

Quality of Life and Sleep Profile in Relapsing Remitting Multiple Sclerosis Patients

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Abstract:

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Received: 11 October 2023

Accepted: 14 February 2024

Background: Multiple sclerosis (MS) is the most common demyelinating autoimmune disease affecting the central nervous system (CNS) which can present by various neurological symptoms including visual impairment, numbness and tingling, focal weakness, bladder and bowel incontinence and cognitive dysfunction. Patients with MS rate their health-related quality of life (HRQOL) to be lower than that of the general populations and also lower than patients with other chronic diseases such as epilepsy and diabetes. Patients with multiple sclerosis (MS) frequently report poor sleep, and sleep disorders are more common in MS patients compared to the healthy group. **Aim of the work:** The aim of the current study was to assess the quality of life and sleep profile in patients with relapsing remitting multiple sclerosis (RRMS). **Methods:** The study was descriptive comparative case control study which included 40 patients and 40 controls; HRQOL was assessed using the Arabic version of the Multiple Sclerosis Quality of Life-54 questionnaire in RRMS patients. Sleep quality was assessed for both patients and control group using the Arabic version of The Pittsburgh Sleep Quality Index. To measure patients' degree of disability, the Expanded Disability Status Scale (EDSS) was used. **Results:** The results showed that RRMS patients have low mean physical and mental composite score. The results also showed that RRMS patients have high global sleep index indicating poor sleep quality. **Conclusion:** MS patients have limitations as regard physical and cognitive functions in addition to poor sleep quality, which lead to low health related quality of life.

Keywords: multiple sclerosis, health related quality of life, sleep quality, disease severity.

Introduction:

Multiple sclerosis is an autoimmune-mediated disorder that affects the central nervous system (CNS) which is considered a leading neurological cause of disability in some populations (1). The incidence and prevalence of MS has been on an alarming rise (2).

The causes of the disease are not exactly known, but there are genetic and environmental factors such as vitamin D deficiency, Epstein-Barr virus, and Herpes virus infections that activate T cells and lead to myelin sheath destruction (3).

The clinical manifestations differ depending on the site of the lesion in the CNS and the phenotype of MS. The common clinical presentations are visual loss, sensory loss including numbness and tingling, weakness, incoordination, imbalance, gait impairment and bladder/bowel dysfunction (4).

Types of MS depend on the progression, deterioration and remission of the disease. They include the relapsing-remitting form multiple sclerosis (RRMS), primary progressive MS (PPMS), secondary progressive MS (SPMS), clinically isolated syndrome and radiological isolated syndrome. The most common type is the relapsing remitting type (RRMS) as it affects approximately 85% of the MS population (5).

Studies involving MS patients have shown that wellbeing is not a simple manifestation of impairment or disability (6). The quality of life in multiple

sclerosis patients depends on many factors such as the type of MS, type of treatment, social relationships, social support and psychological (7).

MS patients rate their health related QOL lower than general populations and also lower than patients with other chronic diseases such as epilepsy and diabetes (8). There is a growing interest in how different problems associated with MS, such as fatigue and depression, impact different dimensions of QOL independent of the contribution of physical disability (9).

Multiple sclerosis patients frequently report poor sleep and many studies revealed that sleep disorders are more common in MS patients compared to healthy individuals (10). Causes of poor sleep in MS are multifactorial including adverse effects from immunotherapy, symptomatic medications, MS-associated symptoms such as pain and fatigue (11).

Patients suffering from sleep disturbance have an increased risk of developing comorbid conditions such as heart disease, obesity and diabetes that may have a profound impact on long-term health. In order to improve sleep and possibly reduce long-term health consequences of poor sleep in MS, identification of modifying risk factors of poor sleep is needed (12).

