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Research Article

Sleep Disturbance and Related Factors in the Patients with Relapsing-Remitting Multiple Sclerosis

Izabela Sempik,[1] Edyta Dziadkowiak,[2] Małgorzata Wieczorek,[3] and Anna Pokryszko–Dragan[2]

[1]*Department of Neurology, Regional Hospital in Legnica, Iwaszkiewicza 5, 59-220 Legnica, Poland*
[2]*Department of Neurology, Wroclaw Medical University, Borowska 213, 50-556 Wroclaw, Poland*
[3]*Faculty of Earth Sciences and Environmental Management, University of Wroclaw, Uniwersytecki 1, 50-137 Wroclaw, Poland*

Correspondence should be addressed to Edyta Dziadkowiak; edyta.dziadkowiak@umw.edu.pl

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Background. Sleep disturbances are commonly reported, although underestimated complaints from people with multiple sclerosis (MS). The aim of the study was to analyze the frequency and type of sleep disturbances in MS patients and to evaluate their relationships with demographics and clinical data. *Methods*. The study group consisted of 178 patients with relapsing-remitting MS: 130 females and 48 males. Clinical measures (disease duration, disability level in Expanded Disability Status Scale (EDSS), and treatment) were acquired from medical records. The questionnaire was applied, containing questions about sleep disturbances, somatic complaints, perception of fatigue, depression, anxiety, and problems at work and in social/family life. Athens Insomnia Scale (AIS) and Karolinska Sleepiness Scale (KSS) were performed to quantify sleep problems and Hamilton Depression Rating Scale (HDRS) and Addenbrooke's Cognitive Examination (Mini-ACE) to assess level of depression and cognitive performance. Electroencephalography was recorded to identify electrophysiological indices of sleep. *Results*. 109 patients (61%) reported sleep disturbances, most frequently insomnia, snoring, and parasomnias. This subgroup had significantly higher scores in AIS ($p < 0.0001$) and KSS ($p = 0.010$) and slightly higher EDSS score ($p = 0.048$) and more often complained of fatigue (71% vs. 53%, $p = 0.0148$), involuntary limb movement (42% vs. 25, $p = 0.0170$), and breathing disturbances (10% vs. 0%). There was a significant correlation between the results of AIS and HDRS ($Rs = 0.715$, $p < 0.05$). *Conclusion*. Sleep disturbances, predominantly insomnia, are reported by more than a half of the patients with relapsing-remitting MS. Significant associations were found between sleep problems and MS-related clinical symptoms and psychosocial issues.

1. Introduction

Multiple sclerosis (MS) is a long-lasting, multifocal demyelinative disease of the central nervous system (CNS). According to the current state-of-the-art knowledge, complex etiology of MS includes genetic predisposition and impact of environmental factors, which contribute to the major pathomechanism associated with autoreactive immune-mediated response against components of CNS myelin. Exacerbating inflammatory demyelination is accompanied by slowly evolving process of neurodegeneration with axonal loss [1, 2].

MS-related lesions disseminated throughout the brain and spinal cord result in a wide range of symptoms which show temporary fluctuations (especially in the relapsing-remitting type of disease).

The most common symptoms include motor deficit with disturbances of gait, optic neuritis with impaired vision, ataxia, vertigo and dizziness, sensory impairment, and bladder dysfunction. There are also other conditions which may become a serious burden for patients with MS, but due to their subjective and chronic characteristics, they are underestimated (and thus called "invisible disability"): e.g., fatigue, cognitive impairment, and sleep disturbances [1, 3, 4]. Sleep

problems have been described in up to 60% of patients with MS, with inconsistencies in their type and frequency across the studies [5]. Among these, main complaints include insomnia, disturbances in the circadian wake-sleep cycle, and restless legs syndrome; hypersomnia, different kinds of parasomnias (night terrors, nightmares, somnambulism), and obstructive sleep apnea have been also occasionally reported [5]. Sleep disturbances in MS may be reciprocally associated with somatic symptoms of neurological deficit, as well as with mental health issues. They play an important role in MS impact upon patients' daily functioning, social participation, and quality of life [6, 7]. Thus, in clinical practice, there is a need for their proper evaluation and management.

