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Depression severity and its predictors among multiple sclerosis patients in Saudi Arabia: a cross-sectional study

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Abstract

Aim: To assess depression severity among multiple sclerosis (MS) patients.

Methods: Our survey was carried out among a sample of 598 MS patients (35.8% were males and 64.2% were females) from all different regions of KSA. A self-administered questionnaire was used for data collection. The Chi-square test was applied to examine the association between demographic factors, depression severity and level of disability.

Results: The mean age of patients at the time of diagnosis was 26.1 4 7.9 years (range 15 to 60 years). The mean duration of the disease was 6.6 4 4.8 years. More than quarter of patients (27.1%) were admitted during last year. Our results revealed that 9.7% of MS patients had a positive family history of MS, 27.8% of patients were also suffering from different chronic diseases. A large proportion of patients were receiving drugs for MS (e.g. interferon-β by 26.2% of patients). Among respondents, the majority (53.2%) were likely to have a mild level of disability and mild depression severity (30.8%), with a significant relationship between the level of disability and depression severity.

Conclusion: Severity of depression is mostly mild among MS patients, while only some have severe depression. Depression severity is significantly related to the level of MS patients' disability. Early support of MS patients, especially

newly diagnosed ones, is strongly advised in order to ensure a better quality of life. It is recommended to conduct a nationwide study to explore severity of depression among MS patients in Saudi Arabia.

Keywords: Depression, multiple sclerosis, Saudi Arabia

INTRODUCTION

Multiple sclerosis (MS) is a chronic autoimmune disease, with variable severity and evolution[1]. It is a disease that affects the central nervous system, especially the brain, optic nerves and the spinal cord[2,3]. Most commonly, MS evolves in relapses[4] during symptoms recur or new symptoms occur[5]. After a few years, the relapses leave sequelae[2] (i.e. permanent symptoms), which can become severe disability. The disease can affect many functions, e.g. movement control, sensory perception, memory, speech, *etc*.[6].

In term of MS epidemiology, there were few studies about the situation in Arabian Gulf countries. Bohlega *et al*.[7] reported an increasing incidence of MS, designating the Gulf region as a moderate to high-prevalence zone. The results from studies that focused on MS patients showed an increasing incidence of the pathology[7-9]. Prevalence of MS was estimated by Bohlega *et al*.[7] to be 40/100,000, who also stated that MS may be under-diagnosed.

Depression has been reported as one of the most common symptoms of MS with a risk of major depressive disorder of 13%-30% and about 50% of lifetime prevalence[10]. A direct physical link between depression and multiple sclerosis has been reported. By studying atrophied areas of the brain of MS patients and healthy people by magnetic resonance imaging, researchers could establish a concrete link. It seems that the hippocampus was of lower volume in patients with MS. By analyzing saliva samples, the researchers also noticed that the level of cortisol was particularly high in people with MS. Atrophy of the hippocampus and a high level of cortisol in the body are biological parameters frequently associated with major depressive episodes[11].

The importance of depression among MS patients is unquestionable[12], as this symptom influences the general health and the quality of life of MS patients[13]. Therefore, focusing on studying the association between MS and depression seems quite important.

This study aimed to assess the severity of depression and its predictors among multiple sclerosis patients in Saudi Arabia.

METHODS

This study followed a cross-sectional study which design to test the hypothesis that some patients' sociodemographic (e.g. age, gender, nationality, marital status, monthly income) and other characteristics (e.g. received treatment or grade of disability) may be associated with higher grades of severity of depression among MS patients.

Study area

During the period from November 2016 to May 2017, this study has been conducted by all geographical regions of Saudi Arabia (i.e. the Southern, Northern, Eastern, Western, and Middle regions).

Study population and sampling

According to the Saudi Arabian National Multiple Sclerosis Registry[14], there are 2313 MS patients in Saudi Arabia. Following a simple random sample, with a sampling fraction of 1/3, we invited 763 patients (coverage = 33%), only 598 MS patients participated in this study (response rate = 78.4%).

