



## Psychiatric Comorbidities among University Students with Relapsing-Remitting Multiple Sclerosis

Wessam Mustafa <sup>a≡</sup>, Samer Salama <sup>a∞\*</sup>, Mohamed Jawad <sup>b#</sup>, Ibrahim Elkalla <sup>c†</sup>,  
Shady El Rashedy <sup>d‡</sup> and Mohammed Abbas <sup>a‡</sup>

<sup>a</sup> Department of Neurology, Mansoura University, Mansoura, Egypt.

<sup>b</sup> Mansoura University, Mansoura, Egypt.

<sup>c</sup> Department of Psychiatry, Mansoura University, Mansoura, Egypt.

<sup>d</sup> Ministry of Health, Egypt.

### Authors' contributions

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

### Article Information

DOI: 10.9734/INDJ/2022/v17i130192

### Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/84827>

Original Research Article

Received 03 January 2022

Accepted 19 February 2022

Published 20 February 2022

### ABSTRACT

**Background:** Multiple sclerosis (MS) has been reported to be associated with psychological manifestations like depression, anxiety, and depression. Its presence in university students may impact their academic performance. As the relapsing-remitting type (RRMS) is the commonest MS type, we conducted this study to evaluate the prevalence and severity of the previous psychological manifestations in University students diagnosed with RRMS. The impact of MS on their academic performance was also assessed.

**Patients and Methods:** This case-control study included 65 students diagnosed with RRMS in addition to the same number of healthy controls. Psychological manifestations were evaluated via the Arabic form of DASS (depression, anxiety, and stress score), while academic performance was assessed via the GPA (grade point average).

<sup>≡</sup> Associate Professor of Neurology;

<sup>∞</sup> Assistant Lecturer of Neurology;

<sup>#</sup> Inter Doctor;

<sup>†</sup> Lecturer of Psychiatry;

<sup>‡</sup> Consultant of Neurology;

<sup>‡</sup> Lecturer of Neurology;

\*Corresponding author: E-mail: [samer\\_salama@yahoo.com](mailto:samer_salama@yahoo.com), [samer\\_salama@mans.edu.eg](mailto:samer_salama@mans.edu.eg);

**Results:** Patient criteria, including age and gender, were statistically comparable between the two groups. The three components of DASS expressed significantly higher values in cases compared to controls, indicating increased prevalence and severity of psychological issues in association with RRMS. MS was associated with a significant decline in the student's academic performance as had median values of 1 and 3 in cases and controls, respectively.

**Conclusion:** MS is associated with a significant increase in both prevalence and severity of depression, anxiety, and depression compared to the normal healthy population. MS also has a significant negative impact on the academic performance of these students.

*Keywords: Depression; multiple sclerosis; academic performance.*

## 1. INTRODUCTION

Multiple sclerosis (MS) represents a chronic inflammatory autoimmune central nervous system disease, which is characterized by neuronal demyelination, gliosis, and neuronal loss [1,2]. In 2016, a previous Egyptian study, including data from the Red Sea Governorate, reported that the prevalence of MS was 13.7/100,000 [3]. MS patients represent about 0.5% - 3.7% of patients attending the Egyptian outpatient neurology clinics [4].

The clinical spectrum of this clinical entity is widely variable. It can include numbness, tingling, focal motor weakness, visual impairment, cognitive impairment, and bladder or fecal incontinence [5]. MS can be classified into seven categories based on the disease course. This includes the relapsing-remitting, primary progressive, secondary progressive, progressive relapsing, clinically isolated syndrome, fulminant, and benign types [6,7].

Relapsing-remitting MS (RRMS), the most frequent type of MS at the time of diagnosis, is characterized by clearly defined relapses (attacks or exacerbations) followed by partial or complete recovery [8,9].

Psychological troubles represent one of the major problems encountered in MS patients [10-12]. Previous reports have confirmed that MS is associated with an increased risk of depression, stress, and anxiety [13,14]. Each of these psychiatric symptoms is a negative load on MS patients and could negatively affect their quality of life [15].

