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ORIGINAL ARTICLE

Prevalence and factors associated with disturbed sleep in outpatients with ankylosing spondylitis

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Abstract

Sleep disturbance is prevalent among patients with ankylosing spondylitis (AS) and is considered a multifactorial issue. The study was designed to investigate sleep disturbance and its associated factors in AS outpatients in Southwest China. Patients were recruited by convenience sampling in this cross-sectional study. The Pittsburgh Sleep Quality Index (PSQI), the Bath AS Disease Activity Index (BASDAI), the Bath AS Functional Index (BASFI), the Bath AS Patient Global Score (BAS-G), and the Hospital Anxiety and Depression Scale (HADS) were used to assess sleep quality, disease activity, function status, global well-being, depression, and anxiety. Spearman's correlation, *t* test, ANOVA, and multiple linear regression analysis were used to explore the associated factors of sleep disturbance. Of the 281 outpatients included in the study, 190 (67.6%) patients had sleep disturbance. The married patients, the patients with extra-spinal manifestation, depression and anxiety, longer duration of diagnostic delay, higher disease activity, worse functional status and global well-being, high level of pain, and fatigue, had poorer sleep quality ($P < 0.05$). Multiple linear regression analysis revealed age ($\beta = 0.087$, $P = 0.102$), BAS-G ($\beta = 0.181$, $P = 0.003$), fatigue ($\beta = 0.170$, $P = 0.002$), anxiety ($\beta = 0.151$, $P = 0.002$) and nocturnal back pain ($\beta = 0.192$, $P = 0.001$), extra-spinal manifestation ($\beta = 0.120$, $P = 0.012$), and duration of diagnostic delay ($\beta = 0.174$, $P = 0.001$) were the contributors to PSQI. Sleep disturbance is common in AS patients in Southwest China. It may be useful to keep regular exercise, strengthen the management of pain, relieve anxiety, and prevent and treat extra-spinal manifestation for improving sleep quality.

Keywords Ankylosing spondylitis · China · Sleep disturbance · Sleep quality

Introduction

Ankylosing spondylitis (AS) is a chronic, progressive, and systemic inflammatory disease of unknown cause. It primarily affects the sacroiliac joints and may attack the axial skeleton at the advanced stage of disease [1, 2]. AS has caused a series of significant problems, such as pain, fatigue, functional impairment, and sleep disturbance [3–5]. It has been reported that sleep disorders in AS patients are more frequent than that in normal population [2, 6]. The prevalence of sleep disturbance has been reported to occur in 50 to 64.5% of AS patients [1, 7, 8]. Patients often complain about poor sleep quality, sleep onset insomnia, difficulty awakening, and obstructive sleep apnea syndrome [9]. Sleep disturbance would cause adverse physical, psychological, and social effects, such as psychological stress, attention deficit, and learning difficulties [10, 11]. Studies [12, 13] indicated that sleep disturbance was an important risk factor for depression and anxiety. Moreover, sleep disorder would aggravate the disease symptoms and reduce general well-being [14, 15]. In addition, AS patients reported higher priority for improvement in sleep problem than by the patients with other rheumatic diseases [16]. Therefore, it is necessary to explore the sleep-related factors in AS patients for improving their sleep quality.

Sleep disturbance in AS patients was caused by multiple causes. Pain was considered to be one of the most important factors of sleep quality [14, 17, 18]. Poor sleep quality was proved to be associated with increased disease activity, gradually deteriorated function, and more severe fatigue in AS

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patients [6, 7, 19]. A number of studies [20–22] found that depression and anxiety also played an important role in sleep disturbance in AS patients. However, some factors that may affect sleep quality, such as extra-spinal manifestation, duration of diagnostic delay, and global well-being, have been rarely studied before. Moreover, there is a lack of study on the prevalence and associated factors of sleep disturbance in AS outpatients in Southwest China.

Hence, the objectives of this study were (1) to estimate the prevalence of sleep disturbance in AS outpatient in Southwest China and (2) to explore the association between demographic variables, disease-specific variables, psychological variables, and sleep quality.