Data collection tool

This study used a pretested, pre-coded, self-administered questionnaire that included sociodemographic patients' characteristics and Patient Determined Disease Steps (PDDS) to quantify disability in MS patients as well as the Patient Health Questionnaire (PHQ) for quick assessment of depression score among MS patients.

The severity of the illness was measured using the PDDS[15]. It is a 9-item patient-administered measure of MS-related disability. Its content validity is indicated by the consistency of the items with the Expanded Disability Status Scale (EDSS)[16]. The PDDS scores range from 0 to 8, and can be used to categorize participants into 3 groups according to level of disability: a score of 0 to 2 indicates mild disability, represented by sensory symptoms but no limitations on walking; a score of 3 to 5 indicates moderate disability, represented by symptoms that interfere with daily activities, especially walking, and the need for a cane; and a score of 6 to 8 indicates severe disability, represented by the need for bilateral support, the use of a wheelchair, or being bed-ridden[17].

Learmonth *et al.*[15] reported that the PDDS had a strong correlation with the EDSS, supporting criterion aspects of validity. The magnitude and pattern of correlations between PDDS and EDSS scores were consistent between persons with mild and moderate-to-severe disability. Such results provide evidence for the validity of PDDS scores as a patient-reported outcome of disability in persons with MS.

Kroenke *et al.*[18] stated that the PHQ is a reliable and valid measure of depression severity. It scores each of the 9 DSM-IV criteria as "0" (not at all) to "3" (nearly every day).

Data collection method

The questionnaire sheets were personally distributed by researchers to all participant MS patients.

Data analysis

Collected data were analyzed by using the Statistical Package for Social Sciences (SPSS version 22). We used Chi-square test to examine the association between demographic factors, depression severity and level of disability. *P*-values less than 0.05 were considered statistically significant.

Ethical considerations

The ethical approval for conducting this study was obtained from Head of Research Ethics Committee (HA-06-B-001) in King Khalid University (REC) # 2016-08-23.

Prior to interviewing participants, the purpose of the study has been explained briefly and their consent has been obtained and they were informed that they have the full right to withdraw at any point of time. Participants' confidentiality and anonymity were fully secured. Finally, participants have been reassured that they have the right to withdraw at any point of time.

RESULTS

Demographics of the studied subjects

Participants' socio-demographic characteristics are shown in Table 1. Our study included 598 patients with MS. Males constituted 35.8% of patients. Patients' age ranged between 15 and 60 years with a mean age (± SD) of 32.4 ± 8.5 years. Most participants (87%) were Saudi. About two thirds (63.2%) had a Bachelor Degree, while 24.3% were secondary school educated. More than half of respondents (51.8%) were married and the monthly income of 43.5% was less than 3000 Saudi Riyals (SR).

Table 1. Demographic characteristics of the participants

Characteristics		Frequency	Percent (%)
Gender	Male	214	35.8
	Female	384	64.2
Marital status	Single	250	41.8
	Married	310	51.8
	Divorced	36	6.0
	Widower	2	0.3
Nationality	Saudi	520	87.0
	Non-Saudi	78	13.0
Educational level	Illiterate	4	0.7
	Primary	12	2.0
	Intermediate	28	4.7
	Secondary	140	23.4
	University	378	63.2
	Postgraduate	36	6.0
Monthly income	< 3000 SR	260	43.5
	3001-6000 SR	76	12.7
	6001-10,000 SR	130	21.7
	> 10,000 SR	132	22.1
Region	South	170	28.4
	Middle	150	25.1
	East	114	19.1
	North	28	4.7
	West	136	22.7

Clinical variables

Table 2 shows the distribution of participants by their clinical variables. The mean duration of the disease (± SD) was 6.6 ± 4.8 years. More than one-fourth of patients (27.1%) were admitted once during last year. Patients were diagnosed with MS at a mean age (± SD) of 26.1 ± 7.9 years. The great majority of respondents (90.3%) had no family history of MS. About the three-quarters of surveyed patients (74.2%) had no associated chronic diseases, while the rest was reported suffering from asthma (4.7%), hypertension (3%), depression (2.7%), and some of them were taking drugs such as interferon beta-1b (Betaferon) (26.2%), followed by interferon beta-1a (Rebif) (20.4%), Fingolimod (Gilenya) (19%). About one-fourth of patients (27.4%) have been diagnosed with depression before and 18.1% were taking anti-depressant drugs.

