Depression and Anxiety in Spondyloarthritis: Prevalence and Relationship with Clinical Parameters and Self-Reported Outcome Measures

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SUMMARY

Objective: To assess the prevalence of depression and anxiety among patients with spondyloarthritis.

Method: One hundred patients with spondyloarthritis attending the rheumatology outpatient unit were enrolled. Duration of morning stiffness, pain/fatigue visual-analogue-scale, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Functional Index, Metrology Index, Patient Global Score, Hospital Anxiety and Depression Scale (HADS) including depression subscale (HADS-D) and anxiety subscale (HADS-A), Ankylosing Spondylitis Quality of Life (ASQoL) Scale, Short Form 36 Health Survey and Functional Assessment of Chronic Illness Therapy-Fatigue-Scale were used to assess clinical and psychological status.

Results: The HADS-D and HADS-A scores revealed that 31% of the patients were depressed and 39% had anxiety. Multivariate logistic regression analysis revealed that a VAS fatigue >50, morning stiffness >15minutes, BASDAI >4, BASFI >4, BAS-G >50 and high FACIT-Fatigue scale were independent risk factors associated with the risk of both depression and anxiety. A visual-analogue-scale pain >50 was an independent risk factor for only depression. Female gender, disadvantaged social class and MCS <50 seemed to be the independent risk factors associated only with anxiety.

Conclusion: Association of SpA with anxiety and/or depression appear multifactorial including both personal and disease-related factors. Early identification of depressive and anxiety disorders may allow early referral for psychiatric assessment, educational programs and psychopharmacological treatment.

Keywords: Depression, anxiety, spondyloarthritis

INTRODUCTION

Clinical anxiety and depression are two to three times more common in rheumatic diseases than in the general population (Geenen et al. 2012). This is of particular concern since depression and anxiety are negatively associated with chronic diseases, leading to poor adherence to self-care regimens (diet, exercise, quitting smoking) and medical treatment recommendations with increased morbidity (van Melle et al. 2004). Depression and anxiety are also risk factors for increased burden of physical symptom, decreased quality of life as well as increased health care utilization (Katon et al. 2007, Creed et al. 2002). Spondyloarthritis (SpA) can lead to functional impairment, reduced quality of life, sleep disturbances, workforce decline, and psychological distress especially depression and anxiety (Ozgül et al. 2006). Moreover, negative beliefs about illness, disability and side-effects from treatment may lead to the development of psychological disorders. Literature regarding the relation between SpA and depression and/or anxiety is inconclusive (Martindale et al. 2006, Hakkou et al. 2011, McWilliams et al. 2008). In clinical practice, understanding the risk factors that are associated with

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depression and anxiety is important in the management of SpA patients as it offers the opportunity to either identify the subjects at risk for depression and/or anxiety or recognizing and treating the disorder in a timely matter.

In this study we will assess the prevalence of depression and anxiety in Tunisian SpA patients and investigate the factors associated with depression and anxiety. Furthermore, we will examine if HADS is a valued screening tool compared to the diagnostic psychiatric interview which is used as the gold standard.

METHOD

Study Design

This cross-sectional study was conducted at a rheumatology outpatient and/or hospitalized in Charles Nicolle Hospital, Tunisia, from September 2012 to September 2013.

Patient Selection

SpA diagnosis (either peripheral or axial) was based on the criteria of the Assessment of Spondyloarthritis International Society (ASAS) (Figures 1 and 2) (Rudwaleit et al. 2009), (Rudwaleit et al. 2011). Exclusion criteria were as followed: (1) subject younger than 16 years of age, (2) history of psychotic illness, (3) alcohol and/or drug abuse, (4) dementia, (5) current treatment with psychotropic, (6) diabetics and its degenerative complications, (7) progressive visceral complications, (8) cancer, (9) hearing and understanding disorder, and (10) end-stage renal disease.

In patients with ≥3 months back pain (with/ without peripheral manifestations) and age at onset <45 years:

Sacroiliitis on Imaging*	OR	HLA-B27
plus		plus
≥1 SpA feature**		≥2 other SpA features**

* Sacroiliitis on Imaging:
- active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA
Or
Definite radiographic sacroiliitis according to mod. New York Criteria
** SpA features:
Inflammatory back pain; arthritis; enthesitis (heel); uveitis; dactylitis; psoriasis; Crohn's/ulcerative colitis; good response to NSAIDs; family history of SpA; HLA-B27; Elevated CRP

Figure 1. ASAS Classification Criteria for Axial SpA

In patients with peripheral manifestations ONLY:

Arthritis* or Enthesitis or Dactylitis

Plus

≥1 SpA feature		**≥2 other SpA features**
• uveitis		• arthritis
• psoriasis		• enthesitis
• Crohn's/ulcerative colitis	OR	• dactylitis
• preceding infection		• IBP ever
• HLA-B27		• family history for SpA
• sacroiliitis on imaging		

Figure 2. ASAS Classification Criteria for Peripheral SpA

Data Collection

Demographic characteristics and anthropometric measurements were evaluated in all patients. The same physician conducted all assessments including the anthropometric measurements. Standardized case report forms were filled out. Blood collection occurred and baseline values were used in the analyses. Baseline radiographs of the pelvis, lumbar spine and cervical spine were collected from each participant and scored using the Bath Ankylosing Spondylitis Radiographic Index Global (BASRI). The BASRI is a validated method for scoring radiographic severity in Ankylosing Spondylitis (AS) (MacKay et al. 1998).

