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The Effect of Neuropathic Pain on Sleep Quality in Patients with Axial Spondyloarthritis

Esma Demirhan[1]*, Sevgi Atar[1], Nur Ferhatlar[1], Ömer Kuru[1]

1 Prof. Dr. Cemil Taşçıoğlu City Hospital Physical Medicine and Rehabilitation Clinic, İstanbul, TR

*** Corresponding Author:** Esma Demirhan **E-mail:** esmademirhan@gmail.com

ABSTRACT

Objective: This study aims to determine whether neuropathic pain (NP) presence affects sleep quality in patients with axial spondyloarthritis (AxSpA).

Materials and Methods: Demographic data of the patients were documented. The patient's NP was evaluated with painDETECT questionnaire. Pittsburgh Sleep Quality Index (PSQI), Ankylosing Spondylitis Quality of Life (AsQoL), Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP), and visual analog scale (VAS) were used to evaluate sleep quality, quality of life (QoL), pain severity and disease activity, respectively.

Results: Among the 108 patients who participated in the researh, 51 were female and 57 were male. NP was found in 41.7% of them. 65.7% Of all patients had a sleep disorder. AxSpA patients with NP had a statistically significant higher VAS-activity, VAS-night, and VAS-rest scores ($p<0.001$, $p<0.001$, $p=0.002$, respectively). They also had higher ASQoL scores and higher disease activity. ($p=0.008$, $p=0.012$, respectively).

Although impaired sleep was detected in 71.1% of AxSpA patients with NP, it was present in 61.9% of AxSpA patients without NP, and we didn't find a statistically significant difference ($p=0.32$). Total painDETECT scores were correlated with PSQI ASQoL, and VAS scores ($p< 0.001$). But there was no correlation with ASDAS-CRP scores ($p=0.57$).

Conclusion: A large majority of AxSpA patients have a sleep problem, independent of the presence of NP. Not only targeting the inflammatory pain but also targeting NP and sleep disorder together in the follow-up of patients with AxSpA will improve QoL.

Keywords: Axial Spondyloarthritis, Neuropathic Pain, Sleep Quality, Visual Analog Scale, Quality of Life

INTRODUCTION

Axial spondyloarthritis (AxSpA) is one of the chronic rheumatic diseases. Inflammatory back pain is characteristic for AxSpA and usually has an insidious onset. At first, it is intermittent over time it turns into a permanent pain. Patients often feel pain in the lower back and buttocks (1,2). Also, some patients have reported persistent pain while in clinical remission. This condition suggests that pain in AxSpA includes neuropathic and nociceptive components in addition to inflammatory components (3–5).

Neuropathic pain (NP) was explained as ‘’pain that arises as a direct consequence of a lesion or diseases affecting the somatosensory system” (6). It consists of abnormal sensations and unpleasant symptoms (throbbing, stinging or burning, shooting pain, allodynia or hyperalgesia, numbness) (6). In the general population, the prevalance of NP was found to be 6.9% to 10% (7). This rate is increased in chronic inflammatory rheumatic diseases, and NP was reported in 26.7% in spa patients (3).

Sleep disorder was observed in AxSpA patients, at ratings varying between 35.4-50 (8,9). Stiffness and pain and in the axial spine impact sleep. Moreover, poor sleep and decreased QoL have frequently encountered problems in patients with NP (10,11).

We sought to analyze the existence of NP in AxSpA patients and the association between NP and sleep quality, quality of life (QoL), and disease activity. According to our knowledge, the current study is the first to examine how NP presence affects sleep quality in AxSpA.