Table 3 shows that regarding the PDDS calculated score, more than half of patients (53.2%) were likely to have a mild disability, while 35.5% were likely to have a moderate disability and 11.4% to have a severe disability.

Based on the depression score (PHQ), Table 4 shows that almost one-third of patients (30.8%) were likely to have mild depression, 24.7% were likely to have moderate depression, 10.7% were likely to have severe depression, while 2.3% appeared to have no depression.

Relation between patients' sociodemographic factors and depression

Regardless of the type of depression, the prevalence of depression was significantly higher among women than men ($P < 0.001$). Prevalence of depression was significantly higher among patients aged 26-35 years ($P = 0.016$). The severity of depression did not differ significantly according to patients' marital status or nationality. Prevalence of depression differed significantly according to patients' educational level ($P < 0.001$), being higher among those with Bachelor Degree, followed by those with secondary qualification and lower among illiterate patients. Prevalence of depression was significantly higher among patients with the lowest income (< 3000 SR, $P = 0.001$) [Table 5].

Severity of depression among participants differed significantly according to their region ($P < 0.001$). Severe depression was highest among patients living in the northern region (28.6%).

Table 2. Distribution of respondents by clinical variables

Characteristics	Patients (*n* = 598)
Duration of the disease (years), mean ± SD (range)	6.6 ± 4.8 (0.3-30)
Number of admissions during the last year, *n* (%)	
0	234 (39.1)
1	162 (27.1)
2	90 (15.1)
3	42 (7)
4	16 (2.7)
5	16 (2.7)
> 5	38 (6.4)
Total	598 (100.0)
Patient age at time of diagnosis (years), mean ± SD (range)	26.1 ± 7.9 (0-56)
Number of attacks in the last 2 years, mean ± SD (range)	1.9 ± 2 (0-14)
Family history of MS, *n* (%)	
Yes	58 (9.7)
No	540 (90.3)
Chronic disease, *n* (%)	
No	442 (74.2)
DM	16 (2.7)
HTN	18 (3)
Asthma	28 (4.7)
Depression	16 (2.7)
Thyroid disease	18 (3)
SLE	2 (0.3)
Anti phospholipid syndrome	16 (2.7)
Behjet	0 (0.0)
Headache/migraine	16 (2.7)
Shogren syndrome	2 (0.3)
More than 1	38 (6.4)
Current drug, *n* (%)	
Interferon beta-1b (Betaferon)	146 (26.2)
Interferon beta-1a (Rebif)	114 (20.4)
Interferon beta-1a (Avonex)	102 (18.3)
Copaxone (Glatiramer)	0 (0.0)
Teriflunomide (Aubagio)	20 (3.6)
Dimethyl fumarate (Tecfidera)	18 (3.2)
Fingolimod (Gilenya)	106 (19)
Natalizumab (Tysabri)	46 (8.2)
Mitoxantrone	0 (0.0)
Rituximab (Rituxan)	4 (0.7)
Alemtuzumab (Lemetrada)	2 (0.4)
Have been diagnosed with depression before, *n* (%)	
Yes	164 (27.4)
No	434 (72.6)
Use of anti-depressant drugs, *n* (%)	
Yes	108 (18.1)
No	490 (81.9)

MS: multiple sclerosis; DM: diabetes mellitus; HTN: hypertension; SLE: systemic lupus erythematosus

Relation between patients' received medications and depression

The severity of depression differed significantly according to received medications ($P < 0.001$). All patients who received alemtuzumab had severe depression (2, 100%). Moreover, the highest percentages of moderately severe and severe depression were observed among those who received interferon beta-1a (21.1% and 14%, respectively) and dimethyl fumarate (DMF) (22.2% and 11.1%, respectively) [Table 6].

