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Original Article

Anxiety and depression among patients with axial spondyloarthritis

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Abstract

Objective: The axial spondyloarthritis (axSpA) mainly affects young population and often leads to reduced mobility, but less is known about the impact it has on mental health. The objective of this study was to determine the prevalence of symptoms of anxiety and depression among axSpA patients and explore the underlying associated factors.

Methods: A cross sectional survey-based study was conducted from a single center. A convenient sampling was done to include 100 patients. We included questions about disease activity, sleep, fatigue, quality of life (QoL), and work productivity. All patients were asked to fill the patient health questionnaire-9 (PHQ) for depression and general anxiety disorder-7 (GAD) for anxiety. A multivariate binomial logistic regression analysis was performed to determine associations between PHQ-9 and GAD-7 scores with various socio-demographic factors, disease activity scores, and other variables.

Results: Clinically significant symptoms of anxiety and depression were present in 38% and 36% patients, respectively. Both were significantly associated with younger age at disease onset ($P < .05$), high disease activity, sleep disturbances, fatigue, poor QoL, and high impact on work productivity. Misbeliefs that "doctors hide side-effects of medicines" and "all modern medicine used in treatment of axSpA causes side-effects" were also related to higher anxiety and depression scores. Depression was also found to be associated with female patients.

Conclusion: Anxiety and depression are common in axSpA. They are associated with high disease activity and reduced work productivity. Patients should be regularly screened for these symptoms.

Keywords: Ankylosing spondylitis, anxiety, depression, GAD-7, PHQ-9

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Introduction

Chronic diseases such as axial spondyloarthritis (axSpA) can significantly influence a patient's life that may result in negative effects on their wellbeing and quality of life (QoL).[1] The axSpA can promote inflammation in the entheses, joints, and spine gradually leading to reduced spinal mobility, stiffness, fatigue, and sleep disturbances. These physical manifestations may further result in psychological consequences, including distress, depression, and anxiety.[2]

Apart from clinical implications, depression in ankylosing spondylitis (AS) leads to economic strain by increasing rates of hospitalization and work disability.[3] Furthermore, the disease activity scores used in axSpA such as Bath AS disease activity index (BASDAI) and Bath AS functional index (BASFI) are subjective. The important treatment-related decisions are made based on these patients reported outcomes. Psychological disorders can potentially influence these outcomes. Patients with severe disease have a higher risk of developing anxiety and depression,[2,4] and higher levels of disease activity can be used as an indicator to identify risks of these psychological illness.[5] Therefore, screening for anxiety and depression among axSpA in routine clinical practice is important. This is endorsed by recent European League Against Rheumatism recommendations for patients with chronic inflammatory rheumatic diseases.

Studies from various parts of the world have reported a huge impact of axSpA on a patient's mental health. The Europe and the UK have well established the impact of axSpA on patient's mental health and have identified factors associated with them.[3,4,6] While nonradiographic axSpA may have less incapacity in spinal mobility compared to AS, both are associated with similar burden on physical function, mood disturbance, work effect, and QoL disability.[7] In a Chinese study, major depressive disorder and anxiety disorder were present in 10.6% and 15.6% axSpA patients, respectively.[8] Turkey reported depression in

44% and anxiety in 22.5% of axSpA patients, while 25% of AS patients from Northern Taiwan reported mild to moderate depression.[9,10] There is a lack of such robust data from Indian population.

It has been observed that the psychological impact of AS is more severe than rheumatoid arthritis (RA). AS carries an increased risk of serious mental health issues such as self-harm but no such risk was observed in RA.[11] Prior literature from other countries has reported the various predictors of psychological distress among axSpA patients, including high disease activity, decreased functionality,[6] impaired QoL,[9] poor work productivity,[10] fatigue,[12] and sleep disturbances.[13] However, due to differences in the cultural and social dynamics of India,[14] there is a need to verify whether the same predictive factors are applicable for Indians.

The primary objective of our study was to determine the prevalence of anxiety and depression symptoms in axSpA patients. The secondary objective was to identify the underlying factors associated with it. To the best of our knowledge, this is the first study from India to determine the potential influencers of psychological distress among axSpA patients.

Main Points

- The high prevalence of anxiety and depression highlights the need for regular screening for these symptoms in axSpA patients.
- The associated factors were younger age at disease onset, female gender, high disease activity, sleep disturbances, fatigue, poor QoL, high impact on work productivity, and misbeliefs related to medications.
- Many associated factors are similar to those observed in other parts of the world. Adopting and implementing the interventions done in those regions might help to improve disease outcomes in India as well.
- Patient education about the modern medicine and nonpharmacological interventions such as psychological counseling should be integral part of the management of axSpA.
- There is also a need to set up appropriate employment policies for axSpA patients to reduce their psychological distress.