Patient Characteristics

Socio-demographic data, including age, sex, marital status, number of children, education level (illiterate, primary, secondary, university), social class (disadvantaged, fair, good), occupation, living arrangement (urban or rural areas) were collected.

Clinical data including date of onset of SpA, disease duration, smoking, extra-articular symptoms and details of pharmacological treatments were determined from participants' self reports. Medications included non-steroidal anti-inflammatory drugs (NSAIDs), disease-modifying anti-rheumatic drugs (sDMARD), and tumor necrosis factor inhibitors (TNFi).

Assessment Tools for Clinical and Biological Status

Each patient recorded the severity of pain/fatigue on a visual analogue scale (VAS) from 0 to 100 (0: no pain/fatigue - 100: the worst imaginable pain/fatigue). Duration of morning stiffness was noted. Erythrocyte sedimentation rate (ESR) and C-Reactive Protein (CRP) were measured.

Assessment of Disease Status and Physical Functioning

The Tunisian versions of Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) were used to assess disease activity and functional status for patients with axial or mixed pattern of joint involvement (Kchir et al. 2009). Spinal limitation was assessed by using the Bath Ankylosing Spondylitis Metrology Index (BASMI) (Jenkinson et al. 1994). The Bath Ankylosing Spondylitis Patient Global Score (BAS-G) gives a global assessment of the patient's well-being for the last 6 months (Jones et al. 1996).

In order to determine the severity of hip osteoarthritis, Lequesne Algofunctional Index was used. All questionnaires

are scored and the total score reveals the level of osteoarthritis reached.

Assessment of Quality of Life

The psychometric evaluation includes the following self reported questionnaires: the Short Form 36 Health Survey (SF-36), the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) Scale, and the Ankylosing Spondylitis Quality of Life (ASQoL). The SF-36 is a generic health status instrument developed for application in primary care and chronic disease populations (Ware et al. 1993). In this study we used the SF-36 Version1 with a 4-week recall period. It contains two summary scores i.e. Mental Component Summary [MCS] and Physical Component Summary [PCS] scores), and eight subscales: (1) physical function, (2) bodily pain, (3) role-physical, (4) general health, (5) vitality, (6) social function, (7) role-emotional, and (8) mental health. The SF-36 subscales and summary scores have excellent reliability and good construct validity across the chronic disease populations, including in patients with AS (Chorus et al. 2003).

Assessment of Psychiatric Status

Psychological status was evaluated by the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith 1983), which is the most commonly used screening tool for identifying clinically anxiety and depression in patients attending a general medical clinic with physical illness (within the non-psychiatric hospital framework). This self-administered scale consists of two subscales i.e. an assessment for anxiety (HADS-A) and an assessment for depression (HADS-D). Each subscale consists of seven items with a score between 0 (no distress) to 3 (maximum distress). The total score ranges from 0 to 21 points for each subscale. A score between 0 to 7 reveals no anxiety or depression, a score between 8 to 10 indicates possible case of anxiety or depression, and a score of 11 or higher indicates the presence of anxious or depressive disorders (Herrmann 1997). Scores for the entire scale (emotional distress) range from 0 to 42.

Patients with HADS-A or HADS-D scores of 10 or higher were consecutively recruited and interviewed separately by a psychiatrist in another clinic visit.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) for Windows, version 11.5.

A descriptive analysis was conducted in order to present the socio-demographic and clinical variables of the study sample. The continuous variables were described in terms of the mean and standard deviation (SD), whereas the categorical variables were summarized by counting up the frequency or the percentages for each category of response. Student's t Test was used to compare two independent variables. Subgroup comparisons (> 2 variables) of independent series were carried out using the F Snedecor test analysis of the parametric variance (one-way ANOVA). If case of significant difference, Bonferroni correction method was performed. Percentages comparisons of independent series were performed by the chi-square test of Pearson and in case of non-validity, the Fisher's exact test was used. Relationship between parameters was analyzed by using Pearson correlation coefficients. The variables with a p value between 0.05 and 0.15 on univariate analysis were subjected to a stepwise multivariate logistic regression analysis to determine which factors were independent predictors of depression or anxiety risk in patients with SpA. Adjusted odds ratios (OR) were recorded with a 95% confidence interval for each. An OR higher than 1 means that the risk is increased, whereas an OR less than 1 means that the risk is reduced. In all cases, a p-value<0.05 was consider statistically significant.

