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RESEARCH ARTICLE

Exploring the Relationship Between Sleep Quality and Fatigue, Quality of Life, Daytime Sleepiness, and Anxiety-depression Levels in Patients with Multiple Sclerosis

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Abstract

Objective: Multiple sclerosis (MS) is a chronic neurological disorder often linked with fatigue and poor sleep quality, both of which significantly affect quality of life and mental health. This study aimed to explore the relationship between sleep quality and fatigue, quality of life, daytime sleepiness, and anxiety-depression in patients with MS (pwMS).

Materials and Methods: A cross-sectional study was conducted with 52 pwMS (16 with poor sleep quality, 36 without), recruited from a neurology clinic. Sleep quality was assessed using the Pittsburgh sleep quality index (PSQI), fatigue with the modified fatigue impact scale (MFIS), daytime sleepiness with the Epworth sleepiness scale (ESS), anxiety and depression using the hospital anxiety and depression scale (HADS), and quality of life with the preference-based multiple sclerosis index (PBMSI). Participants were categorized into two groups based on PSQI scores: Those with poor sleep quality and those without. The groups were compared based on patient-reported outcomes, and correlations between these variables and clinical characteristics (e.g., expanded disability status scale scores, disease duration) were examined.

Results: Participants with poor sleep quality reported higher MFIS scores across the physical, cognitive, and psychosocial domains compared to those without poor sleep quality, though these differences were not statistically significant. Anxiety was significantly higher in the poor sleep quality group ($p=0.043$), and there was a positive correlation between poor sleep quality and increased anxiety ($r=0.336$, $p<0.05$). No significant differences were found in ESS or PBMSI scores between the groups. Additionally, a significant correlation was observed between the number of relapses, and the MFIS-physical, MFIS-cognitive, MFIS-total scores, and the PSQI score.

Conclusion: This study underscores the relationship between sleep quality, fatigue, anxiety, and the number of relapses in pwMS. Improving sleep quality may help reduce fatigue and anxiety, thereby improving overall well-being. The results suggest that these factors should be evaluated and addressed together in managing MS.

Keywords: Fatigue, multiple sclerosis, sleep quality

Introduction

Multiple sclerosis (MS) is a chronic, progressive demyelinating disease that affects more than 2.5 million people globally, typically in young adults aged 20-40, with a higher prevalence in women (1). While the precise incidence in Turkey is unclear, it is estimated to be around 40 per 100,000 individuals. Recent epidemiological studies suggest a rising trend in both prevalence and incidence rates (2).

Sleep disturbances, which encompass a variety of sleep issues, symptoms, and diagnoses, affect more than 50% of patients with MS (pwMS), who report sleep disruptions or poor sleep quality (3). pwMS are more likely to experience conditions such as insomnia, sleep apnea, restless leg syndrome, and narcolepsy compared to the general population (4).

Fatigue and sleep disturbances are frequently reported as co-occurring symptoms in pwMS and can significantly impact

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quality of life (5,6). Fatigue affects up to 90% of pwMS and is characterized by persistent exhaustion, weakness, or tiredness. It is a major cause of unemployment, early retirement, and disability in this group (7). MS-related fatigue is especially difficult to assess and manage due to its multidimensional nature (e.g., physiological, cognitive, and behavioral aspects), its subjective experience, and its overlap with other symptoms and comorbidities, such as sleep disturbances (8).

Depression is commonly associated with MS, with a prevalence rate of up to 50% (9). Depression can present as fatigue, and its symptoms (such as loss of motivation and anhedonia) are often mistaken for MS-related fatigue, making the differential diagnosis more challenging. Research has shown a longitudinal relationship between depression and fatigue (10). Even when depression does not directly contribute to fatigue, addressing and treating it is crucial due to its significant effect on quality of life (11). Additionally, over 60% of pwMS report chronic sleep disturbances, which contribute to daytime sleepiness, worsening both fatigue and depression (12). Studies have also indicated that anxiety levels may be related to sleep quality in pwMS (13).