Relation between patients' level of disability and depression

There was a significant association between patients' level of disability and severity of depression ($P < 0.001$). It is to be noted that none of the patients with absent depression had a moderate or severe disability, while those with moderately severe or severe depression had their highest percentages of severe disability (35.3% and 23.5%, respectively) [Table 6].

Table 3. Distribution of participants by level of disability

Patient determined disease steps score	Frequency	Percent (%)
Mild (0-2)	318	53.2
Moderate (3-5)	212	35.5
Severe (6-8)	68	11.4
Total	598	100.0

Table 4. Distribution of participants by depression severity

Depression score and severity	Frequency	Percent (%)
No (0)	14	2.3
Minimal (1-4)	98	16.4
Mild (5-9)	184	30.8
Moderate (10-14)	148	24.7
Moderately severe (15-19)	90	15.1
Severe (20-27)	64	10.7
Total	598	100.0

DISCUSSION

Our study illustrated the severity MS disease among the surveyed patients using the PDDS score and the depression severity using the PHQ score. Accordingly, almost half of participants had a PDSS score of 3 or more (i.e. considered to have a moderate or severe disability, 35.5%, and 11.4%, respectively) and more than one-fourth of them were considered to have moderately severe or severe depression.

These findings are in accordance with those of Siegert and Abernethy[10], who reported that depression is one of the most frequently discovered psychiatric symptoms among MS patients. Moreover, Kister *et al.*[19] reported that the proportion of MS patients with PDDS score = 3 or more (i.e. moderate to severe disability) reached 50% after 15 years of disease and 75% after 45 years.

Our study showed that about one-third of participants were males. About half of patients were married and the monthly income of almost half of them (43.5%) was less than 3000 SR.

The female predilection observed among participants in the present study has been reported by Kingwell *et al.*[20], who stated that, in the majority of studies, the prevalence of MS was higher in women, with gender ratios ranging from 1.1 to 3. The high prevalence of MS-related disability among our patients may explain why only about half of them are married and almost half of them have low monthly income (i.e. less than 3000 SR).

Results of the present study revealed that prevalence of depression differed significantly with our patients' age and was significantly higher among women than men.

These findings are in accordance with those of Van de Velde *et al.*[21], who noted that depression is significantly associated with gender and age. Women typically have a two-fold higher risk of major depression compared to men. Moreover, Andrade *et al.*[22] reported that prevalence of major depression is significantly associated with younger age.

Findings of the present study revealed that severity of depression differed significantly according to patients' educational level, being higher among those with higher education and lower among less educated patients. Moreover, depression was significantly higher among patients with the lowest income (i.e. with monthly income < 3000 SR).

Similarly, Kessler and Bromet[23] reported that the poorest respondents in the WHO World Mental Health surveys which were carried out in the USA and several European countries, showed about twofold increased

Table 5. Severity of depression among multiple sclerosis patients according to their sociodemographic characteristics