Ethical approval

The study was approved by the Hospital local Ethics Committee. All subjects were previously informed of the study and written consent was obtained.

RESULTS

Patient's Characteristics

One hundred patients were enrolled in the study. Seventy-one percent of the patients were males. Table 1 illustrates the patients' baseline socio-demographic characteristics. Fifty

Table 1. Sociodemographic Background of the Sample (n = 100)

Parameters	Value
Age (years) mean (SD)	41.7 (13.5)
Male gender (%)	71
Marital status (%)	
Single	39
Married	61
Number of children mean (SD)	1.55 (1.7)
Education level (%)	
Illiterate	16
Primary	33
Secondary	35
University	16
Social class (%)	
Disadvantaged	24
Fair	70
Good	6
Employed (%)	51
(manual labor/ hard physical work)	(55/45)
Housing (%)	
Urban	54.5
Rural	45.5

SD: Standard deviation

Table 2. Clinical Parameters and Laboratory Results of the Sample

	Variable
Age of onset of SpA (years) mean (SD)	28.9 (13.5)
Disease duration (years) mean (SD)	11.8 (10.3)
Morning stiffness (minutes) mean	3.2
Current tobacco use (%)	47
Cardiovascular history (%)	8
Diagnosis (N)	
AS	76
PsA	11
SpA/IBD	9
Reactive Arthritis	2
SAPHO	1
uSpA	1
SpA features history (%)	
Inflammatory back pain	100
Peripheral arthritis	77.6
Psoriasis	11
Colitis/Crohn's disease	9
Reactive arthritis	2
Extra-articular symptoms (%)	46.9
Biochemical measures	
Median ESR (mm/h)‡‡	41.5 [2-114]
Median CRP (mg/L)‡‡	24.4 [0-228]
Rating scales	
BASDAI mean (SD)	4.5 (2.3)
BASFI mean (SD)	4.4 (2.7)
BAS-G mean (SD)	56.1 (25.1)
BASMI mean (SD)	4.7 (2.6)
VAS, mm	
Pain mean (SD)	60.3 (28.6)
Fatigue mean (SD)	55.2 (29.2)
Radiological parameters	
Sacroiliitis (%)	75
BASRI mean (SD)	4 (4)
Quality of life	
SF-36 PCS mean‡‡	36.1 [16.1-59.5]
SF-36 MCS mean‡‡	37.9 [9.2-61.9]
FACIT-Fatigue mean‡‡	25.7 [8-52]
ASQoL mean (SD)	43 (21.6)
Current treatments (%)	
NSAIDs	74
sDMARD	56
TNFi	12

AS: ankylosing spondylitis, AsQol : The Ankylosing Spondylitis Quality of Life questionnaire, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, BASMI: Bath ankylosing spondylitis metrology index, BAS-G: Bath Ankylosing Spondylitis Global Score, BASRI: Bath Ankylosing Spondylitis Radiographic Index Global, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, FACIT-F : Functional Assessment of Chronic Illness Therapy-Fatigue, MCS: Mental Component Summary score, PCS: Physical Component Summary score, NSAIDs: Non-steroidal Anti-inflammatory Drugs, PsA: psoriatic arthritis, SpA: spondyloarthritis, SpA/IBD: Enteropathic Spondyloarthritis, SAPHO: Synovitis–acne–pustulosis–hyperostosis–osteitis, USpA: undifferentiated spondyloarthritis, sDMARD: disease-modifying anti-rheumatic drugs, TNFi: tumor necrosis factor inhibitors, VAS: visual analogue scale,*SD: standard deviation,‡‡:interquartile range (IQR).

Table 3. HADS Anxiety and Depression Scores and Categories Based on Cutoff Scores

HADS-D	
Mean (SD)	7.2 (5.2) [0-18]
Depression status	
I Normal (0–7) (%)	54
II Possible (8–10) (%)	15
III Certain (11–21) (%)	31
HADS-A	
Mean (SD)	8.9 (5.1) [0-20]
Anxiety status	
I Normal (0–7) (%)	43
II Possible (8–10) (%)	18
III Certain (11–21) (%)	39
HADS mean (SD)	16.3 (9.2)

HADS-D: Hospital Anxiety and Depression Scale (depression) subscale, HADS-A: Hospital Anxiety and Depression Scale (anxiety) subscale, HADS: Hospital Anxiety and Depression Scale, SD: standard deviation, [ ]:interquartile range

percent of the patients were unemployed because of SpA and nearly a quarter of the patients felt they were not married because of their SpA. Furthermore forty-seven percent of patients were smokers and 8 patients were diagnosed with cardiovascular disease.

Measures

At baseline, the BASDAI score was 4.5±2.3, the BASFI score was 4.4±2.7, the BAS-G score was 56.1±25.1 and the BASMI score was 4.74±2.6. The pain VAS score was 60.3±2,66 (Table 2). Fifty-seven present of the patients had a BASDAI greater than or equal to 4 and 59% of the patients had a BASFI greater than or equal to 4 (Table 2).