Methods

Study participants

A cross-sectional study was conducted on axSpA patients attending a private rheumatology center. A convenient sampling method was implemented to include 100 patients. This study was explained to patients by the attending rheumatologist, and a written informed consent was obtained from all participants. This study received ethical approval from the Institutional Ethics Committee of Bharati Vidyapeeth (Deemed to be University) Medical College, Pune, via a letter BVDUMC/IEC/59 dated July 27, 2020. All the participants were adults (age ≥18) and met Assessment of Spondyloarthritis International Society (ASAS) classification criteria for axial SpA. None of the participants had a history of psychiatric illness.

Psychological factors were measured by the following instruments

The patients were asked to complete the generalized anxiety disorder scale (GAD-7)[15] for anxiety. The GAD-7 classifies patients as having mild (5-9), moderate (10-14), and severe anxiety (15-21) symptoms. A cutoff score of ≥10 on GAD-7 has a specificity of 82% and sensitivity of 89% to detect generalized anxiety disorders.[15]

The patient health questionnaire (PHQ-9)[16] was used for depression. It classifies patients as having mild (5-9), moderate (10-14), moderately severe (15-19), and severe (20-27) depression symptoms. A cutoff of ≥10 on PHQ-9 has 88% specificity and sensitivity for identifying major depression.[16]

Due to a high specificity and sensitivity for identifying anxiety and depression, patients with a score ≥10 on GAD-7 and PHQ-9 were defined as having clinically significant symptoms of anxiety and depression, respectively. These scales are based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria for major depression and generalized anxiety disorder. Both scales are validated for use in specialty and general practice.

Demographic and clinical variables

1. Disease activity was recorded using BASDAI and BASFI. Patients having a score of ≥4 were considered to have high disease activity.
2. QoL was assessed using AS quality of life (ASQoL), which is an index containing 18 questions with a dichotomous response (yes = 1, no = 0) having a score range of 0-18. The higher the score, the poor the QoL.
3. Problems associated with sleep pattern were assessed using Jenkin's sleep questionnaire that consists of four items rated on a 6-point scale. A dichotomous scoring system was used, wherein the responses were coded as 1 if any of the sleep disturbances occurred for 15 nights or more during 1 month and 0 if not. The criteria for this cutoff were based on the Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition, Text Revision (DSM-IV-TR). This states that sleep disorders such as difficulty in maintaining or initiating sleep should be present for three or more nights/week for at least a month.
4. Fatigue was measured using functional assessment of chronic illness therapy-fatigue (FACIT-F) scale, which is a 13-item scale and asks respondents to rate fatigue-related questions using a 5-point rating scale. The lower the score, the greater the fatigue. This scale has been validated to identify fatigue in AS[17] and general population.[18]
5. Impact on work productivity was assessed using work productivity and activity impairment questionnaire that has six sets of questions.
6. Various demographics as well as the data related to disease characteristics were collected from patients to determine associations with anxiety and depression. The disease characteristics obtained were age at disease onset, disease duration, delay in diagnosis, delay in reaching a rheumatologist, and initiating treatment. Disease onset refers to the time at which the first symptom of axSpA was experienced. The time between the first symptom onset and correct diagnosis of axSpA is termed as delay in diagnosis, whereas time to reach rheumatologist refers to the interval between symptom onset and first visit to a rheumatologist. Duration of the disease refers to time from symptom onset to when the study was conducted. Data on complementary and alternative medicine (CAM) use, the presence of extra-spinal manifestations (ESMs), and comorbidities were also obtained.

Statistical analysis

Normality of data was checked using Kolmogorov–Smirnov test. For normally and non-normally distributed data, variables were presented as mean with standard deviation and median with interquartile range (IQR), respectively. Normally distributed data were compared using a student's t test and non-normally distributed data via nonparametric test (Mann–Whitney U test). A multivariate binomial logistic regression analysis was performed to determine the associations between GAD-7 anxiety symptoms and PHQ-9 depression symptoms with a priori chosen set of clinical and demographic variables. For BASDAI, scores above 4 were computed as 1

Table 1. Demographic details of patients without anxiety and clinically significant anxiety.