Characteristics	Severity of depression, *n* (%)						*P* value
	Absent	Minimal	Mild	Moderate	Moderately severe	Severe	
Gender							< 0.001
Male	8 (3.7)	32 (15.0)	80 (37.4)	62 (29.0)	26 (12.1)	6 (2.8)	
Female	6 (1.6)	66 (17.2)	104 (27.1)	86 (22.4)	64 (16.7)	58 (15.1)	
Age groups							0.016
15-25 years	2 (1.4)	24 (17.4)	42 (30.4)	30 (21.7)	22 (15.9)	18 (13.0)	
26-35 years	8 (3.3)	40 (16.3)	82 (33.3)	62 (25.2)	34 (13.8)	20 (8.1)	
36-45 years	4 (2.3)	24 (13.8)	54 (31.0)	48 (27.6)	30 (17.2)	14 (8.0)	
> 45 years	0 (0.0)	10 (25.0)	6 (15.0)	8 (20.0)	4 (10.0)	12 (30.0)	
Marital status							0.585
Single	6 (2.4)	40 (16.0)	72 (28.8)	68 (27.2)	40 (16.0)	24 (9.6)	
Married	8 (2.9)	54 (17.4)	98 (31.6)	72 (23.2)	42 (13.5)	36 (11.6)	
Divorced	0 (0.0)	4 (11.1)	14 (38.9)	6 (16.7)	8 (22.2)	4 (11.1)	
Widow	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	0 (0.0)	0 (0.0)	
Nationality							0.340
Saudi	12 (2.3)	84 (16.2)	160 (30.8)	136 (26.2)	76 (14.6)	52 (10.0)	
Non-Saudi	2 (2.6)	14 (17.9)	24 (30.8)	12 (15.4)	14 (17.9)	12 (15.4)	
Education							< 0.001
Illiterate	0 (0.0)	0 (0.0)	2 (50.0)	0 (0.0)	0 (0.0)	2 (50.0)	
Primary	0 (0.0)	6 (50.0)	0 (0.0)	0 (0.0)	4 (33.3)	2 (16.7)	
Intermediate	0 (0.0)	10 (35.7)	2 (7.1)	8 (28.6)	6 (21.4)	2 (7.1)	
Secondary	0 (0.0)	20 (14.3)	46 (32.9)	26 (18.6)	28 (20.0)	20 (14.3)	
University	14 (3.7)	50 (13.2)	122 (32.3)	108 (28.6)	50 (13.2)	34 (9.0)	
Postgraduate	0 (0.0)	12 (33.3)	12 (33.3)	6 (16.7)	2 (5.6)	4 (11.1)	
Monthly income							< 0.001
< 3000 SR	0 (0.0)	32 (12.3)	60 (23.1)	74 (28.5)	52 (20.0)	42 (16.2)	
3001-6000 SR	2 (14.3)	16 (21.1)	22 (28.9)	12 (15.8)	16 (21.1)	8 (10.5)	
6001-10,000 SR	8 (57.1)	20 (15.4)	56 (43.1)	30 (23.1)	8 (6.2)	8 (6.5)	
> 10,000 SR	4 (28.6)	30 (22.7)	46 (34.8)	32 (24.2)	14 (10.6)	6 (4.5)	
Region							< 0.001
Southern	6 (3.5)	28 (16.5)	58 (34.1)	30 (17.6)	26 (15.3)	22 (12.9)	
Middle	4 (2.7)	38 (25.3)	42 (28.0)	38 (25.3)	22 (14.7)	6 (4.0)	
Eastern	4 (3.5)	20 (17.5)	28 (24.6)	28 (24.6)	20 (17.5)	14 (12.3)	
Northern	0 (0.0)	0 (0.0)	10 (35.7)	8 (28.6)	2 (7.1)	8 (28.6)	
Western	0 (0.0)	12 (8.8)	46 (33.8)	44 (32.4)	20 (14.7)	14 (10.3)	

SR: Saudi Riyals

odds of major depressive episodes compared with those in the highest income group. Moreover, in Japan and China (Shenzhen) the least educated had the lowest risk of depression.

The present study showed that severity of depression among MS patients differed significantly according to their region, with the highest percentage of severe depression among those living in the northern region.

These findings necessitate further studies to explore the reason for the significant differences in severity of depression among MS patients according to their location within Saudi Arabia.

Results of the present study showed that severity of depression differed significantly according to received medications. The patients in two cases who received alemtuzumab had severe depression, while the highest percentages of those with moderately severe and severe depression were among those who received interferon beta-1a and DMF.

The significant differences in severity of depression among our MS patients according to the received medication may be attributed to the depression-related side effects associated with those medications.

The current study revealed a significantly positive association between patients' level of disability and the severity of depression.