The aim of the study was to analyze the frequency and type of sleep disturbances in MS patients and to evaluate their relationships with demographics and clinical MS-related data.

2. Materials

Participants were recruited from the patients with MS, hospitalized or consulted in the Department of Neurology, Specialist Hospital in Legnica, between 1 January and 30 June 2022.

Inclusion criteria comprised the diagnosis of relapsing-remitting MS (according to McDonald's criteria—revision 2017) [8] and availability of complete medical records from regular outpatient follow-up with documented course of disease. Exclusion criteria included primary or secondary progressive MS, recent relapse and treatment with corticosteroids within preceding 2 months, moderate-to-severe bladder dysfunction, coexisting uncompensated chronic conditions (e.g., diabetes, hypertension, and renal or liver failure), and severe cognitive impairment which would prevent from providing informed consent and/or completion of the study questionnaires. The flow chart illustrating recruitment for the study group is presented in Figure 1.

The ultimate group consisted of 178 patients, including 130 females (73%) and 48 males (27%), with the mean age 43 years.

3. Methods

The design of the study was cross-sectional. Completion of the patients' medical history and all the procedures was performed during one session, in morning hours (between 9 and 12 AM).

3.1. Demographic and Clinical Characteristic. The demographics and clinical data concerning MS (disease duration, type of MS, and disease-modifying and symptomatic treatment) and comorbidities were established on the basis of the medical records. In addition, on the basis of neurological examination, the current degree of disability was evaluated using Expanded Disability Status Scale (EDSS) [9].

3.2. The Questionnaire on Sleep Disturbances and Psychosocial Issues. In the first part of the study questionnaire, the participants were asked about occurrence of any sleep disorders since the onset of the disease, their specific types and any medications taken to relieve the sleep problems.

Further questions concerned are somatic complaints potentially associated with sleep problems (pain, involuntary limb movements—clonic jerks or muscle cramps—and nycturia), subjective perception of fatigue, depression and anxiety, and problems at work and in social/family life.

The second part of the questionnaire contained the following self-assessment scales:

(1) The Athens Insomnia Scale (AIS)—for the quantitative measurement of insomnia [10]

(2) The Karolinska Sleepiness Scale (KSS)—a measure of the subjective level of sleepiness at a particular time during a day [11]

Following completion of the questionnaire, the two tests were performed by one of the investigators:

(1) Hamilton Depression Rating Scale (HDRS)—to assess the level of depression [12]

(2) Addenbrooke's Cognitive Examination (Mini-ACE) test—as a brief screening test for cognitive functions [13]

3.3. Electroencephalography. Electroencephalography (EEG) was conducted to evaluate bioelectrical activity of the brain, especially with regard to sleep-wake cycle. EEG was performed with the use of ELMIKO Digi Track (version14) device, with 21 electrodes placed on the patient's head according to the international "10-20" system. The raw signal was filtered with the use of FFT filters (settings: 70 Hz for high pass frequencies and 0.3 Hz for low-pass frequencies) and processed. The amplifier sensitivity was calibrated within the range of 20-100 μV/cm. The unified standardized protocol was applied to data recording, artifact control, and signal processing.

The patients were lying in the semidarkened room with their eyes closed and allowed to fall asleep. During 30 minutes of recording, hyperventilation was applied for 3 minutes and intermittent photic stimulation for 4 minutes. After automatic rejection of artifacts, the recordings were visually analyzed and investigated for any abnormalities of the background activity and physiological elements of sleep; sleep latency was determined as the time from the onset of recording to the identification of the I stage of sleep. The recordings were analyzed by a qualified neurophysiologist, blinded to the other results of study.

3.4. Ethical Standards. The study was carried out in accordance with Declaration of Helsinki and Good Clinical Practice guidelines. The design of the study was approved by the Bioethics Committee of Wroclaw Medical University. Participation in the study was voluntary and without compensation. After obtaining a thorough information about the aim and design of the study, followed by necessary explanations, the patients provided their written consent prior to participating in the study.

