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ORIGINAL ARTICLE

# Prevalence of psychological disorders, sleep disturbance and stressful life events and their relationships with disease parameters in Chinese patients with ankylosing spondylitis

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**Abstract** Our aim was to investigate the prevalence of psychological disorders, sleep disturbance, and stressful life events in Chinese patients with ankylosing spondylitis (AS) and healthy controls, to assess the correlation between psychological and disease-related variables, and finally to detect powerful factors in predicting anxiety and depression. AS patients diagnosed with the modified New York criteria and healthy controls were enrolled from China. Participants completed a set of questionnaires, including demographic and disease parameters, Zung self-rating anxiety scale (SAS), Zung self-rating depression scale (SDS), the Pittsburgh Sleep Quality Index questionnaire (PSQI), and the Social Readjustment Rating Scale (SRRS). The relationship between psychological and other variables was explored. Stepwise multiple regression was used to determine the contributors to each disorder. Of all the 2772 AS patients, 79.1% were male. Mean age was 28.99 ± 8.87 years. Prevalence of anxiety, depression, and sleep disturbance was 31.6% (95% CI, 29.9, to 33.4), 59.3% (95% CI, 57.5, to 61.2), and 31.0% (95% CI, 29.3, to 36.7), respectively. 35.3% had stimulus of psychological and social elements (SPSE). Compared with healthy controls, AS patients had more severe psychological disorders, sleep disturbance, and stressful life events ($P < 0.01$). SDS, overall pain, BASFI, and sleep disturbance were significant contributors of the SAS scores ($P < 0.03$). SAS, less years of education, and sleep duration were significant contributors of SDS ($P < 0.01$). AS patients had more anxiety, depression, stressful life events, and sleep disturbance than healthy controls. Pain, functional limitation, sleep disturbance, and education were major contributors to psychological disorders.

**Keywords** Ankylosing spondylitis · Anxiety · Depression · Psychological status · Sleep disturbance · Stressful life events

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## Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease which mainly involves the spine and sacroiliac joints. Major clinical manifestations of AS include inflammatory back pain, morning stiffness, limited spinal activity, and even spinal deformity or ankylosis at the advanced stage [1].

Psychological symptoms not only have a substantial negative impact on the quality of life, but also on the course and outcome of the chronic disorder [2]. Anxiety and depression are common among people with arthritis and interplay independently and synergistically with clinical outcomes such as pain and disability [3]. Psychological variables can be found either within the body functions or within the personal factors [4]. Depression can be the direct consequence of the health condition or an emotional reaction to the presence of the disease [5]. Existing research suggests that psychological factors not only affect self-reported physical health in ankylosing spondylitis, but also mental health and worker participation, pointing to the societal relevance of the issue [6].

AS patients may suffer from various sleep problems, including poor quality of sleep, sleep onset insomnia, and other sleep disturbance. In a Chinese study, half of the patients with AS are reported to have sleep disturbances [7]. Pain intensity, anxiety, and depression correlated significantly with poorer sleep quality [8]. Some previous studies have proved that psychological disorders have a negative influence on sleep problem in the patients with arthritis [9, 10].

Stress has been recognized as a significant risk factor in the etiology of inflammatory rheumatic diseases [11]. An adaptational stress response involves the activation of both the hypothalamus-pituitary-adrenal axis (HPA axis) [12] and the autonomic nervous system (ANS) [13], and both stress axes are related to communication with the immune system. Stressful life events have a substantial association with psychological disorders, and early life stress constitutes a major risk factor for the subsequent development of mental disorder [14]. It has reported that psychological disorders may increase exposure or reactivity to stress and thereby increase reports of pain [15]. However, stressful life events have been rarely taken into consideration in the patients with AS. It is necessary to unveil the relationship between psychological disorder, sleep problems, and stressful life events in AS patients.

The objectives of this study were to determine the prevalence of anxiety, depression, sleep disorder, and stressful life events in AS patients in a large sample number and then to assess the correlation between anxiety, depression, sleep disturbance, and stressful life events.

## Materials and methods

### Participants

Study participants and healthy controls were recruited from rheumatology department of 7 hospitals all over China, including the Third Affiliated Hospital of Sun Yat-sen University, Beijing Jishuitan Hospital, Tongji Hospital, Union Hospital, the First Affiliated Hospital of Zhengzhou University, Hainan Provincial People's Hospital, and Fuzhou General Hospital of Nanjing Military Command. All the patients met the Modified New York Classification Criteria for AS. People with concomitant disorders like serious infections or systemic diseases (cardiac, respiratory, gastrointestinal, neurological, endocrine, etc.) were excluded. This study was conducted in compliance with the Helsinki Declaration to protect human subjects and was approved by the Third Affiliated Hospital of Sun Yat-sen University ethics committee. All the participants gave written informed consent.

