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➜ **Original Article**

Epidemiological Study of Myasthenia Gravis in Patients Referring to Farshchian Hospital in Hamadan

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Abstract

Background: Myasthenia gravis (MG) is an autoimmune disease that leads to fatigue and weakness after voluntary activities. If early diagnosed, MG can be treated, and a person's performance and quality of life can be greatly improved as well.

Materials and Methods: The study population of the present cross-sectional study included 80 patients with MG referring to Sina (Farshchian) hospital in Hamadan, Iran. The inclusion criterion included complete medical files. Finally, the variables were investigated using the chi-square test and two-sample t test by SPSS, version 16.

Results: The mean (standard deviation) of the patients' age was 45.6 ± 15.8 years and most patients (55.5%) were females and 72.5% of them were married. In addition, weakness, lethargy, and premature fatigue were the most common symptoms (47.5%) in patients while unsteady gait was the lowest prevalent symptom (11.3%). There was no significant relationship between gender and the incidence of symptoms in patients ($P>0.05$). However, a significant relationship was found between patients' age with the shortness of breath and unsteady gait ($P<0.05$). Eventually, most women, especially married and elderly ones, contracted the disease.

Conclusion: In general, there is a proper treatment for MG considering its early diagnosis. Accordingly, it is recommended that the level of awareness should be increased about the disease and provide appropriate medical and therapeutic facilities in this regard.

Keywords: Myasthenia gravis, Neuromuscular disorder, Epidemiology

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Introduction

Myasthenia gravis (MG), which manifests as muscle weakness, is caused by a neuromuscular disorder (1). Neuromuscular disorders are conditions leading to muscle and nerve injury pain and discomfort in the limbs (2). Muscle disorders reduce a person's quality of life (3, 4). MG, which is a neurological type of muscle paralysis, is an autoimmune disease occurring at the neuromuscular junction and is often caused by an anti-acetylcholine receptor antibody (5-8). Problems in the body structure interfere with the functioning of various organs of the body (9). The disease is characterized by fluctuating muscle weakness and premature fatigue of voluntary muscles (10). In addition, MG is due to an autoimmune attack on the components of the postsynaptic muscle membrane, which is an antibody against muscle nicotinic acetylcholine receptors in most patients (11). This process causes a kind of muscle weakness following voluntary activities and is exacerbated by physical activity while it is improved by rest (12). Different clinical symptoms occur depending on the extent of striated muscle involvement. The main finding of this disease is extreme fatigue following repeated activities. Thus, the symptoms gradually begin in the morning and worsen at nights (12) although these symptoms improve by rest or may become progressive (13, 14). It should be mentioned that MG usually weakens the eye muscles and causes ptosis and meiosis. It also impairs chewing, voice change, and respiratory distress (15), bulbar weakness, and consequently dysphagia and dysarthria (16). Both males and females may contract MG in any age group, but recent studies have shown that its peak in women is in the second and third decades of life while the peak in men is in the fifth and sixth decades. Further, it is more

common in women than men (17). More precisely, the prevalence of MG in women is 1.5 times more than that of men (18, 19). Furthermore, the incidence of the disease has been reported to be 14 individuals per 100 000 people (20) and its diagnosis may take more than one year. Moreover, critical MG may lead to limb paralysis and death, if it is left undiagnosed. Disability caused by such diseases weakens individual and social functioning, followed by physical and mental problems (21) because human activities are carried out to meet physical and psychological needs through physiological activities (22). Nonetheless, there are some treatments that can greatly control the disease and improve one's performance.

In other words, treatments control the disease to a great extent. There are currently four treatments for this disease, including anticholinergic drugs, immunosuppressive drugs, thymectomy, and short-term immunotherapy, which encompass the replacement of the patient's plasma and intravenous immunoglobulins (11). Concerning drug therapy, acetylcholinesterase inhibitors are the first choice that inhibit enzyme activity by binding to it. If more drug therapy is needed, immunosuppressive drugs are the second choice. These drugs are associated with severe side effects and thus they should be controlled carefully. Plasmapheresis and immunoglobulin are used in severe cases such as MG and in acute cases where there is a poor response to standard drug therapies. Additionally, thymectomy is widely used in patients, especially in generalized MG, with an early onset and thymomas in MG (2). A few studies have focused on the prevalence of this disease in Iran. Overall, the results of recent studies show that most patients are women (6, 11, 12). In addition, people may be affected at any age, but the prevalence is higher in people aged 30-40 years (1, 6). The most common symptoms of this disease are swallowing disorders, breathing difficulty, and the like (7). If diagnosed, it does not lead to death (1). Conventional treatments include immunotherapy, and thymectomy (8). Considering that the prevalence of the disease has increased in recent years and it affects more people at young ages, successful treatments can be selected to improve the symptoms, if it is diagnosed timely. Hence, the present study attempted to identify the patients' age and gender structure, as well as their symptoms and influential factors to take necessary measures for better diagnosis and treatment. To the best of our knowledge, no study has addressed MG epidemiology in Hamadan in recent years. Therefore, the present study investigated the epidemiology of MG in Hamadan during 2006-2014.

