Psychiatric comorbidities Among university Students with Relapsing-**Remitting Multiple Sclerosis**

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).

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.

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.

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 oral 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.

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
Gender			
-Male	48 (73.85%)	50 (76.92%)	0.684
-Female	17 (26.15%)	15 (23.08%)	
Disease duration	5 (2 – 7)		

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.

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*
Depression			
category	17 (26.15%)	54 (83.08%)	< 0.001*
-No	12 (18.46%)	5 (7.69%)	

-Mild	15 (23.08%)	2 (3.08%)	
-Moderate	12 (18.46%)	3 (4.62%)	
-Severe	9 (13.85%)	1 (1.53%)	
-Very severe			
Anxiety category			
-No	18 (27.69%)	46 (70.77%)	
-Mild	13 (20%)	9 (13.85%)	< 0.001*
-Moderate	14 (21.54%)	4 (6.15%)	< 0.001**
-Severe	11 (16.92%)	4 (6.15%)	
-Very severe	9 (13.85%)	2 (3.08%)	
Stress category			
-No	20 (30.77%)	42 (64.62%)	
-Mild	12 (18.46%)	15 (23.08%)	. 0. 0014
-Moderate	15 (23.08%)	4 (6.15%)	< 0.001*
-Severe	11 (16.92%)	3 (4.62%)	
-Very severe	7 (10.77%)	1 (1.53%)	

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).

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*
GPA category			
4	0 (0%)	4 (6.15%)	< 0.001*
3	9 (13.85%)	32 (49.23%)	
2	21 (32.31%)	18 (27.69%)	
1	28 (43.08%)	9 (13.85%)	
0	7 (10.77%)	2 (3.08%)	

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.

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.

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