Subjects and methods:

This was a descriptive comparative case control study carried out among RRMS patients from the MS outpatient clinic at

Benha University Hospitals and from MS committee at Benha insurance hospital, from the end of 2021 till the end of March 2023. Patients between 18 and 60 years with RRMS according to McDonald criteria (13) were included in the study. Other types of MS patients, patients who had relapse within the last 3 months and patients with comorbid diseases were excluded. As for the control group, a matched sample for age and sex were selected. The included patients filled a semi structured interview containing questions about age, sex, marital status, educational level and employment status. To measure patients' disability status, we used the Expanded Disability Status Scale (EDSS) (14). Patients were categorized according to the total EDSS score as having mild (0–2.5), moderate (3.0–6.0), and severe (6.5– 9.5) disability. HRQOL was assessed using the MSQoL-54 questionnaire which is a disease-specific instrument to measure the QOL of MS patients, which was based on the generic SF-36 QOL instrument. Two composite scores can be obtained on the MSQOL-54, physical health composite and mental health composite (15). Quality of sleep was assessed in both patients and controls using the Pittsburgh Sleep Quality Index (PSQI) (16) which assesses sleep quality over a 1-month time interval. The Arabic version of this questionnaire was used (17). The measure consists of 19 individual items, creating 7 components each weighted equally on 0-3 scale. They are summed to yield a global PSQI score which has a range of 0-21; higher scores indicated worse sleep quality.

Research ethics committee: Ms.44.12.2021.

Statistical analysis:

The collected data was revised, coded and tabulated using Statistical package for Social Science (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Data were presented and suitable analysis was done according to the type of data obtained for each parameter.

Descriptive statistics such as Mean, standard deviation (\pm SD), median, standard error (\pm SE), and range were used for numerical data. Frequency and percentage were used for non-numerical data. Student T Test was used to assess the statistical significance of the difference of parametric variable between two study group means. Mann Whitney Test was used to assess the statistical significance of the difference of a non-parametric variable between two study groups.

Results:

This study presents comparative statistics for the socio demographic data including age, sex, marital status, educational level and occupation between the two groups. The majority of MS patients were females (72.5%), below the age of 40 (67.5%), married (62.5%). The study showed no statistically significant difference between patients with multiple sclerosis and control group regarding age, sex and marital status. The results also show that most of MS patients were university graduate (52.5%) and had professional job (42.5%).

There was no significant difference between the MS and control groups regarding education and occupation ($p \geq 0.05$) (**Table 1**). The majority of the MS group (75.0%) lived in urban areas in contrast to the control group in which the majority (62.5%) lived in rural areas with a high statistical significant difference.

The mean duration of illness in the studied MS group was 5.26 ± 0.57 years. The median of the duration of illness was 5 years, and the range was from 0.5 to 19.0 years (**Table 2**).

The results also revealed that the most commonly used medication is Fingolimod (47.5%) followed by Interferon b 1a (17.5%) then Rituximab (12.5%) (**Table 3**).

The mean EDSS score for the MS patients was 1.91 ± 0.30 , with 85% having mild disability, while the remaining 15% had moderate disability. The functional systems with the highest mean scores were pyramidal and mental, with scores of 0.95 ± 0.22 and 0.63 ± 0.11 , respectively (**Table 4**).

The mean physical composite score for the MS patients were 50.28 ± 3.47 . As for its the subscales; the lowest mean scores were role limitation due to physical problem, health distress due to

physical problems and energy, with scores of 3.0 ± 0.75 , 5.57 ± 0.50 and 5.72 ± 0.41 , respectively. The subscales with the highest mean scores were physical function, health perception and social function, with scores of 7.88 ± 0.87 , 8.05 ± 0.51 and 7.48 ± 0.47 , respectively as shown in **table 5**.

Regarding the mental composite score, the mean was of 46.42 ± 3.36 . As for its subscales, the lowest mean score was cognitive function 5.44 ± 0.56 and the highest was emotional well-being (13.57 ± 1.05) as shown in **table 6**.

PQSI questionnaire scores from both MS patients and the control group were compared. MS patients had a higher mean global PSQI score (7.40 ± 0.66) compared to controls (5.98 ± 0.54), indicating poorer sleep quality. There was a significant difference ($p=0.031$) between the two groups in terms of sleep efficiency, with the MS group reporting a higher mean score (0.58 ± 0.15) compared to the control group (0.20 ± 0.09). Most of MS patients (75%) were classified as poor sleeper which was insignificantly higher than the control group (67.5%). There were also no significant differences between the two groups in terms of subjective sleep quality, sleep latency, sleep duration, sleep disturbance, sleep medication, and daytime dysfunction (**Table 7**).

