$<0.001^{b}$	0.540	$<0.001^a$
HADS-D	0.483	<0.001a	0.490	$<0.001^a$	0.446	<0.001a	0.431	$<0.001^a$
HADS-A	0.333	$0.003^{b}$	0.373	0.001 <sup>b</sup>	0.389	0.001 <sup>b</sup>	0.337	$0.003^{a}$

VAS: Visual analogue score, Pt-VAS: Patient Visual analogue score, ASQoL: Ankylosing Spondylitis Quality of Life, FAIR: Fear Assessment in Inflammatory Rheumatic Diseases Questionnaire, HADS: Hospital Anxiety and Depression Scale, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, <sup>a</sup> Spearman rank correlation test, <sup>b</sup> Pearson Correlation

Table 3: The association between FAIR scores and FSS, ASQoL, HADS-D, and HADS-A.

	rs	P-value
FSS	0.490	< 0.001
ASQoL	0.592	< 0.001
HADS-D	0.577	< 0.001
HADS-A	0.651	< 0.001

ASQoL: Ankylosing Spondylitis Quality of Life, FAIR: Fear Assessment in Inflammatory Rheumatic Diseases Questionnaire, HADS: Hospital Anxiety and Depression Scale, Spearman rank correlation test.

The patients were grouped according to their BASDAI scores. The patients with BASDAI scores < 4 were categorized as "inactive disease activity" (n = 20), and patients with BASDAI  $\geq$  4 were accepted as "active disease activity" (n = 59). The demographic and clinical features of AS patients with BASDAI < 4 and  $\geq$  4 are shown in Table 4. Even though there were no differences between the two groups in terms of age, disease duration, and treatment features, the FSS, HADS-D, HADS-A, and ASQoL scores were significantly higher in the active group compared to the inactive group. The number of patients with severe fatigue (FSS  $\geq$  4) was significantly higher in the active group. Additionally, the FAIR score was statistically higher in the active group compared to the inactive group. Most active patients (89.8%) had FAIR scores above the estimated cutoff level of 50.

Table 4: The clinical, laboratory, and psychological features of AS patients with remission-to-low disease activity and moderate-to-high disease activity.

	BASDAI < 4 $(n=20)$	BASDAI $\geq$ 4 (n=59)	P-value
Age (years)*	39(14.5)	42.6(10)	0.30a
Male +	18 (90)	31 (52.5)	0.003b
Disease Duration <sup>¥</sup> (months)	60 (12-96)	36 (12-84)	0.36°
Treatment features <sup>+</sup>	00 ( > 0)	()	
Concomitant NSAIDs	10 (50)	27 (45.8)	$0.74^{b}$
Concomitant cDMARDs	4 (20)	19 (32.2)	$0.30^{b}$
bDMARDs	12 (60)	28 (47.5)	$0.33^{b}$
Disease Activity Status	` ′		
VAS Pain <sup>¥</sup> (0-10)	3.5 (2-5)	7 (6-9)	<0.001°
PtVAS¥ (0-10)	3 (2-4.8)	8 (7-10)	<0.001°
BASDAI¥	2.5 (1.53-3.45)	6.62 (4.8-7.8)	<0.001°
BASFI¥	1.6 (0.3-2.7)	4.9 (3.3-6.7)	<0.001°
ASDAS-CRP*	2.29(0.9)	4.38(1.1)	<0.001a
Laboratory Features			
ESR <sup>¥</sup> (mm/h)	4 (2-8)	10 (3-19)	$0.017^{c}$
$CRP^{\Psi}$ (mg/L)	2.6 (1.2-7.1)	6.8 (1.2-14.8)	$0.16^{c}$
Psychological Status			
Overall Fatigue Severity Score <sup>¥</sup>	3.2 (2.2-4.4)	6 (5-7)	<0.001°
< 4+	12 (60)	4 (6.9)	$<0.001^{d}$
$\geq 4^+$	8 (40)	54 (93.1)	$<0.001^{d}$
$ASQOL^*$	4.9(4.7)	11.2(4.3)	<0.001a
Overall FAIR score <sup>¥</sup>	48 (33-79)	78 (62-93)	$0.002^{c}$
< 50	11 (55)	6 (10.2)	$< 0.001^{d}$
≥ 50	9 (45)	53 (89.8)	$<0.001^{d}$
HADS-Depression Score*	4.1(3.5)	8.9(4)	<0.001a
0-7+	16 (84.2)	22 (38.6)	$0.002^{b}$
8-10 <sup>+</sup>	2 (10.5)	16 (28.1)	$0.002^{b}$
≥ 11+	1 (5.3)	19 (33.3)	$0.002^{b}$
HADS-Anxiety Score*	6.7 (4.4)	10.9 (4.6)	0.001a
0-7+	9 (47.4)	13 (22.8)	0.041 <sup>b</sup>
8-10+	6 (31.6)	14 (24.6)	0.041 <sup>b</sup>
≥ 11+	4 (21.1)	30 (52.6)	0.041 <sup>b</sup>