Cognitive impairment is another problem that is frequently encountered in such patients, as about 65% of them express a marked decrease in mental functions [16,17]. Multiple sclerosis has been shown to have a negative impact on academic performance in children and adolescents. MS has been shown to have a

negative impact on the academic performance of both children and adolescents [18].

According to our research, there is a clear paucity of Egyptian studies handling the prevalence of these psychological manifestations in university students with RRMS. Also, the effect of MS on the academic performance in such a population is lacking. This was a good motive for us to conduct this study.

## 2. PATIENTS AND METHODS

The current prospective case-control study was conducted at the University Hospitals after approval from the local ethical committee and Institutional Review Board of our medical school. The study was conducted over a period of six months, from June 2021 till December 2021. Based on our medical records at University Students Hospital, there are 65 students diagnosed with RRMS and registered to the neurology clinic database. Their diagnosis has been established via history taking, clinical assessment, magnetic resonance imaging, and McDonald's diagnostic criteria [19]. According to our hospital protocol, regular follow-up visits are scheduled for these patients for frequent examination and treatment monitoring.

After gaining written consent from these 65 patients, their depression, anxiety, stress, as well as academic performance were assessed and compared with the data of other age and sex-matched healthy 65 university students who presented to the same hospital during the same period for Covid-19 vaccination. Of course, all controls accepted to participate in our study.

We used the Arabic validation of DASS-21 (depression, anxiety, and stress score) to assess the former three items. This score has 21 items (seven questions for each component, and each question is graded from 0 to 3) [20]. The score of each component is multiplied by two to compare the net result with the normal DASS. According

to that net result, each component was graded into normal, mild, moderate, severe, and extremely severe. This was categorized as follows; for the depression component (normal for 0 - 9, mild for 10 - 13, moderate for 14 - 20, severe for 21 - 27, and extremely severe for 28 or more), for the anxiety component (normal for 0 - 7, mild for 8 - 9, moderate for 10 - 14, severe for 15 - 19, and extremely severe for 20 or more), and for the stress component (normal for 0 - 14, mild for 15 - 18, moderate for 19 - 25, severe for 26 - 33, and extremely severe for 34 or more) [13].

The academic performance of the included participants was graded according to the GPA (grade point average) on a 4.0 scale. The GPA score ranged between 0 and 4 according to the reported numeric grade as follows; 4 for 90 - 100, 3 for 80 - 89, 2 for 70 - 79, a for 60 - 69, and 0 for below 60.

For data tabulation and analysis, the Statistical Package for Social Science for Windows was

used. The median and range were used to express quantitative data. The independent samples t-test was developed to compare two independent sets of parametric quantitative data. Numbers and relative percentages were used to express qualitative data. To compare two independent groups of qualitative data, the chi-square or Fischer's exact test was used. Significant was defined as a p-value of less than 0.05.

### 3. RESULTS

In the cases and control groups, the average age of the participants was 23 and 22 years, respectively. Female predominance was evident in both groups, as they constituted 73.85% and 76.92% of subjects in the same groups, respectively. Both age and gender showed no significant difference between cases and controls. In the cases group, disease duration ranged between two and seven years (median = 5 years). Table 1 illustrates the previous data.

**Table 1. Demographics of the study participants**

Variable	Cases (n = 65)	Controls (n = 65)	P value
Age (years)	23 (20 - 25)	22 (20 - 25)	0.065
<b>Gender</b>			
-Male	48 (73.85%)	50 (76.92%)	0.684
-Female	17 (26.15%)	15 (23.08%)	
Disease duration	5 (2 - 7)		