Considering the negative impact of symptoms like fatigue, anxiety-depression, and daytime sleepiness on functionality, it is important to understand the role of sleep quality as a potential contributing factor. Thus, this study aimed to explore the relationship between sleep quality and factors such as fatigue, quality of life, daytime sleepiness, and anxiety-depression levels in pwMS while identifying contributing factors. Moreover, examining the differences and relationships between sleep quality and clinical characteristics, such as disability level, disease duration, and number of relapses, could provide insights into the sleep disturbances experienced by pwMS.

Materials and Methods

Study Design

This cross-sectional study involved pwMS who voluntarily participated during routine check-ups at MS Clinic of the Neurology Department at Van Yuzuncu Yil University Medical Faculty Hospital. Ethical approval was granted by the Non-Invasive Research Ethics Committee of Van Yuzuncu Yil University Faculty of Health Sciences on October 18, 2024, under approval number 2024/11-26.

Participants

The study by Al-dughmi and Siengsukon (14) examined the relationship between sleep quality and fatigue. The study found a correlation of r^2=0.388 (p=0.005) between the total Pittsburgh sleep quality index (PSQI) score, used to assess sleep quality, and fatigue levels. The effect size of this relationship was calculated to be 0.62. Using G*Power (version 3.1) software, the minimum required sample size was determined to be at least 20 patients, with an effect size of 0.62, a power of 95%, and an error probability of 0.05.

Inclusion criteria were a confirmed MS diagnosis, age between 18 and 65 years, no relapses in the past 3 months, and willingness to participate. Exclusion criteria included severe musculoskeletal, cardiovascular, pulmonary, or metabolic conditions that could prevent participation, other neurological disorders, severe cognitive impairments that might interfere with completing the tests, or the use of sleep-related or sleep-inducing medications.

Outcomes

Demographic Data

Data was gathered on age, gender, weight, height, body mass index, education level, occupation, employment status, marital status, and clinical factors (e.g., MS type, Expanded Disability Status Scale (EDSS) score, time since diagnosis, relapse history, and medications).

EDSS

The EDSS is a widely recognized scale used to evaluate neurological disability in pwMS through clinical evaluations and mobility tests. Scores range from 0 (normal) to 10.0 (death due to MS). Scores from 1.0 to 4.5 reflect full ambulation, while scores between 5.0 and 9.5 indicate various degrees of mobility impairment. Scores above 7.0 suggest the patient is wheelchair or bed-bound. The EDSS assesses functions such as pyramidal, cerebellar, sensory, visual, brainstem, bladder, bowel, and cerebral (15).

PSQI

The PSQI, developed by Buysse et al. (16) and adapted into Turkish by Ağargün et al. (17), is a self-report tool used to evaluate sleep quality over the past month. It includes 19 items across 7 components, each scored from 0 to 3, with a total range of 0-21. A score above 5 indicates poor sleep quality (16,17).

Epworth Sleepiness Scale (ESS)

The ESS evaluates daytime sleepiness with eight questions rated from 0 to 3, evaluating the likelihood of dozing off in various daily situations. A score of 10 or higher indicates excessive daytime sleepiness (18). The Turkish version has been validated (19).

Modified Fatigue Impact Scale (MFIS)

The MFIS, commonly used in clinical research, measures the impact of fatigue on physical, cognitive, and social functioning through 21 questions rated from 0 to 4. Lower scores indicate less fatigue (20). The Turkish version has been validated for use with Turkish pwMS (21).

Hospital Anxiety and Depression Scale (HADS)

The HADS evaluates anxiety and depression in pwMS using 14 items (7 for anxiety and 7 for depression), scored on a 0-3

Likert scale. Higher scores indicate greater severity (22). The Turkish version was validated by Aydemir (23), confirming its appropriateness for pwMS.