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MATERIAL and METHODs

Study Design and Participants: This cross-sectional study was established between May 2020 and November 2020. Patients with AxSpA who met the ASAS AxSpA criteria were enrolled in the research (12). The local ethics committee (NO: 2020/76) gave its approval to the study protocol. All patients who participated in this study gave written, informed consent in accordance with the principles of the Declaration of Helsinki. Patients under the age of 18 and above the age of 65 were not allowed to participate in the trial. Other exclusion standards included past or present neurological, psychiatric or other chronic inflammatory diseases, acute post-acute infectious diseases, pregnancy or current breastfeeding, malignancy, and substance abuse. Patients who took part in the study underwent an interview and completed the questionnaires in the same session. Age, gender, body mass index (BMI), education level, smoking status, and treatments were among the demographic information. The patients' sleep quality, disease activity, pain severity and QoL at the outpatient admission were questioned. Two groups of patients were formed based on the existence of NP as detected by painDETECT. Accordingly, Group 1 (n = 45) was classified as those with NP (painDETECT score > 13), and Group 2 (n = 63) as without NP. The groups' quality of life, disease activity, sleep quality, and pain intensity were compared.

Materials: PainDETECT: NP symptoms were assessed by the painDETECT questionnaire. It evaluates pain qualities, pain radiation, and course of pain. Score between 0 and 12 are thought to be unlikely NP, the score between 13 and 18 is considered as possible NP, and those between 19 and 38 to be likely NP (13).

Pittsburgh Sleep Quality Index (PSQI): The index distinguishes “poor” sleep from “good” sleep. A “poor” sleeper is one with a total score of 5 or higher (14).

Ankylosing Spondylitis Quality of Life (ASQoL): It evaluates the effect of ankylosing spondylitis (AS) on patient-reported health-related QoL. A high score indicates a decreased quality of life (15).

Ankylosing Spondylitis Disease Activity Score (ASDAS): Both the subjective and objective components of disease activity are assessed by the ASDAS. It includes acute-phase reactants and patient-reported metrics (16).

Visual Analog Scale (VAS): Patients rate their level of discomfort on a scale from 0 (no pain) to 10 (the most intense pain possible) (17).

Statistical Analysis: The Statistical Package for the Social Sciences, version 25.0, for Windows (SPSS Inc; Chicago, IL, USA) was used for statistical analysis. The data were reported as mean ± standard deviation for continuous variables, and for categorical variables, as number (n) and percentage (%). The normal distribution was analyzed using the Shapiro-Wilk and Kolmogorov-Smirnov tests, however the data were not normally distributed. For intergroup analysis, Mann-Whitney U tests were used. Comparing qualitative data was done using the chi-square test. According to the data distribution, Spearman correlation analysis was used to assess the correlation between the variables. Statistical significance was defined as p 0.05.

RESULTS

A total of 108 patients—51 female and 57 male—were evaluated. **Table 1** displays the clinical data of individuals with AxSpA. In 41.7% of the patients, NP was found (23,1% had possible NP components, and 18.5% had likely NP components). 65.7% of the patients had a sleep issue. The VAS activity, VAS night, and VAS rest, scores were all statistically significantly higher in AxSpA patients with NP (p<0.001, p<0.001 and p=0.002, respectively). They also had higher ASQoL scores and higher disease activity. (p=0.008, p=0.012, respectively)

Table 1. Patient characteristics

		n (%) // median (min-max) / mean±sd
Gender	female	51 (47.2%)
	male	57 (52.8%)
Age		40 (23-65) / 41.6±10
BMI		26.3 (18-39) / 26.8±4.6
Smoking status	smoker	52 (48.1%)
	nonsmoker	56 (51.9%)
Education	primary	71 (65.7%)
	secondary	25 (23.1%)
	university	12 (11.1%)
Disease duration		48 (4-384) / 74.10±72.7
	<10years	81 (75%)
	>10years	27 (25%)
B-DMARD	none	5 (4.6%)
	adalimumab	39 (36.1%)
	etanercept	22 (20.4%)
	golimumab	14 (13%)
	sekukinumab	17 (15.7%)
	sertolizumab	11 (10.2%)
ASDAScrp		3.1 (0.4-6.0) / 3.1±1.1
	<2.1	37 (34.3%)
	>2.1	88 (81.5%)
PainDETECT		11 (0-35) / 11.4±7.8
Neuropathic pain	None (<13)	63 (58.3%)
	Likely (13-18)	25 (23.1%)
	Probable (>18)	20 (18.5%)
PSQI		6 (0-20) / 7.1±4.3
Sleep disorder	Present(PSQI≥5	71 (65.7%)
	Not present PSQI<5	37 (34.3%)
VASr		6 (0-10) / 5.5±2.7
VASa		5 (0-10) / 5.3±2.8
VASn		5 (0-10) / 5.5±2.8