Parameters	No anxiety (n = 62)	Clinically significant anxiety (n = 38)	*P*
Age at disease onset (mean ± SD)	30 ± 12.00	23 ± 5.8	.002*
Median current age (IQR)	33 (27, 47)	29 (25, 33)	.010†
Median disease duration (IQR)	5.0 (1.0, 10.0)	3.0 (0.5, 5.0)	.872†
Median delay in diagnosis (IQR)	1.5 (0.5, 5.0)	3.0 (1.25, 5.0)	.949†
Median delay in reaching rheumatologist (IQR)	2.0 (0.5, 5.0)	4.0 (2.0, 5.0)	.060†

SD, standard deviation; IQR, interquartile range.
**P* value using Student "t" test.
†*P* value using Mann–Whitney U test.

Table 2. Multiple logistic regression analysis of GAD-7 anxiety score and clinical variables.

Parameters	No anxiety (n = 62)	Clinically significant anxiety (n = 38)	*P*
Female, % (n)	27 (17)	39 (15)	.210
Psychological believes, % (n)			
Doctors hide side-effects	19 (12)	42 (16)	.014
AS medicines cause side-effects in all patients	55 (34)	79 (30)	.015
BASDAI (mean ± SD)	2.59 ± 2.04	5.27 ± 2.01	.001
BASFI (mean ± SD)	2.59 ± 2.31	4.49 ± 2.73	.012
Jenki's Sleep Scale Median (IQR)	1.0 (0, 4.0)	18 (14, 22)	.001
FACIT Fatigue Median (IQR)	38.5 (32.0, 44.0)	25.0 (19.5, 32.0)	.001
ASQoL (mean ± SD)	5.25 ± 4.76	12.65 ± 3.48	.001
Impact on work productivity, n = 57 Median (IQR)	10.0 (0, 32.0)	53.42 (19.37, 79.87)	.004
Daily activities affected Median (IQR)	20.0 (0, 47.5)	48.25 (40.5, 71.0)	.001
Extra-spinal manifestations, % (n)	45.16 (28)	44.73 (17)	.92
Concurrent illness, % (n)	35.48 (22)	26.31 (8)	.24
Complementary medicines, % (n)	45.16 (28)	47.36 (15)	.83
Tobacco consumption, % (n)	17.74 (11)	18.42 (6)	.70

SD, standard deviation; IQR, interquartile range; BASDAI, Bath ankylosing spondylitis disease activity index; BASFI, Bath ankylosing spondylitis functional index; ASQoL, ankylosing spondylitis quality of life; FACIT, functional assessment of chronic illness therapy.

and rest as 0; for ASQoL and impact on work productivity, the median scores were taken as cutoff and values above this cutoff were coded as 1 and below as 0. FACIT-F scores higher than 30 were coded 0 and below as 1. The presence of ESM, comorbidities, CAM use, tobacco consumption in any form (chewing/sniffing), misbelief that doctors hide side-effects, and all AS medicines cause side-effects were computed as 1. *P* values <.05 were considered as statistically significant. All statistical tests were performed using SPSS version 20.00 (IBM Corp, Armonk, NY, USA).

Results

Characteristics of study population

Out of 100 patients enrolled in the study, 68% were male. Clinically significant symptoms of anxiety and depression were present in 38% and 36% patients, respectively. About 57% of patients were employed, 18% were housewives, and 17% were full-time students. Eight percent of patients had to terminate employment due to axSpA-related disability. The work disability in these patients was mainly a result of severe disease, which caused physical disability in the form of kyphosis and osteoarthritis of the hip or knee joint. The median age of patients at the time of study was 32.00 years (IQR: 26.0, 36.7). The median disease duration, delay in diagnosis, and delay in reaching to a rheumatologist was 5.00 years (IQR: 2.0, 10.0), 2 years (IQR: 0.5, 5.0), and 3.00 years (IQR: 0.6, 5.0), respectively. Peripheral arthritis was the most common ESM present in 40 patients followed by uveitis (n = 11), psoriasis (n = 3), and inflammatory bowel disease (n = 2). Comorbidities were present in 30 patients with type 2 diabetes mellitus as the commonest (n = 10), followed by hypertension (n = 5), hypothyroidism (n = 5), fibromyalgia (n = 4), anemia (n = 3), osteoarthritis of knee (n = 2), and IHD (n = 1).

Disease status and association with clinically significant anxiety symptoms

Patients having clinically significant anxiety symptoms were younger at the age of disease onset (*P* < .05). Table 1 compares the journey from symptom onset to reaching a rheumatologist among patients with anxiety symptoms and those not having anxiety symptoms. Although there was no statistically significant difference, the delay in diagnosis and delay in reaching a rheumatologist were longer in patients present with anxiety symptoms. In a multivariate binomial regression analysis, strong associations of GAD-7 were found with various factors. These included high disease activity, sleep disturbances, high level of fatigue, poor QoL, misbelief that doctors hide side-effects of medicines, and all allopathy medicines used in the treatment of axSpA cause side-effects (Table 2). There was no association of gender with anxiety. Higher GAD-7 scores were observed in patients whose work productivity and daily activities were greatly affected due to axSpA.