NSAID: Non-steroidal anti-inflammatory drug, cDMARD: conventional disease modifying anti-rheumatic drug, bDMARD: biological disease modifying anti-rheumatic drug, VAS: Visual analogue score, ESR: Erythrocyte-sedimentation rate, CRP:C-reactive protein, Pt-VAS: Patient Visual analogue score, ASQOL: Ankylosing Spondylitis Quality of Life, FAIR: Fear Assessment in Inflammatory Rheumatic Diseases Questionnaire, HADS: Hospital Anxiety and Depression Scale, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, ASDAS: Ankylosing Spondylitis Disease Activity Score, "mean (SD), \*n (%), \*median (Q1-Q3), \*Independent-Samples T Test, \*b Chi-Square, \*Mann-Whitney-U, \*d Fisher's Exact Test.

## **Discussion**

In this study, we show that AS patients have high fear scores, which were well correlated with disease activity scores, and patients with a higher disease burden face a higher degree of fear. Additionally, patients with higher disease activity have significantly increased fatigue, anxiety, depression, and lower quality of life. Fear scores were not only significantly correlated with disease activity indices but also with fatigue, anxiety, depression, and quality of life scores.

Due to their chronic and unpredictable course, patients with CIRDs, such as RA and spondyloarthritis, encounter psychological distress as well as fear about the prognosis of the disease, limitation in daily activities, risk of dependence on other people, and their roles in work, family and social life [8, 21]. Understanding the level and the reasons for fear in these patients and counseling towards it allows for optimizing treatment adherence and improving the quality of care given via advanced patient-physician dialogue [21]. Until recently, there was no measure to specifically assess the CIRD-related fear even though there are many patient-reported outcome measures to evaluate psychological states like anxiety and depression. Gossec et al. [8] developed and validated the patient-reported outcome measure of fear assessment in patients with CIRD, namely the FAIR questionnaire, in 2018. This study included a total of 432 RA patients and 240 axial spondyloarthritis patients to whom a 10item questionnaire was applied. In this study, patients were classified due to their fear scores as high (mean score: 87.0 [7.9], n = 116; 17.2%), moderate (mean score: 65.8 [11.4], n = 276; 41.1%) and low (mean score: 31.1 [14.7], n = 280; 41.7%) in

which the distinguishing cut-off level for high and low fear was found as 77 and 51, respectively [8].

In our study, the optimal cut-off level distinguishing high and low fear levels in patients with AS was 50 out of 100 points. However, we showed that AS patients with active disease (BASDAI  $\geq$  4) had a median fear score of 78 (62–93), which is in the group of high fear in the study stated above. The other study that assessed the utility of FAIR in CIRD is the validation study of the FAIR questionnaire in the Turkish language which included 58 AS and 57 RA patients [4]. In this study by Küçükakkaş et al. [4], the authors found that the mean FAIR score of AS patients was 49.3 (22.7), which was similar to our study. In both studies, no correlations were found between BASDAI and FAIR scores; however, Gossec et al. [8] stated that people with severer perceived disease activity were mostly in the high fear group. Our study showed significant correlations in patients' visual analog scores of global assessment and pain and in objective disease activity scores of BASDAI and BASFI. We also confirmed that patients with higher BASDAI scores have significantly higher FAIR scores compared to the low disease activity group and that they can be classified as the high fear cluster group based on Gossec et al. [8] study. One of the reasons why we showed a correlation between disease activity indices and fear degree may be due to the larger number of patients recruited, and secondly, we involved only patients with radiographic axial spondyloarthritis (i.e., AS), whereas the study of Gossec et al. [8], included patients also non-radiographic axial spondyloarthritis patients. Similar to the other two studies, our results showed a significant correlation between fear levels with HADS anxiety and depression scores [4, 8]. As a result, it is noteworthy that our study is the first study to assess the magnitude of fear in AS patients and its good relationship with disease activity indices, quality of life, and psychiatric status.

