Araştırma Makalesi / *Research Article*

İzmir Eğitim ve Araştırma Hastanesi Tıp Dergisi (Medical Journal of İzmir Hospital) 26 (4): 425-433, 2022

DOES SLEEP QUALITY ASSOCIATE WITH COGNITIVE FUNCTIONS AND CLINICAL PARAMETERS IN ANKYLOSING SPONDYLITIS?

ANKİLOZAN SPONDİLİTTE UYKU KALİTESİ KOGNİTİF FONKSİYONLAR VE KLİNİK PARAMETRELERLE İLİŞKİLİ MİDİR?

Mahmut EREN[1] Seniz AKCAY[2] Taciser KAYA[2]
Altinay GOKSEL KARATEPE[2] Bugra INCE[2]

[1]Edremit State Hospital Physical Medicine and Rehabilitation Department, Balıkesir, Turkey
[2]University of Health Sciences Izmir Bozyaka Training and Research Hospital Physical Medicine and Rehabilitation Department, Izmir, Turkey

Keywords: Spondylitis, Ankylosing, sleep, cognition, pain
Anahtar Sözcükler: Spondilit, ankilozan, uyku, kognisyon, ağrı

Yazının alınma tarihi: 14.03.2022 Yazının kabul tarihi: 17.04.2022 Online basım: 04.10.2022

SUMMARY

Introduction: *Sleep disturbance is prevalent in rheumatic diseases. However, some studies have reported cognitive impairment in rheumatic diseases, and the cognitive impairment associated factors in Ankylosing Spondylitis (AS) patients have not been studied yet. We aimed to explore the prevalence of sleep disturbance and investigate the association between sleep quality, cognitive functions, and disease-specific parameters in AS patients.*

Material and Methods: *Seventy AS participants enrolled in the study. Participants were divided into two groups by using the Pittsburgh sleep quality index (PSQI) as good and poor quality sleepers. Pain severity was assessed with visual analogue scale, disease activity with Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), mobility with Bath Ankylosing Spondylitis Metrology Index (BASMI), and functionality with Bath Ankylosing Spondylitis Functional Index (BASFI). Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) were used for assessing depressive symptoms and anxiety severity. Montreal Cognitive Assessment Test was used to assess cognitive functions. Correlation analysis was performed between sleep quality, cognitive functions, and clinical parameters.*

Results: *Morning stiffness duration, C-reactive protein (CRP) level were higher, disease activity, mobility, and functionality index were worse in poor sleepers. All of the participants with poor sleep quality had cognitive impairment. Cognitive function was significantly correlated with education, morning stiffness duration, CRP, VAS, BASDAI, BASFI, BASMI, PSQI, BAI, and BDI.*

Conclusion: *Cognitive impairment is frequent in AS patients with sleep disturbance. There are significant correlations between sleep quality, clinical parameters, and cognitive functions. The relationship between cognitive functions and disease activity changes in the AS patient population needs to be evaluated in prospective studies.*

ÖZ

Giriş: *Romatizmal hastalıklarda uyku bozuklukları sıktır. Bazı çalışmalarda romatizmal hastalıklarda kognitif bozulma bildirilmiş olmasına rağmen Ankilozan Spondilit (AS) hastalarında kognitif bozulma ile ilişkili faktörler henüz çalışılmamıştır. Bu araştırmada, AS hastalarında uyku bozukluğu prevalansını ve uyku kalitesi, kognitif fonksiyonlar ve hastalığa özgü parametreler arasındaki ilişkiyi değerlendirmeyi amaçladık.*

Gereç ve Yöntem: *Araştırmaya yetmiş AS katılımcı dahil edildi. Katılımcılar Pittsburgh Uyku Kalite İndeksine (PUKİ) göre iyi ve kötü uyku kalitesi olanlar şeklinde ikiye ayrıldı. Ağrı şiddeti görsel analog skala (VAS) ile; hastalık aktivitesi Bath Ankilozan Spondilit Hastalık Aktivite İndeksi (BASDAI) ile; mobilte, Bath Ankilozan Spondilit Metroloji İndeksi (BASMI) ile; fonksiyonellik Bath Ankilozan Spondilit Fonksiyonel İndeksi (BASFI) ile değerlendirildi. Depresif semptom şiddeti ve anksiyete düzeyi ise Beck Depresyon (BDÖ) ve Beck Anksiyete Ölçeği (BAÖ) ile değerlendirildi. Kognitif fonksiyonları değerlendirmek için Montreal Bilişsel Değerlendirme Ölçeği kullanıldı. Uyku kalitesi, kognitif fonksiyonlar ve klinik parametreler arasında korelasyon analizi gerçekleştirildi.*