Materials and methods

Study design

The study was a cross-sectional study. It was approved by West China Hospital Medical Ethics Committee, and informed consent was received from all participants.

Participants

Patients were recruited by convenience sampling from Rheumatic Outpatient Clinic of West China Hospital, Sichuan University between July and October 2015. Patients were enrolled if they fulfilled the modified New York criteria for the classification of AS [23]. Patients who were 14 years old or above and had no difficulty in communicating were included. Patients who had other diseases that may cause sleep disturbance, such as psychiatric disease, malignancy, and other chronic diseases, were excluded from the study. Demographic characteristics (age, gender, marital status, educational level, employment status, smoking status, family history, household income monthly per capita (HIMPC)) and past medical history (disease duration, duration of diagnostic delay, and extra-spinal manifestation) were documented for each participant. Disease duration was defined as the time from the onset of first symptoms to the investigation. Duration of diagnostic delay was defined as the time from the onset of first symptoms to the time of diagnosis. Extra-spinal manifestation included peripheral joint involvement and extra-articular manifestation, which was diagnosed by rheumatologists. A rheumatologist on our research team asked AS patients questions and determined whether they had extra-spinal manifestation or not.

Sleep disturbance

Sleep quality was measured by the Pittsburgh Sleep Quality Index Questionnaire (PSQI) [24]. The Chinese version [25] has been assessed for its validity and reliability. The questionnaire consists of 19 items and was divided into seven dimensions: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disorders, use of hypnotics, and daytime dysfunction. The average score of the seven components is the final PSQI score (0–21) that higher scores indicate poor sleep quality. A PSQI score >5 indicates that a participant had sleep disturbance.

Pain

The nocturnal back pain and total back pain were measured by a 10-cm horizontal visual analog scale (VAS) that a higher score indicates a higher level of pain.

Disease activity

The disease activity was evaluated by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [26]. The BASDAI is a self-administered instrument consists of five domains and relating six questions: (1) Fatigue, (2) Spinal pain, (3) Joint pain/swelling, (4) Localized tenderness, (5) Morning stiffness duration, and (6) Morning stiffness severity. Then, the average score of the 5th and 6th questions is the score of morning stiffness. The average score of five domains is the final BASDAI score (0–10) that a higher score represents more severe disease activity.

Functional status

The Bath Ankylosing Spondylitis Functional Index (BASFI) was used to assess functional status [27]. This scale consists of eight specific questions regarding function and two questions reflecting the patient's ability to cope with daily life. Each question is scored on a 10-cm horizontal VAS range from 0 (easy) to 10 (impossible). The mean of the 10 questions was calculated to give the final BASFI score (0–10) that a higher score indicates worse functional status.

Global well-being

The Bath Ankylosing Spondylitis Patient Global Score (BAS-G) reflects the effect of AS on patient's well-being over the last week/6 months. The test-retest reliability of BAS-G was good (1 week $r=0.84$, 6 months $r=0.93$) [28].The scale includes two questions based on a 10-cm horizontal VAS. The mean of the two questions was the final BAS-G score that a higher score indicates that AS had a more serious impact on patients' well-being.

Depression and anxiety

The Hospital Anxiety and Depression Scale (HADS) was used to assess anxiety and depression. This scale was developed by Zigmond and Snaith [29], and the Chinese version [30] has been assessed for its reliability and validity. The HADS is a 4-Likert self-evaluation scale that consists of 14 items: seven to investigate the depression symptoms (HADS-D) and the other seven to investigate the anxiety symptoms (HADS-A). The subscale score ≥ 8 indicates depression symptoms or anxiety symptoms in the participants.

Data analysis

Descriptive statistics analysis was performed by mean ± standard deviation (SD), frequency, and percentage. Spearman's rank correlation, independent sample *t* test, and one-way ANOVA were used to describe the relationship between PSQI and other variables. The differences in terms of variables that were studied in poor and good sleepers were analyzed by independent sample *t* test. Multiple linear regression analysis was used to explore the predictors of sleep disturbances. All statistical analysis was carried out by SPSS 22.0, and a $P < 0.05$ was considered to be statistically significant.

