# The Correlation Between Daytime Sleepiness and Physical Fatigue in Multiple Sclerosis Patients

Original Article

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## ABSTRACT

**Background:** Multiple sclerosis (MS) is a chronic disease that affects the central nervous system and causes a variety of physical and mental disabilities. Several studies have found that comorbid neurologic disorders such as fatigue, migraine, seizure disorders, and sleep disorders are more common in MS patients than in the general population.

**Objective:** To investigate the relationship between daytime sleepiness and physical fatigue in patients with multiple sclerosis.

**Patients and Methods:** Forty relapsing-remitting RRMS patients of both sexes were recruited from the outpatient clinic of the Faculty of Physiotherapy as well as the Kasr Al-Ain Multiple Sclerosis Unit (KAMSU) at the Faculty of Medicine, Cairo University.

All patients were diagnosed and referred by a neurologist as clinically defined multiple sclerosis (CDMS) according to the revised McDonald's criteria. The study was applied during a period of remission. Patients were selected according to the following criteria: patient age ranged from 20 to 40 years, patients with EDSS no more than four, and patients who have not had relapses for the previous four months, and patients who have sufficient cognitive abilities to be able to understand and follow instructions with a score greater than 24 according to the Miniature Mental State Examination Scale (MMSE). Using Epworth sleepiness scale for daytime sleepiness and Fatigue severity scale for fatigue.

**Results:** There was no association between the Epworth score for drowsiness (ESS) and fatigue severity scale (FSS). Relation between patient's results and types of graft used showed no statistically significant differences between them. **Conclusion:** It is important to reveal that there is no relationship between daytime sleepiness and the severity or degree of physical fatigue.

Key Words: Daytime sleepiness, multiple sclerosis, physical fatigue.

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## **INTRODUCTION**

Multiple sclerosis (MS) is a chronic disease that affects the central nervous system leading to various physical and psychiatric disabilities [1]. Multiple sclerosis patients suffer from several neurological deficits and impairments as motor disorders, sensory disorders, communication disorders and cognitive deficits [2].

Comorbid neurologic problems such as tiredness, migraine, seizure disorders, and sleep disturbances have been found to be more common in MS patients than in the general population in several studies. Although the influence of these disorders on disability, survival, and quality of life is unclear, existing research suggests that several neurologic comorbidities exacerbate these outcomes [3].

Sleep disorders are common in MS patients compared to normal subjects [4]. Causes of poor sleeping in MS are

likely multifactorial and could be related to the adverse effects of immunotherapy and symptomatic medications as well as to other MS-associated symptoms, such as pain, anxiety and fatigue [5]. Patients with sleep disturbances are more likely to develop co-morbid illnesses such as heart disease, obesity, and diabetes, which can have a significant influence on long-term health [4].

Patients mainly suffer also from fatigue and inability to work especially chronic patients however those changes of physical abilities and easy fatigability are not directly related to the site of lesion rather than there is suggestion that immune system has a big role [6].

Fatigue in MS is defined as a "subjective lack of physical and/or mental energy that is seen by the individual or caregiver to interfere with regular and desired activities," according to the 1998 Multiple Sclerosis Council for Clinical Practice Guidelines [6].

**Epworth Sleepiness Scale (ESS):** - Is a self-reporting questionnaire that measures the general level of daytime sleepiness. It consists of eight elements that must be rated on a four-point scale (0–3). A higher score suggests more sleepiness during the day. Individuals with excessive daytime sleepiness can be identified using a cut-off score > 10. A score of >16 implies that you are sleepy all of the time [7].

The fatigue severity scale (FSS) is a self-report scale with nine items that assess the degree of physical fatigue over the previous week. For clinically relevant fatigue, most studies use a cut-off of 4.0 [8-11,1].

The FSS is a self-reported questionnaire that is straightforward to complete. It consists of nine statements that rank the intensity of the patient's tiredness symptoms in terms of their impact on motivation, exercise, physical function, and everyday activities [12].

This study aims to found if there is relationship between daytime sleepiness and fatigue in multiple sclerosis patients.

## **PATIENTS AND METHODS:**

#### **Participants:**

Forty patients with Remitting Relapsing (RRMS) from both sexes will be recruited from the outpatient clinic at Faculty of Physical Therapy as well as the Kasr Alainy Multiple Sclerosis Unit (KAMSU) at the Faculty of Medicine, Cairo University. All patients will be diagnosed and referred by a neurologist as clinically definite multiple sclerosis (CDMS) according to the revised MCDonald's criteria. The study will be applied during the remission period.