Materials and Methods
The study population included all people with MG in Hamadan, Iran. This cross-sectional study was carried out at the Health Care Center of Farshchian hospital, Hamadan University of Medical Sciences from February 2006 to February 2015. All MG patients referring to Farshchian hospital were assessed according to international diagnostic criteria and clinical symptoms over a period of 8 years. Patients' information was collected from their medical files including their medical histories based on a checklist designed for this purpose. The collected information encompassed gender, age, the length of hospital stay, patients' age, clinical symptoms such as early symptoms and neurological findings during the treatment course, laboratory findings, and other medical conditions, as well as specific treatments such as plasma and intravenous immunoglobulin treatment, and thymectomy. The exclusion criterion was patients' incomplete profiles and these medical files were removed from the study. All archived patient reports were investigated and the necessary information was extracted accordingly. The obtained data were described using graphs, tables, and numerical indicators, and the chi-square test and a two-sample t test. Finally, data analysis was performed using SPSS version 16 and a P value of 0.05 was considered as a statistically significant level.

Results
The present study was carried out on 80 patients with MG who had complete medical files and referred to Farshchian hospital in Hamadan from 2006 to 2014. The results showed that most patients were females, married, and had an average age of infection and diagnosis of 42.13 and 45.63 years, respectively. The most common symptoms included swallowing disorder, shortness of breath, and premature fatigue. The most commonly used medications or treatments were prednisolone, intravenous immunoglobulin, and corticosteroid drugs, respectively. Table 1 demonstrates the age profile of these patients.

The youngest and the oldest patients aged 16 and 83 years old, respectively. Similarly, the minimum and maximum age of the infection was 14 and 82 years, respectively. In addition, the average age of diagnosis and infection was 45 and 42 years, respectively.

As mentioned earlier, the disease can be treated if it is diagnosed early, therefore, the age distribution of infection was examined according to different variables. Table 2 provides the age distribution of infection based on

Table 1. Age of Infection and Diagnosis of Patients With MG

	Maximum	Minimum	Standard Deviation	Mean
Age of diagnosis (y)	45.6	15.8	16	83
Age of infection	42.1	15.9	14	82

Note. MG: myasthenia gravis.

Table 2. The Frequency Distribution of Gender and Marital Status and the Average Age of Infection Based on These 2 Variables

Variables	Categories	Frequency	Percentage	Age of Infection	P Value
Gender	Female	45	55.7	36.34	0.001
	Male	35	44.3	48.82	
Marital status	Single	22	27.5	29.64	<0.001
	Married	58	72.5	47.22	

gender and marital status.

Forty-five (55.7%) and 35 (44.3%) patients were females and males, respectively. Further, 22 (27.5%) and 58 (72.5%) of them were single and married, respectively. The results also indicated that the average age of infection was less in women and single people compared to men and married people. There was also a significant relationship between gender and marital status with the age of infection (P < 0.05).

According to Table 3 the frequency and percentage of MG symptoms were 15 (18.8%), 36 (45%), 16 (20%), 14 (17.5%), 26 (32.5%), 9 (11.3%), and 25 (31.3%) for speech impairment, swallowing disorder, drooping eyelids, premature fatigue, shortness of breath, unsteady gait, and

diplopia, respectively. The results further revealed that the lowest and highest average age of infection belonged to diplopia (37.65 years) and swallowing disorder (44.10 years), respectively. There was no significant relationship between age and all the seven studied symptoms (P > 0.05).

After diagnosing the disease, medications and treatments were used to improve the disease, including IVIg (n = 42, 52.5%), plasmapheresis (n = 26, 32.5%), thymectomy (n = 12, 15%), and corticosteroids (n = 38, 47.5%) such as azathioprine, pyridostigmine bromide, and prednisolone (Table 4). Concerning the studied medications and treatments in patients with MG, the results showed that the lowest and highest average age of infection were related to azathioprine (32 years) and IVIg

Table 3. The Frequency Distribution of Disease Symptoms and the Average Age of Infection in Patients According to the Symptoms of MG in the Subjects

Symptoms	Categories	Frequency	Percentage	The Average Age of Infection	P Value
Speech impairment	Yes	15	18.8	44.00	0.614
	No	65	81.2	41.67	
Swallowing disorder	Yes	36	45.00	44.10	0.332
	No	44	55.00	40.49	
Drooping eyelids	Yes	16	20.00	43.86	0.656
	No	64	80.00	41.74	
Premature fatigue	Yes	14	17.50	43.93	0.642
	No	66	82.50	41.73	
Shortness of breath	Yes	26	32.50	41.42	0.781
	No	54	67.50	42.50	
Unsteady gait	Yes	8	11.30	40.00	0.691
	No	68	88.7	42.38	
Diplopia	Yes	23	31.3	37.65	0.106
	No	53	68.7	44.10	

Note. MG: Myasthenia gravis.