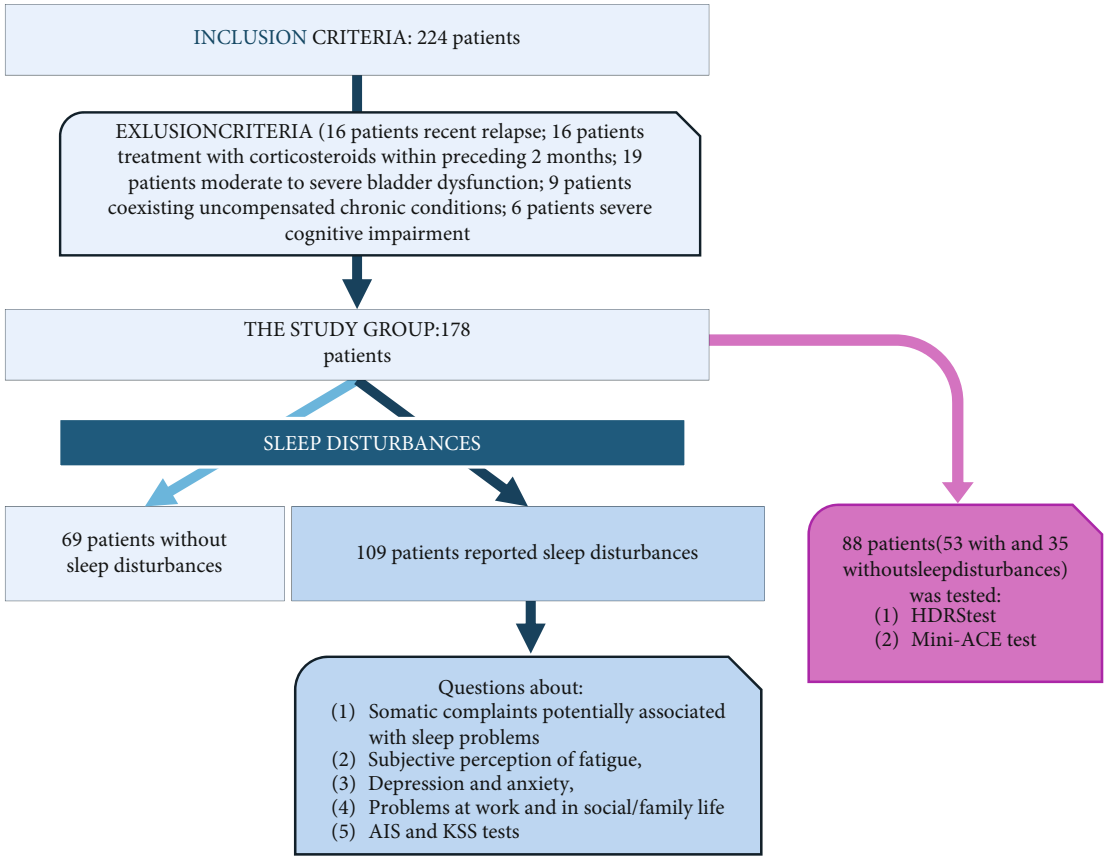

Figure 1: The flowchart of the selected patients for the study.

3.5. The Statistical Analysis. On the basis of responses to the questionnaire, the patients were divided into subgroups with or without sleep disturbances. Relationships were searched between the presence and type of sleep disturbances (including AIS and KSS scores) and demographics, MS-related clinical data, and results of HDRS and Mini-ACE. Statistical analysis was performed using STATISTICA 13 software, for all tests assuming alpha = 0.05. The normality of the distributions of the variables was tested using the Shapiro-Wilk test. Descriptive statistics were used to determine the mean, standard deviation, and abundance of individual variables. A comparison of the significance of differences was made using the Mann–Whitney U test (due to the nonnormality of the distribution) in subgroups with and without sleep disturbances. For analysis of relationships between sleep disturbances and MS treatment, Z-score ratio test was performed when the counts of individual fractions > 10 or the chi-square test with the Yates correction, respectively, when the count criterion was not met.