Table 6. Severity of depression among multiple sclerosis patients according to their received drugs and disability level

Variables	Severity of depression, *n* (%)						*P* value
	Absent	Minimal	Mild	Moderate	Moderately severe	Severe	
Drugs							< 0.001
Betaferon	8 (5.5)	28 (19.2)	44 (30.1)	32 (21.9)	22 (15.1)	12 (8.2)	
Rebif	2 (1.8)	18 (15.8)	30 (26.3)	24 (21.1)	24 (21.1)	16 (14.0)	
Avonex	0 (0.0)	24 (23.5)	28 (27.5)	20 (19.6)	16 (15.7)	14 (13.7)	
Aubagio	0 (0.0)	0 (0.0)	6 (30.0)	12 (60.0)	2 (10.0)	0 (0.0)	
Tecfidera	0 (0.0)	4 (22.2)	4 (22.2)	4 (22.2)	4 (22.2)	2 (11.1)	
Gilenya	4 (3.8)	10 (9.4)	44 (41.5)	22 (20.8)	14 (13.2)	12 (11.3)	
Tysabri	0 (0.0)	2 (4.3)	14 (30.4)	24 (52.2)	4 (8.7)	2 (4.3)	
Rituxan	0 (0.0)	0 (0.0)	2 (50.0)	2 (50.0)	0 (0.0)	0 (0.0)	
Lemetrada	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	
Disability level							< 0.001
Mild	14 (4.4)	78 (24.5)	98 (30.8)	76 (23.9)	38 (11.9)	14 (4.4)	
Moderate	0 (0.0)	16 (7.5)	74 (34.9)	60 (28.3)	28 (13.2)	34 (16.0)	
Severe	0 (0.0)	4 (5.9)	12 (17.6)	12 (17.6)	24 (35.3)	16 (23.5)	

The significant association between disability and depression has been emphasized by several studies. Noh *et al*.[24] noted that physical disability is significantly related to depressive symptoms. People with physical disability experience multiple risk factors for depressive symptoms, including stereotypic social and personal attitude, abuse, loss of roles, and stressors related to poverty, environmental barriers, and/or lack of access to appropriate health care. Hughes *et al*.[25] added that substantial evidence shows that people living with physical disabilities are at least three times more likely to experience depression compared to the general population.

In conclusion, the severity of depression is mostly mild among MS patients, while only some have severe depression. Depression severity is significantly related to the level of MS patients' disability. Early support of MS patients, especially newly diagnosed ones, is strongly advised in order to ensure a better quality of life. It is recommended to conduct a nationwide study to explore severity of depression among MS patients in Saudi Arabia.

DECLARATIONS

Authors' contributions

Conception: Alhazzani AA, Ogran H, Abuhawi OH, Al-Hanash AM
Design: Alhazzani AA, Alqahtani MS
Supervision: Alhazzani AA
Materials: Alqahtani MS, AlQahtany RA, Alfaifi AA, Asiri AA, Asiri MA,
Data collection and/or processing: Abuhawi OH, Asiri AY, Al-Hanash AM, AlQahtany RA, Alfaifi AA, Asiri AA
Analysis and/or interpretation: Alqahtani MS, Ogran H, Abuhawi OH, Al-Hanash AM, AlQahtany RA, Asiri AA, Asiri MA
Literature review: Ogran H, Asiri AY, Alfaifi AA, Asiri AA, Asiri MA
Manuscript writing: Alhazzani AA, Asiri AY, AlQahtani MS
Critical review: Alhazzani AA

Data source and availability

Corresponding author may be contacted for any data inquiries.

Financial support and sponsorship

None.

Conflicts of interest

There are no conflicts of interest.

Patient consent

Consent has been obtained from all participants prior to interviewing. Participants' confidentiality and anonymity were fully secured.

Ethics approval

The ethical approval for conducting this study was obtained from Head of Research Ethics Committee (HA-06-B-001) in King Khalid University (REC) # 2016-08-23.

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