Psychological Variables

The HADS-A score was 8.9±5.08. Based on the HADS-A score, 39% of the patients had prevalence of anxious symptomatology (Table 3). The mean HADS-D was 7.23±5.27. Based on HADS-D scores, 31% of the patients presented symptoms of depression and 15% possible depression (Table 3).

Independent Variables Associated with Higher Scoring on the HADS Univariate Analyses

Both HADS-D and HADS-A scores positively correlated with VAS fatigue, morning stiffness, BASDAI, BASFI, BASG-s and Lequesne Algofunctional Index. PCS, MCS and AsQoL were negatively correlated with HADS-D and HADS-A scores. Disease duration was only positively correlated with HADS-A whereas VAS pain was only positively correlated with HADS-D.

Table 4. Correlation Between the Psychological Scores and the Clinical and Laboratory Results in Patients with Spondyloarthritis

Variables	HADS-D		HADS-A	
	r	p	r	p
Age (years)	0.201	0.062	0.198	0.066
Disease duration (years)	0.159	0.143	0.251	0.02
Delay in diagnosis of SpA (years)	0.122	0.262	0.073	0.502
Age at onset of SpA (years)	0.06	0.58	-0.010	0.928
VAS pain (mm)	0.262(*)	0.014	0.262(*)	0.014
VAS fatigue	0.459(*)	<0.0001	0.356(*)	0.001
Morning stiffness	0.233(*)	0.03	0.320(*)	0.003
BASFI	0.436(*)	<0.0001	0.341(*)	0.001
BASDAI	0.505(*)	<0.0001	0.425(*)	<0.0001
BAS-G	0.518(*)	<0.0001	0.508(*)	<0.0001
BASMI	0.180	0.096	0.159	0.141
BASRI	-0.064	0.595	-0.049	0.684
PCS	-0.336(*)	0.002	-0.345(*)	0.001
MCS	-0.712(*)	<0.0001	-0.556(*)	<0.0001
Lequesne Algofunctional Index	0.321(*)	0.003	0.368(*)	0.001
ESR (mm/h)	-0.028	0.808	-0.005	0.968
CRP (mg/L)	-0.010	0.931	-0.074	0.529
ASQoL	-0.352(*)	0.003	-0.336(*)	0.005

ASQoL: Ankylosing Spondylitis Quality of Life questionnaire. BASDAI: Bath Ankylosing Spondylitis Activity Disease Activity Index. BASFI: Bath Ankylosing Spondylitis Functional Index. BASMI: Bath Ankylosing Spondylitis Metrology Index. BAS-G: Bath Ankylosing Spondylitis Global Score. BASRI: Bath Ankylosing Spondylitis Radiographic Index Global. CRP: C-reactive protein. ESR: erythrocyte sedimentation rate. HADS-A: Hospital Anxiety Depression Scale-Anxiety. HADS-D: Hospital Anxiety Depression Scale-Depression. MCS: Mental Component Summary score. PCS: Physical Component Summary score. SpA: spondyloarthritis. VAS: visual analogue scale. r: Pearson's correlation
*Correlation is significant at the 0.05 level.

A gender difference was found for anxious symptomatology [anxious symptomatology: women, 64%; men, 31%; p=0.006]. Disadvantaged social class played also a role in anxious symptomatology [anxious symptomatology: Fair, 71%; good, 29%; p<0.001]. Interestingly, gender and social class did not influence the HADS-D score. Marital status, educational level, the presence of peripheral arthritis and extra-articular symptoms, hip osteoarthritis, habitat, sacroiliitis and current treatments were not significantly associated with higher scoring on HADS-A and HADS-D, respectively. The correlation coefficients are summarized in Table 4.

ANOVA analysis was performed for patients with HADS-D≥11 and HADS-A≥11 (Table 5). Depression and anxiety were significantly associated with morning stiffness>15 minutes, VAS fatigue>50, BASDAI>4, BASFI>4 and BAS-G>50. Vas pain>50 was significantly associated with depression.

VAS fatigue>50, Morning stiffness>15mn, BASDAI>4, BASFI>4, BAS-G>50 and high FACIT-Fatigue scale were independent risk factors associated with the risk of both depression and anxiety as determined by multivariate logistic regression analysis.

Whereas gender, disadvantaged social class and MCS <50 were independent risk factors associated with the risk of anxiety (Table 6).

Psychiatric Assessment

Forty-one patients with HADS-D and/or HADS-A scores greater than 10 accepted a psychiatric interview. Respectively, twenty-two patients (53.7%) were diagnosed with depression and five patients (12.2%) were diagnosed with anxiety disorders. Mean HADS-D was significantly higher in subjects with confirmed depression (p=0.02). However, HADS-A did not demonstrated diagnostic value (p=0.55).

