

Prevalence of depression among Iranian patients with myasthenia gravis during 2017-2018

Received: 28 May 2020
Accepted: 03 Aug. 2020

Kiana Amani¹, Payam Sarraf¹, Alireza Abkhoo¹, Abbas Tafakhori¹, Farzad Fatehi¹, Sama Bitarafan¹, Elmira Agah¹, Mamak Shariat^{2,3}

¹ Iranian Center for Neurological Research, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran

² Fetal and Neonatal Research Center, Tehran University of Medical Sciences, Tehran, Iran

³ Breast Feeding Research Center, Tehran University of Medical Sciences, Tehran, Iran

Keywords

Myasthenia Gravis; Depression; Iran

Abstract

Background: Myasthenia gravis (MG) is a chronic neuromuscular disease, which physically and mentally affects the patient's life, with depression being one of the most important psychological complications in these patients. This study aims to investigate the prevalence of depression and its associated factors in a group of Iranian patients with MG.

Methods: This was a cross-sectional study in which consecutive patients diagnosed with MG who referred to two referral neuromuscular clinics affiliated to the Tehran University of Medical Sciences, Tehran, Iran, were evaluated for eligibility. Patients with a previously known psychiatric disorder and those with a family history of mental disorders were excluded. Eligible patients were interviewed and screened for depression through the administration of the Hamilton Depression Rating Scale (HDRS) and the Iranian version of Beck Depression Inventory-II (BDI-II).

Results: A total of 62 patients participated in this study. The total prevalence of depression according

to the HDRS and BDI-II scores was 64.5% and 53.2%, respectively. The mild depression was the most frequent level of depression based on the HDRS (33.9%) and BDI-II (22.6%) scores. None of the variables, including age, sex, duration of the disease, and dosages of prednisolone, pyridostigmine, and azathioprine, were correlated with the severity of depression. The number of academic years was the only variable associated with the lower HDRS score ($P = 0.037$).

Conclusion: Based on the current findings, depression was common among Iranian patients with MG. The severity of depressive symptoms was unrelated to age, sex, marital status, duration of the disease, the daily dosage of medications, and thymectomy status. Further investigations are needed to reveal the exact burden of depression in patients with MG and address the importance of preventive interventions for improving the quality of life (QOL) in these patients.

How to cite this article: Amani K, Sarraf P, Abkhoo A, Tafakhori A, Fatehi F, Bitarafan S, et al. Prevalence of depression among Iranian patients with myasthenia gravis during 2017-2018. Curr J Neurol 2020; 19(4): ???-??.

Introduction

Myasthenia Gravis (MG) is a chronic autoimmune neuromuscular disease, usually presenting with fluctuating weakness of skeletal muscles and fatigue. Its prevalence has been estimated to be about 77.7 per million population.¹

MG can negatively impact the mental health of the affected patients both directly and indirectly by involving the central nervous system (CNS),² as well as weakness, fatigue, chronic medication dependence, frequent hospitalization, and complications caused by the disease. In addition, psychological complications may also affect patients' motivation to continue treatment and the treatment outcomes as well.³ It has been reported that depression is one of the most important psychological complications in patients with MG,^{4,8} and it might be even more prominent than physical complications.⁹

Similar to other chronic diseases, factors affecting the quality of life (QOL) should be considered in patients with MG. According to previous studies, psychological factors have significant effects on the QOL of patients affected with MG.¹⁰

This study aims to determine the prevalence of depression and its associated factors in Iranian patients with MG.

Materials and Methods

Patients: This was a cross-sectional study in which 62 patients diagnosed with MG who referred to two referral neuromuscular clinics affiliated to the Tehran University of Medical Sciences, Tehran, Iran, were evaluated for eligibility. The protocol of this study was reviewed and approved by the ethics committee of Tehran University of Medical Sciences. Signed informed consent was obtained from all participants.