Patients will be selected according to the following criteria:

#### Inclusion criteria:

1. Patient's age ranges from 20-40 years.

2. Patient with EDSS not more than four.

3. Patients who have no relapses for the previous four months.

4. Patients with sufficient cognitive capacity, as measured by a score of more than 24 on the Mini-Mental State Examination scale (MMSE), who can understand and follow instructions.

## **Exclusion Criteria**:

The patients will be excluded if they have any of the followings:

1. Musculoskeletal disorders such Leg length difference, severe arthritis, knee surgery, total hip joint replacement, lower limb fractures less than 6 months or contractures of fixed deformity.

2. Cardiovascular disease or pulmonary disease (unstable angina, recent myocardial infarction within the last three months, congestive heart failure, severe heart valve malfunction, or unstable hypertension).

3. Auditory problems.

4. Cognitive impairment (a score less than 24 according to the MMSE).

5. Sensory impairment caused by other diseases except the MS such as diabetes mellitus.

6. Vestibular impairment and vertigo caused by other diseases except the MS such as peripheral vestibulopathy.

- 7. Basal ganglia affection.
- 8. Heavy Smoker.
- 9. Excessive caffeine intake specially before sleeping.

#### Procedures:

Study objectives and procedures were explained to each participant before starting the study, and a consent form was filled by each participant. Also, they were informed that data collected would be used for publication. Demographic data was collected from all participants regarding age, height in centimeter, weight in kilogram, and BMI.

We used for measurement of fatigue: Fatigue severity scale (Arabic version) [13].

We used for measurement of daytime sleepiness: Epworth Sleepiness Scale (Arabic versions).

**Epworth Sleepiness Scale (ESS):** - In this scale there is question asks if the person is likely to doze off while lying down to rest in the afternoon if the circumstances allow. Normal people, it was assumed, would, and drowsy people would almost surely doze off in that situation. Never doing so would imply an unusually low level of tiredness, as some insomniacs describe. Other scenarios were included in the questionnaire because it was assumed that only the sleepiest people would complete it. would dose off in them while sitting and talking to someone, even in a car while stopped in traffic for a few minutes [7].

The FSS is a self-report scale with nine items that assess the degree of physical fatigue over the previous week. For clinically relevant fatigue, most studies use a cut-off of 4.0 [8-11,1].

The FSS is a straightforward self-report questionnaire. It consists of nine statements that assess the severity of the patient's tiredness symptoms in terms of how they affect motivation, exercise, physical function, and everyday activities [12].

## **Outcomes:**

This study aimed to found if there is correlation between daytime sleepiness and fatigue in multiple sclerosis patients.

#### STATISTICAL ANALYSIS:

This study used a bivariate correlational research design (Spearman rank correlation coefficient). The main purpose of this study was to investigate the relationship between daytime sleepiness and fatigue in patients with multiple sclerosis.

Statistical analysis was conducted using SPSS for windows, version 26 (SPSS, Inc., Chicago, IL). Prior to final analysis, data were checked for normality assumption, variance homogeneity, and the existence of extreme scores. This investigation was carried out as a prerequisite for parametric analysis of difference calculations. Preliminary assumption testing found that data for all measured variables was not normally distributed, as determined by the Shapiro-Wilk test ((p > 0.05)). According to Levene's test of variance homogeneity, there was homogeneity of variances (p > 0.05) and covariances (p > 0.05). As a result, non-parametric statistics were employed. Quantitative factors were expressed as mean

Table 1: Demographic	characteristics	of patients
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 $\pm$  standard deviation (X  $\pm$  SD) and qualitative variables as percent (%). The association between the tiredness severity scale and daytime drowsiness as measured by the Epworth Sleepiness Scale was investigated using the Spearman rank correlation coefficient. The alpha level was set at 0.05, and the correlation coefficients were reported as 0-0.1 = extremely low, 0.10-0.30 = low, 0.30-0.50 = moderate, 0.50-0.70 = high, 0.70-0.90 = extremely high, and 0.90-1.0 = strong.

#### **RESULTS:**

## General characteristics of participants

## - Demographic data

Forty patients (10 males and 30 females) were included in this study. The mean values of their age, height, weight and BMI were  $27.86 \pm 1.68$  years,  $174.13 \pm 11.59$  cm,  $86.86 \pm 13.52$  kg and  $28.42 \pm 1.33$  Kg/m<sup>2</sup> respectively. (Table 1).