Table 5. Bivariate Analysis

Clinical Severity Measure	Patient-Reported Outcome Measure	
	HADS-D ≥ 11	HADS-A ≥ 11
Morning stiffness (minutes)		
> 15	52.6%	52.6%
≤ 15	14.3%	28.6%
p-value	<0.0001	0.023
BASDAI (0-10)		
> 4	55.8%	55.8%
≤ 4	6.8%	22.7%
p-value	<0.0001	0.001
BASFI (0-10)		
> 4	45.7%	50%
≤ 4	14.6%	26.8%
p-value	<0.0001	0.016
BAS-G (0-100)		
> 50	47.8%	52.2%
≤ 50	12.2%	24.4%
p-value	<0.0001	0.001
VAS fatigue (0-100) (mm)		
> 50	51.2%	48.8%
≤ 50	11.4%	29.5%
p-value	<0.0001	0.006
VAS pain (0-100) (mm)		
> 50	41.2%	45.1%
≤ 50	16.7%	30.6%
p-value	0.033	NS
SF-36 MCS (0-100)		
> 50	0%	13%
≤ 50	49.2%	49.2%
p-value	<0.0001	<0.0001
SF-36 PCS (0-100)		
> 50	0%	25%
≤ 50	34.6%	41.0%
p-value	NS	NS

BASDAI: Bath Ankylosing Spondylitis Activity Disease Activity Index. BASFI: Bath Ankylosing Spondylitis Functional Index. BAS-G: Bath Ankylosing Spondylitis Global Score. HADS-A: Hospital Anxiety Depression Scale-Anxiety. HADS-D: Hospital Anxiety Depression Scale-Depression. MCS: Mental Component Summary score. PCS: Physical Component Summary score. VAS: visual analogue scale. NS: not significant

DISCUSSION

In our cohort, the prevalence of depression and anxiety in patients with SpA was higher than the Tunisian general population (8.2% for depression and between 4 to 6% for anxiety (Douki et al. 2003) which is consistent with a Turkish and Chinese studies (Martindale et al. 2006, Chan et al. 2014). They showed that patients with AS had 2 to 3 fold higher rate of anxiety and depression symptoms than the general population (Martindale et al. 2006, Chan et al. 2014). As shown before anxiety was more prevalent in SpA patients than depression (Martindale et al. 2006, Hakkou et al. 2011, Baysal et al. 2011, Gniadecki et al. 2012). In this study the HADS was chosen because of the availability of a validated Arabic version and its reliability, sensitivity, specificity and severity assessment in the detection of anxiety and depression (Bjelland et al. 2002, Malasi et al. 1991). The majority of somatic symptoms related to depression and anxiety, such as fatigue and pain have been omitted in HADS in order to prevent false-positive cases. Furthermore, the HADS is a patient-reported test. SpA patients can suffer from silent anxiety or depression that could be undiagnosed by a physician but probably detected by the extensively validated HADS. Indeed, we found higher prevalence of anxious (39%) and depressive (31%) symptomatology in SpA patients, which are close to the reported prevalence of anxiety and depression by others Turkish, Moroccan and English studies (rates ranging between 33% and 60%) but higher than observed in a representative national survey of the Spanish and Greece (anxious, 14.8% and depression, 27.4%) (Hakkou et al. 2011, Baysal et al. 2011, Jiang et al. 2015, Barlow et al. 1993, Kilic et al. 2014, Günaydin et al. 2009). In our study population the mean HADS-A was 8.9 and the mean HASD-D was 7.23. Previous reports have shown that the HADS-A score can varied between 6.7 and 9.5 and the HADS-D score between 5.5 and 9.1 (Martindale et al. 2006, Hakkou et al. 2011, Chan et al. 2014, Baysal et al. 2011, Gniadecki et al. 2012, Mercedes et al. 2011, Packham

Table 6. Multivariate Analysis (Binary logistic regression): Adjusted Odds Ratio and 95% Confidence İnterval for the Factors Influencing Depression and Anxiety Risk in Patients with Spondyloarthritis

	Factors for Depression			Factors for Anxiety		
Independent Factors	aOR	95% CI	p	aOR	95% CI	p
VAS pain > 50	3.5	1.2 - 9.9	0.015	-	-	-
VAS Fatigue > 50	8.2	2.7 – 24.7	<0.0001	2.3	0.9- 5.5	0.07
BASFI > 4	4.9	1.7 – 13.9	0.002	2.7	1.1 – 6.7	0.027
BASDAI > 4	17.3	4.6 – 64.5	<0.0001	4.3	1.7 – 10.8	0.002
BAS-G > 50	6.6	2.2 – 19.8	<0.0001	3.4	1.4 - 8.5	0.008
MSC ≤ 50	Undefined	-	<0.0001	6.5	1.7 – 23.9	0.002
Morning stiffness >15 minutes	6.7	2.4 – 18.5	<0.0001	2.8	1.1 – 6.8	0.023
Sex (F)	-	-	-	3.9	1.4 – 10.9	0.006
Disadvantaged Social class	-	-	-	6.2	2.1 - 18.3	<0.0001

BASDAI: Bath Ankylosing Spondylitis Activity Disease Activity Index. BASFI: Bath Ankylosing Spondylitis Functional Index. BAS-G: Bath Ankylosing Spondylitis Global Score. F: female. MCS: Mental Component Summary score. VAS: visual analogue scale. CI: confidence interval. aOR: adjusted odds ratio

et al. 2012). The differences in scores between studies might be attributed to data recording, definition of depression, instruments, cut-off values used for assessing depression and demographic diversities. There is a need for detailed interview structures for assessing depression in SpA.