Result

Patients' characteristics

Of the 291 distributed questionnaires, 286 questionnaires were collected back. Five questionnaires with up to 10% missed items were excluded. Finally, 281 outpatients (the available rate was 98.28%) were included in the analysis.

The clinical and demographic characteristics of the patients are listed in Tables 1 and 2. The participants were aged between 14 and 61, with an average age of 31.71 ± 9.80 years, 32% participants were female, and 47.3% participants were unemployed. 39.1% of patients had a college education or above, and 61.2% participants had extra-spinal manifestation, and most of patients were married (170, 60.5%). 32.7% of the patients received anti-TNF, 62.3% received NSAID or DMARD, and 5% of the patients received no medication. The disease duration and duration of diagnostic delay was 7.94 ± 7.36 years and 4.30 ± 5.33 years, respectively. The mean score of nocturnal back pain and total back pain was 3.09 ± 3.10 and 3.19 ± 3.03, respectively. The mean scores of BASDAI, fatigue, BASFI, BAS-G, HADS-D, and HADS-A were 3.40 ± 2.20, 4.37 ± 2.83, 1.79 ± 2.15, 4.30 ± 2.92, 5.67 ± 3.63, and 7.53 ± 3.87, respectively. The prevalence of depression and anxiety was 30.2 and 48.0%, respectively. In addition, PSQI score was 7.48 ± 3.84, with 67.6% of the participants identified as poor sleepers (PSQI score > 5).

The comparison between good and poor sleepers is displayed in Table 3. Poor sleepers were older and had significantly higher level of disease activity, nocturnal pain, total back pain, anxiety, depression, worse functional status and global well-being, longer disease duration, and diagnostic delay ($P < 0.05$).

Associated factors with sleep quality

In *t* test and one-way ANOVA, sleep quality was worse in married, anxious and depressed patients, and those who had extra-spinal manifestations, but no significant association was found between gender, employment status, educational level, HIMPC, smoking status, family history, and sleep quality. The results are displayed in Table 1.

The correlations between PSQI and other variables are displayed in Table 2. According to Spearman's correlation analysis, poor sleep quality was positively related to longer duration of diagnostic delay, higher BASDAI, BASFI and BAS-G scores, high level of pain, and fatigue (all $P < 0.05$).

The results of the multiple linear regression analysis are shown in Table 4. Categorical variables were transformed into dummy variables. Older age ($\beta = 0.087$, $P = 0.102$), higher BAS-G score($\beta = 0.181$, $P = 0.003$), higher level of fatigue ($\beta = 0.170$, $P = 0.002$) and nocturnal back pain ($\beta = 0.192$, $P = 0.001$), longer duration of diagnostic delay ($\beta = 0.174$, $P = 0.001$), anxiety($\beta = 0.151$, $P = 0.002$), and extra-spinal manifestation ($\beta = 0.120$, $P = 0.015$) were found to be significantly associated with sleep disturbances. The $R^2 = 0.418$ indicated about 41.8% variation of sleep disturbances could be explained by these variables.

Discussion

In the present study, the PSQI score was 7.48 ± 3.84, with 67.6% of the AS outpatients were defined as poor sleepers. The prevalence of sleep disturbance in AS patients was much higher than that in the normal population [31]. We observed that sleep quality was associated with age, global well-being, nocturnal pain, anxiety, fatigue, duration of delayed diagnosis, and extra-spinal manifestation.

Increasing age has been shown to be correlated with a significant increase in subjective experience of disturbed sleep [2, 7]. Actually, sleep quality decreases across the lifespan in both patients and normal people [32]. For health providers, an accurate understanding of sleep quality is essential to assess and improve sleep quality in AS patients. It was reported that the decrease in physical activity was one of the causes of decline in sleep quality in older people [33]. For AS patients, regular and effective exercise is an important way to alleviate disease severity. Therefore, it is useful for AS patients to keep regular exercise to slow down the progression of the disease and improve the sleep quality.