Bulgular: *Kötü uyku kalitesi olanlarda sabah tutukluğu süresi, C-reaktif protein (CRP) düzeyi daha yüksek, hastalık aktivitesi, mobilite ve fonksiyonellik indeksi daha kötüydü. Uyku kalitesi kötü olanların tamamında kognitif yetersizlik vardı. Kognitif fonksiyonlar, eğitim, sabah tutukluğu süresi, CRP, VAS, BASDAI, BASFI, BASMI, PUKİ, BAÖ, BDÖ ile anlamlı ilişkiliydi.*

Sonuç: *Uyku bozukluğu olan AS hastalarında kognitif bozukluk sık görülür. Uyku kalitesi, klinik parametreler ve kognitif fonksiyonlar arasında anlamlı ilişki vardır. AS hasta popülasyonunda, hastalık aktivitesi değişiklikleri ile kognitif fonksiyonlar arasındaki ilişkinin prospektif araştırmalarla değerlendirilmesi gerekmektedir.*

INTRODUCTION

Ankylosing spondylitis (AS) is one of the progressive rheumatological diseases that is manifested with inflammatory back pain, functional impairment, and a decrease in quality of life. The prevalence of sleep problems can reach up to 80% in rheumatological diseases, due to the nature of inflammatory pain and reduced mobility overnight (1-4). Among AS treatment choices, sleep quality has become one of the outcome measurement parameters of both exercise and pharmacological treatments (5,6).

Sleep quality has been associated with neuropsychiatric conditions and its relationship with cognitive functions and disease-related clinical parameters in inflammatory rheumatological diseases are limited (7,8). The relationship between sleep quality, disease activity, and cognitive functions in inflammatory rheumatic diseases is scarce. Although there is an increasing number of studies that reported the burden of cognitive impairment in rheumatic diseases, the cognitive impairment in AS patients are contradictory (9,10). Neurodegenerative effects of systemic inflammation on the central nerve system, medications, cardiovascular risk, and chronic pain are indicated among the causes of cognitive impairment in chronic inflammatory rheumatic diseases (11-14). Investigating cognitive impairment in these patients by documenting the disease-related factors affecting cognitive functions would have provided more than an estimation of the causes.

The purpose of this study was to explore the prevalence of sleep disturbance and cognitive impairment in a cohort of individuals with AS and to identify the specific factors that are associated with cognitive impairment. The sleep quality was not included in the studies investigating cognitive dysfunction and dementia risk in chronic inflammatory rheumatic diseases (9-11). Although there have been studies evaluating the relationship between sleep disturbance and disease activity; cognitive functions in rheumatic diseases; no study has assessed the association between sleep disturbance and cognitive functions in AS population yet (15-17).

In this study, we hypothesized that cognitive impairment is frequent in AS patients with sleep disturbance and is related to disease-specific clinical parameters.

MATERIALS AND METHODS

We carried out a cross-sectional, single-center study composed of consecutive patients with AS who were under regular clinical follow-up in the Physical Medicine and Rehabilitation Department. The study was approved by the University of Health Sciences Bozyaka Training and Research Hospital Ethics Committee (Date: 03.05.2017 Decision No:5) The study was conducted according to the Declaration of Helsinki. Each patient gave written informed consent before enrollment. Seventy patients with AS diagnosis according to Modified New York or ASAS Spondyloarthritis Classification Criteria were used in the study.

The patients aged 18 or older who had been diagnosed with AS were considered eligible for

the study. Patients with severe systemic infections, psychiatric disease, obstructive sleep apnea syndrome, illiterate, mental retardation, and dementia were excluded from the study.

Demographic data, clinical characteristics, treatment modalities, morning stiffness duration time (min), pain intensity (visual analogue scale 0-10 cm (VAS)], disease activity [(Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)], functional impairment level [(Bath Ankylosing Spondylitis Functional Index (BASFI)], axial mobility [Bath Ankylosing Spondylitis Metrology Index (BASMI)], Erythrocyte sedimentation rate (ESR), serum C-reactive protein (CRP) level, Pittsburgh sleep index score (PSQI), Montreal Cognitive Assessment score (MoCA), Beck Depression Scale (BDI), Beck Anxiety Scale (BAI) scores were recorded.