The substantial higher scoring for anxiety and depression found in our cohort could be due partly by the fact that our patients were enrolled during their visit at the hospital leading to a broad spectrum of SpA patients including severe cases. Also our cohort was older and the disease duration was longer compared to other studies. Interestingly, disease duration was positively correlated to anxiety whereas no correlation was found between age, anxiety and depression. However, Geenen et al. reported an associated with age, anxiety and depression in rheumatic diseases (Geenen et al. 2012). Martindale et al. and Baysal et al. have demonstrated that disease duration was not associated with anxiety and depression (Martindale et al. 2006, Baysal et al. 2011).

Female gender was a predictor for anxiety as previously reported (Mercedes et al. 2011, McDonough et al. 2014). Moreover, other studies have reported higher rates of depression in female with SpA (Barlow et al. 1993, McDonough et al. 2014, Meesters et al. 2014a). The disadvantaged social class was also an independent risk factor associated with anxiety. Our results regarding the educational level of our patients are in contrast with the literature. In fact, many authors reported that the educational level is negatively correlated with both HADS-D and HADS-A scores and lower educational levels are independent risk factors for anxiety and depression in SpA (Kilic et al. 2014, Mercedes et al. 2014, Meesters et al. 2014b, Bjelland et al. 2008). Indeed, a recent report demonstrated that patients with increased education levels were more informed about their disease and therefore managed their disease better leading to less vulnerable to psychological impact (Baysal et al. 2011, Bjelland et al. 2008).

We showed that VAS pain was a risk factor for depression (Baysal et al. 2011, Kilic et al. 2014, Mercedes et al. 2014, McDonough et al. 2014, Meesters et al. 2014b). Previous reports have shown that VAS pain correlated with high HADS-A, however, we could not confirm that finding in this cohort (Baysal et al. 2011, Kilic et al. 2014, Mercedes et al. 2014, McDonough et al. 2014, Meesters et al. 2014b). We identified that BASDAI and BASFI were independent risk factors for anxiety and depression (Martindale et al. 2006, Hakkou et al. 2011, Baysal et al. 2011, Jiang et al. 2015, Kilic et al. 2014, Mercedes et al. 2014, Meesters et al. 2014b, Brionez et al. 2010a, Brionez et al. 2009b, Jang et al. 2011). Brionez et al (Brionez et al. 2010a, Brionez et al. 2009b) found a significant correlation between BASDAI/BASFI and psychological variables including arthritis, helplessness, passive coping, and depression. Kilic et al. (Kilic et al. 2014) showed that both HADS-D and HADS-A scores correlated with BASDAI, ASDAS-CRP and BASFI in axial SpA.

Some researchers (Baysal et al. 2011, Kilic et al. 2014) found no evidence of any association between anxiety and/or depression and BASMI, whereas others did find a correlation (Martindale et al. 2006). BASMI wasn't identified as a risk factor for depression or anxiety in our patients.

Quality of life was negatively correlated with HADS-A and HADS-D in our study. The multivariate regression analysis revealed that only MCS<50 was an independent risk factor for anxiety. However, several reports confirmed that quality of life was significantly associated with symptoms of anxiety and/or depression (Baysal et al. 2011, Kilic et al. 2014, Mercedes et al. 2011, Meesters et al. 2014b, Husted et al. 2012). These results may be related to a potential loss of independence or mobility, functional disability and accompanying feelings of failure, helplessness and low self-esteem

In our cohort, we identified that high FACIT-Fatigue score, VAS fatigue (>50) and morning stiffness (>15 minutes) were independent risk factors for anxiety and depression. Hence, other reports have shown that fatigue was significantly associated with higher levels of anxiety and depression (Kilic et al. 2014, Mc Donough et al. 2014, Meesters et al. 2014b). Günaydin et al. showed that the contribution of depression on fatigue was 12% in AS (Günaydin et al. 2009). We found only one study verifying the correlation with morning stiffness (Baysal et al. 2011).

The inflammatory markers, ESR and CRP were no risk factors for psychological status (Kilic et al. 2014). Recently there has been growing interest in the roles of inflammation in contributing to the development of depression in people with physical illness (Valkanova et al. 2013). In fact, proinflammatory cytokines (PIC) such as IL-1, TNFα and interferon gamma (IFN-γ) release in inflammation might be involved in the pathogenesis of depression.