**Table 2. DASS among the study participants**

Variable	Cases (n = 65)	Controls (n = 65)	P value
Depression score	15 (0 - 32)	6 (0 - 29)	< 0.001*
Anxiety score	11 (1 - 23)	5 (0 - 22)	< 0.001*
Stress score	20 (1 - 38)	10 (0 - 35)	< 0.001*
<b>Depression category</b>			
-No	17 (26.15%)	54 (83.08%)	< 0.001*
-Mild	12 (18.46%)	5 (7.69%)	
-Moderate	15 (23.08%)	2 (3.08%)	
-Severe	12 (18.46%)	3 (4.62%)	
-Very severe	9 (13.85%)	1 (1.53%)	
<b>Anxiety category</b>			
-No	18 (27.69%)	46 (70.77%)	
-Mild	13 (20%)	9 (13.85%)	
-Moderate	14 (21.54%)	4 (6.15%)	< 0.001*
-Severe	11 (16.92%)	4 (6.15%)	
-Very severe	9 (13.85%)	2 (3.08%)	
<b>Stress category</b>			
-No	20 (30.77%)	42 (64.62%)	
-Mild	12 (18.46%)	15 (23.08%)	
-Moderate	15 (23.08%)	4 (6.15%)	< 0.001*
-Severe	11 (16.92%)	3 (4.62%)	
-Very severe	7 (10.77%)	1 (1.53%)	

**Table 3. Academic performance in the study participants**

Variable	Cases (n = 65)	Controls (n = 65)	P value
GPA	1 (0 – 3)	3 (0 – 4)	< 0.001*
<b>GPA category</b>			
4	0 (0%)	4 (6.15%)	
3	9 (13.85%)	32 (49.23%)	
2	21 (32.31%)	18 (27.69%)	< 0.001*
1	28 (43.08%)	9 (13.85%)	
0	7 (10.77%)	2 (3.08%)	

As shown in Table 2, the three components of DASS showed a significant increase in cases compared to controls ( $p < 0.001$ ). Depression score had median values of 15 and 6, while anxiety score had median values of 11 and 5 in cases and controls, respectively. In addition, the stress score had median values of 20 and 10 in the same groups, respectively. Furthermore, the prevalence and severity of these psychological comorbidities showed a significant increase in cases compared to controls.

It was evident that MS was associated with a significant decline in the student's academic performance, as illustrated in Table 3, via the GPA. It had median values of 1 and 3 in cases and controls, respectively ( $p < 0.001$ ).

#### 4. DISCUSSION

This study was conducted to estimate the prevalence and severity of depression, anxiety, and depression among university students with RRMS. Starting with controls, the three psychological symptoms were present in 16.92%, 29.23%, and 35.38% of them, respectively. One should also notice that the mild form of each symptom was the most prevalent severity in the control group.

The presence of depression, anxiety, and stress among controls could be explained by several factors; university students are often exposed to geographic challenges, academic stress, and financial problems. Additionally, this age group represents a transient period between adolescence and adulthood, through which the individual is subjected to endocrine changes, identity development as well as emotional changes [21]. This makes this specific age group at higher risk for having depression [22]. In addition, the Covid-19 outbreak had a negative impact on the mental health of this population, as proved by many studies [23,24].

Multiple studies have reported that the prevalence of depression among university

students varies between 4% and 79.2% [21,25], and our prevalence rate lies within the previous range. A previous Iranian study reported that the prevalence of such a psychiatric disorder was 33% [26], whereas different American studies reported a prevalence between 33% and 41% [27,28]. In addition, reports from different European countries showed that about 6.1% - 34.2% of their university students had depression [29,30].

Moreover, the previous literature reported that about 25% - 44% of university students suffer from anxiety [31-33], whereas psychological stress has been reported in about 27% - 53% of college students according to previous studies [34,35]. Our prevalence of both anxiety and stress lies within the previously reported ranges.

In the current study, the depression score showed a significant increase in cases compared to controls (15 vs. 6 respectively –  $p < 0.001$ ). RRMS was associated with a significant increase in the prevalence and severity of depression compared to controls. Only 26.15% of MS cases were free from depression compared to 83.08% of controls.