Table 4. The Average Age of the Infection of Patients Based on Medications and Treatments

Treatments	Categories	Frequency	Percentage	The Average Age of Infection	P Value
IVIg	Yes	42	52.5	42.17	0.982
	No	38	47.50	42.10	
Plasmapheresis	Yes	26	32.50	40.88	0.625
	No	54	67.50	42.78	
Thymectomy	Yes	12	15.00	32.50	0.021
	No	68	85.00	43.94	
Corticosteroid medications	Yes	38	47.50	41.47	0.663
	No	42	52.50	43.10	
Azathioprine	Yes	1	1.3	32.00	0.524
	No	79	98.70	42.27	
Pyridostigmine Bromide	Yes	8	10.00	33.63	0.110
	No	72	90.00	43.13	
Prednisolone	Yes	45	56.30	41.26	0.587
	No	35	43.70	43.27	

Note. IVIg: Intravenous immunoglobulin.

(42.17 years), respectively. It should also be noted that age was only significantly related to thymectomy ($P < 0.05$).

Based on the results (Table 5), no significant statistical relationship was observed between gender and any of the seven symptoms of MG ($P > 0.05$).

Finally, the relationship between patients' age and the symptoms of their disease was examined using a two-sample t test. Based on the finding of Table 6, no significant relationship was found between age and the other symptoms of MG ($P > 0.05$).

Discussion

People of both genders and in any age group can contract the disease. The results of recent studies showed that the peak of the disease occurs in the second and third decades in women, and the fifth and sixth decades in men. Based on the results of the present study, no significant difference was detected between the patient's age and the age of infection, which is consistent with those of Vahabi et al(23) and Lindstrom et al (5). In their study, Guillermo et al compared the seropositive and seronegative groups and showed that the age of infection and diagnosis was higher in seronegative patients (24). However, Palace et al demonstrated that the age of infection and diagnosis was lower in the seronegative group (25). In the present study, the mean age of the patients and the average age of infection were 46 and 42 years, respectively. Further, the minimum age of MG infection was 14 years, which is in line with the findings of Aghajanzadeh et al where the minimum age of the patients was 14 years while their maximum age was 83 years in the epidemiological study of patients with MG (12). The maximum age of the patients was not similar to the sample studied in the above-mentioned study. With regard to gender, the majority of patients with MG were women, which corroborates with

Table 5. Frequency Distribution of Disease Symptoms and Gender of Patients and the Relationship Between Disease Symptoms and Patients' Gender

		Gender		Chi-square Statistics	P Value
		Female	Male		
Speech impairment	Yes	9	6	0.139	0.469
	No	35	29		
Swallowing disorder	Yes	21	14	0.472	0.324
	No	23	21		
Drooping eyelids	Yes	10	6	0.376	0.373
	No	34	29		
Premature fatigue	Yes	9	5	0.509	0.341
	No	35	30		
Shortness of breath	Yes	14	11	0.001	0.583
	No	30	24		
Unsteady gait	Yes	6	3	0.495	0.369
	No	38	32		
Diplopia	Yes	13	12	0.202	0.417
	No	31	23		

Table 6. Relationship Between Age and Disease Symptoms

Symptoms	T Statistics	P Value
Speech impairment	0.282	0.779
Swallowing disorder	1.146	0.255
Drooping eyelids	0.810	0.420
Premature fatigue	0.675	0.502
Shortness of breath	-0.081	0.936
Unsteady gait	-0.327	0.744
Diplopia	-1.491	0.140

the results of Vahabi et al and Aghajanzadeh et al (12, 23). This result can be justified by the autoimmune nature of the disease and its higher prevalence in women.

In the present study, the average age of patients was 45 years. However, it was 34 and 37.6 years in studies by Aghajanzadeh et al (12) and Vahabi et al (23). The chi-square test was used to investigate the relationship between the patients' gender and their symptoms. The results suggested no significant relationship between gender and any of the observed symptoms in the patients. However, Vahabi et al found a significant relationship between the severity of the disease in patients with seropositive MG and patients' gender (23). Critical MG may lead to limb paralysis. The results of the present study also showed a significant relationship only between age with the symptoms of the shortness of breath and unsteady gait while no significant relationship was observed between age and the other symptoms of MG. However, Sanders et al reported that the severity of MG was higher in women compared to men, and it seemed that increasing age and female hormones could make a person prone to infection (22).

Conclusion

According to the results of the present study and those of other similar studies, the prevalence of MG is higher in women, especially at a young age. Therefore, women need to pay more attention to the risk factors of this disease in addition to effective methods and pharmacological and therapeutic measures. There are appropriate pharmacological and therapeutic measures to treat MG if it is early diagnosed, thus it is recommended to increase the level of awareness about this disease and related factors.

Ethical Statement

The current study protocol was approved by the Research Council of Hamadan University of Medical Sciences with the plan number of 940201311.

Author's Contribution

All the authors made contributions to the proposal and design of the study, the acquisition of the data, as well as the analysis and interpretation of the data.

Informed Consent

In this study, information was collected from the health records of the households in bulk (general) and without mentioning the names and details of the individuals.

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