Protocol: The protocol included patients aged 18 to 65 years who referred to the neuromuscular clinic of our center in 2017-2018 with clinical and laboratory criteria including pharmacological test with edrophonium chloride that leads to a significant improvement in muscle strength and repetitive nerve stimulation (RNS) electrophysiological test or single-fiber electromyography to show an early disruption of the nerve-muscle junction.

The diagnosis of MG was confirmed by the clinical, laboratory, and electrophysiological studies, including the edrophonium test, RNS test, electromyography (EMG), and positive acetylcholine receptor (AChR) or anti muscle-

specific tyrosine kinase (Anti-MuSK) autoantibodies. Patients with a previously known psychiatric disorder and those with a family history of mental disorders were excluded.

Eligible patients were interviewed and screened for depression through the administration of the Hamilton Depression Rating Scale (HDRS) and the Iranian version of Beck Depression Inventory-II (BDI-II). The HDRS scale consists of five categories as normal, mild depression, moderate depression, severe depression, and very severe depression with scores 0-7, 8-13, 14-18, 19-23, and more than 23, respectively.¹¹ Moreover, the BDI-II scale score is divided into four categories of without depression, mild depression, moderate depression, and severe depression with scores 0-13, 14-19, 20-28, and 29-63, respectively.¹²

Data were analyzed by SPSS software (version 16.0, SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean with standard deviation (SD), and categorical variables were expressed as frequencies and percentages. T-test and chi-square test scores were used for comparison between two variables. Besides, Pearson's correlation coefficient and linear regression were applied to evaluate the association between two numeric variables. A P-value < 0.050 was considered statistically significant.

Results

A total of 62 patients participated in this study, of whom 22 (35.5%) patients were male and 40 (64.5%) patients were female. The mean age of the subjects was 41.59 ± 13.30 years (range, 20-65 years). Additionally, 11 (17.7%) and 49 (79.0%) were respectively single and married; 1 (1.6%) and (1.6%) were divorced and widow, respectively.

The average number of academic years of education of the participants was 10.33 ± 4.46 years (range, 0-18 years). The mean duration of MG in the patients was 6.22 ± 6.64 years (range, 1-33 years). At the time of interview, 29 (46.8%) patients were thymectomized.

Based on the HDRS, 22 (35.5%) patients were not depressed and 40 (64.5%) patients were suffering from different levels of depression. The mean HDRS score in our sample was 11.09 ± 7.31 (Table 1).

According to BDI-II, 29 (46.8%) patients were not depressed and 33 (53.2%) patients had depression. The mean BDI-II score in our sample was 16.83 ± 10.98 . The severity of depression in patients based on HDRS and BDI-II is shown in table 2.

Table 1. Demographic information of the study subjects

Variable	Value
Age (mean $\pm$ SD)	41.59 $\pm$ 13.30
Gender [n (%)]	Male 22 (35.5)
	Female 40 (64.5)
Marital status	Married 49 (79.0)
[n (%)]	Single 11 (17.7)
	Divorced 1 (1.6)
	Widow 1 (1.6)
Years of education (mean $\pm$ SD)	10.33 $\pm$ 4.46
Duration of disease (mean $\pm$ SD)	6.62 $\pm$ 6.64
Presentation	Petosis 24 (38.7)
[n (%)]	Muscle weakness 15 (24.2)
	Diplopia 11 (17.7)
	Bulbar sign 11 (17.7)
	Respiratory failure 1 (1.6)

SD: Standard deviation

The compatibility and correlation of more than 68% were found between HDRS and BDI-II ($P < 0.0001$). Based on the Pearson's correlation test, there was no correlation between age and the HDRS and BDI-II scores ($P = 0.901$ and $P = 0.565$, respectively).

There was a weak reverse correlation between the number of academic years and the HDRS score ($P = 0.037$). In contrast, there was no correlation between the BDI-II score and the number of academic years. The association between the ages of patients and the number of academic years based on the severity of depression is shown in table 2.

Gender showed no correlation with HDRS ($P = 0.769$) or BDI-II ($P = 0.0307$) scores, and there was no correlation between marital status and HDRS ($P = 0.158$) or BDI-II ($P = 0.374$) scores.