### Study design

Baseline assessments were completed by trained investigators using identical structured questionnaires including demographic information (age, gender, year of education, occupation, marital status) and disease-related characteristics (age of onset, disease duration), measurements of disease status using Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [16], Bath Ankylosing Spondylitis Functional Index (BASFI) [17]. Several self-reported questionnaires were completed by the participants, including Zung self-rating anxiety scale (SAS), and Zung self-rating depression scale (SDS), Social Readjustment Rating Scale (SRRS) used to assess stressful life event and the Pittsburgh Sleep Quality Index (PSQI) for sleep quality.

### Psychological status

Psychological status was assessed by Zung self-rating anxiety scale (SAS) and Zung self-rating depression scale (SDS). SAS is a 20-item self-administrated scale to measure anxiety. Each question is scored on a scale of 1 to 4 (rarely, sometimes, frequently, and always). The total score ranges between 20 and 80. The total score multiplied by 1.25 equals the standard score. Higher score indicates more severe anxiety. Anxiety index is obtained by total score divided by 80, ranging from 0 to 1. There is no anxiety if anxiety index is less than 0.50, while 0.50–0.59 refers to little anxiety, 0.60–0.69 meaning moderate anxiety, and more than 0.70 indicating severe anxiety. SDS is a 20-item scale to assess depression. Half of the items are scored positively and half negatively. Each item is scored on a scale of 1 to 4, and the total score varies between 20 and 80. Higher score reflects more severe depression.

Standard score of SDS and depression index are obtained in a similar way [18, 19].

### Sleep quality

Sleep quality was measured by the Pittsburgh Sleep Quality Index (PSQI) questionnaire. It includes 19 questions in seven components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disorders, sleep medication, and daytime dysfunction. Each component is assessed by one or several questions. Subjective sleep, sleep duration, sleep medication, and poor daytime functioning are evaluated individually by a 4-point Likert scale. Sleep latency is measured according to time to fall asleep and sleep efficiency by hours asleep divided by total of hours in bed. Sleep disturbance is assessed by nine questions. These components are scored from 0 (no difficulty) to 3 (severe difficulty) individually, and then summed to give a score ranging from 0 to 21. If the PSQI is over 7.0, it means a poor sleeper while if the PSQI was less than 7.0, it means a good sleeper [20].

### Stressful life events

Social Readjustment Rating Scale (SRRS) is applied to assess stressful life events. It is a standardized measure of stress based on the occurrence of life events over the past 12 months. This self-administered questionnaire covers 43 items (i.e., death of a close family member, divorce). Each event in the questionnaire is given a score from 100 to 11, and the sum represents the quantity of stress experienced by a person over the recent year. If the sum is over 150, that means stimulus of psychological and social elements exists. Mild stimulus of psychological and social elements refers to a score of 150 to 199, moderated one referring to 200 to 299, and severe one with a score of more than 300. Higher score indicates more possibility to get sick or mental disorders in the next year [21].

### Statistical analysis

The Statistical Package for Social Sciences (SPSS) software version 21 was used for all data management and analysis. The Kolmogorov–Smirnov test was used to confirm that data were within the ranges of normal distribution. A nonparametric test was employed for the variables outside the normal distribution. First, descriptive statistics were performed to assess participants' characteristics. Second, the Mann-Whitney *U* test and Student's *t* test were used to compare the patients and controls and to compare the patients with and without anxiety or depression. Third, the relationship between psychological variables, sleep parameters, and stressful life events was examined with Spearman rank correlation analysis. Finally, stepwise linear multiple regression was used to determine the contributors to SAS, SDS, and SRRS scores (Tables 4, 5, 6). The level of significance was set at $P < 0.05$.

## Result

### 1. Sample characteristics

The characteristics of the 2772 AS patients were summarized in Table 1. 79.1% were male patients. 79.5% were employed. 48.4% were married. Mean age was 28.99 ± 8.87. 79.5% of the participants had a job at the time of survey and 15.5% were students. 26.2% of the participants had more than 12 years of education, while 5.6% did not receive primary education. Mean disease duration at study baseline was 6.84 ± 6.78 years.