Bath Ankylosing Spondylitis Functionality Index (BASFI)

BASFI was used to determine daily functional status. It includes 10 questions; 8 for measuring activities related to daily life (bending, reaching, changing position, standing, turning, and climbing steps) and 2 for coping ability for everyday life. It was measured on a scale of 0 (easy) to 10 (impossible), and higher scores indicate worse function (18). The validity and reliability of the Turkish version have been previously demonstrated (19).

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

Disease activity was assessed by BASDAI, which consists of six questions related to 5 main symptoms in the last week (weakness/fatigue, spinal pain intensity, joint pain intensity/swelling, localized sensitive body areas sensitive to touch, morning stiffness). The questions were answered on a VAS, between labels ‘none’ and ‘very severe’ for the first five items and ‘0 hour’ and ‘2 or more hours for the duration of morning stiffness. The mean score of the two items for morning stiffness is considered one variable. The final score is then divided by 5 to give the final BASDAI score (20). The validity and reliability of the Turkish version have been demonstrated (21).

Bath Ankylosing Spondylitis Disease Metrology Index (BASMI)

Axial skeletal mobility was assessed by BASMI, which consists of the cervical rotation angle, tragus wall distance, lumbar flexion (Modified Schober test), lumbar lateral flexion, and measurement of intermalleolar space. Each measure was scored between 0-2 (with a total score of 0-10). Higher scores indicate greater impaired mobility (22).

Pittsburgh sleep quality index (PSQI)

Sleep quality during the last month was assessed by the Pittsburgh Sleep Quality Index (PSQI). PSQI is a self-reported assessment questionnaire that consists of 19 items including seven components of sleep quality: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. Each question is scored between 0-3 with a total score of 0-21. The PSQI global score distinguishes ‘good sleepers’ (PSQI total score ≤5) from ‘poor sleepers’ (PSQI>5). In this study, we used the threshold values mentioned above to categorize good and bad sleepers (23). The validity and reliability of the Turkish version have been demonstrated (24).

Beck Depression Inventory (BDI)

Beck Depression Inventory (BDI), a 21-item self-administered measure, was used to rate depressive symptomatology. Each item was scored between 0 and 3 points. A higher BDI score indicates that depressive symptom severity is higher (25). The validity and reliability of the Turkish version have been demonstrated (26).

Beck Anxiety Inventory (BAI)

Beck Anxiety Inventory (BAI), a 21-item self-administered measure, was used to assess the anxiety of the patients. Each item was scored between 0 and 3 points. A higher BAI score indicates more severe anxiety (27). The validity and reliability of the Turkish version have been demonstrated (28).

Montreal Cognitive Assessment Test (MoCA)

The MoCA scale has been used to distinguish healthy individuals from individuals with mild

cognitive impairment assesses attention and concentration, executive functions, memory, language, visual-spatial skills, abstract thinking, computing, and orientation. The total score is calculated out of 30 points. A score of 25 and below is considered to be cognitive dysfunction (29). The validity and reliability of the Turkish version have been demonstrated (30).

Serum C-reactive protein (CRP) was measured by the immunoturbidimetric method (mg/dL) and erythrocyte sedimentation rate (ESR) was measured through the Westergren method (mm/h).

Statistical Analysis

The statistical analysis of data was performed by using SPSS version 20.0 for the Windows package program (SPSS Inc., Chicago, IL, USA).

The Kolmogorov–Smirnov test was used to determine whether data were within the ranges of normal distribution. Comparisons of numerical variables between sleep quality groups were evaluated by t-test or Mann Whitney U test accordingly. The difference in categorical variables between groups was investigated using the chi-square test. The associations of PSQI and MoCA, with the variables age, gender, education level, study, duration of diagnosis, laboratory parameters, BDI, BASMI, and BASDAI, were analyzed using the Spearman correlation test. Statistical significance was based on a value of $p<0.05$

RESULTS

Seventy AS patients (18 female, 52 male) enrolled in the study. The age of participants was between 27 and 65 years (min-max). The frequency of the patients with poor sleep quality was 44.25%. The mean disease duration was 10.9 ±8.2 years (minimum 0.1; maximum 36 years).