4. Results

4.1. Clinical Characteristics of the Study Group. Mean duration of disease in the study group was 9.48 ± 6.8 years, and median EDSS score is 1.5 (interquartile range = 2.0). All the patients were currently being treated with disease-modifying therapies (DMT): interferon beta, 72 persons; glatiramer acetate, 25; dimethyl fumarate, 50; teriflunomide, 19; fingolimod, 7; natalizumab, 2; and ocrelizumab, 3 persons, respectively. Mean duration of treatment with DMT was 6.24 ± 4.4 years.

As for coexisting diseases, 6 patients had been diagnosed with hypothyroidism and 12 with depression. All of them were being treated appropriately for these conditions and regarded as stable.

4.2. Sleep Disturbances. Responding to the questionnaire, 109 participants (61%) reported occurrence of sleep disturbances, while 69 ones denied them. 102 persons (57%) usually considered their sleep as effective, and 82 (46%) claimed that they usually wake up fully rested. According to the respondents, their average time to falling asleep was estimated at 35 minutes. For further analysis, the study group was divided into two subgroups: with ($n = 109$) and without ($n = 69$) sleep disturbances.

The most common type of sleep disturbances was insomnia (reported in 57 cases), followed by snoring (41 patients), parasomnias (38 patients), and hypersomnia (30 ones). The least common disturbances included sleep dyspnea (11 patients), uncontrolled sudden falling asleep (3 subjects), and somnambulism (2 subjects).

In the subgroup with sleep problems, 69 subjects reported only one type of these, while the others complained of more coexisting disturbances (2 types, 26 persons; 3 types, 9 persons; and more than 3 types, 4 persons).

4.2.1. Sleep Disturbances—Contributing Factors. Somatic complaints potentially associated with sleep problems were analyzed and compared between the subgroups. In the whole study group, fatigue was the most frequent complaint (reported by 115 respondents), followed by pain and involuntary limb movement; nycturia and respiratory distress were the least frequent ones (Table 1). Out of these, significant differences between the subgroups with and without sleep disturbances were found for fatigue (71% vs. 53%, $p = 0.0148$), involuntary limb movement (42% vs. 25, $p = 0.0170$), and breathing disturbances (10% vs. 0%, $p = 0.0162$) (Table 1).

4.2.2. Management of Sleep Disturbances. Seven participants reported the use of medications to relieve sleep disturbances: zolpidem in 2 cases, hydroxyzine in 2, bromazepam in 1 (prescribed by a physician), and melatonin (available over-the-counter) in 2. Besides, those diagnosed with depression were being treated with antidepressants (5 with trazodone, 1 with mianserin, 1 with venlafaxine, and 10 with SSRI), which could also affect their quality of sleep. Seventeen participants declared regular use and/or abuse of alcohol.

4.2.3. Self-Assessment Scales. According to the results of AIS, the scores of 121 patients indicated lack of insomnia, while in 57 cases, they corresponded with mild (41), moderate (12), or severe (4) insomnia. Mean AIS result for the whole study group was 6.80 points (SD 4.88) with the significant difference between the subgroups with and without sleep disturbances (Table 2).

The result of KSS ranged from 1 to 5. In 67 persons, the result could be interpreted as "very alert," in 78 as "alert", and in 33 as "neither alert nor sleepy." Mean KSS result was significantly higher in the subgroup with sleep disturbances, indicating higher degree of daily sleepiness (Table 2).

4.2.4. Sleep Disturbances vs. Demographic and MS-Related Data. The subgroups with and without sleep disturbances were compared with regard to demographic and clinical data. The subgroups did not differ significantly in age. With regard to sex, in the subgroup with sleep disturbances, the proportion of women and men was 3 : 1 and in the other subgroup 2 : 1 (Table 1). Mean EDSS was significantly higher in the subgroup with sleep disturbances. No differences were found between the subgroups in duration of the disease or treatment. (Table 1).

Table 3 shows the use of DMT in the subgroups with and without sleep disturbances. No significant differences were found between these subgroups in distribution of DMT.

4.2.5. Sleep Disturbances vs. Psychosocial Issues. The results of Mini-ACE, evaluating cognitive performance, were obtained only for 88 participants (53 with and 35 without sleep disturbances). The remaining ones either withdrawn their consent to undergo the test or provided incomplete responses. The subgroups of patients with or without completed Mini-ACE did not differ significantly in demographics (age, sex distribution) or MS-related variables (disease duration, EDSS).