Preference-based Multiple Sclerosis Index (PBMSI)

The PBMSI is a patient-reported measure that covers five areas: Walking, fatigue, mood, concentration, and roles. Each item has three response options, scoring between 0 (worst) and 1 (best) (24). The Turkish version was validated by Kahraman et al. (25).

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics (Version 25.0, Armonk, NY, IBM Corp.). The normality of the data distribution was assessed using the Kolmogorov-Smirnov test and histograms. Since continuous variables showed normal distribution, the mean and standard deviation were reported with a 95% confidence interval. For categorical variables, frequency and percentage values were provided. Comparisons of clinical and demographic factors and patient-reported outcomes between the groups (with and without poor sleep quality) were made using an independent samples t-test for continuous data and the chi-squared test for categorical data. The relationship between sleep quality and other variables was evaluated using Pearson correlation coefficients. Correlation values were interpreted as small (≤0.30), moderate (0.31-0.59), or strong (≥0.60). Statistical significance was set at $p<0.05$ (26).

Results

Table 1 displays the demographic and clinical characteristics of pwMS, categorized into two groups based on the presence or absence of poor sleep quality. The group with poor sleep quality (n=16) had a mean age of 32.50±10.12 years, while the group without poor sleep quality (n=36) had a slightly lower mean age of 29.69±8.36 years (p=0.301). In terms of gender, females made up a larger proportion in both groups, with 87.5% in the poor sleep quality group and 63.9% in the group without poor sleep quality. The mean EDSS score was higher in the poor sleep quality group (1.59±1.54) compared to the group without poor sleep quality (1.08±1.23). Disease duration was also slightly longer in the poor sleep quality group (7.13±5.27 years) than in the other group (5.89±4.32 years). Similarly, the number of relapses was higher in the poor sleep quality group (3.94±2.49) compared to the group without poor sleep quality (2.64±1.64). Although some differences in demographic and clinical characteristics were observed between the groups, none of these differences reached statistical significance, indicating similar baseline characteristics in terms of age, gender, EDSS scores, disease duration, and MS type.

Table 2 presents a comparison of patient-reported outcomes between pwMS with poor sleep quality (n=16) and those without (n=36). There was no significant difference in PBMSI scores between the groups, with the mean score being 0.64±0.24 for the poor sleep quality group and 0.70±0.18 for the group without poor sleep quality (F=0.836, p=0.243). In the MFIS domains, participants with poor sleep quality reported higher scores in the physical (15.13±11.36 vs. 10.56±8.50, p=0.114), cognitive (17.69±12.85 vs. 12.75±9.23, p=0.122), and psychosocial (3.19 3.06 vs. 2.06±2.29, p=0.145) subscales compared to those without poor sleep quality. Although these differences suggest higher fatigue in the poor sleep quality group, none were statistically significant. The MFIS-total score also suggested higher overall fatigue in the poor sleep quality group (36.0±26.85) compared to the group without poor sleep quality (25.33±18.06), but this difference was not statistically significant (F=6.789, p=0.098). The ESS score was slightly lower in the poor sleep quality group (3.88±3.84) compared to the non-poor sleep quality group (4.61±4.79), with no significant difference (p=0.591). Regarding psychological outcomes, the HADS results showed that depression scores (HADS-D) were

Table 1. Demographic and clinical characteristics of the participants

	pwMS with poor sleep quality (n=16)	pwMS without poor sleep quality (n=36)	p-value
Age (years)	32.50±10.12	29.69±8.36	0.301
Gender, n (%)			
Female	14 (87.5%)	23 (63.9%)	0.083
Male	2 (12.5%)	13 (36.1%)	
EDSS score (Min.-Max.)	1.59±1.54 (0-5.5)	1.08±1.23 (0-5.0)	0.208
Disease duration of MS (years)	7.13±5.27	5.89±4.32	0.377
Number of relapses	3.94±2.49	2.64±1.64	0.070
MS type, n (%)			
RRMS	15 (93.8%)	35 (97.2%)	0.548
PPMS	1 (6.2%)	1 (2.8%)	

EDSS: Expanded disability status scale, MS: Multiple sclerosis, RRMS: Relapsing-remitting MS, PPMS: Primary progressive MS, pwMS: Patients with multiple sclerosis, Min.-Max.: Minimum-maximum

higher in the poor sleep quality group (8.0±4.87) than in the non-poor sleep quality group (6.22±4.15), but the difference was not significant (p=0.183). However, anxiety scores (HADS-A) were significantly higher in the poor sleep quality group (9.13±5.24) compared to the non-poor sleep quality group (6.25±4.29), with a statistically significant difference (p=0.043).