Comparison of demographic characteristics, and clinical parameters with sleep quality

There was no significant difference between good sleepers and poor sleepers regarding socio-demographic features, disease duration, medication, ESR level. The poor sleepers had higher serum CRP level, longer morning stiffness duration, and higher BASDAI, BASMI, BASFI, VAS, BDI, BAI than the good sleepers ($p=0.016$, $p<0.001$, $p<0.001$, $p=0.012$, $p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, respectively). The number of smokers was significantly higher in the poor sleepers group than in good sleepers ($p=0.04$). The MoCA score was significantly lower in the poor sleepers group than in good sleepers ($p<0.001$). The demographic and clinical characteristics of the patients are detailed in Table 1.

All of the participants in the poor sleepers group were cognitively impaired (Table 2).

Correlation analysis between sleep quality, clinical parameters, and cognitive functions

The correlation analysis results between sleep quality, MoCA, and clinical characteristics are detailed in Table 3.

According to Spearman correlation analysis, neither sleep quality, nor cognitive function was correlated with age, gender, disease duration, and ESR).

Poor sleep quality was significantly positively correlated with serum CRP ($p=0.017$, $r=0.283$) and clinical parameters (pain intensity, BASDAI, BASFI, BASMI scores), ($p<0.001$, $r= 0.812$; $p<0.001$, $r=0.824$; $p<0.001$, $r=0.617$; $p=0.003$, $r=0.354$, respectively). Poor sleep quality was found to be significantly positively correlated with depressive symptom and anxiety severity ($p<0.001$, $r= 0.690$; $p<0.001$, $r=0.741$, respectively).

A significant positive correlation was found between MoCA score and employment ($p=0.027$). There were significant negative correlation between MoCA score and morning stiffness duration, serum CRP level, pain intensity, BASDAI, BASMI, BASFI, depressive symptom and anxiety severity ($p<0.001$, $r=-0.441$; $p<0.001$,$r=-0.307$; $p<0.001$, $r=-0.706$; $p<0.001$, $r=-0.725$, $p<0.001$, $r=-0.297$; $p<0.001$, $r=-0.547$; $p<0.001$, $r=-0.633$; $p<0.001$, $r=-0.605$, respectively). MoCA score was found to be significantly negatively correlated with PSQI score ($p<0.001$, $r=-0.846$). When BDI and BAI were controlled with partial correlation analysis PSQI score was still in correlation with MoCA score ($p < 0.001$, $r= -0,622^{**}$).

Table 1. Demographic, clinical parameters, and intergroup comparison of patients with normal and poor sleep quality.

	Participants (n=70)	Poorsleepers (n=31)	Goodsleepers (n=39)	p
Age, year (mean±SD)	43.3±9.8	41 ± 9.3	44.9 ± 10,	0.956¶
Gender, Female (n, %)	18 (25.71%)	8 (25.8%)	10 (25.6)	0.60†
BMI, kg/m^2 (mean±SD)	26.5 ±4.3	26.4 ± 5	26.7 ±3.2	0.630¶
Smoking status	34 (48.57%)	19 (61.2%)	15 (38.4%)	0.04*†
Education (year) (mean±SD)	9,3 ± 4,6	8.7 ± 3.7	9.7 ± 5.2	0.821¶
Employement (n,%)	31 (44.28%)	21 (67.7%)	30 (76.9)	0.27†
Disease duration, year (mean±SD)	10.9 ±8.2	10.5 ± 9.2	11.2 ± 7.5	0.308¶
Morning stiffness, min (mean±SD)	30.5 ±43.5	53 ± 55.1	12.3 ± 16.5	< 0.001¶*
NSAID	54 (77.14%)	26 (83.9%)	28 (71.8)	0.18†
DMARDs	9(12.85%)	4 (12.9)	5 (12.8)	0.63†
Anti TNFα	47 (67.14)	19 (61.2%)	28 (71.8)	0.25†
CRP (mg/L) (mean±SD)	10.7 ±17.8	14 ± 21.2	7.9 ± 14,	0.016¶*
ESR (mm/saat) (mean±SD))	24.1 ± 20	25 ± 21.8	23 ± 18.7	1.000¶
VAS (mean±SD)	3.7±2.7	6.1±1.9	1.8±1.4	<0.001¶*
BASDAI (mean±SD)	3.3 ±2.3	5.2 ± 1.7	1.8 ± 1.3	< 0.001¶*
BASFI (mean±SD)	3.1 ±2.4	4.6 ± 2,	1.9 ± 1.9	< 0.001¶*
BASMI (mean±SD)	2.4 ±2.1	3.3 ± 2.5	1.6 ± 1.4	0.012¶*
BDI (mean±SD)	12.7 ±9.2	19.4 ± 8.1	7.4 ± 6.3	< 0.001¶*
BAI (mean±SD)	13.7 ± 11	22.3 ± 10.1	6.8 ± 5.5	< 0.001*
MoCA	22.2 ±3.2	19.5 ± 1.5	24.4 ± 2.3	< 0.001¶*