BMI: body mass index; B-DMARD: biological disease-modifying antirheumatic drugs; ASDAS-crp: Ankylosing Spondylitis Disease Activity Score-crp; PSQI: the Pittsburgh Sleep Quality Index; VAS: visual analog scale (r:rest, a: activity, n: night)

The comparison of AxSpA patients according to NP presence is shown in **Table 2**. Although impaired sleep was detected in 71.1% of AxSpA+ NP patients, it was present in 61.9% of AxSpA patients without NP, which wasn’t statistically significant (p=0.32). Total painDETECT scores correlated moderately with ASQoL scores (r = 0.360, p< 0.001), VAS rest scores (r = 0.313, p<0.001), VAS activity (r = 0.437, p < 0.001), VAS night scores (r = 0.355, p<0.001) and PSQI scores (r=0.283, p<0.001). There was no correlation between painDETECT scores and ASDAS-CRP scores (r=0.183, p=0.57) (**Table 3**).

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Table 2: Comparison of groups according to neuropathic pain presence. (a) median (minimum–maximum), (b) number (percentage)

		NP (+) 45 (41.7%)	NP (-) 63 (58.3%)	p
Age[a]		42.0 (23-65)	40.0 (26-58)	0.345
Gender	Male[b]	25 (55.6%)	32 (50.8%)	0.625
	Female[b]	20 (44.4%)	31 (49.2%)	0.625
BMI [a]		26.6 (19-39)	26.2 (18-39)	0.876
Disease duration[a]		60 (6-360)	42 (4-384)	0.171
	<10years[b]	32 (77.8%)	49 (71.1%)	0.430
	>10years[b]	13 (22.2%)	14 (28.9%)	0.430
Smoking	Present[b]	22 (48.9%)	30 (47.6%)	0.896
	Not present[b]	23 (51.1%)	33 (52.4%)	0.896
ASDAScrp[a]		3.2 (1.3-6.0)	2.8 (0.4-5.0)	**0.012**
ASQOL[a]		7.0 (0-12)	5.0 (0-12)	**0.008**
VASr[a]		7.0 (0-10)	5.0 (0-10)	**0.002**
VASa[a]		8.0 (0-10)	4.0 (0-10)	**<0.001**
VASn[a]		8.0 (0-10)	6.0 (0-10)	**<0.001**
PSQI [a]		7.0 (0-20)	6.0 (0-19)	0.177
Sleep disorder	Present[b] PSQI≥5	32 (71.1%)	39 (61.9%)	0.320
	Not present[b] PSQI<5	13 (28.9%)	24 (38.1%)	

NP: neuropathic pain; BMI: body mass index; ASDAS-crp: Ankylosing Spondylitis Disease Activity Score-crp; ASQoL: Ankylosing Spondylitis Quality of Life; VAS: visual analog scale (r:rest, a: activity, n: night) PSQI: the Pittsburgh Sleep Quality Index

Table 3: Correlation between outcome parameters

		ASQOL	ASDAS crp	PSQI	PAINDETECT
yaş	rho	0,068	-0,036	,222*	0,012
	p	0,486	0,709	0,021	0,901
BMI	rho	-0,077	-0,040	0,017	-0,002
	p	0,425	0,678	0,861	0,982
disease duration	rho	0,037	0,105	0,096	0,057
	p	0,701	0,278	0,320	0,555
ASQOL	rho	1,000	,381**	,483**	,360**
	p		0,000	0,000	0,000
ASDAScrp	rho	,381**	1,000	0,120	0,183
	p	0,000		0,216	0,057
PSQI	rho	,483**	0,120	1,000	,283**
	p	0,000	0,216		0,003
PinDETECT	rho	,360**	0,183	,283**	1,000
	p	0,000	0,057	0,003	
VASr	rho	,404**	,642**	0,156	,313**
	p	0,000	0,000	0,108	0,001
VASa	rho	,447**	,595**	,275**	,437**
	p	0,000	0,000	0,004	0,000
VASn	rho	,413**	,562**	,302**	,355**
	p	0,000	0,000	0,001	0,000