Table 1. Comparison between age, sex and marital status of both the studied group of relapsing remitting multiple sclerosis and control group:

	MS N = 40	patients	Control N = 40	Test	P
Age (years)					
Mean ± SD.	35.23 ± 10.96		31.53 ± 8.86	t=	0.101
Median	37.0		28.50	1.660	
Min. – Max.	17.0 – 63.0		18.0 – 53.0		
≤40 year	27 (67.5%)		31 (77.5%)	X ² =1.003	0.317
>40 year	13 (32.5%)		9 (22.5%)		
Sex	N	%	N	%	
Male	11	27.5	14	35.0	x ² =
Female	29	72.5	26	65.0	0.524
Marital status					
Single	12	30.0	15	37.5	x ² =
Married	25	62.5	25	62.5	2.907
Widow	1	2.5	0	0.0	
Divorced	2	5.0	0	0.0	
Residence					
Rural	10	25.0	25	62.5	x ² =
Urban	30	75.0	15	37.5	11.429
Education					
University graduate	21	52.5	23	57.5	x ² =
University student	7	17.5	5	12.5	2.269
Technical graduate	10	25.0	12	30.0	
Technical student	2	5.0	0	0.0	
Occupation					
Professional	17	42.5	24	60.0	x ² =
Clerk	4	10.0	3	7.5	5.592
Student	9	22.5	5	12.5	
Craftsman	4	10.0	5	12.5	
Unemployed	3	7.5	0	0.0	
Housewife	3	7.5	3	7.5	

P: Comparing between MS patients and control; *, significant, p <0.05; ** high significant, p<0.01; *** very high significant, p<0.001.

Table 2. Duration of illness in the studied patients with relapsing remitting multiple sclerosis:

Duration of illness	MS patients N = 40
Mean ± SE.	5.26 ± 0.57
Median (Min. – Max.)	5.0 (0.50 – 19.0)

Min.: Minimum, Max.: Maximum, SE: Standard Error.

Table 3. Medications used in the studied patients with relapsing remitting multiple sclerosis:

Medication	MS patients N = 40	
	No.	%
No medication	2	5.0
Dimethyl Fumerate	3	7.5
Fingolimod	19	47.5
Interferon b 1a	7	17.5
Interferon b 1b	1	2.5
Natalizumab	1	2.5
Ocrelizumab	1	2.5
Rituximab	5	12.5
Teriflunamide	1	2.5

Table 4. The Expanded Disability Status Scale in the studied patients with relapsing remitting multiple sclerosis:

EDSS	MS patients N = 40		
	Mean \pm SE.	Median	Min. – Max.
	1.91 \pm 0.30	1.50	0.0 – 6.0
Visual	0.18 \pm 0.07	0.0	0.0 – 2.0
Brainstem	0.0 \pm 0.0	0.0	0.0 – 0.0
Cerebellar	0.13 \pm 0.06	0.0	0.0 – 2.0
Sensory	0.33 \pm 0.08	0.0	0.0 – 2.0
Sphincter	0.50 \pm 0.08	0.50	0.0 – 1.0
Mental	0.63 \pm 0.11	1.0	0.0 – 2.0
Pyramidal	0.95 \pm 0.22	2.0	0.0 – 4.0
Mild disability (0–2.5)		34 (85%)	
Moderate disability (3.0–6.0)		6 (15%)	

Min.: Minimum, Max.: Maximum, SE.: Standard Error

Table 5. The physical health composite score and its subscales of the multiple sclerosis quality of life 54 questionnaire (MSQOL-54) in the studied patients with relapsing remitting multiple sclerosis :

Physical composite score of the MSQOL-54 (PCS)	MS patients N = 40		Max score
	Mean \pm SE.	Median (Min. – Max.)	
	50.28 \pm 3.47	45.85 (8.80 – 100.0)	100.0
Physical function	7.88 \pm 0.87	8.50 (0.0 – 17.0)	17.0
Role limitation due to physical problem	3.0 \pm 0.75	0.0 (0.0 – 12.0)	12.0
Pain	5.81 \pm 0.51	5.31 (0.0 – 11.0)	11.0
Energy	5.72 \pm 0.41	5.76 (1.44 – 12.0)	12.0
Health perception	8.05 \pm 0.51	7.65 (2.55 – 17.0)	17.0
Social function	7.48 \pm 0.47	7.99 (1.99 – 12.0)	12.0
Sexual function	6.70 \pm 0.40	8.0 (0.0 – 8.0)	8.0
Health distress due to physical problem	5.57 \pm 0.50	4.40 (0.0 – 11.0)	11.0