There was no correlation between the severity of depression and thymectomy status based on the HDRS ($P = 0.074$) or BDI-II ($P = 0.634$).

The results of the Pearson's correlation test indicated that there was no correlation between the daily dosages of prednisolone ($P = 0.539$), pyridostigmine ($P = 0.168$), or azathioprine ($P = 0.883$) and the HDRS scores. There was also

no correlation between the daily dosage of prednisolone ($P = 0.641$), pyridostigmine ($P = 0.193$), or azathioprine ($P = 0.623$) and the BDI-II scores. There was no significant difference between the severity of depression and the daily dosages of these medications (Table 3).

The linear regression analysis was used in order to eliminate the confounding factors affecting depression in patients with MG and also to determine the predictive factors. Based on the BDI-II score, none of the variables, including age ($P = 0.726$), the number of academic years ($P = 0.095$), daily dosages of medications [prednisolone ($P = 0.782$), pyridostigmine ($P = 0.315$), and azathioprine ($P = 0.549$)], and duration of the disease ($P = 0.523$) were significant variables affecting the depression.

The number of academic years was the only predictive variable ($P = 0.046$), and it was also found that by increasing the educational level, HDRS score experienced a decrease of about 0.278, however the age ($P = 0.433$), daily dosages of medications [prednisolone ($P = 0.755$), pyridostigmine ($P = 0.296$), and azathioprine ($P = 0.775$)], and duration of the disease ($P = 0.627$) had no significant effects on depression.

Discussion

This study evaluated the prevalence of depression and its associated factors in 62 patients with MG referred to two referral centers using the HDRS and BDI-II. The total prevalence of depression in these patients based on the HDRS and BDI-II scores was 64.5 and 53.2, respectively. The severity of depression was mild in the majority of cases. There was high compatibility between the HDRS and BDI-II scores. We found no correlation between the severity of depression and age, sex, marital status, duration of the disease, daily dosages of medications, and thymectomy status. The number of academic years was the only factor poorly correlated with the HDRS score.

Table 2. Frequency of depression, mean age, and academic years of the subjects based on the Hamilton Depression Rating Scale (HDRS) and Beck's Depression Inventory-II (BDI-II)

Depression levels	HDRS [n (%)]	Age (mean $\pm$ SD)	Academic years (mean $\pm$ SD)	BDI-II [n (%)]	Age (mean $\pm$ SD)	Academic years (mean $\pm$ SD)
No depression	22 (35.5)	37.72 $\pm$ 12.46	12.72 $\pm$ 2.47	29 (46.8)	41.72 $\pm$ 13.84	11.31 $\pm$ 4.39
Mild depression	21 (33.9)	46.04 $\pm$ 14.18	9.09 $\pm$ 4.83	14 (22.6)	38.07 $\pm$ 11.79	10.57 $\pm$ 3.95
Moderate depression	9 (14.5)	44.22 $\pm$ 12.90	8.00 $\pm$ 5.45	11 (17.7)	45.00 $\pm$ 15.13	8.18 $\pm$ 5.41
Severe depression	5 (8.1)	34.60 $\pm$ 9.98	11.60 $\pm$ 1.81	8 (12.9)	42.62 $\pm$ 12.09	9.37 $\pm$ 3.62
Very severe depression	5 (8.1)	42.20 $\pm$ 13.47	8.00 $\pm$ 5.61	-	-	-
Total	62 (100)	41.59 $\pm$ 13.30	10.33 $\pm$ 4.46	62 (100)	41.59 $\pm$ 13.30	10.33 $\pm$ 4.46

HDRS: Hamilton Depression Rating Scale; BDI-II: Beck's Depression Inventory-II; SD: Standard deviation

Table 3. The correlation between the daily dosage of medications and depression levels based on the Hamilton Depression Rating Scale (HDRS) and Beck's Depression Inventory-II (BDI-II)