While several measures, particularly related to fatigue and depression, indicated higher symptom burdens in pwMS with poor sleep quality, only the HADS-A showed a statistically significant difference between the groups.

Table 3 shows the correlation coefficients between sleep quality, patient-reported outcomes, and clinical characteristics in pwMS. Notably, HADS-A was positively correlated with the PSQI (r=0.336, p<0.05), indicating that poorer sleep quality is linked to higher anxiety. Additionally, the number of relapses showed a moderate correlation with the PSQI score (r=343, p<0.05). A small correlation was found between the MFIS-physical, MFIS-cognitive, and MFIS-total scores with the PSQI score (p<0.05).

Discussion

This study examined the relationship between sleep quality, fatigue, quality of life, daytime sleepiness, and anxiety-depression levels in pwMS. The results indicated a connection between sleep quality and fatigue (physical, cognitive, and total MFIS scores), the number of relapses, and anxiety levels in pwMS. A significant difference was observed between the groups in terms of anxiety levels.

Although both groups (with and without poor sleep quality) shared similar demographic and clinical characteristics, those with poor sleep quality reported higher levels of fatigue in the physical, cognitive, and psychosocial domains. While the differences in MFIS scores were not statistically significant, the trend suggests that poor sleep quality may worsen fatigue in pwMS. This finding is consistent with previous studies that show poor sleep quality can exacerbate fatigue, likely due to disrupted restorative sleep processes (27,28).

A key finding of this study was the higher anxiety levels in pwMS with poor sleep quality, as measured by the HADS-A. The correlation between poor sleep quality and increased anxiety (r=0.336, p<0.05) highlights the bidirectional relationship between sleep and mental health. Anxiety may contribute to poor sleep quality by increasing arousal, while poor sleep may worsen anxiety symptoms (29). AlSaeed et al. (30) explored factors that could reduce anxiety levels and identified MS relapse, physical inactivity, and fatigue as influential factors in anxiety. In our study, we found that anxiety, fatigue, and the number of relapses were related to sleep quality. Based on these results, we hypothesize that these factors interact in a cyclical manner. While depression scores were higher in the poor sleep quality group, the difference was not statistically significant, suggesting that the relationship between depression and poor sleep quality in MS may be more complex or influenced by other factors.

Interestingly, no significant differences in daytime sleepiness (ESS scores) or quality of life (PBMSI scores) were found between the groups. This suggests that the effects of poor sleep quality may be more evident in terms of fatigue and psychological distress rather than noticeable daytime sleepiness. However, the positive correlation between ESS scores and MFIS subscales, despite not reaching statistical significance, indicates that individuals with higher daytime sleepiness tend to report more fatigue.

These findings emphasize the need for comprehensive management strategies in MS care. Addressing poor sleep quality could help reduce fatigue and anxiety, potentially improving overall quality of life. Clinicians should consider regularly screening for sleep issues and conducting mental health assessments as part of MS management, especially for patients with high fatigue or anxiety levels. Interventions aimed at improving sleep quality, such as cognitive-behavioral therapy for insomnia or relaxation techniques, may provide beneficial outcomes.