Overall results showed good performance in attention and memory domains and impairment in the field of visuospatial abilities (clock-drawing test), verbal fluency, and memory recall.

According to KSS scores, all the patients remained "very alert" while completing Mini-ACE.

On comparison of subgroups with and without sleep problems, there were no significant differences in particular domain subscores or total Mini-ACE result (Table 4). No significant correlations were found between Mini-ACE result and AIS or KSS scores either.

The result of HDRS in the study group ranged from 0 to 24, with the mean value 9.48 points. In 17 persons, the score corresponded with the mild depression, in 7 with moderate, and in 4 with severe depression. Mean HDRS score was significantly higher in the subgroup with sleep disturbances (12.19 ± 6.83 vs. 4.94 ± 4.57, $p < 0.00001$).

There was a significant correlation between HDRS and AIS scores ($R = 0.71$, $p < 0.05$) (Figure 2).

As mentioned before, 12 patients had been previously diagnosed with depression. 11 of them were assigned to the subgroup with sleep disorders and only one to the subgroup without sleep disturbances. Subjective perception of depressed mood and anxiety was reported by 43 patients, more frequently in the subgroup with sleep disturbances (34% vs. 7%, $p = 0.0001$).

Out of 55 patients, who reported problems at work and/or family life, 38 (69%) belonged to the subgroup with sleep disturbances.

4.2.6. Sleep Disturbances vs. EEG Findings. EEG was recorded only in 99 participants (54 from the subgroup with sleep problems, 45 without sleep problems); the remaining ones withdrawn their consent and resigned from this procedure. None of the participants who had EEG performed had been diagnosed with epilepsy or had experienced a seizure before. Epileptiform discharges were recorded in 2 patients: generalized in one case and focal in another one.

In 52 subjects, electrophysiological features of somnolence were noted, and in 18, I and II stages of sleep were recorded. No significant difference was found in the presence of sleep in EEG recording between the study subgroups.

For those who fell asleep during EEG recording, mean sleep-onset latency was 6 minutes.

The mean KSS score for these patients was higher (on the edge of significance) than for those who did not fall asleep during EEG (3.36 vs. 2.78, $p = 0.05$).

5. Discussion

According to literature resources, 47-62% of MS patients suffer from sleep disorders, which can seriously affect their overall condition. The results of our study are consistent with these findings, as 61% of participants reported some kind of sleep disturbances throughout the disease. Similarly, insomnia—the most frequently reported complaint (32%) by our respondents—has been observed in up to 28% of patients in other studies [14–17].

However, our results differed from literature data with regard to occurrence of other sleep disturbances. Our patients often complained of snoring (23%) and parasomnias (21%),

Table 1: Demographic and MS-related clinical data: a comparison between the study subgroups.

	Study group ($n = 178$) Mean ± SD	Subgroup with sleep disturbances ($n = 109$) Mean ± SD	Subgroup without sleep disturbances ($n = 69$) Mean ± SD	p value
Age	43.28 ± 11.45	44.02 ± 11.54	42.17 ± 11.31	0.503
Sex (F/M)	130/48	83/26	47/22	0.876
Duration of disease	9.51 ± 6.84	10.01 ± 6.98	8.74 ± 6.60	0.294
Duration of treatment	6.24 ± 4.41	6.24 ± 4.72	6.23 ± 3.93	0.561
EDSS	2.00 ± 1.46	2.20 ± 1.47	1.70 ± 1.40	**0.048**
Pain	76 (42.7%)	52 (47.7%)	24 (34.8%)	0.0894
Nycturia	10 (5.6%)	8 (7.3%)	2 (2.9%)	0.3578
Involuntary limb movements	63 (35.4%)	46 (42.2%)	17 (24.6%)	**0.0170**
Respiratory disturbances	11 (6.2%)	11 (10.1%)	0 (0.0%)	**0.0162**
Fatigue	115 (64.6%)	78 (71.6%)	37 (53.6%)	**0.0148**

Statistically significant values are indicated in bold.