Numeric variables are presented as mean (±SD), categorical variables are presented as n (%).

†: Chi-square test

¶: Mann-Whitney U test

Abbreviations: SD: Standart deviation; BMI: Body Mass Index; CRP: c-reactive protein; ESR: Erythrocyte sedimentation rate; VAS: Visual analog scale; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; MoCA: Montreal Cognitive Assessment Test; DMARD: Disease-Modifying Anti-RheumaticDrugs; Anti-TNF: Anti-Tumor necrosis factor medication

Table 2. The frequency of cognitive dysfunction in Ankylosing Spondylitis patients with poor and good sleepers.

		MOCA≤ 25	MOCA > 25
PSQI	Poor sleepers	n = 31 (100%)	n = 0
	Good sleepers	n = 23 (58.97%)	n = 16 (41.02%)

Abbreviations: PSQI: Pittsburgh Sleep Quality Index; MOCA: Montreal CognitiveAssessment Test

Table 3. Relationship of sleep quality, clinical parameters, and cognitive functions with sociodemographic and clinical parameters in patients with ankylosing spondylitis.

	PSQI		MOCA	
	r	p	r	p
Age	- 0.121	0.319	0.066	0.586
Gender	-	0.987 ‡	-	0.209 §
Education	- 0.076	0.534	0.348**	0.003
Employment	-	0.391‡	-	0.027§
Disease duration	- 0.099	0.413	0.136	0.261
Morning stiffness	0.674**	<0.001	-0.441**	<0.001
CRP	0.283*	0.017	- 0.307**	0.010
ESH	0.148	0.223	- 0.177	0.144
VAS	0.812**	<0.001	-0.706**	<0.001
BASDAI	0.824**	< 0.001	- 0.725**	<0.001
BASMI	0.354**	0.003	-0.297*	0.012
BASFI	0.617	<0.001	-0.547**	<0.001
BDI	0.690**	< 0.001	- 0.633**	< 0.001
BAI	0.741**	< 0.001	- 0.605**	< 0.001
PSQI	-	-	-0.846**	-<0.001
MoCA	-0.846**	<0.001	-	-

Abbreviations: BMI: Body Mass Index; CRP: c-reactive protein; ESR: Erythrocyte sedimentation rate; VAS: Visual analog scale; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; PSQI: Pittsburgh Sleep Quality Index; MoCA: Montreal Cognitive Assessment Test

§: Fisher exact test;‡: Chi-square test

DISCUSSION

In this study, nearly half of the patients with AS had poor sleep quality. All of the patients with poor sleep quality were with cognitive impairment however the frequency of normal and impaired cognitive functions in those with good sleep quality were close to each other. The study results indicated that sleep quality and cognitive functions were associated with disease activity, mobility, functionality, serum CRP level, and psychiatric symptom severity.

Sleep disturbance is a prevalent problem in AS patients. According to our data, the prevalence of sleep quality disorders in AS patients, which we found to be 44.28% that is ranged from 35.4% to 67.6% in different studies (1,15–17,31).

The study results indicated that neither sleep quality, nor cognitive functions were associated with, age and disease duration. The results were similar to previous studies that had reported that age and disease duration were similar among good and poor sleepers (31,32). We didn't find an association between age and gender either for sleep quality or cognitive functions. The studies reported conflicting results about the association between sleep disturbance and gender (1,31,32). It is acceptable that the results of studies examining the general population may differ from the results of data in specific diseases. It supports that disease-specific parameters may override the predictable parameters that generally determine sleep quality and cognitive functions.