Table 1 Demographic characteristics of AS patients and the univariate analysis of sleep quality

Variable	Frequency (%)	PSQI (mean ± SD)	t/*F*	*P*
Gender			$t = -1.114$	0.266
Male	191 (68.0)	7.31 ± 3.76		
Female	90 (32.0)	7.86 ± 3.99		
Age (years)			$F = 5.060$	0.001
14–20	30 (10.7)	5.90 ± 2.90		
20–30	115 (40.9)	6.82 ± 3.16		
30–40	82 (29.2)	7.96 ± 3.92		
40–50	43 (15.3)	8.93 ± 4.60		
> 50	11 (3.9)	9.55 ± 5.73		
Employment status			$t = 1.203$	0.230
Unemployment	133 (47.3)	7.77 ± 3.93		
Employment	148 (52.7)	7.22 ± 3.75		
Educational level			$F = 1.011$	0.388
Primary school	33 (11.7)	8.55 ± 4.50		
Middle school	112 (39.9)	7.25 ± 3.98		
High school	26 (9.3)	7.58 ± 3.40		
College and above	110 (39.1)	7.22 ± 3.55		
Marital status			$t = 3.526$	< 0.001
Single	111 (39.5)	6.50 ± 3.22		
Married	170 (60.5)	8.12 ± 4.08		
HIMPC ($)			$F = 2.273$	0.062
< 77	39 (13.9)	8.00 ± 3.78		
77–153	37 (13.2)	8.73 ± 4.27		
153–306	49 (17.4)	7.84 ± 3.94		
306–459	70 (24.9)	6.63 ± 3.73		
> 459	86 (30.6)	7.21 ± 3.58		
Medication			$F = 1.326$	0.267
Anti-TNF	92 (32.7)	7.16 ± 3.87		
NSAID or DMARD	175 (62.3)	7.74 ± 3.85		
No medication	14 (5.0)	6.36 ± 3.30		
Extra-spinal manifestation			$t = 2.834$	0.005
Yes	172 (61.2)	7.99 ± 3.93		
No	109 (38.8)	6.68 ± 3.56		
Anxiety			$t = -5.341$	< 0.001
Yes	135 (48.0)	8.70 ± 3.92		
No	146 (52.0)	6.36 ± 3.41		
Depression			$t = -4.507$	< 0.001
Yes	85 (30.2)	9.00 ± 3.87		
No	196 (69.8)	6.83 ± 3.64		
Smoking status				
Yes	77 (27.4)	7.14 ± 3.34	$t = -0.994$	0.322
No	204 (72.6)	7.61 ± 4.01		
Family history				
Yes	51 (18.1)	8.12 ± 4.43	$t = -1.162$	0.250
No	230 (81.9)	7.34 ± 3.69		

HIMPC household income monthly per capita, *PSQI* Pittsburgh Sleep Quality Index, *TNF* tumor necrosis factor, *DMARD* disease modifying anti-rheumatic drug, *NSAID* non-steroidal anti-inflammatory drug

Table 2 Correlation between disease-related variables and PSQI

Variable	Mean ± SD	*r*	*P*
Disease duration (years)	7.94 ± 7.36	0.223	< 0.01
Duration of diagnostic delay (years)	4.30 ± 5.33	0.240	< 0.01
BASDAI (0–10 cm VAS)	3.40 ± 2.20	0.452	< 0.01
Fatigue (0–10 cm VAS)	4.37 ± 2.83	0.419	< 0.01
BASFI (0–10 cm VAS)	1.79 ± 2.15	0.433	< 0.01
Nocturnal back pain (0–10 cm VAS)	3.09 ± 3.10	0.456	< 0.01
Total back pain (0–10 cm VAS)	3.19 ± 3.03	0.437	< 0.01
BAS-G (0–10 cm VAS)	4.30 ± 2.92	0.491	< 0.01