Prevalence of anxiety was 31.6% (95% CI, 29.9, to 33.4). Mean SAS score was 49.32 ± 18.75, and 10.8% of the patients

**Table 1** Demographic features and self-administrated questionnaire results in AS patients

| Variables | AS patients $N = 2772$ |
|---|---|
| Age (years) | 28.99 ± 8.87 |
| Gender (male, %) | 79.1 |
| Marital status (%) | |
| Single | 50.4 |
| Married | 48.8 |
| Divorced | 0.8 |
| Number employed, *n* (%) | 79.5 |
| Student, *n* (%) | 15.5 |
| Disease duration (years) | 6.84 ± 6.78 |
| SAS | 49.32 ± 18.75 |
| SDS | 54.87 ± 16.67 |
| Subjective sleep quality | 1.24 ± 0.89 |
| Sleep latency | 1.14 ± 1.03 |
| Sleep duration | 0.91 ± 0.91 |
| Sleep efficiency | 0.81 ± 1.08 |
| Sleep disturbance | 1.00 ± 0.75 |
| Sleep medication | 0.19 ± 0.70 |
| Daytime dysfunction | 1.19 ± 0.93 |
| PSQI | 6.48 ± 4.32 |
| Poor sleepers (%) | 31.0 |
| SRRS | 129.33 ± 145.06 |
| Without SPSE, *n* (%) | 64.7 |
| With SPSE, *n* (%) | 35.3 |
| Mild SPSE, *n* (%) | 9.6 |
| Moderate SPSE, *n* (%) | 11.3 |
| Severe SPSE, *n* (%) | 14.4 |

*SAS* self-rating anxiety scale, *SDS* self-rating depression scale, *SRRS* Social Readjustment Rating Scale, *SPSE* stimulus of psychological and social elements, *PSQI* Pittsburgh Sleep Quality Index

had severe anxiety. Prevalence of depression was 59.3% (95% CI, 57.5, to 61.2). Mean SDS score was 54.97 ± 16.67, and 11.3% of the sample had severe depression. Mean PSQI score was 6.48 ± 4.32. Prevalence of sleep disturbance was 31.0% (95% CI, 29.3, to 36.7). Mean SRRS score was 129.33 ± 145.06. 35.3% (95% CI, 33.5, to 37.1) of the patients had stimulus of psychological and social elements (SPSE), while 14.4% came across severe SPSE.

Among all the patients, only 683 patients completed both the measurement of disease activity and questionnaires. The characteristics of the 683 patients with AS were summarized in Table 2.

**Table 2** Demographic features, clinical, and laboratory results of the 683 patients with AS

| Variables | Values (means ± SD, or percentage) |
|---|---|
| Age (years) | 27.33 ± 8.67 |
| Gender (male, %) | 80.4 |
| Marital status (%) | |
| Single | 38.9 |
| Married | 60.6 |
| Divorced | 0.4 |
| Years of education | |
| Illiterate | 4(0.6%) |
| < 6 years | 42(6.1%) |
| 7–9 years | 145(21.2%) |
| 10–12 years | 180(26.4%) |
| 13–16 years | 287(42.0%) |
| > 16 years | 25(3.7%) |
| Number employed, *n* (%) | 68.2 |
| Student, *n* (%) | 9.5 |
| Current smoker, *n* (%) | 24.5 |
| Disease duration (years) | 6.47 ± 6.47 |
| < 5 | 51.4 |
| 5–9 | 22.1 |
| 10–14 | 14.6 |
| 15–19 | 6 |
| 20–24 | 3.9 |
| > 24 | 2 |
| Morning stiffness (VAS, cm) | 3.12 ± 2.86 |
| Duration of morning stiffness (min) | 37.9 ± 155.92 |
| Overall pain (VAS, cm) | 3.97 ± 2.77 |
| Nocturnal back pain (VAS, cm) | 2.93 ± 2.96 |
| Overall back pain (VAS, cm) | 2.99 ± 2.93 |
| ESR (mm/h) | 20.94 ± 21.71 |
| CRP (mg/dl) | 18.4 ± 26.01 |
| BASDAI | 3.36 ± 2.03 |
| BASFI | 1.50 ± 1.95 |

*BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *VAS* Visual Analogue Scale, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *BASFI* Bath Ankylosing Spondylitis Functional Index

Five hundred forty-nine men and 134 women completed all the questionnaires and examination. Mean age of the patients was 27.33 ± 8.67 years. Mean disease duration at study baseline was 6.47 ± 6.47 years.

### The differences of psychological status, stressful life events, and sleep disturbance between patients and controls

Significant differences were found between patient group and healthy controls in anxiety, depression, and SRRS ($P < 0.01$), indicating that AS patients had significantly higher scores in anxiety and depression, and had more severe life events than healthy controls, as shown in Table 3. Overall sleep quality, subjective sleep quality, sleep latency, sleep efficiency, sleep disturbance, and daytime dysfunction were significantly worse than those of the controls, while there were no significantly differences between two groups in the aspects of sleep duration and sleep medication statistically. PSQI scores revealed that AS patients suffered from worse sleep quality and the percentage of poorer sleeper (37.3%) was higher than healthy controls (9.5%).