Table 2: Results of Athens Insomnia Scale (AIS) and Karolinska Sleepiness Scale (KSS): a comparison between the study subgroups.

	Study group ($n = 178$)		Subgroup with sleep disturbances ($n = 109$)		Subgroup without sleep disturbances ($n = 69$)		p value
	Mean	SD	Mean	SD	Mean	SD	
Athens Insomnia Scale (AIS)	6.80	4.88	8.67	4.91	4.04	3.29	**<0.00001**
Karolinska Sleepiness Scale (KSS)	2.76	1.07	2.94	1.14	2.48	0.87	**0.009**

Statistically significant values are indicated in bold.

Table 3: The use of DMT: a comparison between the study subgroups.

		Subgroup with sleep disturbances ($n = 109$)	Subgroup without sleep disturbances ($n = 69$)	p value
DMT	Fingolimod	4	3	0.866
	Dimethyl fumarate	25	25	0.054
	Interferon beta-1a	8	5	0.981
	Interferon beta-1b	30	23	0.409
	Natalizumab	2	0	—
	Ocrelizumab	2	1	—
	Glatiramer acetate	19	6	0.103
	Peginterferon beta-1a	4	2	—
	Teriflunomide	15	4	0.095

while nocturnal involuntary movements, breathing disturbances, and REM-sleep behavioral disorders, frequently described in MS population [5, 12, 18], occurred in our survey only occasionally.

Almost two-thirds of our patients with sleep disturbances declared more than one type of these: most frequently insomnia combined with night terrors, snoring, or hypersomnia. Night terrors or snoring indeed may cause insomnia, further resulting in daily hypersomnia. Such a complex character of sleep disturbances is often highlighted in CNS diseases, due to their causal link or coexistence [19, 20]. Importantly, our patients were inquired about sleep problems at any time since the onset of MS, and it was not specified when their particular types had occurred. Thus, it is difficult to conclude about relationships between sleep disturbances, and the recall bias has to be taken into account. To diminish the effect of the latter, AIS and KSS were applied to evaluate a current degree of insomnia and daily sleepiness in the study group. Based on the subject's subjective perception, they are considered as effective tools for quantitative assessment of sleep problems, useful in research and clinical settings [17, 21, 22]. We chose these scales out of the available ones because of their simplicity and convenience for the patients. The results of both AIS and KSS differed significantly between the subgroups with and without sleep disturbances, which additionally supports their distinction, based on the responses to the questionnaire. In the patients with insomnia, AIS scores mostly indicated its mild level, which corresponded with perception of efficient sleep reported by ca. 50% of respondents. Furthermore, the results of KSS were consistent with EEG findings: those who fell asleep during EEG (with electrophysiological patterns of

Table 4: Mini-ACE results vs. sleep disturbances in the study group.

	Total group ($n = 88$)		Subgroup with sleep disturbances ($n = 53$)		Subgroup without sleep disturbances ($n = 35$)		p value
	Mean	SD	Mean	SD	Mean	SD	
Attention	4.00	0.00	4.00	0.00	4.00	0.00	
Memory	7.00	0.00	7.00	0.00	7.00	0.00	
Fluency	5.61	1.79	5.58	1.41	5.66	2.27	0.864
Visuospatial	3.88	1.94	3.79	2.03	4.03	1.81	0.750
Memory recall	4.63	1.52	4.53	1.64	4.77	1.33	0.779
Total score	25.13	3.37	24.91	3.42	25.46	3.32	0.897