Depression and anxiety are known to be associated with sleep disturbances (15,31,32). Sleep characteristics may contribute to cognitive decline (33). In the relevant study, we used the severity of depressive symptoms and anxiety, however, their relationship with sleep quality and cognitive functions is predictable, we purposed to examine the relationship between sleep quality and cognitive functions even when we suppressed depression and anxiety and found a significant correlation between sleep quality and cognitive function even when psychiatric symptom severity were suppressed.

The high disease activity in poor sleepers and the strong relationship between sleep quality and disease activity may point out that the impaired sleep quality is an indicator of high disease activity or inadequate treatment in AS patients. Consistent with previous reports, we also found that the poor sleepers group had higher pain intensity and disease activity scores, prolonged morning stiffness, worse functionality, and axial mobility scores than good sleepers (1,15–17,32).

Poor sleep quality is associated with high serum CRP levels, but not ESR. Serum CRP level and sleep quality are related and may negatively affect sleep quality indirectly due to its relationship with the pain threshold (31,34). The studies that had investigated sleep quality and inflammation markers in patients with AS reported conflicting results (1,15,16,31,32,35). The conflicting results among studies may be related to the controversial validity of these markers in determining disease activity in AS (35,36).

Recent studies had focused on the cognitive functions in inflammatory rheumatic diseases have suggested the definition of 'rheumatic dementia' in inflammatory rheumatic diseases. Before the diagnosis of 'rheumatic dementia', it is important to investigate the relationship between disease-specific parameters and cognitive functions, clearly (11). It has been suggested that inflammatory mediators increase the permeability of the blood-brain barrier and cause central nervous system inflammation and vascular dementia (37). Systemic Lupus Erythematosus, RA, AS, and psoriatic arthritis (PsA) are diseases for which there are little data on cognitive impairment. Cognitive impairment was found to be prevalent in patients with PsA

(11). A previous study including RA patients reported that there was no significant difference between good and poor sleepers in terms of cognitive functions, but also a significant correlation between sleep quality and cognitive functions (38). Cognitive impairment was found to be frequent in RA patient cohort. Nevertheless, AS patients did not significantly increase the risk of dementia, but the study included National Health Insurance International Classification of Diseases records of dementia (10). It would be better, to investigate dementia in AS patients in a longitudinal cohort study. Our results showed that patients with higher disease activity were of greater alteration in sleep quality and worse

cognitive functions. Screening patients with sensitive tests such as MoCA is a means to identify the patients who may require more specific neuropsychological testing for the diagnosis of dementia.

Sleep duration, fragmentation, and sleep-disordered breathing are important factors for the development of cognitive impairment. People with sleep disturbance are at risk of cognitive decline (39). Prospective studies are required in patients with sleep disturbance and cognitive functions. All the patients with poor sleepers are classified as impaired cognitive functions considering that there is a strong relationship between sleep quality and cognitive functions and that the improvement in sleep quality may alleviate cognitive functions. When sleep quality and cognitive dysfunction are evaluated together, it is seen that cognitive impairment is evident in patients with high pain severity and disease activity level. Markers such as functional limitation and mobility are strongly associated with cognitive impairment. Demographic factors, habits (smoking), and disease-specific characteristics may influence sleep quality in AS patients, and exposure to cognitive decline should not be ignored in these patients. Due to the cross-sectional nature of our study, we cannot comment on the effect of changes in disease activity on sleep quality and cognitive functions during follow-up. However, in our opinion, the obtained findings may lead to the importance of a holistic approach beyond disease-specific parameters and to further follow-up studies.

The main limitation of this study is the cross-sectional design and assessment of sleep quality by subjective measurement parameters. Prospectively designed studies are required to prove the relationship between functional and cognitive change over time. The study didn't include a healthy control group, as the main aim of the study was to compare the effect of the parameters on cognitive functions among AS patients with and without sleep disturbances. Although MoCA is a sensitive test to detect mild cognitive impairment, more extensive neuropsychiatric batteries could be used. Participants were obtained from AS patients who were followed up in the same tertiary health center. Neurologic history, cognitive assessment tests, and disease-specific parameters were evaluated by the same examiner. It proves that before evaluating cognitive impairment in chronic rheumatic diseases, sleep quality, as well as disease-related parameters associated with cognitive impairment, must be included in the variables.