### Comparisons of subgroups with/without anxiety or depression

We divided the 683 patients into four subgroups according to the patients with or without anxiety and/or depression (Table 4). The Mann-Whitney *U* test and a Student's *t* test were performed in these subgroups. Patients with higher SAS scores had significantly higher degree and longer duration of morning stiffness, more overall pain and back pain, higher ESR, BASDAI, BASFI, and worse sleep quality ($P < 0.05$). No statistically significant differences were found between the two subgroups in the following aspects, including CRP and SRRS. Meanwhile, patients with higher SDS scores had more overall pain, back pain, higher BASDAI, BASFI, and worse sleep quality ($P < 0.05$). There were no statistically significant differences between two subgroups in the following aspects, including degree and duration of morning stiffness, CRP, ESR, and SRRS.

The results of subgroup comparison of 2772 AS patients were shown in Supplementary Table 1. Patients with anxiety had older age, less education, more depression, and more stressful life events ($P < 0.05$). Patients with depression had older age, less education, more anxiety and more SRRS scores. ($P < 0.05$). However, disease duration and sleep quality did not differ in subgroups significantly.

### The associations of disease status and psychological status

The results of 683 patients were displayed in Table 5. Spearman correlation analysis found the following variables to be significantly associated with the SAS scores: disease duration, morning stiffness and duration, overall pain, back pain, BASDAI, BASFI,

**Table 3** The differences of psychological status, stressful life events, and sleep disturbance between patients and controls

| Variables | AS patients $N = 683$ | Controls $N = 697$ | $P$ |
|---|---|---|---|
| Age (years) | 27.33 ± 8.67 | 27.47 ± 7.71 | 0.26 |
| Gender (male, %) | 80.4 | 76.9 | 0.09 |
| SAS | 45.41 ± 9.86 | 41.93 ± 9.26 | 0.000 |
| Without anxiety, *n* (%) | 69 | 48.8 | |
| With anxiety | 31 | 51.2 | |
| Mild anxiety, *n* (%) | 22.9 | 36.7 | |
| Moderate anxiety, *n* (%) | 6.3 | 13.9 | |
| Severe anxiety, *n* (%) | 1.8 | 0.6 | |
| SDS | 52.08 ± 9.21 | 49.75 ± 9.24 | 0.000 |
| Without depression, *n* (%) | 35.9 | 76.3 | |
| With depression, *n* (%) | 64.1 | 23.7 | |
| Mild depression, *n* (%) | 44.1 | 16.2 | |
| Moderate depression, *n* (%) | 15.6 | 7.0 | |
| Severe depression, *n* (%) | 4.1 | 0.4 | |
| SRRS | 120.41 ± 149.46 | 94.78 ± 123.68 | 0.000 |
| Without SPSE, *n* (%) | 68 | 73.9 | |
| With SPSE, *n* (%) | 32 | 26.1 | |
| Mild SPSE, *n* (%) | 9.6 | 9.2 | |
| Moderate SPSE, *n* (%) | 9.6 | 8.6 | |
| Severe SPSE, *n* (%) | 12.4 | 8.3 | |
| Subjective sleep quality | 1.41 ± 0.88 | 0.83 ± 0.75 | 0.000 |
| Sleep latency | 1.30 ± 1.05 | 1.30 ± 1.05 | 0.000 |
| Sleep duration | 0.95 ± 0.93 | 0.90 ± 0.80 | 0.698 |
| Sleep efficiency | 0.81 ± 1.07 | 0.21 ± 0.63 | 0.000 |
| Sleep disorders | 1.08 ± 0.72 | 0.59 ± 0.55 | 0.000 |
| Sleep medication | 0.15 ± 0.62 | 0.08 ± 0.36 | 0.357 |
| Daytime dysfunction | 1.30 ± 0.89 | 0.81 ± 0.67 | 0.000 |
| PSQI | 7.00 ± 4.21 | 4.21 ± 2.68 | 0.000 |
| Poor sleepers (%) | 37.3 | 9.5 | |

*SAS* anxiety scale, *SDS* self-rating depression scale, *SRRS* Social Readjustment Rating Scale, *SPSE* stimulus of psychological and social elements, *PSQI* Pittsburgh Sleep Quality Index

SDS score and all components of the PSQI score positively, and years of education negatively ($P < 0.05$). On the contrary, the other variables, including age, ESR, CRP, and SRRS, did not significantly correlate with the SAS scores. The SDS scores were significantly associated with degree and duration of morning stiffness, overall pain, back pain, BASDAI, BASFI, SAS and all components of the PSQI score positively, and years of education negatively ($P < 0.05$), but there was no association between SDS and age, disease duration, ESR, CRP, and SRRS. The results of 2772 patients were shown in Supplementary Table 2.