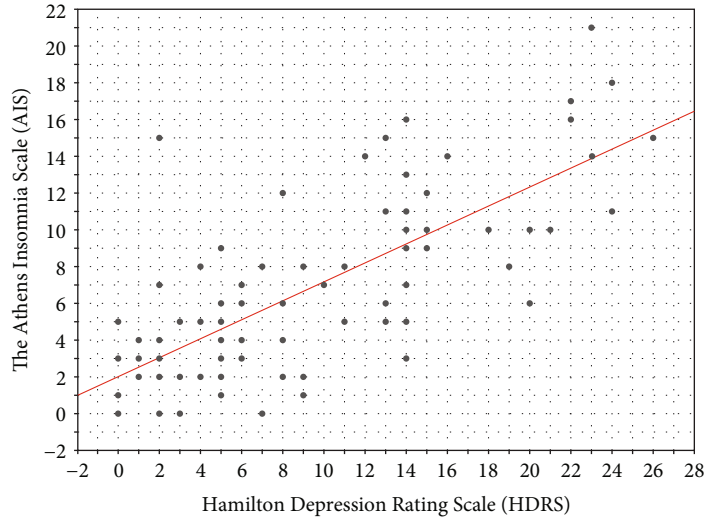

Figure 2: Scatter diagram of the correlation between AIS and HDRS scores in the study group.

sleep recorded) had significantly higher KSS scores. Overall, AIS and KSS are worth considering in the basic follow-up of the MS patients, to include sleep quality in the complex evaluation of their condition. Those identified with particular sleep disturbances might be qualified for more advanced EEG diagnostics (e.g., multiple sleep latency test or polysomnography).

With regard to demographics, sleep disorders in multiple sclerosis have been associated with older age and female sex [15–17, 23–25]. In our study, no significant differences were found in age or sex structure between the subgroups with and without sleep disturbances. There was a marked predominance of women in the whole study group, but this is commonly observed in MS populations.

Among MS-related clinical factors, relationships have been described between sleep disturbances and higher EDSS score and longer duration of disease [15, 26, 27]. The effect of DMT on sleep quality (with regard to the outcomes or side effects of treatment) has been also investigated. IFN-β and glatiramer acetate were found to prolong sleep-onset latency and cause frequent awakenings at night with poor sleep efficiency and daily somnolence [28, 29]. On the contrary, natalizumab was shown to have a positive effect upon fatigue and daytime sleepiness [29] and dimethyl fumarate to ameliorate sleep problems [30]. Our findings demonstrated only slightly higher (on the edge of significance) EDSS score in the subgroup with sleep problems, and distribution of DMT did not differ between the subgroups. However, it should be stressed that median of disability level in the study group was relatively low and only a small percentage of patients were being treated with high-efficacy therapies (presumably due to greater activity of disease). While it is difficult to consider the impact of the disease course and DMT upon sleep quality separately, our observations seem relevant for RRMS patients with mild-to-moderate disease activity and cannot be generalized for all types and stages of MS.

With regard to specific symptoms of neurological deficit, we inquired the patients about the complaints, most often identified as associated with sleep problems [26, 31]. Indeed, pain, involuntary limb movement (clonus or muscle cramps), and breathing disorders turned out to be more frequent in the subgroup with sleep disturbances. The same was noted for nycturia, which needs to be stressed, because subjects with severe bladder dysfunction had been deliberately excluded from the study. All these symptoms might impede falling asleep and cause awakenings during the night.

Some links have been established between sleep disturbances and fatigue, a common and burdensome symptom of MS, which may be distinctive but also overlapping problems. Association was shown between the results of Modified

Fatigue Impact Scale and polysomnography, as well as between Epworth Sleepiness Scale and Fatigue Severity Scale scores [6, 16, 32, 33]. Although we did not use any of the quantitative fatigue scales, the participants were asked about their subjective perception of fatigue, and the frequency of these complaints differed significantly between the subgroups with and without sleep disturbances.

Even more complex interplay can be observed for sleep disturbances and mental health issues, especially depression [15, 17, 18, 33–35]. These relationships seem reciprocal, because sleep disturbances can predict mood disorders and anxiety, but also, affective disorders often result in sleep problems. Insomnia occurs in more than half of patients with depression, while excessive daily sleepiness is less frequently reported [36]. Polysomnographic studies in the patients with depression showed altered sleep architecture: difficulties with falling asleep, fragmentation of sleep, and changes in proportion and timing of particular sleep stages (e.g., REM) [36, 37]. Possible pathomechanisms shared by MS, depression, and sleep disorders include dysregulation of hypothalamic-pituitary-adrenal axis (with exaggerated reactivity of cortisol production to stress), changes in function of neurons and oligodendrocytes related to circadian rhythm, and modified neurotransmission [38–40].