The presence of depression in MS cases could be explained by both psychological and biological factors. The unpredictability of the disease course, unknown prognosis, and lack of definitive treatment could be possible psychological factors. The biological component could be explained by the affection of certain brain regions by the disease itself with its inflammatory and degenerative nature. These areas include the temporal lobe, left arcuate fasciculus, and periventricular regions [36].

In line with our findings, Karimi and his associates reported that depression was present in 71.2% of the included patients diagnosed with MS (47.1% had moderate depression while 24.1% had severe depression) [13]. Patten et al. reported that up to 50% of MS patients could

develop depression, with a 2 or 3 times increased risk compared to the general population [37]. Other studies reported a lower prevalence of depression in such cases (30 – 40%) [38,39].

It's worth noting that severe depression is more common in MS (15.7%) than other chronic diseases (9.1%) and the general population (7.4%). This should also imply that the disease itself has a direct impact on the development of depression [40,41].

Our findings showed a significant increase in the prevalence of anxiety in cases compared to controls ( $p < 0.001$ ). Only 27.69% of cases were free from anxiety compared to 70.77% of controls. The anxiety component of DASS had median values of 11 and 5 in cases and controls, respectively.

As MS is a chronic disease, fear of progression itself may make the patient anxious, and this has been found to be the main source of anxiety in patients with chronic diseases like cancer and diabetes mellitus [42,43]. Besides, the fear from relapse in RRMS might also contribute to patient anxiety. Patients usually do not know the time, severity, duration, or consequences of the next relapse [44].

Karimi et al. confirmed our findings regarding the increased prevalence of anxiety in MS patients. Authors reported that moderate and severe anxiety were detected in 39.1% and 34.5% of MS patients [13].

In our study, the stress component of DASS had median values of 20 and 10 in the cases and control groups, respectively ( $p < 0.001$ ). In subjects with stress, the severity was markedly increased in cases compared to controls ( $p < 0.001$ ).

Some symptoms, which are not visible to the surrounding people, can cause MS patients to feel misunderstood by others, like fatigue and pain. These problems in daily life can lead to anxiety and impaired quality of life [45,46].

In 2020, Karimi and his colleagues reported that only 32.2% of the included MS patients were free from stress manifestations. Nevertheless, moderate and severe stress were encountered in 44.8% and 23% of MS patients, respectively [13]. Additionally, other studies demonstrated that MS

patients with higher levels of disability had higher stress intensity [46,47].

In the current study, it was evident that MS was associated with a significant decline in the student's academic performance. GPA had median values of 1 and 3 in cases and controls, respectively.

This could be attributed to multiple facts; first of all, impaired vision in MS patients negatively affects attention, reading, and writing [48]. In addition, learning and memory are negatively affected by the cognitive impairment associated with MS [49]. Furthermore, socialization problems also play a part in this problem. MS patients find some difficulty in learning social skills, as they feel different from their colleagues. MS patients often express physical symptoms like fatigue, and the presence of incontinence could exaggerate this problem of socialization [50].

In accordance with our findings, Sinay and his colleagues reported that school performance was poorer in MS patients compared to controls, and this significance was noticed even before developing MS manifestations. The poor performance was noticed in both language and math [51]. Additionally, about 39% of adolescents with MS discontinued their high school education, according to a previous report [52]. This implies the necessity of academic achievement assessment in MS patients.

There are certain limitations to our research. It consisted of a small group of patients drawn from a single facility. As a result, new research with a larger number of patients from various neurology facilities should be carried out in the near future.

## 5. CONCLUSION

When compared to a healthy population, MS is linked to a considerable increase in the prevalence and severity of depression, anxiety, and depression. MS has a severe negative impact on these students' academic performance.

## CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

1. Hauser SL, Cree BAC. Treatment of Multiple Sclerosis: A Review. *Am J Med.* 2020;133(12):1380-90.e2. Available: <https://doi.org/10.1016/j.amjmed.2020.05.049>
2. Dobson R, Giovannoni G. Multiple sclerosis - a review. *Eur J Neurol.* 2019; 26(1):27-40. Available: <https://doi.org/10.1111/ene.13819>.
3. El-Tallawy HN, Farghaly WM, Badry R, Metwally NA, Shehata GA, Rageh TA, et al. Prevalence of multiple sclerosis in Al Quseir city, Red Sea Governorate, Egypt. *Neuropsychiatr Dis Treat.* 2016;12:155-8. Available: <https://doi.org/10.2147/ndt.S87348>.
4. Hashem S. MS in Egypt. *Multiple Sclerosis and Related Disorders.* 2014;3(6):768-9. Available: <https://doi.org/10.1016/j.msard.2014.09.018>.
5. Thompson AJ, Baranzini SE, Geurts J, Hemmer B, Ciccarelli O. Multiple sclerosis. *Lancet.* 2018;391(10130):1622-36. Available: [https://doi.org/10.1016/s0140-6736\(18\)30481-1](https://doi.org/10.1016/s0140-6736(18)30481-1).
6. Baldassari LE, Paz Soldán MM. Natural History of Multiple Sclerosis. In: Piquet AL, Alvarez E, editors. *Neuroimmunology: Multiple Sclerosis, Autoimmune Neurology and Related Diseases.* Cham: Springer International Publishing. 2021;89-104.
7. Tafti D, Ehsan M, Xixis KL. Multiple Sclerosis. *StatPearls.* Treasure Island (FL): StatPearls Publishing Copyright © 2022, StatPearls Publishing LLC.; 2022.
8. Syed YY. Alemtuzumab: A Review in Relapsing Remitting Multiple Sclerosis. *Drugs.* 2021;81(1):157-68. Available: <https://doi.org/10.1007/s40265-020-01437-2>.
9. Deleu D, Canibaño B, Mesraoua B, Adeli G, Abdelmoneim MS, Ali Y, et al. Management of relapsing-remitting multiple sclerosis in Qatar: an expert consensus. *Curr Med Res Opin.* 2020; 36(2):251-60. Available: <https://doi.org/10.1080/03007995.2019.1669378>.
10. Giordano A, Granella F, Lugaresi A, Martinelli V, Trojano M, Confalonieri P, et al. Anxiety and depression in multiple sclerosis patients around diagnosis. *J Neurol Sci.* 2011;307(1-2):86-91. Available: <https://doi.org/10.1016/j.jns.2011.05.008>.
11. Tauil CB, Rocha-Lima AD, Ferrari BB, Silva FMD, Machado LA, Ramari C, et al. Depression and anxiety disorders in patients with multiple sclerosis: association with neurodegeneration and neurofilaments. *Braz J Med Biol Res.* 2021;54(3):e10428. Available: <https://doi.org/10.1590/1414-431x202010428>.
12. Tauil CB, Grippe TC, Dias RM, Dias-Carneiro RPC, Carneiro NM, Aguilar ACR, et al. Suicidal ideation, anxiety, and depression in patients with multiple sclerosis. *Arq Neuropsiquiatr.* 2018;76(5): 296-301. Available: <https://doi.org/10.1590/0004-282x20180036>.
13. Karimi S, Andayeshgar B, Khatony A. Prevalence of anxiety, depression, and stress in patients with multiple sclerosis in Kermanshah-Iran: a cross-sectional study. *BMC Psychiatry.* 2020;20(1):166. Available: <https://doi.org/10.1186/s12888-020-02579-z>.
14. Pham T, Jetté N, Bulloch AGM, Burton JM, Wiebe S, Patten SB. The prevalence of anxiety and associated factors in persons with multiple sclerosis. *Mult Scler Relat Disord.* 2018;19:35-9. Available: <https://doi.org/10.1016/j.msard.2017.11.003>.
15. Bhattacharjee S, Goldstone L, Ip Q, Warholak T. Depression Treatment among Adults with Multiple Sclerosis and Depression in Ambulatory Care Settings in the United States. *Mult Scler Int.* 2017; 2017:3175358. Available: <https://doi.org/10.1155/2017/3175358>.
16. Reuter F, Zaaoui W, Crespy L, Faivre A, Rico A, Malikova I, et al. Frequency of cognitive impairment dramatically increases during the first 5 years of

- multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2011;82(10):1157-9.  
Available:<https://doi.org/10.1136/jnnp.2010.213744>.
17. Amato MP, Zipoli V, Portaccio E. Cognitive changes in multiple sclerosis. *Expert Rev Neurother*. 2008;8(10):1585-96.  
Available:<https://doi.org/10.1586/14737175.8.10.1585>.
  18. Amato MP, Goretti B, Ghezzi A, Lori S, Zipoli V, Moiola L, et al. Cognitive and psychosocial features in childhood and juvenile MS: two-year follow-up. *Neurology*. 2010;75(13):1134-40.  
Available:<https://doi.org/10.1212/WNL.0b013e3181f4d821>.
  19. Thompson AJ, Banwell BL, Barkhof F, Carroll WM, Coetzee T, Comi G, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol*. 2018;17(2):162-73.  
Available:[https://doi.org/10.1016/s1474-4422\(17\)30470-2](https://doi.org/10.1016/s1474-4422(17)30470-2).
  20. Ali AM, Ahmed A, Sharaf A, Kawakami N, Abdeldayem SM, Green J. The Arabic Version of The Depression Anxiety Stress Scale-21: Cumulative scaling and discriminant-validation testing. *Asian J Psychiatr*. 2017;30:56-8.  
Available:<https://doi.org/10.1016/j.ajp.2017.07.018>.
  21. Ahmed G, Negash A, Kerebih H, Alemu D, Tesfaye Y. Prevalence and associated factors of depression among Jimma University students. A cross-sectional study. *Int J Ment Health Syst*. 2020;14:52.  
Available:<https://doi.org/10.1186/s13033-020-00384-5>.
  22. Hakami RM. Prevalence of Psychological Distress Among Undergraduate Students at Jazan University: A Cross-Sectional Study. *Saudi J Med Med Sci*. 2018;6(2):82-8.  
Available:[https://doi.org/10.4103/sjmms.sjmms\\_73\\_17](https://doi.org/10.4103/sjmms.sjmms_73_17).
  23. Son C, Hegde S, Smith A, Wang X, Sasangohar F. Effects of COVID-19 on College Students' Mental Health in the United States: Interview Survey Study. *J Med Internet Res*. 2020;22(9):e21279.  
Available:<https://doi.org/10.2196/21279>.
  24. Odriozola-González P, Planchuelo-Gómez Á, Irurtia MJ, de Luis-García R. Psychological effects of the COVID-19 outbreak and lockdown among students and workers of a Spanish university. *Psychiatry Res*. 2020;290:113108.  
Available:<https://doi.org/10.1016/j.psychres.2020.113108>.
  25. Chen L, Wang L, Qiu XH, Yang XX, Qiao ZX, Yang YJ, et al. Depression among Chinese university students: prevalence and socio-demographic correlates. *PLoS One*. 2013;8(3):e58379.  
Available:<https://doi.org/10.1371/journal.pone.0058379>.
  26. Sarokhani D, Delpisheh A, Veisani Y, Sarokhani MT, Manesh RE, Sayehmiri K. Prevalence of Depression among University Students: A Systematic Review and Meta-Analysis Study. *Depression Research and Treatment*. 2013;2013:373857.  
Available:<https://doi.org/10.1155/2013/373857>.
  27. Brenneisen Mayer F, Souza Santos I, Silveira PS, Itaquí Lopes MH, de Souza AR, Campos EP, et al. Factors associated to depression and anxiety in medical students: a multicenter study. *BMC Med Educ*. 2016;16(1):282.  
Available:<https://doi.org/10.1186/s12909-016-0791-1>.
  28. Peluso DL, Carleton RN, Asmundson GJG. Depression symptoms in Canadian psychology graduate students: Do research productivity, funding, and the academic advisory relationship play a role? *Canadian Journal of Behavioural Science / Revue Canadienne des Sciences du Comportement*. 2011;43(2):119-27.  
Available:<https://doi.org/10.1037/a0022624>.
  29. Sokratous S, Merkouris A, Middleton N, Karanikola M. The prevalence and socio-demographic correlates of depressive symptoms among Cypriot university students: a cross-sectional descriptive correlational study. *BMC Psychiatry*. 2014;14:235.  
Available:<https://doi.org/10.1186/s12888-014-0235-6>.
  30. Mojs E, Warchol-Biedermann K, Głowacka MD, Strzelecki W, Ziemska B, Marcinkowski JT. Are students prone to depression and suicidal thoughts? Assessment of the risk of depression in university students from rural and urban areas. *Ann Agric Environ Med*. 2012;19(4):770-4.
  31. Zhang L, Zhao S, Lin Q, Song M, Wu S, Zheng H. Algorithms to Predict Anxiety and Depression Among University Students in China After Analyzing Lifestyles and Sport