ASQoL is an 18 dichotomous questionnaire first developed in 2002 to assess the impact of the disease and treatment from the patient's perspective [19]. It was translated and validated in the Turkish language in 2013 by Duruöz et al. [20]. ASQoL evaluates the pain, energy, physical mobility, emotional status, sleep, and social interactions, which are all components of quality of life. Our study showed a statistically significant correlation of ASQoL with BASDAI, BASFI, patient assessment of disease activity, and pain. Duruöz et al. [20] also found a mild to moderate correlation between ASQoL and BASDAI, BASFI, and VAS-Pain. In the study of Bodur et al. with a total of 962 AS patients, the mean ASQoL was 7.1 (5.7), and ASQoL was strongly associated with BASDAI, BASFI, pain, and fatigue [22]. In our study, the mean ASQoL level was 4.9 (4.7) in AS patients with BASDAI < 4 and 11.2 (4.3) in patients with BASDAI  $\geq 4$ , similar to our results, in the study of Bodur et al. [22], mean ASQoL in patients BASDAI < 4 was 4.56 (4.32) whereas mean ASQoL was 11.19 (5.13) in patients with BASDAI  $\geq$  4. Likewise, in other studies evaluating the association of ASQoL with BASDAI, BASFI, and total pain, strong correlations between the mentioned parameters were shown [23-25]. Our study is the first to evaluate the association between ASQoL and fear levels in AS patients and demonstrated that higher fear levels were associated with higher ASQoL, which results in poorer quality of life.

Several studies focused on the psychological status of patients with AS and found an increased risk of depression and anxiety [26]. In a recent meta-analysis, Park et al. [2] showed a 51% higher risk of depression among AS patients compared to a healthy population. Zhang et al. [27] found the prevalence of depression in AS patients ranges from 3% to 66%, and the prevalence of major depressive disorder was 13%. Increased disease activity, sleep problems, fatigue, and poorer quality of life are more common in AS patients with depression.

Indeed, studies showed that BASDAI, BASFI, ASQoL, and ASDAS-CRP were independent factors for depression [2, 26]. Additionally, an 85% increased risk of anxiety was demonstrated in AS patients compared to healthy controls [28]. Similarly, in our study, we found overall depression and anxiety scores of 7.7 (4.4) and 9.8 (4.9), respectively. Moreover, HADS-D and HADS-A scores were not only correlated with BASDAI, BASFI, and pain assessments but also with FAIR scores. Furthermore, the prevalence of fatigue ranged from 53 to 65% in AS patients [29, 30]. Zhou et al. [29] reported an incidence of fatigue in Chinese AS patients of 48.7% and showed BASDAI as an independent risk factor for fatigue severity. Likewise, in our study, AS patients had higher fatigue levels on the FSS scale, and FSS scores correlated positively with BASDAI, BASFI, and pain scores. Besides, FAIR scores correlated significantly with fatigue severity.

#### Limitations

The study's cross-sectional design restricted the interpretation of psychological status change after successful treatment. The second limitation was the relatively small number of AS patients included, hence, a lower number of patients with inactive disease activity. On the other hand, the current study is unique as it is the first study evaluating the association of fear by using the FAIR questionnaire, which specifically assesses the fear level in AS patients with disease activity indices as well as depression, anxiety, and fatigue status. Prospective studies are needed to evaluate more thoroughly the fear degree in spondyloarthritis patients and also the change in fear scores after especially bDMRD initiation with a larger cohort.

# Conclusion

This study shows that the FAIR and ASQoL scores are associated with disease activity and depression, anxiety, and fatigue scores. Also, patients with higher disease activity face more fear about their disease, physical disability, and social life. As a result, physicians should adopt a holistic approach when treating patients with inflammatory rheumatic diseases, focusing on controlling disease activity and handling psychological status.

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