Level of depression	Kind of scale	Prednisolone (mean $\pm$ SD)	Pyridostigmine (mean $\pm$ SD)	Azathioprine (mean $\pm$ SD)
No depression	HDRS	18.40 $\pm$ 21.63	169.09 $\pm$ 113.59	51.13 $\pm$ 76.17
	BDI-II	15.43 $\pm$ 19.57	177.93 $\pm$ 102.02	60.34 $\pm$ 74.25
Mild depression	HDRS	8.92 $\pm$ 8.19	182.85 $\pm$ 83.73	64.28 $\pm$ 81.22
	BDI-II	11.25 $\pm$ 11.25	175.71 $\pm$ 92.54	32.14 $\pm$ 63.87
Moderate depression	HDRS	14.16 $\pm$ 14.03	253.33 $\pm$ 65.57	58.33 $\pm$ 70.71
	BDI-II	17.04 $\pm$ 16.57	234.54 $\pm$ 102.01	86.36 $\pm$ 90.39
Severe depression	HDRS	14.00 $\pm$ 12.57	228.00 $\pm$ 115.41	90.00 $\pm$ 89.44
	BDI-II	16.87 $\pm$ 22.54	225.00 $\pm$ 62.10	62.50 $\pm$ 79.05
Very severe depression	HDRS	27.50 $\pm$ 30.61	204.00 $\pm$ 68.41	40.00 $\pm$ 65.19
	BDI-II	-	-	-
P	HDRS	0.210	0.217	0.839
	BDI-II	0.835	0.260	0.367

HDRS: Hamilton Depression Rating Scale; BDI-II: Beck's Depression Inventory-II; SD: Standard deviation

In a study conducted by Suzuki et al.,¹³ the prevalence of depression among 287 patients with MG was reported to be 13.6%, which is less than that of the present study (53.2%). Unlike our study, the authors of this found that higher prednisolone dosage and early disease stage were significantly associated with depression.¹³ Similarly, Freeman et al. reported that there was a correlation between severity and duration of MG and severity of depression.¹⁴ However, unlike the latter study, no association was found between the dose of prednisolone and neuropsychological symptoms in the current investigation.¹⁴

In another similar study conducted on 45 patients with MG, Fisher et al. reported that based on BDI-II results, the prevalence of depression was about 33.0%, and most patients had mild depression (about 24),¹⁵ which is consistent with our findings.

Aysal et al. studied depression in patients with MG through both HDRS and BDI-II and reported its prevalence as 52.4 and 40.5%, respectively.¹⁶ Consistent with our results, the prevalence of depression based on HDRS was slightly higher than BDI-II.¹⁶

No correlation was observed between the level of depression and thymectomy status in our patients.

According to a review by Montazeri et al., the prevalence of depression in different groups of the Iranian population ranged from 5.69 to 73.0%.¹⁷ Modabernia et al. evaluated 4,020

individuals in Rasht (a northern city of Iran) and reported depression in about 9.5% of cases.¹⁸ According to our study it seems that the prevalence of depression in patients with MG is higher than the healthy Iranian population.

A small sample size, no classification of the type of depression by a psychiatrist interview, as well as no comparison between the severity of depression and severity of MG were some of the limitations faced by the researchers of the study. However, evaluating depression by two validated scales (HDRS and BDI-II) can be considered as its strength.

Conclusion

Our findings indicate that depression was common among Iranian patients with MG. The severity of depressive symptoms was unrelated to age, sex, marital status, duration of the disease, daily dosages of medications, and thymectomy status. Further investigations are needed to reveal the exact burden of depression in patients with MG and address the importance of preventive interventions for improving the QOL in these patients.

Conflict of Interests

The authors declare no conflict of interest in this study.

Acknowledgments

None.