The strengths of this study are as followed: we recruited a large group of Tunisian patients that were from Tunisia's largest tertiary teaching hospital, department of rheumatology. Therefore, the sample size was optimally estimated to give adequate power, allowed us statistically reliable results. Validated questionnaires were used to assess anxiety and depression (HAD scale).

This study has limitations. First this is a cross-sectional study design, which provided only correlation findings and therefore we cannot determined whether higher depression scores caused a heightened perception of disease activity or vice versa. It is difficult to distinguish whether the burden of psychological distress is a consequence of the adverse impact of the disease-related problems, underlying inflammatory processes, or other factors associated with SpA. Second, in patients with psoriatic arthritis (PsA) and SpA/ inflammatory bowel disease (IBD), no

measures of IBD activity or psoriasis were performed. Active IBD and psoriasis could influence anxiety and depression. It is a well-known fact that patients with psoriasis often suffer from psychological disorders (Biljan et al. 2009, Esposito et al. 2006, Akay et al. 2002). Therefore, anxiety and depression are not necessarily related to SpA. Third, we did not assess ASDAS-CRP, which is currently being used as an outcome measure replacing BASDAI. Finally, the study does not have a matched control group or diseased control such as chronic mechanical back pain.

This study provides important information regarding the psycho-affective involvement of patients with SpA within the setting of rheumatology clinics in a large Tunisian SpA sample. The prevalence of anxiety and depression according to HADS was high in SpA patients. The use of HADS as a screening tool for depressive and anxiety disorders aids rheumatologists in identifying patients for further psychiatric evaluation. Disease severity, functional limitation, VAS fatigue and worse quality of life were independent risk factors for anxiety and depression. Therefore, psychological status of the patient is needed with the assessment of patients with SpA. Early identification of depressive and anxiety disorders may allow early referral for psychiatric assessment, psychological counseling, educational programs and even psychopharmacological treatment, to complement their medical therapy. Longitudinal studies are needed to determine the degree of causality and intervention studies to evaluate the effect of such screening.

REFERENCES

Akay A, Pekcanlar A, Bozdag KE et al (2002) Assessment of depression in subjects with psoriasis vulgaris in lichen planus. J Eur Acad Dermatol Venereol 16:347-52.

Baysal O, Durmuş B, Ersoy Y et al (2011) Relationship between psychological status and disease activity and quality of life in ankylosing spondylitis. Rheumatol Int 31:795–800

Barlow JH, Macey SJ, Struthers GR (1993) Gender, depression, and ankylosing spondylitis. Arthritis Care Res 6:45–51.

Biljan D, Laufer D, Filakovic P et al (2009) Psoriasis, mental disorders and stress. Coll Antropol 33:889-92.

Bjelland I, Krokstad S, Mykletun A et al (2008) Does a higher educational level protect against anxiety and depression? The HUNT study. Soc Sci Med 66:1334–45.

Bjelland I, Dahl AA, Haug TT et al (2002) The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res 52:69-77.

Brionez TF, Assassi S, Reveille JD et al (2010a) Psychological Correlates of Self-Reported Disease Activity in Ankylosing Spondylitis. J Rheumatol 37:829–34.

Brionez TF, Assassi S, Reveille JD et al (2009b) Psychological correlates of self-reported functional limitation in patients with ankylosing spondylitis. Arthritis Res Ther 11:R182.

Chan CYY, Tsang HH, Lau CS et al (2017) Prevalence of depressive and anxiety disorders and validation of the Hospital Anxiety and Depression Scale as a screening tool in axial spondyloarthritis patients. Int J Rheum Dis 20:317-25.

Chorus AM, Miedema HS, Boonen A et al (2003) Quality of life and work in patients with rheumatoid arthritis and ankylosing spondylitis of working age. Ann Rheum Dis 62:1178-84.

Creed F,Morgan R, Fiddler M,Marshall S, Guthrie E et al (2002) Depression and anxiety impair health-related quality of life and are associated with increased costs in general medical inpatients. Psychosomatics 43:302–9.

Douki S, Taktak MJ HZ (2003) Prevalence of depression in developing countries: the example of Tunisia. WPA Bull Depress 6:1-3.

Esposito M, Saraceno R, Giunta A et al (2006) An italian study on psoriasis and depression. Dermatology 212:123-7

Geenen R, Newman S, Bossema ER et al (2012) Psychological interventions for patients with rheumatic diseases and anxiety or depression. Best Pract Res Clin Rheumatol 26:305–19.

Gniadecki R, Robertson D, Molta CT et al (2012) Self-reported health outcomes in patients with psoriasis and psoriatic arthritis randomized to two etanercept regimens. J Eur Acad Dermatol Venereol 26:1436–43.

Günaydin R, Göksel Karatepe A, Ceşmeli N et al (2009) Fatigue in patients with ankylosing spondylitis: relationships with disease-specific variables, depression, and sleep disturbance. Clin Rheumatol 28:1045-51.

Hakkou J, Rostom S, Aissaoui N et al (2011) Psychological status in Moroccan patients with ankylosing spondylitis and its relationships with disease parameters and quality of life. J Clin Rheumatol 17:424–28.