Min.: Minimum, Max.: Maximum, SE.: Standard Error

Table 6. The mental health composite score and its subscales of the multiple sclerosis quality of life 54 questionnaire (MSQOL-54) in the studied patients with relapsing remitting multiple sclerosis:

Mental composite of the MSQOL-54	MS patients N = 40		Max score
	Mean \pm SE.	Median (Min. – Max.)	
	46.42 \pm 3.36	39.3 (16.81 – 100.0)	100.0
Cognitive function	5.44 \pm 0.56	5.25 (0.0 – 15.0)	15.0
Health distress due to emotional problems	7.09 \pm 0.64	5.60 (0.0 – 14.0)	14.0
Role limitation due to emotional problems	10.0 \pm 1.85	0.0 (0.0 – 24.0)	24.0
Emotional well being	13.57 \pm 1.05	12.76 (1.16 – 29.0)	29.0
Overall quality of life	11.19 \pm 3.15	10.7 (4.5 – 18.0)	18.0

Min.: Minimum, Max.: Maximum, SE.: Standard Error, U: Mann-Whitney,

Table 7. Comparison between the studied patients with relapsing remitting multiple sclerosis and control group regarding The Pittsburgh Sleep Quality Index (PSQI):

PSQI	MS N = 40	patients	Control N = 40	Test	P
Global sleep index					
Mean ± SE.	7.40 ± 0.66		5.98 ± 0.54	U=	0.130
Median (Min. – Max.)	8.0 (0.0 – 17.0)		6.0 (1.0 – 16.0)	643.5	
Good sleepers <5	10	25.0%	13	32.5%	X²=0.549
Bad sleepers ≥5	30	75%	27	67.5%	0.459
Subjective sleep quality					
Mean ± SE.	1.53 ± 0.15		1.23 ± 0.15	U=	0.202
Median (Min. – Max.)	1.0 (0.0 – 3.0)		1.0 (0.0 – 3.0)	674.5	
Sleep latency					
Mean ± SE.	1.70 ± 0.17		1.55 ± 0.19	U=	0.346
Median (Min. – Max.)	2.0 (0.0 – 3.0)		1.50 (0.0 – 6.0)	705.5	
Sleep duration					
Mean ± SE.	0.98 ± 0.16		0.85 ± 0.15	U=	0.603
Median (Min. – Max.)	1.0 (0.0 – 3.0)		1.0 (0.0 – 3.0)	749.5	
Sleep efficiency					
Mean ± SE.	0.58 ± 0.15		0.20 ± 0.09	U=	0.031*
Median (Min. – Max.)	0.0 (0.0 – 3.0)		0.0 (0.0 – 3.0)	630.5	
Sleep disturbance					
Mean ± SE.	0.88 ± 0.11		1.13 ± 0.11	U=	0.116
Median (Min. – Max.)	1.0 (0.0 – 2.0)		1.0 (0.0 – 2.0)	950.0	
Sleep medication					
Mean ± SE.	0.30 ± 0.12		0.30 ± 0.13	U=	0.609
Median (Min. – Max.)	0.0 (0.0 – 3.0)		0.0 (0.0 – 3.0)	767.0	
Daytime dysfunction					
Mean ± SE.	0.95 ± 0.13		0.73 ± 0.13	U=	0.130
Median (Min. – Max.)	1.0 (0.0 – 3.0)		1.0 (0.0 – 3.0)	656.0	

Min.: Minimum, Max.: Maximum, SE.: Standard Error, U: Mann-Whitney, *, significant, p <0.05; ** high significant, p<0.01; *** very high significant, p<0.001.