BASDAI Bath Ankylosing Spondylitis Disease Activity Index, *BASFI* Bath Ankylosing Spondylitis Functional Index, *VAS* visual analog scale, *BAS-G* Bath Ankylosing Spondylitis Patient Global Score

Previous studies [14, 17, 34] have reported that pain is one important factor associated with sleep disturbance in AS patients. In the study, nocturnal back pain was an important contributor to sleep disturbance, which was consistent with another study [35]. The reason may be that pain during the pre-sleep period and during the night would lead to difficulty falling asleep, sleep duration decreased, and sleep quality decline. Deodhar et al. [36] reported that relieving the pain occurred at night in AS patients was the most important measure to improve sleep quality. Some methods have been proposed to reduce pain severity and improve sleep quality, such as cognitive-behavioral therapies [37] and pain management [38], and proved to be effectively. Health care providers could take measures to relieve pain, especially the nocturnal back pain, to improve sleep quality in AS patients.

Psychological disorders are the risk factor for sleep quality. In the present study, the prevalence of depression and anxiety in AS outpatients was 30.2 and 48.0%, respectively. And we found patients with anxiety had worse sleep quality than those patients without anxiety, which was consistent with previous study [14, 39]. It was worth mentioning that the average age of patients in the study was 31.71 years. In China, people at this age are the mainstay of the family. The combination of patient role and family mainstay role made them more anxious, which may lead to difficulty in falling asleep. Meanwhile, sleep disturbance could aggravate anxiety [40, 41]. Thus, the AS patients with anxiety need not only psychological treatment, but also the support of family members.

The relationship between extra-spinal manifestations and sleep disturbance has rarely been studied before. With the progression of AS, extra-spinal manifestation such as uveitis, bowel disease, and heart involvement may occur in AS patients [42]. Of the participants in the study, 61.2% had extra-spinal manifestations. And we found that patients with extra-spinal manifestations had poorer sleep quality. Extra-spinal manifestation imposed more burdens on AS patients, which may affect sleep quality. However, it was reported that 59.5% of the patients had low awareness about the nature and complications of the disease [43]. For AS patients, it was not conducive to disease control and sleep quality improvement. Health providers could emphasize the harm of extra-spinal manifestations to AS patients to raise their awareness and take measures to prevent and treat extra-spinal manifestation.

We detected that the longer the duration of diagnostic delay, the worse the sleep quality in AS patients. It has been reported that AS has the longest duration of diagnostic delay among rheumatic diseases [44]. The new and effective therapies, such as anti-TNF therapy, make it possible to reduce destructions of the disease in early stage [45]. Ibn et al. [46] found an increase in structural damage and spinal functional limitation in AS patients with a diagnostic delay over 5 years. Early diagnosis and interventions are especially important for reducing destruction of disease and improving the sleep quality in AS patients. Besides, some studies [44, 46] suggested

Table 3 Comparison between poor and good sleepers

Variables	PSQI ≤ 5 (*n* = 91)	PSQI > 5 (*n* = 190)	*t*	*P*
Age (years)	29.47 ± 9.12	32.78 ± 9.95	− 2.672	0.008
Disease duration (years)	6.30 ± 5.86	8.73 ± 7.87	− 2.904	0.004
Duration of diagnostic delay (years)	2.95 ± 3.54	4.95 ± 5.89	− 3.545	< 0.001
BASDAI (0–10 cm VAS)	2.25 ± 1.96	3.95 ± 2.10	− 6.473	< 0.001
Fatigue (0–10 cm VAS)	3.06 ± 2.64	5.00 ± 2.70	− 5.672	< 0.001
BASFI (0–10 cm VAS)	1.00 ± 1.78	2.17 ± 2.21	− 4.749	< 0.001
Nocturnal back pain (0–10 cm VAS)	1.37 ± 2.21	3.92 ± 3.14	− 7.837	< 0.001
Total back pain (0–10 cm VAS)	1.60 ± 2.34	3.95 ± 3.04	− 7.119	< 0.001
BAS-G (0–10 cm VAS)	2.75 ± 2.67	5.03 ± 2.74	− 6.582	< 0.001
HADS-A	5.60 ± 3.39	8.45 ± 3.75	− 6.113	< 0.001
HADS-D	4.40 ± 3.48	6.28 ± 3.54	− 4.204	< 0.001