Table 2. Comparison of patient-reported outcomes between the groups

	pwMS with poor sleep quality (n=16)	pwMS without poor sleep quality (n=36)	F	p-value
ESS	3.88±3.84	4.61±4.79	0.761	0.591
MFIS-physical	15.13±11.36	10.56±8.50	3.192	0.114
MFIS-cognitive	17.69±12.85	12.75±9.23	4.896	0.122
MFIS-psychosocial	3.19±3.06	2.06±2.29	2.965	0.145
MFIS-total score	36.0±26.85	25.33±18.06	6.789	0.098
HADS-D	8.0±4.87	6.22±4.15	0.445	0.183
HADS-A	9.13±5.24	6.25±4.29	0.339	0.043
PBMSI	0.64±0.24	0.70±0.18	0.836	0.243

ESS: Epworth sleepiness scale, pwMS: patients with multiple sclerosis, MFIS: Modified fatigue impact scale, HADS: Hospital anxiety and depression scale, PBMSI: Preference-based multiple sclerosis index

Table 3. Correlation coefficients between sleep quality, patient-reported outcome measures, and participant characteristics

Variables	Age	Disease duration	EDSS	Number of relapses	MFIS-physical	MFIS-cognitive	MFIS-psychosocial	MFIS-total score	PBMSI	ESS	HADS-A	HADS-D	PSQI-total
Age	1												
Disease duration	0.371**	1											
EDSS	0.376**	0.322*	1										
Number of relapses	-0.042	0.382**	0.251	1									
MFIS-physical	0.081	0.173	0.487**	0.243	1								
MFIS-cognitive	0.032	0.189	0.346*	0.286*	0.836**	1							
MFIS-psychosocial	0.178	0.180	0.445**	0.160	0.805**	0.714**	1						
MFIS-total score	0.074	0.192	0.443**	0.270	0.958**	0.953**	0.834**	1					
PBMSI	0.179	0.064	-0.087	-0.208	-0.547**	-0.556**	-0.527**	-0.583**	1				
ESS	-0.289*	-0.125	0.142	0.070	0.467*	0.420**	0.298*	0.452**	-0.207	1			
HADS-A	-0.078	-0.039	0.252	0.113	0.638**	0.554**	0.693**	0.643**	-0.614**	0.257	1		
HADS-D	0.021	0.145	0.309*	0.034	0.559**	0.516**	0.501**	0.565**	-0.304**	0.066	0.558**	1	
PSQI-total	0.023	0.116	0.133	0.343*	0.303*	0.297*	0.205	0.308*	-0.210	0.069	0.336*	0.243	1

EDSS: Expanded disability status scale, HADS: Hospital anxiety and depression scale, MFIS: Modified fatigue impact scale, PSQI: Pittsburgh sleep quality index, PBMSI: Preference-based multiple sclerosis index, ESS: Epworth sleepiness scale, *: Correlation is significant at the 0.05 level (2-tailed), **: Correlation is significant at the 0.01 level (2-tailed)

Study Limitations

The relatively small sample size may have limited the statistical power to detect significant differences in some measures. Future studies with larger cohorts could provide more insight into the relationships between these variables. Additionally, longitudinal studies are needed to examine the causal relationships and the effects of interventions targeting sleep quality on fatigue and mental health outcomes.

Conclusion

In conclusion, our study highlights the complex relationship between sleep quality, number of relapses, fatigue, and anxiety in pwMS. Our results identified factors that could influence sleep quality and emphasize the importance of evaluating and addressing them together.

Ethics

Ethics Committee Approval: Ethical approval was granted by the Non-Invasive Research Ethics Committee of Van Yuzuncu Yil University Faculty of Health Sciences on October 18, 2024, under approval number 2024/11-26.

Informed Consent: Informed consent was obtained.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.T.O., E.A., P.Y., V.C., Concept: A.T.O., E.A., P.Y., V.C., Design: A.T.O., E.A., P.Y., V.C., Data Collection or Processing: A.T.O., E.A., P.Y., V.C., Analysis or Interpretation: A.T.O., E.A., P.Y., V.C., Literature Search: A.T.O., E.A., P.Y., V.C., Writing: A.T.O., E.A., P.Y., V.C.

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