Discussion:

Multiple sclerosis (MS) is a chronic autoimmune central nervous disease (CNS) characterized by inflammation, demyelination, gliosis and neuronal loss. Pathological perivascular lymphocytic infiltrates and macrophages produce degradation of myelin sheaths that surround neurons (18). Neurological symptoms vary depending on lesion location and can include visual impairment, numbness and tingling, focal weakness, bladder and bowel incontinence and cognitive dysfunction (19).

MS affects the quality of life of patients compared to the general population and those with other chronic diseases. Lower QOL interferes with a patient's ability to work, pursue leisurely activities and perform daily life tasks. Sleep disturbances are observed four times more frequently in MS patients compared to the general population. The estimated prevalence ranged from 25% to 62%, with a higher prevalence in women. Appropriate sleep regularity, duration and absence of sleep disturbances are important for healthy sleep and good quality of life (20).

The current study demonstrated that the mean age of MS patients was 35.23 years and the majority of MS patients (67.5%) were ≤ 40 years old and the remaining (32.5%) were >40 years old. The results also revealed that 72.5% of MS patients were females while 27.5% were males. There was no statistically significant difference between MS patients and control group regarding age, sex and marital status as shown in **table**

1. This could be explained by the fact that MS onset occurs typically in adults with peak age at onset between 20–40 years and there is a female predominance of up to 3:1 ratio (21). The present results also indicated that there was no significant difference between MS patients and the control group regarding education and occupation (**Table 1**).

The current study showed that the majority of the MS group (75.0%) lived in urban areas in contrast to the control group in which the majority (62.5%) lived in rural areas with a high statistical significant difference (**Table 1**). This is explained by the fact that living in urban areas increases the incidence for MS disease due to environmental factors such as lack of sun exposure and CO pollution, also urban living allows better access to health care facilities.

In the same line with the present results, a study had revealed that in a total of 1557 patients with MS; 81.7% were female, 18.3% were male, with a minimum of 18 years, maximum of 76 years and mean of 46 years (22).

The present results were also in same line with the study which identified 82 patients with MS, it revealed that the majority of cases were married and their education level was that of high school with no significant difference regarding marital status and education level as well as occupation (23) (**Table 1**).

The present study also revealed that the mean duration of illness was 5.26 ± 0.57

years, ranged from 0.5 to 19.0 years (**Table 2**). **Al-Abdullah et al. (23)** had similar results were obtained from the study done in 2018 as the mean disease duration was 4.07 ± 3.65 years. This could be due to the advances in recent years in the diagnosis and increasing awareness among medical staff and the community which lead to diagnosing the disease at a younger age.

The most commonly prescribed medication in the studied RRMS patients was the oral treatment Fingolimod (47.5%), followed by the injection of Interferon β 1a (17.5%) and Rituximab (12.5%). The remaining medications were used by fewer than five individuals in the sample (**Table 3**).

In a recent study in 2023 it was revealed that in cases with RRMS, an injection of interferon (IFN)- β 1b was the most commonly used drug among 107 of their patients, IFN- β 1a in 94 patients, and glatiramer acetate in 34 patients. The oral treatment includes teriflunomide in 14 patients, dimethyl fumarate in 86 patients, and fingolimod in nine patients (24).

The discrepancy with the current results may be due to the recommendation of the Egyptian society of MS which guide the prescription of medication according to the clinical picture, number of relapses among RRMS patients, availability and cost of the medications.

The mean EDSS score for the sample was 1.91 ± 0.30 . The median EDSS score was 1.50, and the range was from 0 to 6. The functional systems with the highest mean scores were pyramidal and mental, with scores of 0.95 ± 0.22 and

0.63 ± 0.11 , respectively, followed by sphincter, sensory, visual, cerebellar and brainstem with scores of 0.50 ± 0.08 , 0.33 ± 0.08 , 0.18 ± 0.07 , 0.13 ± 0.06 and 0.0 ± 0.0 respectively. The majority of MS patients in the sample 85% had mild disability, while the remaining 15% had moderate disability (**Table 4**).

In another Egyptian study it had been revealed that the mean EDSS score was 2.93 ± 1.86 SD with a range of 0.50 to 6.50, with the most common initial presenting symptom was motor symptoms related to the pyramidal system involvement which agreed with the results of this research, followed by sensory symptoms and optic nerve involvement (**25**).