Herrmann C (1997) International experiences with the Hospital Anxiety and Depression Scale-a review of validation data and clinical results. J Psychosom Res 42:17–41.

Husted JA, Tom BD, Farewell VT et al (2012) Longitudinal study of the bidirectional association between pain and depressive symptoms in patients with psoriatic arthritis. Arthritis Care Res 64:758-65.

Jang JH, Green CE, Assassi S et al (2011) The contribution of disease activity on functional limitations over time through psychological mediators: a 12-month longitudinal study in patients with ankylosing spondylitis. Rheumatology 50:2087-92.

Jenkinson TR, Mallorie PA, Whitelock HC et al (1994) Defining spinal mobility in ankylosing spondylitis (AS). The Bath AS Metrology Index. J Rheumatol 21:1694–8.

Jiang Y, Yang M, Wu H et al (2015) The relationship between disease activity measured by the BASDAI and psychological status, stressful life events, and sleep quality in ankylosing spondylitis. Clin Rheumatol 34:503-10.

Jones SD, Steiner A, Garrett SL et al (1996) The Bath Ankylosing Spondylitis Patient Global Score (BAS-G). Br J Rheumatol 35:66-71.

Katon W, Lin EH, Kroenke K (2007) The association of depression and anxiety with medical symptom burden in patients with chronic medical illness. Gen Hosp Psychiatry 29:147–55.

Kilic G, Kilic E, Ozgocmen S (2014) Relationship between psychiatric status, self-reported outcome measures, and clinical parameters in axial spondyloarthritis. Medicine 93:e337.

Kchir MM, Hamdi W, Kochbati S et al (2009) Validation of the Tunisian versions of Bath Ankylosing Spondylitis Functional Index (BASFI) and Disease Activity Index (BASDAI). Tunis Med 87:527–30.

MacKay K, Mack C, Brophy S et al (1998) The Bath Ankylosing Spondylitis Radiology Index (BASRI): a new, validated approach to disease assessment. Arthritis Rheum 41:2263–70.

Martindale J, Smith J, Sutton CJ et al (2006) Disease and psychological status in ankylosing spondylitis. Rheumatology 45:1288–93.

Malasi TH, Mirza IA, el-Islam MF (1991) Validation of the Hospital Anxiety and Depression Scale in Arab patients. Acta Psychiatr Scand 84:323-6.

Mercedes F, Jesus R, Ingrid M et al (2011) Prevalence of symptoms of anxiety and depression in patients with psoriatic arthritis attending rheumatology clinics. Reumatol Clin 7:20–6.

McWilliams LA, Clara IP, Murphy PD et al (2008) Associations between arthritis and a broad range of psychiatric disorders: findings from a nationally representative sample. J Pain 9:37–44.

McDonough E, Ayearst R, Eder L et al (2014) Depression and anxiety in psoriatic disease: prevalence and associated factors. J Rheumatol 41:887-96.

Meesters JJ, Bremander A, Bergman S et al (2014a) The risk for depression

in patients with ankylosing spondylitis: a population-based cohort study. Arthritis Res Ther 16:418.

Meesters JJ, Petersson IF, Bergman S et al (2014b) Sociodemographic and disease-related factors are associated with patient-reported anxiety and depression in spondyloarthritis patients in the Swedish SpAScania cohort. Clin Rheumatol 33:1649-56.

Ozgül A, Peker F, Taskaynatan MA et al (2006) Effect of ankylosing spondylitis on health-related quality of life and different aspects of social life in young patients. Clin Rheumatol 25:168–74.

Packham JC, Jordan KP, Haywood KL et al (2012) Evaluation of Ankylosing Spondylitis Quality of Life questionnaire: responsiveness of a new patient-reported outcome measure. Rheumatology 51:707-14.

Rudwaleit M, van der Heijde D, Landewé R et al (2009) The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection.Ann Rheum Dis 68:777-83.

Rudwaleit M, van der Heijde D, Landewé R et al (2011) The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. Ann Rheum Dis 70:25-31.

Valkanova V, Ebmeier KP, Allan CL (2013) CRP, IL-6 and depression: a systematic review and meta-analysis of longitudinal studies. J Affect Disord 150:736–44.

van Melle JP, de Jonge P, Spijkerman TA et al (2004) Prognostic association of depression following myocardial infarction with mortality and cardiovascular events: a meta-analysis. Psychosom Med 66:814–22.

Ware JE Jr, Snow KK, Kosinski M et al (1993) SF-36 Health Survey: Manual and Interpretation Guide. Boston: The Health Institute, New England Medical Center.

Zigmond AS, Snaith RP (1983) The hospital anxiety and depression scale. Acta Psychiatr Scand 67:361–70.

Zhu CB, Blakely RD, Hewlett WA (2006) The proinflammatory cytokines interleukin-1beta and tumor necrosis factor-alpha activate serotonin transporters. Neuropsychopharmacol 31:2121–31.