- Habits. *Neuropsychiatr Dis Treat.* 2021;17:2011-25.  
Available:<https://doi.org/10.2147/ndt.S315148>.
32. Eisenberg D, Gollust SE, Golberstein E, Hefner JL. Prevalence and correlates of depression, anxiety, and suicidality among university students. *Am J Orthopsychiatry.* 2007;77(4):534-42.  
Available:<https://doi.org/10.1037/0002-9432.77.4.534>.
  33. Saravanan C, Wilks R. Medical students' experience of and reaction to stress: the role of depression and anxiety. *Scientific World Journal.* 2014;2014:737382.  
Available:<https://doi.org/10.1155/2014/737382>.
  34. Iqbal S, Gupta S, Venkatarao E. Stress, anxiety and depression among medical undergraduate students and their socio-demographic correlates. *Indian J Med Res.* 2015;141(3):354-7.  
Available:<https://doi.org/10.4103/0971-5916.156571>.
  35. Bayram N, Bilgel N. The prevalence and socio-demographic correlations of depression, anxiety and stress among a group of university students. *Soc Psychiatry Psychiatr Epidemiol.* 2008;43(8):667-72.  
Available:<https://doi.org/10.1007/s00127-008-0345-x>.
  36. Hanna M, Strober LB. Anxiety and depression in Multiple Sclerosis (MS): Antecedents, consequences, and differential impact on well-being and quality of life. *Mult Scler Relat Disord.* 2020;44:102261.  
Available:<https://doi.org/10.1016/j.msard.2020.102261>.
  37. Patten SB, Marrie RA, Carta MG. Depression in multiple sclerosis. *Int Rev Psychiatry.* 2017;29(5):463-72.  
Available:<https://doi.org/10.1080/09540261.2017.1322555>.
  38. Boeschoten RE, Braamse AMJ, Beekman ATF, Cuijpers P, van Oppen P, Dekker J, et al. Prevalence of depression and anxiety in Multiple Sclerosis: A systematic review and meta-analysis. *J Neurol Sci.* 2017;372:331-41.  
Available:<https://doi.org/10.1016/j.jns.2016.11.067>.
  39. Marrie RA, Walld R, Bolton JM, Sareen J, Walker JR, Patten SB, et al. Estimating annual prevalence of depression and anxiety disorder in multiple sclerosis using administrative data. *BMC Res Notes.* 2017;10(1):619.  
Available:<https://doi.org/10.1186/s13104-017-2958-1>.
  40. Chwastiak L, Ehde DM, Gibbons LE, Sullivan M, Bowen JD, Kraft GH. Depressive symptoms and severity of illness in multiple sclerosis: epidemiologic study of a large community sample. *Am J Psychiatry.* 2002;159(11):1862-8.  
Available:<https://doi.org/10.1176/appi.ajp.159.11.1862>.
  41. Patten SB, Fridhandler S, Beck CA, Metz LM. Depressive symptoms in a treated multiple sclerosis cohort. *Mult Scler.* 2003;9(6):616-20.  
Available:<https://doi.org/10.1191/1352458503ms960oa>.
  42. Herschbach P, Berg P, Dankert A, Duran G, Engst-Hastreiter U, Waadt S, et al. Fear of progression in chronic diseases: psychometric properties of the Fear of Progression Questionnaire. *J Psychosom Res.* 2005;58(6):505-11.  
Available:<https://doi.org/10.1016/j.jpsychores.2005.02.007>.
  43. Herschbach P, Duran G, Waadt S, Zettler A, Amm C, Marten-Mittag B. Psychometric properties of the Questionnaire on Stress in Patients with Diabetes--Revised (QSD-R). *Health Psychol.* 1997;16(2):171-4.  
Available:<https://doi.org/10.1037//0278-6133.16.2.171>.
  44. Khatibi A, Moradi N, Rahbari N, Salehi T, Dehghani M. Development and Validation of Fear of Relapse Scale for Relapsing-Remitting Multiple Sclerosis: Understanding Stressors in Patients. *Front Psychiatry.* 2020;11:226.  
Available:<https://doi.org/10.3389/fpsy.2020.00226>.
  45. Labuz-Roszak B, Kubicka-Bączek K, Pierzchała K, Machowska-Majchrzak A, Skrzypek M. Fatigue and its association with sleep disorders, depressive symptoms and anxiety in patients with multiple sclerosis. *Neurol Neurochir Pol.* 2012;46(4):309-17.  
Available:<https://doi.org/10.5114/ninp.2012.30261>.
  46. Kołtuniuk A, Kazimierska-Zajac M, Cisek K, Chojdak-Łukasiewicz J. The Role of Stress Perception and Coping with Stress and the Quality of Life Among Multiple Sclerosis Patients. *Psychol Res Behav Manag.* 2021;14:805-15.