Disease Status and Association with Clinically Significant Depression Symptoms

Similar to anxiety, clinically significant depression symptoms were present in patients with younger age of disease onset (*P* < .05). The delay in diagnosis and delay in reaching

Table 3. Demographic details of patients without depression and clinically significant depression.

Parameters	No depression (n = 64)	Depression (n = 36)	*P*
Age at disease onset (mean ± SD)	30 ± 12	24 ± 7	.004*
Median current age (IQR)	33 (27, 46)	29 (26, 32)	.006†
Median disease duration (IQR)	5.0 (1.75, 10.0)	4.5 (2.0, 6.25)	.398†
Median delay in diagnosis (IQR)	1.5 (0.5, 5)	3.0 (1.75, 5.0)	.091†
Median delay in reaching rheumatologist (IQR)	2.0 (0.5, 5.0)	4.0 (2.0, 5.0)	.158†

SD, standard deviation; IQR, interquartile range.
**P* value using Student's "t" test.
†*P* value using Mann–Whitney U test.

Table 4. Multiple logistic regression analysis of PHQ-9 depression score and clinical variables.

Parameters	No depression (n = 64)	Depression (n = 36)	*P*
Female, % (n)	25 (16)	44.44 (16)	.045
Psychological believes, % (n)			
Doctors hide side-effects	18.03 (12)	35.42 (13)	.105
AS medicines cause side-effects in all patients	60.00 (38)	83.33 (30)	.031
BASDAI (mean ± SD)	3.68 ± 2.32	5.32 ± 2.01	.001
BASFI (mean ± SD)	3.21 ± 3.08	4.42 ± 2.88	.026
Jenki's Sleep Scale Median (IQR)	1.0 (0, 4.0)	7.0 (5.0, 11.0)	.001
FACIT Fatigue Median (IQR)	38.5 (33.0, 44.0)	25.0 (20.5, 27.0)	.001
ASQoL (mean ± SD)	5.56 ± 5.04	12.52 ± 3.38	.001
Impact on work productivity Median (IQR)	10.0 (0.0, 32.5)	40.37 (20.0, 70.0)	.003
Daily activities affected Median (IQR)	20.0 (0.0, 50.0)	60.0 (40.0, 80.0)	.179
Extra-spinal manifestations, % (n)	20.31 (13)	13.88 (5)	.70
Concurrent illness, % (n)	31.12 (20)	27.77 (10)	.97
Complementary medicines, % (n)	27.77 (18)	34.37 (12)	.35
Tobacco consumption, % (n)	46.87 (30)	44.44 (16)	.81

SD, standard deviation; IQR, interquartile range; BASDAI, Bath ankylosing spondylitis disease activity index; BASFI, Bath ankylosing spondylitis functional index; ASQoL, ankylosing spondylitis quality of life; FACIT, functional assessment of chronic illness therapy.

rheumatologist were also more in patients with depression (Table 3). Table 4 represents the multivariate regression analysis examining associations between various variables and PHQ-9 depression symptoms. Higher levels of depression were strongly associated with female gender, high disease activity, sleep disturbances, fatigue, and poor QoL. Up to 40% impact on work productivity was associated with clinically significant depression symptoms. Depression was significantly common among patients who had a misbelief that all medicines used in the treatment of axSpA cause side-effects.

The presence of ESMs, tobacco consumption, and use of CAM were not associated with either depression or anxiety.

Discussion

The present study identified that more than one-third of axSpA patients experience anxiety and depressive symptoms. The associated factors include younger age at disease onset, female gender, high disease activity, poor QoL, and high impact on work productivity.

There is a wide variation in the reported prevalence of anxiety and depression in different regions of the world.[7,19,20] According to the data from the 2016 Atlas survey, 45.6% of patients with axSpA are at a risk of developing mental disorder.[5] In the study of Baysal et al[19] among 243 patients with AS, 39.8% had a high risk for depression and 19.5% for anxiety symptoms, whereas Hakkou et al[20] found depression in 55.5% and anxiety in 60% among AS patients, higher than that observed in the present study.