### The contributors of anxiety and depression

The results of stepwise multiple regression analysis were shown in Table 6. Higher SDS ($B = 0.640$, $P < 0.001$), overall pain ($B = 0.382$, $P < 0.001$), subjective sleep quality ($B = 1.112$, $P < 0.001$), BASFI ($B = 0.445$, $P < 0.001$), sleep disturbance ($B = 0.981$, $P < 0.001$), and daytime dysfunction ($B = 0.767$, $P < 0.001$) were significant contributors of SAS. These variables could explain 56.3% of variance in SAS. This analysis revealed that SDS (standardized coefficient, 0.598) contributed most in the SAS score statistically. In the same way did we discover that higher SAS ($B = 0.629$, $P < 0.001$), sleep duration ($B = 0.858$, $P < 0.001$), and less years of education ($B = -1.869$, $P < 0.001$) contributed significantly to SDS and could explain 51.2% of variance in the SDS score. This analysis revealed that SAS was the maximum contributor of SDS statistically (standardized coefficient, 0.674). The results of 2772 patients were shown in Supplementary Table 3.

**Table 4** Clinical and laboratory results in 683 patients with AS subgroups with/without depression/anxiety

| | Anxiety | | | Depression | | |
|---|---|---|---|---|---|---|
| | SAS ≥ 50 ($n$ = 212) | SAS< 50 ($n$ = 471) | $P$ | SDS ≥ 50 ($n$ = 437) | SDS < 50 ($n$ = 246) | $P$ |
| Current smoker (yes) | 0.27 ± 0.45 | 0.23 ± 0.42 | 0.236 | 0.26 ± 0.44 | 0.21 ± 0.41 | 0.131 |
| Disease duration (years) | 6.75 ± 6.24 | 6.35 ± 6.57 | 0.215 | 6.57 ± 6.72 | 6.29 ± 6.01 | 0.795 |
| Morning stiffness (VAS) | 3.70 ± 3.06 | 2.86 ± 2.73 | 0.001 | 3.23 ± 2.91 | 2.92 ± 2.77 | 0.235 |
| Duration of morning stiffness (min) | 47.03 ± 170.91 | 33.82 ± 148.69 | 0.011 | 32.02 ± 121.69 | 48.40 ± 202.85 | 0.902 |
| Overall Pain (VAS) | 5.16 ± 2.81 | 3.44 ± 2.58 | 0.000 | 4.29 ± 2.81 | 3.41 ± 2.60 | 0.000 |
| Back pain (VAS) | 4.10 ± 3.17 | 2.49 ± 2.67 | 0.000 | 3.29 ± 3.07 | 2.47 ± 2.59 | 0.002 |
| ESR (mm/h) | 24.99 ± 26.36 | 19.12 ± 19.01 | 0.040 | 21.67 ± 23.40 | 19.65 ± 18.31 | 0.908 |
| CRP (mg/dl) | 21.48 ± 31.07 | 17.01 ± 23.28 | 0.160 | 19.74 ± 28.45 | 16.00 ± 20.82 | 0.306 |
| BASDAI | 4.37 ± 2.15 | 2.90 ± 1.79 | 0.000 | 3.68 ± 2.07 | 2.78 ± 1.81 | 0.000 |
| BASFI | 2.34 ± 2.39 | 1.13 ± 1.58 | 0.000 | 1.80 ± 2.13 | 0.99 ± 1.45 | 0.000 |
| SAS | 69.39 ± 21.49 | 40.04 ± 5.30 | 0.000 | 49.31 ± 9.19 | 38.48 ± 6.71 | 0.000 |
| SDS | 59.05 ± 8.10 | 48.96 ± 7.86 | 0.000 | 63.31 ± 16.73 | 42.55 ± 4.39 | 0.000 |
| SRRS | 111.93 ± 143.06 | 124.70 ± 150.23 | 0.286 | 117.05 ± 127.28 | 127.28 ± 160.39 | 0.789 |
| Subjective sleep quality | 1.88 ± 0.89 | 1.20 ± 0.78 | 0.000 | 1.55 ± 0.90 | 1.15 ± 0.78 | 0.000 |
| Sleep latency | 1.69 ± 1.02 | 1.12 ± 1.02 | 0.000 | 1.42 ± 1.06 | 1.07 ± 1.00 | 0.000 |
| Sleep duration | 1.16 ± 0.85 | 1.01 ± 0.88 | 0.000 | 1.07 ± 0.98 | 0.74 ± 0.80 | 0.000 |
| Sleep efficiency | 1.09 ± 1.17 | 0.68 ± 1.00 | 0.000 | 0.92 ± 1.14 | 0.60 ± 0.91 | 0.001 |
| Sleep disorders | 1.39 ± 0.72 | 0.94 ± 0.67 | 0.000 | 1.15 ± 0.75 | 0.96 ± 0.63 | 0.001 |
| Sleep medication | 0.27 ± 0.80 | 1.72 ± 0.87 | 0.000 | 0.21 ± 0.73 | 0.05 ± 0.36 | 0.000 |
| Daytime dysfunction | 1.72 ± 0.87 | 1.12 ± 0.84 | 0.000 | 1.44 ± 0.92 | 1.07 ± 0.80 | 0.000 |
| PSQI | 9.21 ± 4.28 | 6.01 ± 3.66 | 0.000 | 7.77 ± 4.38 | 5.64 ± 3.25 | 0.000 |