BMI: body mass index; ASDAS-crp: Ankylosing Spondylitis Disease Activity Score-crp; ASQoL: Ankylosing Spondylitis Quality of Life; VAS: visual analog scale (r:rest, a: activity, n: night) PSQI: the Pittsburgh Sleep Quality Index;

DISCUSSION

Chronic inflammatory back pain with nociceptive and neuropathic components is characteristic for AxSpA. We evaluated AxSpA patients with and without NP according to the PainDETECT scale regarding disease duration, pain intensity, QoL, and sleep disorder. In 108 AxSpA patients, 41.7% had NP, which was associated with significantly worse pain, more active disease, and poor QoL than those without NP. However PSQI scores, did not differ between the NP and non-NP groups.

Wu et al was the first who demonstrated NP in patients with AS using neuroimaging studies in addition to the painDETECT score (4). In previous studies that used painDETECT scores, NP rates were found to be 25%-37.9% in AxSpA patients (18–20). Compared to these results, our study showed a higher NP rate of 41.7%. We found that among AxSpA patients 23.1% had possible, 18.5% had likely NP components. Similar to our results Rifberg et al. found 21% of SpA patients had possible NP, and 24% had likely NP (21).

In inflammatory rheumatic disorders such as rheumatoid arthritis, ankylosing spondylitis (AS), osteoarthritis and others, it has been demonstrated that NP's existence is related to poor QoL (22). In addition to low QoL, patients with AxSpA who had NP also had high disease activity and high VAS scores (18,19,21). It was found that as PainDETECT scores increased, VAS scores also increased. VAS scores of patients with NP were twice as severe as patients without NP (23). And also higher BASDAI scores were obtained in patients with NP (20,21). In our study, pain intensity and disease activity were increased, and QoL was significantly impaired with NP presence.

Sleep disturbance has been reported in a range of 58-90% in AxSpA patients (24,25). We found 65.7% of the AxSpA patients had a sleep disorder. Poor sleep was associated with depression, anxiety, active disease, higher pain levels, and nocturnal pain within AxSpA patients (9,26–28). Pain impairs sleep quality independently of the others (8). There is a bidirectional association between pain and poor sleep (30). Chronic pain is thought to impair sleep quality while poor sleep quality worsens the pain (29). Poor sleepers have been shown to have more back pain during the night (26). We also found that poor sleep correlated with nocturnal pain and activity pain but no correlation with disease activity. Pain caused by inflammation and sleep disturbance in AS are related to each other, affecting the patient's functional status, disease activity and QoL (30).

Sleep disorders and decreased QoL have frequently encountered problems in patients with NP (7). NP alone causes poor sleep, and either NP or poor sleep significantly reduces the patient's QoL (31). In a study among the patients with NP 80% of them had poor sleep quality, while the rate was found to be 37% in healthy controls (10). In our study, 71.1% of AxSpA patients with NP had a poor sleep, while 61.9% of AxSpA without NP had a poor sleep. Despite the NP group having higher PSQI values, there was no statistically significant difference between the groups.

Previous studies found poor sleep quality and high disease activity to be positively correlated. (8,26,32). In contrast to these findings we found that poor sleep was not associated with disease activity. Sleep disturbance, mood, and generalized pain all had independent negative effects on QoL of patients with AxSpA in addition to high disease activity (33). Additionally, we observed that poor QoL was associated with worse sleep, severe pain, and high disease activity.

Study Limitations:

The current study has several limitations. First, other possible relationships between NP and sleep quality or QoL could not be established because of the cross-sectional design. Second, our results were based on patients' self-reported data. Also we could assess anxiety/depression with a disease specific questionnaire since these impact QoL and sleep quality negatively.