We have explored the relationship between age and psychological distress. There are studies that did not find significant association between the two.[2,21] However, similar to a German study of 1,736 patients, we found a strong association between higher depression scores and young age.[6] Anxiety was also observed among younger population in our study. This might indicate that with increasing age, patients learn to cope with the disease better.[6] Depression was also associated with female gender. This may be due to comparatively poorer QoL in females than males due to the inflammatory disease.[22] Even in our study, the AsQoL scores indicated poor QoL among women compared to men. BASDAI and BASFI include patients' perceptions of morning stiffness, pain, and fatigue. This reporting can get influenced by patient's depressive symptoms and anxiety.[23] Similar to various studies, a strong association between high disease activity and psychological distress was observed in our study as well.[6,21] The severity of the disease affects the individual's QoL[1] and increases the risk of depression and anxiety.[19] The results of the present study also indicate that the psychological distress is strongly linked to QoL of the patients. Effective disease management, exercise, physiotherapy, and rehabilitation programs have proven not only to mitigate the disease activity but also to maintain and increase spinal function and physical activities.[24,25] These programs should be implemented to decrease the intensity of the disease. This would likewise reduce the psychological distress as systemic inflammation and proinflammatory cytokines are also associated with depression.[26] There is also a strong association between sleep disturbances and anxiety/depression. Due to stiffness and restricted

spinal movements, sleep is often disturbed in patients with axSpA. Patients experience difficulty in getting and maintaining sleep further resulting in poor quality of sleep.[27] Poor quality of sleep is a predictor of depression and anxiety.[13] Poor sleep in patients with high disease activity leads to fatigue.[27,28] Higher fatigue level has been reported in patients with clinically significant anxiety and depression.

In our study, the majority of patients (76%) had a sedentary office job. Sitting for long in a static position in AS patients can adversely affect the ability to concentrate, thereby affecting work productivity.[29] Restrictions or disability in physical functioning may make one incompetent to work. Withdrawal from work due to axSpA was seen in eight patients in our study. Patients exhibiting poor functional outcome at work, and their consequent socioeconomic status might influence the prevalence of depression.[29] Difficulties in everyday life due to limited motoric activity make self-functioning difficult and affect negatively the emotional state of patients as well as their QoL. The presence of anxiety and depression also has a negative impact on patient's self-esteem, which is associated with further impairment of daily activities.[30] Patients with worse affected work productivity and daily activities had higher PHQ-9 and GAD-7 scores. Depression and anxiety can then further influence daily life and work productivity, thereby creating a vicious cycle negatively impacting QoL and wellbeing.

Patients often have several misconceptions about the modern medicine. Significant associations between various misbeliefs for modern medicines and higher anxiety, and depression scores were observed in the present study. These misconceptions are important to address because they might not only cause psychological distress but also influence a patient's decision about adhering to the prescribed medicines.

The strengths of our study include the use of a well-defined axSpA cohort with detailed baseline data on important confounders as well as data on disease activity. Our survey tool included disease-specific questions, which helped to collect a reasonably homogenous data. Additionally, we used validated measures of anxiety and depression. The PHQ-9 and GAD-7 have been validated in local languages like Marathi and Hindi. We also acknowledge that there are various limitations of our study. The small sample size, the use of convenient sampling, and the absence of a control group do impose some limitation to our data interpretation. Being a cross sectional observational study, it is limited to a specific time interval. Though GAD-7 and PHQ-9 questionnaires are validated to assess anxiety and depression, these are self-reported screening tools. The final scores do not indicate confirmed diagnoses of anxiety and depression. Another important limitation of our study is recall bias with respect to symptom onset and duration of disease as our data relied on available patient records and memory. Furthermore, the information on work absenteeism was recorded as reported by the patient. Ideally, this would be verified from the employer, in order for quantification. We have mainly focused on identifying disease-related factors. However, psychiatric disorders have multifactorial origin. The contextual factors, such as education, employment, and coping skills, level of education, and income can also contribute to the development of anxiety and depression. The link between inflammation and depression is complex. Unfortunately, we did not have data on inflammatory markers (C-reactive protein or erythrocyte sedimentation rate) for all patients to explore the relationship between inflammation and depression. Further longitudinal studies are required to explore the impact of anxiety and depression on treatment outcomes and axSpA treatment on symptoms of anxiety and depression.

Ethics Committee Approval: Ethics committee approval was received for this study from the Institutional Ethics Committee of Bharati Vidyapeeth (Deemed to be University) Medical College (Approval Date: July 27, 2020; Approval Number: BVDUMC/IEC/59).

Informed Consent: Written Informed consent was obtained from the the patients who participated in this study.

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