#### - Gender distribution

As shown in (Table 2), the frequency distribution of gender in the study revealed that there were 10 males with percentage of 25 % and 30 females with percentage of 75%. (Table 2).

Correlation between Epworth sleepiness scale (ESS) & Fatigue severity scale (FSS).

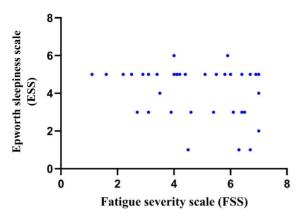
As shown in (Table 3) and (Fig. 1) the correlation between Epworth sleepiness scale (ESS) & Fatigue severity scale (FSS), there was no correlation between the two variables as (R= - 0.238 & p = 0.151).

	$\bar{x} \pm SD$	Minimum	Maximum	Std. Error
Age (years)	$27.86 \pm 1.68$	23	35	0.26
Height (cm)	$174.13 \pm 11.59$	153	188	1.69
Weight (kg)	$86.86 \pm 13.52$	65	106	1.99
BMI (Kg/m <sup>2</sup> )	$28.42 \pm 1.33$	26.20	29.90	0.20

 $\overline{x}$ : Mean MD : Mean Difference SD: Standard Deviation

Table 2: The frequency distribution of gender in both groups

		Gender			
	Male No (%)	Female No (%	)	Total	
Patients	10 (25 %)	30 (75 %)	2	40 (100 %)	
able 3: Correlation between Epworth	sleepiness scale (ESS) & Fati	que severity scale (FSS)			
	Mean ±		r R - Value	p- Value	
Epworth sleepiness scale (	Mean ±	SD Std Error	r R - Value - 0.238	<i>p- Value</i> 0.151	
Å	$\frac{Mean \pm 2}{ESS} = 3.92 \pm 2$	SD Std Error   1.42 0.22		<i>p- Value</i> 0.151	



**Fig. 1:** Correlation between Epworth sleepiness scale (ESS) & Fatigue severity scale (FSS)

#### DISCUSSION

This study discovered evidence that, while sleep deprivation is not associated with physical fatigue, so why this disagreement may come from? The answer of this question underlies in that there is weakness in this study due to the researcher include in his study peoples have different types of multiple sclerosis and didn't determine whether there is inflammatory process (active stage) or not, so if inflammation has a role in physical fatigue this will be confounder variable that may disturb the outcome variable.

There is evidence that inflammatory process has a significant impact on physical fatigue in multiple sclerosis patients was approved by the review article done by Karshikoff [14].

There is also another confounder variable that can disturb the outcome variable (Physical fatigue), this is the EDSS whereas the researcher included patients that have EDSS up to 6 and we know that EDSS has scores start from 0 to 10, so what is the issue?

To answer this question firstly remember that The EDSS is used in clinical studies to describe disease progression in MS patients and to assess the efficacy of treatment therapies. It consists of an ordinal rating system with 0.5 increments ranging from 0 (normal neurological condition) to 10 (death due to MS). The lower scale values of the EDSS measure impairments based on neurological testing, whereas the upper range of the scale (> EDSS 6) measures handicaps of MS patients. The EDSS 4-6 scale is highly influenced by factors of walking ability [15]. So, there were patients in this study that lie in this range (4-6) so there was variety in patient ability to walk with or without assistant that has a significant impact on physical fatigue according to study done by Ghajarzadeh [16] that conclude patients with a higher EDSS experience more weariness than those with a lower EDSS.

In my study I included patients that have EDSS not more than 4 to eliminate the factor of physical disability especially the walking task from contributing to physical fatigue. Also, I included only patients with remission-relapse type in remission period to prevent the inflammatory process from contributing also to physical fatigue.

## LIMITATIONS OF THE STUDY

This study needs to use more objective measurement tools for assessment of fatigue and daytime sleepiness. Also, to be done on large sample.

#### CONCLUSION

It is very important also to reveal that there is no relationship between daytime sleepiness and the severity or degree of physical fatigue.

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## **CONFLICT OF INTEREST**

There are no conflicts of interest.