CONCLUSION

Our study provides evidence that cognitive impairment is more prevalent in patients with sleep disturbance in AS patients than the good sleepers. Both sleep quality and cognitive functions are associated with pain intensity, inflammation, functionality, mobility, and disease activity. To explain the impact on cognitive functions such as chronic systemic inflammation and pain in systemic rheumatic diseases, parameters belonging to or not belonging to the disease should be evaluated together. Sleep quality and disease-specific activity parameters are important parameters associated with cognitive functions in AS patients.

REFERENCES

1. Nie A, Wang C, Song Y, Xie X, Yang H, Chen H. Prevalence and factors associated with disturbed sleep in outpatients with ankylosing spondylitis. Clin Rheumatol 2018;37(8):2161–8.
2. Hakkou J, Rostom S, Mengat M, Aissaoui N, Bahiri R, Hajjaj-Hassouni N. Sleep disturbance in Moroccan patients with ankylosing spondylitis: Prevalence and relationships with disease-specific variables, psychological status and quality of life. Rheumatol Int 2013;33(2):285–90.
3. Hultgren S, Broman JE, Gudbjörnsson B, Hetta J, Lindqvist U. Sleep disturbances in outpatients with ankylosing spondylitis - A questionnaire study with gender implications. Scand J Rheumatol 2000;29(6):365–9.
4. LeBlanc M, Beaulieu-Bonneau S, Mérette C, Savard J, Ivers H, Morin CM. Psychological and health-related quality of life factors associated with insomnia in a population-based sample. J Psychosom Res 2007;63(2):157–66.
5. Mease P, Walsh JA, Baraliakos X, Inman R, de Vlam K, Wei JC-C, et al. Translating Improvements with Ixekizumab in Clinical Trial Outcomes into Clinical Practice: ASAS40, Pain, Fatigue, and Sleep in Ankylosing Spondylitis. Rheumatol Ther 2019;6(3):435–50.

6. Coksevim NH, Durmus D, Kuru O. Effects of global postural reeducation exercise and anti-TNF treatments on disease activity, function, fatigue, mobility, sleep quality and depression in patients with active Ankylosing spondylitis: A prospective follow-up study. J Back Musculoskelet Rehabil 2018;31(6):1005–12.

7. Jansson-Fröjmark M, Lindblom K. A bidirectional relationship between anxiety and depression, and insomnia? A prospective study in the general population. J Psychosom Res 2008;64(4):443–9.

8. Thomas ML, Sing HC, Belenky G, Holcomb HH, Mayberg HS, Dannals RF, et al. Neural basis of alertness and cognitive performance impairments during sleepiness II. Effects of 48 and 72 h of sleep deprivation on waking human regional brain activity. Thalamus Relat Syst 2003;2(3):199–229.

9. Vitturi BK, Nascimento BAC, Alves BR, de Campos FSC, Torigoe DY. Cognitive impairment in patients with rheumatoid arthritis. J Clin Neurosci 2019;69:81–7.

10. Chen KT, Chen YC, Fan YH, Lin WX, Lin WC, Wang YH, et al. Rheumatic diseases are associated with a higher risk of dementia: A nation-wide, population-based, case-control study. Int J Rheum Dis 2018;21(2):373–80.

11. Garcia LOKL, Júnior ATS, Gómez DC dos S, Yoshikawa GSS, Kamikoga CK, Vitturi BK. Cognitive impairment in patients with psoriatic arthritis. Acta Neurol Belg 2021;(0123456789):3–8.

12. Gisondi P, Sala F, Alessandrini F, Avesani V, Zoccatelli G, Beltramello A, et al. Mild cognitive impairment in patients with moderate to severe chronic plaque psoriasis. Dermatology 2014;228(1):78–85.

13. Ernste FC, Sánchez-Menéndez M, Wilton KM, Crowson CS, Matteson EL, Maradit Kremers H. Cardiovascular risk profile at the onset of psoriatic arthritis: a population-based cohort study. Arthritis Care Res (Hoboken) 2015;67(7):1015–21.

14. Glass CK, Saijo K, Winner B, Marchetto MC, Gage FH. Mechanisms underlying inflammation in neurodegeneration. Cell 2010;140(6):918–34.

15. Batmaz I, Sariyildiz 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.

16. Aydin E, Bayraktar K, Turan Y, Omurlu I, Tastaban E, Sendur OF. Qualidade do sono em pacientes com espondilite anquilosante. Rev Bras Reumatol 2015;55(4):340–5.