CONCLUSION

AxSpA Patients with NP had considerably worse QoL, more active disease, and more severe pain than those without NP. And also, a large majority of AxSpA patients have a sleep problem, independent of the presence of NP. Sleep disturbance and the presence of NP independently impair QoL.

In cases where the pain cannot be controlled despite the suppression of inflammation in patients with AxSpA, the presence of a neuropathic component should also be considered. Not only targeting the inflammatory pain but also targeting NP and sleep disorder together in the follow-up of patients with AxSpA will lead to an improvement in QoL.

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REFERENCES

1. Taurog JD, Chhabra A, Colbert RA. Ankylosing Spondylitis and Axial Spondyloarthritis. N Engl J Med. 2016 Jun 30;374(26):2563–74.

2. Sieper J, Poddubnyy D. Axial spondyloarthritis. The Lancet. 2017 Jul 1;390(10089):73–84.

3. Mathieu S, Couderc M, Pereira B, Dubost J-J, Malochet-Guinamand S, Tournadre A, et al. Prevalence of migraine and neuropathic pain in rheumatic diseases. J Clin Med. 2020;9(6):1890.

4. Wu Q, Inman RD, Davis KD. Neuropathic pain in ankylosing spondylitis: a psychophysics and brain imaging study. Arthritis Rheum. 2013;65(6):1494–503.

5. Bidad K, Gracey E, Hemington KS, Mapplebeck JCS, Davis KD, Inman RD. Pain in ankylosing spondylitis: a neuro-immune collaboration. Nat Rev Rheumatol. 2017 Jul;13(7):410–20.

6. Treede R-D, Jensen T, Campbell J, Cruccu G, Dostrovsky J, Griffin J, et al. Neuropathic pain: redefinition and a grading system for clinical and research purposes. Neurology. 2008;70(18):1630–5.

7. Van Hecke O, Austin SK, Khan RA, Smith BH, Torrance N. Neuropathic pain in the general population: A systematic review of epidemiological studies. Pain. 2014;155(4):654–62.

8. Batmaz I, Sarıyıldız MA, Dilek B, Bez Y, Karakoç M, Çevik R. Sleep quality and associated factors in ankylosing spondylitis: relationship with disease parameters, psychological status and quality of life. Rheumatol Int. 2013;33(4):1039–45.

9. Li Y, Zhang S, Zhu J, Du X, Huang F. Sleep disturbances are associated with increased pain, disease activity, depression, and anxiety in ankylosing spondylitis: a case-control study. Arthritis Res Ther. 2012;14(5):1–10.

10. Melikoglu MA, Celik A. Does neuropathic pain affect the quality of sleep? Eurasian J Med. 2017;49(1):40.

11. Smith BH, Hébert HL, Veluchamy A. Neuropathic pain in the community: prevalence, impact, and risk factors. Pain. 2020;161:S127–37.

12. Sieper J, van der Heijde D, Landewe R, Brandt J, Burgos-Vagas R, Collantes-Estevez E, et al. New criteria for inflammatory back pain in patients with chronic back pain: a real patient exercise by experts from the Assessment of SpondyloArthritis international Society (ASAS). Ann Rheum Dis. 2009;68(6):784–8.

13. Freynhagen R, Baron R, Gockel U, Tölle TR. Pain DETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. Curr Med Res Opin. 2006;22(10):1911–20.

14. Buysse DJ, Reynolds III CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28(2):193–213.

15. Doward L, Spoorenberg A, Cook S, Whalley D, Helliwell P, Kay L, et al. Development of the ASQoL: a quality of life instrument specific to ankylosing spondylitis. Ann Rheum Dis. 2003;62(1):20–6.

16. Van der Heijde D, Lie E, Kvien TK, Sieper J, Van den Bosch F, Listing J, et al. ASDAS, a highly discriminatory ASAS-endorsed disease activity score in patients with ankylosing spondylitis. Ann Rheum Dis. 2009;68(12):1811–8.