PSQI Pittsburgh Sleep Quality Index, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BASFI* Bath Ankylosing Spondylitis Functional Index, *BAS-G* Bath Ankylosing Spondylitis Patient Global Score, *HADS-A* Hospital Anxiety and Depression Scale-Anxiety, *HADS-D* Hospital Anxiety and Depression Scale-Anxiety

Table 4 Multiple linear regression analysis of demographic, disease-related variables and psychological variables in relation to PSQI

Predictor	B	SEE	Standardized coefficients (β)	t	95%CI	P
BAS-G	0.239	0.080	0.181	3.000	0.082, 0.395	0.003
Duration of diagnostic delay	0.126	0.038	0.174	3.291	0.050, 0.201	0.001
Fatigue	0.231	0.076	0.170	3.056	0.082, 0.379	0.002
Nocturnal back pain	0.237	0.070	0.192	3.363	0.098, 0.376	0.001
Extra-spinal manifestation (reference: no)	0.942	0.372	0.120	2.534	0.210, 1.674	0.012
Age	0.334	0.203	0.087	1.642	− 0.066, 0.734	0.102
Anxiety (reference: no)	1.161	0.377	0.151	3.081	0.419, 1.902	0.002
Constant	3.229	0.814		3.968	1.627, 4.831	<0.001
$R^2 = 0.418$, Adjusted $R^2 = 0.403$						

SEE standard errors of estimation, *CI* confidence interval, *BAS-G* Bath Ankylosing Spondylitis Patient Global Score

that it was necessary to establish new and applicable criteria to replace the New York criteria for the classification of AS for early diagnosis.

Fatigue is a common complaint in more than half of the AS patients [2, 26]. In present study, fatigue had a negative effect on the sleep quality of AS patients. Actually, fatigue and sleep disturbance were confirmed to effect each other [4, 21]. Furthermore, we found that BAS-G was also an important predictor of sleep disturbance. Abdulaziez et al. [1] also detected that the higher the BAS-G score, the worse the sleep quality in AS patients. Calin et al. [28] suggested that spinal pain and fatigue had a particular significant contribution to patients' well-being. Fatigue as well as pain may influence the global well-being of AS patients and thereby affect sleep quality. It has been reported that pain is the most associated factor with fatigue [47]. Therefore, the strategy for alleviating fatigue and improve patients' global well-being should focus on pain management and inflammation treatment.

The relationships between disease activity, functional status, depression, and sleep disturbance were detected in previous studies [19, 20, 22]. We also found the relationships in univariate analysis, but found no relationship in multivariate analysis. However, these disease markers are also important in clinical practice; thus, further studies could be conducted to explore the relationship between disease activity, functional status, depression, and sleep quality in AS patients in Southwest China.

Limitation

The study had some limitations. Firstly, the study was a cross-sectional survey. Prospective studies are needed in order to fully reveal the relationship between the global well-being, anxiety, pain, fatigue, duration of diagnostic delay, extra-spinal manifestation, and sleep quality. Secondly, we did not recruit a healthy control group of similar age and sex distribution. Thirdly, due to the limited time and financial support, some laboratory parameters that may have an impact on sleep quality, such as ESR and CRP, were not included in the study.

Conclusions

In summary, sleep disturbance is common in AS patients in Southwest China. The factors related to sleep disturbance included age, nocturnal back pain, fatigue, anxiety, duration of diagnostic delay, extra-spinal manifestation, and global well-being. The findings suggest that health care providers should pay more attention to the sleep problems in AS patients, and intervention should be taken. It may be useful to keep regular exercise, strengthen the management of pain, relieve anxiety, and prevent and treat extra-spinal manifestation.

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Compliance with ethical standards

Disclosures None.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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