17. Karatas G, Bal A, Yuceege M, Firat H, Gurcay E, Ardic S, et al. Evaluation of sleep quality in patients with ankylosing spondylitis and efficacy of anti-TNF-α therapy on sleep problems: A polisomnographic study. Int J Rheum Dis 2018;21(6):1263–9.

18. Calin A, Garret S, Whitelock K, Kennedy L, O'Hea J, Mallorie P, et al. A new approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Spondylitis Functional Index. J Rheumatol 1994;21(12):2281–5.

19. Karatepe AG, Akkoc Y, Akar S, Kirazli Y, Akkoc N. The Turkish versions of the Bath Ankylosing Spondylitis and Dougados Functional Indices: reliability and validity. Rheumatol Int 2005;25(8):612–8.

20. Garrett S, Jenkinson T, Kennedy L, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol 1994;21(12):2286–91.

21. Akkoc Y, Karatepe AG, Akar S, Kirazli Y, Akkoc N. A Turkish version of the Bath Ankylosing Spondylitis Disease Activity Index: Reliability and validity. Rheumatol Int 2005;25(4):280–4.

22. Jenkinson TR, Mallorie PA, Whitelock HC, Kennedy LG, Garrett SL, Calin A. Defining spinal mobility in ankylosing spondylitis (AS). The Bath AS Metrology Index. J Rheumatol 1994;21(12):1694–8.

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

24. Agargün M, Kara H AO. Pittsburgh Uyku Kalitesi İndeksi'nin Geçerliği ve Güvenirliği. Turk Psikiyatr Derg 1996;7(2):107–11.

25. Beck AT, Steer RA. Internal consistencies of the original and revised Beck Depression Inventory. J Clin Psychol 1984;40(6):1365–7.

26. Hisli N. Beck depresyon envanterinin üniversite öğrencileri için geçerliği, güvenirliği. Psikol Derg. 1989;7(3):3–13.

27. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol 1988;56(6):893–7.

28. Ulusoy M, Şahin NH, Erkmen H. Turkish Version of the Beck Anxiety Inventory: Psychometric Properties. J Cogn Psychother 1998;12(2):163–72.

29. Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc 2005;53(4):695–9.

30. Selekler K, Cangöz B, Uluç S. Montreal Bilişsel Değerlendirme Ölçeği (MOBİD)'nin hafif bilişsel bozukluk ve Alzheimer hastalarını ayırt edebilme gücünün incelenmesi. Turk J Geriatr 2010;13(3):166–71.

31. 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):R.215.

32. 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.

33. Hu C-P, Zhao Y-H, Zhao X-D, Zhu B-G, Qin H-Y. Correlation between sleep characteristics and cognitive decline in the elderly people: A cross-sectional study in China. Int J Clin Pract 2021;75(7):e14225.

34. Okun ML, Coussons-Read M, Hall M. Disturbed sleep is associated with increased C-reactive protein in young women. Brain Behav Immun 2009;23(3):351–4.

35. 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.

36. Ruof J, Stucki G. Validity aspects of erythrocyte sedimentation rate and C-reactive protein in ankylosing spondylitis: a literature review. J Rheumatol 1999;26(4):966–70.

37. Iadecola C. The pathobiology of vascular dementia. Neuron 2013 Nov;80(4):844–66.

38. Kim SH, Kim H, Kim S, Paek SI, Koh JH, Lee J, et al. Sleep quality independently affects health-related quality of life and cognitive function in Korean female patients with rheumatoid arthritis: A case-control study. J Korean Med Sci 2018;33(35):1–10.

39. Wennberg AM V, Wu MN, Rosenberg PB, Spira AP. Sleep Disturbance, Cognitive Decline, and Dementia: A Review. Semin Neurol 2017;37(4):395–406.

Corresponding Author

Şeniz AKCAY (Assoc. Prof.)
University of Health Sciences Izmir Bozyaka
Training and Research Hospital Physical Medicine and
Rehabilitation Department, Izmir, Turkey
Phone: +90 232 250 50 50
E-mail: senizakcay@hotmail.com
ORCID: 0000-0003-2267-0702

Mahmut EREN (Specialist, MD) ORCID: 0000-0003-1058-5084
Taciser KAYA (Prof. MD)ORCID: 0000-0002-8848-8420
Altinay GOKSEL KARATEPE (Prof. MD) ORCID: 0000-0001-8086-9942
Bugra INCE (Specialist, MD) ORCID: 0000-0001-7467-4073