In our study, 7% of participants had been already diagnosed with depression, but as much as 20% reported subjective feeling of lowered mood and/or anxiety, and HDRS score corresponded with mild-to-severe depression in 28 persons (15%). Furthermore, HDRS score was significantly higher in the subgroup with sleep problems, and it was found to correlate with AIS results as a measure of insomnia. Similar links between depression and sleep disturbances were demonstrated by other authors [17, 27, 41]. These findings indicate the need for screening the evaluation of mood disorders in MS patients, to provide them with adequate support in this field. Moreover, in those diagnosed with depression, recognition of sleep problems is essential with regard to pharmacological treatment: some antidepressants may disrupt sleep, while other improve its quality but may have excessive sedative effect in long-term use [42].

Sleep disturbances in patients with MS may be associated with their cognitive performance. As mentioned above, ineffective night sleep and daytime sleepiness were shown to correlate with cognitive fatigue, but also with the impairment in the field of concentration, memory, visuospatial skills, and executive functions [19, 28]. Sleep problems were also considered as predictors of future cognitive decline in MS [19, 43]. However, some of the studies did not confirm these relationships [21]. In our study, Addenbrooke's Cognitive Examination (Mini-ACE) was used for screening evaluation of cognitive performance of MS patients [44, 45]. The results showed affected domains of verbal fluency, visuospatial functions, and delayed memory, with relatively preserved recent memory and attention. It should be stressed that the patients with severe cognitive decline had been deliberately excluded from the study. Similar to other reports [19], we demonstrated no significant differences in Mini-ACE scores between subgroups with and without sleep disorders. No significant correlations were demonstrated between Mini-ACE total score and AIS or KSS either. However, ca. 45% of the participants did not agree or failed to complete Mini-ACE, so the sample size may have not been sufficient to determine relevant findings in this field.

Apart from impact upon cognition, sleep disturbances in MS patients have been found to interfere with their professional and leisure activities and overall daily functioning [7, 16]. In the study group, ca. 70% of those who reported problems at work and/or family life belonged to the subgroup with sleep disturbances. Surprisingly, only small percentage of this subgroup admitted regular use of sleeping medications, usually prescribed by a physician. Our questionnaire did not include questions about nonpharmacological interventions used to improve quality of sleep, which might be a subject for further investigations. While behavioral/relaxation techniques and change in lifestyle habits are recommended in this field, it would be interesting to find out the MS patients' approach and adherence to these [46].

In our study, we made an attempt of the complex evaluation of sleep problems in the RRMS patients, using a range of tools, with regard to clinical and psychosocial issues. The limitations of the study include potential recall bias associated with construction of the study questionnaire, lack of quantitative assessment of some aspects (fatigue, social functioning), and relatively small sample size for evaluation of Mini-ACE or EEG results. Although low disability level and vast majority of moderate efficacy therapies used in the study group enabled its greater clinical homogeneity, this impeded generalizability of our findings for the whole MS population. However, we managed to identify some relevant contributing factors and consequences of sleep disturbances in MS patients, with potential implications for clinical practice and management of the outcomes of the disease. Our findings encourage further investigation, including larger groups of patients with various types of MS and a wider range of evaluated aspects of sleep problems.

6. Conclusions

Sleep disturbances, predominantly insomnia, are reported by more than a half of the patients with relapsing-remitting MS. Significant associations were found between sleep problems and MS-related clinical symptoms and psychosocial issues. Evaluation of sleep disturbances should be considered in the complex approach to the management of MS outcomes.

Data Availability

The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Approval

The authors had a positive opinion of the Bioethics Committee of the Medical University of Wroclaw No. KB-719/2021 to perform the study. The study was conducted in accordance with the Declaration of Helsinki with amendments of 2013.

Consent

The authors informed the patients and control subjects in detail about the planned study and obtained written consent to conduct it.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

I.S. contributed to the study concept, design, and data analysis and interpretation. E.D. assisted in the design and data analysis and interpretation. M.W. participated in the statistical analysis. A.P.-D. critically revised the manuscript for important intellectual content. All listed authors made a significant scientific contribution to the research in the manuscript, approved its claims, and agreed to be an author. All authors have read and agreed to the published version of the manuscript.

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