*VAS* Visual Analogue Scale, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BASFI* Bath Ankylosing Spondylitis Functional Index, *SAS* self-rating anxiety scale, *SDS* self-rating depression scale, *SRRS* Social Readjustment Rating Scale, *PSQI* Pittsburgh Sleep Quality Index

## Discussion

Psychological disorders often coexist in the patients with AS [22]. Significant differences between AS patients and healthy controls were found in psychological status and sleep disorders. We found that 31.6% of AS patients had come across anxiety, and as much as 10.8% had severe anxiety. 59.3% of the AS patients had suffered from depression, while 11.3% had severe depression. Depression was much more common than anxiety in AS patients. Our result was similar to another study using self-reported questionnaires [23]. But our results were much higher than some previous findings [24, 25].

It is a challenge to deal with the role of psychological variables in self-reported outcomes in ankylosing spondylitis and likely in rheumatology in general [4]. What we need to clarify is that considerable confusion exists in the application of the self-reported instruments according to an Australian study [26]. SDS was reported to have a sensitivity of 93% and specificity of 69%, and SAS had a sensitivity of 89% and specificity of 69%. The rate of false positivity is therefore high, and their use as diagnostic tools invariably leads to an overestimation of anxiety and depression. AS Annelies Boonen wrote, self-reported instruments are not necessarily imperfect; it is rather our means of interpretation and our methods to assess and analyze them that need to be improved [4]. What we should do next is to further evaluate psychiatric status by psychologists after applying self-report questionnaires.

We found that both anxiety and depression were associated with degree and duration of morning stiffness, overall pain, back pain, BASDAI, BASFI, SDS, and PSQI positively, and years of education negatively. Our study was consistent with previous findings, revealing that psychological factors correlated with pain and disease activity [27]. The relationship between psychosocial factors and pain is complex and multidimensional: psychosocial factors influence the perception of pain and the presence of pain influences psychological well-being and social participation [28].

We also discovered that anxiety and depression contributed most to each other. According to Bruce W. Smith, interventions that target anxiety may be the most effective for those who suffer from both anxiety and depression. Our study revealed that depression had an inverse relationship with the

**Table 5** Coefficient of correlations between SAS, SDS and demographic, clinical variables, and sleep and SRRS (Spearman rho)

| Variable | SAS | SDS |
|---|---|---|
| Age | 0.241 | − 0.013 |
| Years of education | − 0.098* | − 0.202** |
| Disease duration (years) | 0.077* | 0.44 |
| Morning stiffness (VAS) | 0.127** | 0.106** |
| Duration of morning stiffness (min) | 0.081* | 0.079* |
| Overall Pain (VAS) | 0.312** | 0.187** |
| Back pain (VAS) | 0.267** | 0.166** |
| ESR | 0.060 | 0.024 |
| CRP | 0.066 | 0.053 |
| BASDAI | 0.361** | 0.263** |
| BASFI | 0.323** | 0.261** |
| SDS | 0.690** | 1 |
| SAS | 1 | 0.690** |
| SRRS | 0.012 | −0.013 |
| Subjective sleep quality | 0.386** | 0.272** |
| Sleep latency | 0.282** | 0.235** |
| Sleep duration | 0.157** | 0.181** |
| Sleep efficiency | 0.158** | 0.167** |
| Sleep disturbance | 0.307** | 0.176** |
| Sleep medication | 0.161** | 0.173** |
| Daytime dysfunction | 0.365** | 0.240** |
| PSQI | 0.406** | 0.320** |

*SAS* self-rating anxiety scale, *SDS* self-rating depression scale, *VAS* Visual Analogue Scale, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BASFI* Bath Ankylosing Spondylitis Functional Index, *SRRS* Social Readjustment Rating Scale, *PSQI* Pittsburgh Sleep Quality Index

*$P < 0.05$; **$P < 0.01$

number of years in education, indicating that knowledge about the disease may help the patients to master their mood in a positive way. And we found no evidence of an effect of disease duration on depression, sleep disturbance, or stressful life events, which was in consistence with some studies [10].