- Available:<https://doi.org/10.2147/prbm.S310664>.
47. Senders A, Bourdette D, Hanes D, Yadav V, Shinto L. Perceived stress in multiple sclerosis: the potential role of mindfulness in health and well-being. *J Evid Based Complementary Altern Med.* 2014;19(2): 104-11.  
Available:<https://doi.org/10.1177/2156587214523291>.
48. Hoff JM, Dhayalan M, Midelfart A, Tharaldsen AR, Bø L. Visual dysfunction in multiple sclerosis. *Tidsskr Nor Laegeforen.* 2019;139(11).  
Available:<https://doi.org/10.4045/tidsskr.18.0786>.
49. Benedict RHB, Amato MP, DeLuca J, Geurts JJG. Cognitive impairment in multiple sclerosis: clinical management, MRI, and therapeutic avenues. *Lancet Neurol.* 2020;19(10):860-71.  
Available:[https://doi.org/10.1016/s1474-4422\(20\)30277-5](https://doi.org/10.1016/s1474-4422(20)30277-5).
50. Giazkoulidou A, Messinis L, Nasios G. Cognitive functions and social cognition in multiple sclerosis: An overview. *Hell J Nucl Med.* 2019;22 Suppl:102-10
51. Sinay V, Perez Akly M, Zanga G, Ciardi C, Racosta JM. School performance as a marker of cognitive decline prior to diagnosis of multiple sclerosis. *Mult Scler.* 2015;21(7):945-52.  
Available:<https://doi.org/10.1177/1352458514554054>.
52. Vargas WS, Noble KG, Banwell B, De Jager P. The educational impact of childhood-onset multiple sclerosis: Why assessing academic achievement is imperative. *Mult Scler.* 2020;26(13): 1633-7.  
Available:<https://doi.org/10.1177/1352458520923946>.

© 2022 Mustafa et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

*Peer-review history:*  
*The peer review history for this paper can be accessed here:*  
<https://www.sdiarticle5.com/review-history/84827>