The current study showed that the mean physical composite score for the MS patients was 50.28 ± 3.47 ; the subscales with the lowest mean scores were role limitation due to physical problem indicating that MS patients experience some limitations in their ability to perform daily physical activities, followed by health distress due to physical problems with scores 3.0 ± 0.75 and 5.57 ± 0.50 respectively. The subscales with the highest mean scores were physical function and health perception with scores 8.05 ± 0.51 and 7.88 ± 0.87 respectively. While the present study revealed that mean scores for energy, pain, sexual function and social function were 5.72 ± 0.41 , 5.81 ± 0.51 , 6.70 ± 0.40 and 7.48 ± 0.47 respectively. This indicates that individuals in the sample experience pain and fatigue related to their MS symptoms (**Table 5**).

As shown in **table 6**, MS patients had a mean mental composite score of 46.42 ± 3.36 ; the subscale with the lowest score was cognitive function with score 5.44 ± 0.56 indicating that MS patients have difficulty concentrating and thinking, troubles keeping their attention for long and troubles with their memory, followed by health distress due to emotional problems with score 7.09 ± 0.64 . The highest mean score was emotional wellbeing with score of 13.57 ± 1.05 . The role limitation due to emotional problem score was 10.0 ± 1.85 , indicating that the patients had cut down the time they spent on work of activities due to emotional problems.

In agreement with the current study a study done in 2021 revealed that the mean MSQOL-54 physical health composite score and mental health composite scale for the MS patients was 42.5 (SD: 17.2) and 58.3 (SD: 21.5), respectively (**26**).

Regarding the mean global sleep index score for the MS group in the present study was 7.40 ± 0.66 , which was insignificantly higher than the control group with a mean score 5.98 ± 0.54 . Most of MS patients (75%) were classified as poor sleeper which was insignificantly higher than the control group (67.5%) (**Table 7**).

This can be explained by the fact that the majority of the control group was students and medical staff with frequently changing sleeping hours which resulted in poor sleep quality. The most frequent causes of poor sleep in the studied group of MS patients are physical complaints such as

musculoskeletal pain and muscular spasticity. Nocturia and urgency lead to interrupted sleep with difficulty falling back into sleep again thus considered major contributing factors to the poor sleep quality (**table 7**).

Going hand in hand with the present research results, it was found that patients with MS showed a higher mean global sleep score than controls (8.6 versus 6.3), and 67.1% of the MS patients compared to 43.9% of the controls were poor sleepers (27). It was also in the same line with an Egyptian study done by **Abd Elsadek et al. (28)** who found that patients with RRMS showed a higher mean global sleep score than controls (6.3 versus 4.5) and Nineteen MS patients (76%) had poor sleep quality.

The present study revealed a significant difference between the two groups in terms of sleep efficiency which is defined as the percentage the number of hours slept divided by the numbers of hours spent in bed, with the MS group reporting a higher mean score (0.58 ± 0.15) compared to the control group (0.20 ± 0.09). There was no significant difference between the two studied groups regarding the subjective sleep quality, sleep latency, sleep duration, sleep disturbance, sleep medication, and daytime dysfunction (**Table 7**).

On the other hand, a study done by **Bøe Lunde et al. (27)** found that PSQI sleep onset latency was significantly higher (1.4 ± 1.1) among patients than controls (1.1 ± 1.1). Another study by **Buratti et al.** found that patients with MS showed a worse sleep quality, in terms of duration,

efficiency, and architecture compared to healthy subjects (29).

That is why early identification and treatment of modifiable risk factors affecting sleep quality in patients suffering from MS is mandatory, in order to improve sleep and quality of life in general.

Conclusion:

In conclusion, multiple sclerosis has negative impact on both physical and mental function. MS patients have limitations as regard physical and cognitive functions which, in addition to poor sleep quality, lead to low health related quality of life. We recommend conducting further research including different types of MS and correlating between duration of illness, number of relapses, medication used, quality of life and quality of sleep.

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To cite this article: Shewikar T. El Bakry, Shaimaa M. Kasem, Shorouk F. Abd-Elmaksoud, Ayatulla E. AbdElhameed. Quality of Life and Sleep Profile in Relapsing Remitting Multiple Sclerosis Patients. *BMFJ* 2024;41(2):93-105.