Sleep disturbance has been shown to be another problem of patients with AS. 31.0% of our study participants suffered from sleep disturbance, less than 50% in previous studies in China [7, 29]. In our study, sleep disorder was among independent variables of anxiety and depression in the multiple regression analysis, which was in consistent with some other studies [30, 31]. Nocturnal pain as a typical symptom of AS often has a negative influence on sleep quality. The relationship between sleep disturbance and psychological disorders in AS needs to be measured in more studies.

Patients suffering from other diseases, such as dermatological disease, have significantly more life event stress in the year preceding the onset or exacerbation of the disease [32]. Zautra AJ et al. proved that interpersonal stressors are predictive of increases in disease activity in rheumatoid diseases [33]. Besides, stressful life events have a substantial association with psychological disorders, and there is some evidence indicating that even early life stress constitutes a major risk factor for the subsequent development of mental disorder [14]. Our study revealed that 35.5% of the AS patients had SPSE, while 14.4% came across severe SPSE. According to Bolger and Zuckerman, anxiety or depression may increase exposure or reactivity to stress [15]. Our study found that patients with AS had more stressful life events than healthy controls, but we failed to prove positive correlation between stressful life events and psychological disorders. How stressful life events impact psychological disorders need to be testified in more studies.

To point out, this study had some limitations and the primary one being its cross-sectional design. It is more convincing to get more information in a longitudinal study when psychological status, sleep, and stressful life events can be monitored over a period of time. Besides, clinical variables were

**Table 6** Stepwise multiple regression of demographic, medical, and other variables in relation to SAS or SDS

| Independent variable | *B* | Standardized coefficient | *t* | *P* | $R^2$ (%) |
|---|---|---|---|---|---|
| Overall model (to SAS) | | | | | 56.3 |
| SDS | 0.640 | 0.598 | 21.80 | 0.000 | |
| Overall pain | 0.382 | 0.107 | 3.78 | 0.000 | |
| Subjective sleep quality | 1.112 | 0.099 | 3.04 | 0.002 | |
| BASFI | 0.445 | 0.088 | 3.12 | 0.002 | |
| Sleep disturbance | 0.981 | 0.071 | 2.29 | 0.022 | |
| Daytime dysfunction | 0.767 | 0.070 | 2.19 | 0.029 | |
| Overall model (to SDS) | | | | | 51.2 |
| SAS | 0.629 | 0.674 | 24.65 | 0.000 | |
| Years of education | − 1.859 | − 0.123 | − 4.57 | 0.000 | |
| Sleep duration | 0.858 | 0.087 | 3.189 | 0.001 | |

*SAS* self-rating anxiety scale, *VAS* Visual Analogue Scale, *BASFI* Bath Ankylosing Spondylitis Functional Index, *SDS* self-rating depression scale

not all recorded properly in the 2772 patients. Only less than 25% of the participants had disease-related variables recorded. Third, SAS, SDS, and some other variables were measured in self-administrated questionnaires, which may not reflect patients' status correctly. We should further evaluate psychiatric status of the patients clinically.

## Conclusion

AS patients had more anxiety, depression, stressful life events, and sleep disturbance than healthy controls. Pain, functional limitation, sleep disturbance, and education were major contributors to psychological disorders.

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**Compliance with ethical standards**