17. Scott J, Huskisson E. Graphic representation of pain. pain. 1976;2(2):175–84.

18. Külcü DG, Batibay S, Öztürk G, Mesci N. The association of neuropathic pain and disease activity, functional level, and quality of life in patients with ankylosing spondylitis: a cross-sectional study. Turk J Med Sci. 2018;48(2):257–65.

19. Gok K, Cengiz G, Erol K, Ozgocmen S. Neuropathic Pain Component in Axial Spondyloarthritis and the Influence on Disease Burden. JCR J Clin Rheumatol. 2018 Sep;24(6):324–7.

20. Zhou L, Li T, Wu X, Lu H, Lin L, Ye L, et al. Assessment of Neuropathic Pain in Ankylosing Spondylitis: Prevalence and Characteristics. Pain Ther. 2021;10(2):1467–79.

21. Rifbjerg-Madsen S, Christensen AW, Christensen R, Hetland ML, Bliddal H, Kristensen LE, et al. Pain and pain mechanisms in patients with inflammatory arthritis: A Danish nationwide cross-sectional DANBIO registry survey. PLOS ONE. 2017 Jul 7;12(7):e0180014.

22. Garip Y, Filiz E, KILIÇARSLAN A, Bodur H. Prevalence of neuropathic pain in rheumatic disorders: association with disease activity, functional status and quality of life. Arch Rheumatol. 2015;30(3):231–7.

23. Freynhagen R, Tölle TR, Gockel U, Baron R. The painDETECT project – far more than a screening tool on neuropathic pain. Curr Med Res Opin. 2016 Jun 2;32(6):1033–57.

24. Aydin E, Bayraktar K, Turan Y, Omurlu I, Tastaban E, Sendur OF. Sleep quality in patients with ankylosing spondylitis. Rev Bras Reumatol. 2015;55:340–5.

25. Abdulaziez O, Asaad T. Sleep problems in ankylosing spondylitis: polysomnographic pattern and disease related variables. Egypt Rheumatol. 2012;34(2):59–65.

26. Wadeley A, Clarke E, Leverment S, Sengupta R. Sleep in ankylosing spondylitis and non-radiographic axial spondyloarthritis: associations with disease activity, gender and mood. Clin Rheumatol. 2018;37(4):1045–52.

27. Deodhar A, Gensler LS, Magrey M, Walsh JA, Winseck A, Grant D, et al. Assessing physical activity and sleep in axial spondyloarthritis: measuring the gap. Rheumatol Ther. 2019;6(4):487–501.

28. Leverment S, Clarke E, Wadeley A, Sengupta R. Prevalence and factors associated with disturbed sleep in patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis: a systematic review. Rheumatol Int. 2017;37(2):257–71.

29. Haack M, Simpson N, Sethna N, Kaur S, Mullington J. Sleep deficiency and chronic pain: potential underlying mechanisms and clinical implications. Neuropsychopharmacology. 2020;45(1):205–16.

30. van Middendorp H, Evers AW. The role of psychological factors in inflammatory rheumatic diseases: From burden to tailored treatment. Best Pract Res Clin Rheumatol. 2016;30(5):932–45.

31. Galer BS, Gianas A, Jensen MP. Painful diabetic polyneuropathy: epidemiology, pain description, and quality of life. Diabetes Res Clin Pract. 2000;47(2):123–8.

32. Tymms K, Butcher BE, Sletten TL, Smith T, O'Sullivan C, Littlejohn G, et al. Prevalence of sleep disturbance and the association between poor disease control in people with ankylosing spondylitis within the Australian clinical setting (ASLEEP study): a real-world observational study using the OPAL dataset. Clin Rheumatol. 2021;1–10.

33. Macfarlane GJ, Rotariu O, Jones GT, Pathan E, Dean LE. Determining factors related to poor quality of life in patients with axial spondyloarthritis: results from the British Society for Rheumatology Biologics Register (BSRBR-AS). Ann Rheum Dis. 2020;79(2):202–8.