## REFERENCES

- Braley, T. J., Kratz, A. L., Kaplish, N., & Chervin, R. D. (2016). Sleep and cognitive function in multiple sclerosis. Sleep, 39(8). https://doi. org/10.5665/sleep.6012.
- Susan. E. B., Francois B., Theodore R. B., Marcia F., Frederick W. F., Rock H., Bianca W. G., (2014). Complex Symptoms and mobility in Multiple sclerosis. International Journal of MS Care, 16, 40.
- Marrie, R. A., Reider, N., Cohen, J., Trojano, M., Sorensen, P. S., Cutter, G., ... Stuve, O. (2015). A systematic review of the incidence and prevalence of sleep disorders and seizure disorders in multiple sclerosis. Multiple Sclerosis Journal, 21(3), 342– 349. https://doi.org/10.1177/1352458514564486
- Bøe Lunde, H. M., Aae, T. F., Indrevåg, W., Aarseth, J., Bjorvatn, B., Myhr, K. M., & Bø, L. (2012). Poor Sleep in Patients with Multiple Sclerosis. PLoS ONE, 7(11), 7–11. https://doi. org/10.1371/journal.pone.0049996.

- Veauthier, C., Radbruch, H., Gaede, G., Pfueller, C. F., Dörr, J., Bellmann-Strobl, J., ... & Sieb, J. P. (2011). Fatigue in multiple sclerosis is closely related to sleep disorders: a polysomnographic cross-sectional study. Multiple Sclerosis Journal, 17(5), 613-622.
- Ormstad, H., Simonsen, C. S., Broch, L., Maes, M., Anderson, G., & Celius, E. (2020). Chronic fatigue and depression due to multiple sclerosis: Immune-inflammatory pathways, tryptophan catabolites and the gut-brain axis as possible shared pathways. Multiple Sclerosis and Related Disorders, 102533.
- Furtado, F., Gonc, S. B., Lopes, I., & Fornercordero, A. (2016). Chronic Low Quality Sleep Impairs Postural Control in Healthy Adults. PLoS ONE, 1–13. https://doi.org/10.1371/journal. pone.0163310.
- Fisk, J. D., Pontefract, A., Ritvo, P. G., Archibald, C. J., & Murray, T. J. (1994). The impact of fatigue on patients with multiple sclerosis. Canadian Journal of Neurological Sciences, 21(1), 9-14.
- Krupp, L. B., LaRocca, N. G., Muir-Nash, J., & Steinberg, A. D. (1989). The fatigue severity scale: application to patients with multiple sclerosis and systemic lupus erythematosus. Archives of neurology, 46(10), 1121-1123.
- Valko, P. O., Bassetti, C. L., Bloch, K. E., Held, U., & Baumann, C. R. (2008). Validation of the fatigue severity scale in a Swiss cohort. Sleep, 31(11), 1601-1607.

- Gavrilov, Y. V., Shkilnyuk, G. G., Valko, P. O., Stolyarov, I. D., Ivashkova, E. V., Ilves, A. G., ... & Valko, Y. (2018). Validation of the Russian version of the Fatigue Impact Scale and Fatigue Severity Scale in multiple sclerosis patients. Acta Neurologica Scandinavica, 138(5), 408-416.
- Al-Sobayel, H. I., Al-Hugail, H. A., AlSaif, R. M., Albawardi, N. M., Alnahdi, A. H., Daif, A. M., & Al-Arfaj, H. F. (2016). Validation of an Arabic version of fatigue severity scale. Saudi medical journal, 37(1), 73.
- 13. Multiple Sclerosis Council for Clinical Practice Guidelines. (1998). Fatigue and Multiple Sclerosis: Evidence-based Management.
- Karshikoff, B., Sundelin, T., & Lasselin, J. (2017). Role of inflammation in human fatigue: relevance of multidimensional assessments and potential neuronal mechanisms. Frontiers in immunology, 8, 21.
- 15. Meyer-Moock, S., Feng, Y. S., Maeurer, M., Dippel, F. W., & Kohlmann, T. (2014). Systematic literature review and validity evaluation of the Expanded Disability Status Scale (EDSS) and the Multiple Sclerosis Functional Composite (MSFC) in patients with multiple sclerosis. BMC neurology, 14(1), 1-10.
- Ghajarzadeh, M., Jalilian, R., Eskandari, G., Sahraian, M. A., Azimi, A., & Mohammadifar, M. (2013). Fatigue in multiple sclerosis: relationship with disease duration, physical disability, disease pattern, age and sex. Acta Neurologica Belgica, 113(4), 411-414.