**Disclosures** None.

## References

1. Braun J, Sieper J (2007) Ankylosing spondylitis. Lancet 369:1379–1390
2. Gladis MM, Gosch EA, Dishuk NM, Crits-Christoph P (1999) Quality of life: expanding the scope of clinical significance. J Consult Clin Psychol 67:320–331
3. McWilliams LA, Cox BJ, Enns MW (2003) Mood and anxiety disorders associated with chronic pain: an examination in a nationally representative sample. Pain 106:127–133
4. Boonen A (2010) Towards a better understanding of the role of psychological variables in arthritis outcome research. Arthritis Res Ther 12:106
5. Brionez TF, Assassi S, Reveille JD et al (2009) Psychological correlates of self-reported functional limitation in patients with ankylosing spondylitis. Arthritis Res Ther 11:R182
6. Boonen A, Chorus A, Miedema H et al (2001) Withdrawal from labour force due to work disability in patients with ankylosing spondylitis. Ann Rheum Dis 60:1033–1039
7. Li Y, Zhang S, Zhu J, Du X, Huang F (2012) Sleep disturbances are associated with increased pain, disease activity, depression, and anxiety in ankylosing spondylitis: a case-control study. Arthritis Res Ther 14:R215
8. Sayar K, Arikan M, Yontem T (2002) Sleep quality in chronic pain patients. Can J Psychiatr 47:844–848
9. Murphy H, Dickens C, Creed F, Bernstein R (1999) Depression, illness perception and coping in rheumatoid arthritis. J Psychosom Res 46:155–164
10. Martindale J, Smith J, Sutton CJ, Grennan D, Goodacre L, Goodacre JA (2006) Disease and psychological status in ankylosing spondylitis. Rheumatology (Oxford) 45:1288–1293
11. Cutolo M, Straub RH (2006) Stress as a risk factor in the pathogenesis of rheumatoid arthritis. Neuroimmunomodulation 13:277–282
12. Miller GE, Chen E, Zhou ES (2007) If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans. Psychol Bull 133:25–45
13. Ader R, Cohen N, Felten D (1995) Psychoneuroimmunology: interactions between the nervous system and the immune system. Lancet 345:99–103
14. Gourion D (2009) Events of life and links with severe depression at different ages. Encéphale 35(Suppl 7):S250–S256
15. Bolger N, Zuckerman A (1995) A framework for studying personality in the stress process. J Pers Soc Psychol 69:890–902
16. Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A (1994) A new approach to defining disease status in ankylosing spondylitis: the bath ankylosing spondylitis disease activity index. J Rheumatol 21:2286–2291
17. Calin A, Garrett S, Het al W (1994) A new approach to defining functional ability in ankylosing spondylitis: the development of the bath ankylosing spondylitis functional index. J Rheumatol 21:2281–2285
18. Zung WW (1971) A rating instrument for anxiety disorders. Psychosomatics 12:371–379
19. Zung WW, Richards CB, Short MJ (1965) Self-rating depression scale in an outpatient clinic. Further validation of the SDS. Arch Gen Psychiatry 13:508–515
20. Tsai PS, Wang SY, al WMY (2005) Psychometric evaluation of the Chinese version of the Pittsburgh Sleep Quality Index (CPSQI) in primary insomnia and control subjects. Qual Life Res 14:1943–1952
21. Holmes TH, Rahe RH (1967) The social readjustment rating scale. J Psychosom Res 11:213–218
22. Ortancil O, Konuk N, May H, Sanli A, Ozturk D, Ankarali H (2010) Psychological status and patient-assessed health instruments in ankylosing spondylitis. J Clin Rheumatol 16:313–316
23. Hakkou J, Rostom S, Mengat M, Aissaoui N, Bahiri R, Hajjaj-Hassouni N (2013) Sleep disturbance in Moroccan patients with ankylosing spondylitis: prevalence and relationships with disease-specific variables, psychological status and quality of life. Rheumatol Int 33:285–290
24. Murphy LB, Sacks JJ, Brady TJ, Hootman JM, Chapman DP (2012) Anxiety and depression among US adults with arthritis: prevalence and correlates. Arthritis Care Res (Hoboken) 64:968–976
25. Baysal O, Durmus B, al EY (2011) Relationship between psychological status and disease activity and quality of life in ankylosing spondylitis. Rheumatol Int 31:795–800
26. Dunstan DA, Scott N, Todd AK (2017) Screening for anxiety and depression: reassessing the utility of the Zung scales. BMC Psychiatry 17:329
27. Smith BW, Zautra AJ (2008) The effects of anxiety and depression on weekly pain in women with arthritis. Pain 138:354–361
28. Backman CL (2006) Arthritis and pain. Psychosocial aspects in the management of arthritis pain. Arthritis Res Ther 8:221
29. Jiang Y, Yang M, Het al W (2015) The relationship between disease activity measured by the BASDAI and psychological status, stressful life events, and sleep quality in ankylosing spondylitis. Clin Rheumatol 34:503–510
30. Batmaz I, Sariyildiz MA, Dilek B, Bez Y, Karakoc M, Cevik R (2013) Sleep quality and associated factors in ankylosing spondylitis: relationship with disease parameters, psychological status and quality of life. Rheumatol Int 33:1039–1045
31. Leverment S, Clarke E, Wadeley A, Sengupta R (2017) Prevalence and factors associated with disturbed sleep in patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis: a systematic review. Rheumatol Int 37:257–271
32. Evers AW, Lu Y, Duller P, van der Valk PG, Kraaimaat FW, van de Kerkhof PC (2005) Common burden of chronic skin diseases? Contributors to psychological distress in adults with psoriasis and atopic dermatitis. Br J Dermatol 152:1275–1281
33. Zautra AJ, Hamilton NA, Potter P, Smith B (1999) Field research on the relationship between stress and disease activity in rheumatoid arthritis. Ann N Y Acad Sci 876:397–412