References

1. Carr AS, Cardwell CR, McCarron PO, McConville J. A systematic review of population based epidemiological studies in Myasthenia Gravis. *BMC Neurol* 2010; 10: 46.
2. Kaltsatou A, Fotiou D, Tsiptsios D, Orologas A. Cognitive impairment as a central cholinergic deficit in patients with Myasthenia Gravis. *BBA Clin* 2015; 3: 299-303.
3. Katon W. The impact of major depression on chronic medical illness. *Gen Hosp*

- Psychiatry 1996; 18(4): 215-9.
4. Basta IZ, Pekmezovic TD, Peric SZ, Kistic-Tepavcevic DB, Rakocevic-Stojanovic VM, Stevic ZD, et al. Assessment of health-related quality of life in patients with myasthenia gravis in Belgrade (Serbia). *Neurol Sci* 2012; 33(6): 1375-81.
 5. Jeong A, Min JH, Kang YK, Kim J, Choi M, Seok JM, et al. Factors associated with quality of life of people with Myasthenia Gravis. *PLoS One* 2018; 13(11): e0206754.
 6. Stankovic M, Peric S, Stojiljkovic TO, Stankovic T, Nikolic A, Lavrnjic D, et al. Quality of life in patients with MuSK positive myasthenia gravis. *Acta Neurol Belg* 2018; 118(3): 423-7.
 7. Yang Y, Zhang M, Guo J, Ma S, Fan L, Wang X, et al. Quality of life in 188 patients with myasthenia gravis in China. *Int J Neurosci* 2016; 126(5): 455-62.
 8. Magni G, Micaglio GF, Lalli R, Bejato L, Candeglio MR, Merskey H, et al. Psychiatric disturbances associated with myasthenia gravis. *Acta Psychiatr Scand* 1988; 77(4): 443-5.
 9. Padua L, Evoli A, Aprile I, Caliendo P, Mazza S, Padua R, et al. Health-related quality of life in patients with myasthenia gravis and the relationship between patient-oriented assessment and conventional measurements. *Neurol Sci* 2001; 22(5): 363-9.
 10. Winter Y, Schepelmann K, Spottke AE, Claus D, Grothe C, Schroder R, et al. Health-related quality of life in ALS, myasthenia gravis and facioscapulohumeral muscular dystrophy. *J Neurol* 2010; 257(9): 1473-81.
 11. HAMILTON M. A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1960; 23: 56-62.
 12. Ghassemzadeh H, Mojtabai R, Karamghadiri N, Ebrahimkhani N. Psychometric properties of a Persian-language version of the Beck Depression Inventory--Second edition: BDI-II-PERSIAN. *Depress Anxiety* 2005; 21(4): 185-92.
 13. Suzuki Y, Utsugisawa K, Suzuki S, Nagane Y, Masuda M, Kabasawa C, et al. Factors associated with depressive state in patients with myasthenia gravis: A multicentre cross-sectional study. *BMJ Open* 2011; 1(2): e000313.
 14. Freeman C, Lewis I, Heckmann J. Neuropsychiatric symptoms in patients with thymoma-associated and non-thymoma myasthenia gravis. *S Afr J Psychiatr* 2014; 20: 4.
 15. Fisher J, Parkinson K, Kothari MJ. Self-reported depressive symptoms in Myasthenia Gravis. *J Clin Neuromuscul Dis* 2003; 4(3): 105-8.
 16. Aysal F, Karamustafalioglu O, Ozcelik B, Yilmaz M, Karamustafalioglu N, Yumrukcal H, et al. The relationship of symptoms of anxiety and depression with disease severity and treatment modality in Myasthenia Gravis: A cross-sectional study. *Noro Psikiyatrisi Ars* 2013; 50(4): 295-300.
 17. Montazeri A, Mousavi SJ, Omidvari S, Tavousi M, Hashemi A, Rostami T. Depression in Iran: A systematic review of the literature (2000-2010). *Payesh* 2013; 12(6): 567-94. [In Persian].
 18. Modabbernia MJ, Tehrani HS, Fallahi M, Shirazi M, Modabbernia AH. Prevalence of depressive disorders in Rasht, Iran: A community based study. *Clin Pract Epidemiol Ment Health* 2008; 4: 20.