

Short Communication**Clinical Manifestations, Accompanying Diseases, Complications, and Thymus Pathologies in 102 Patients with Myasthenia Gravis**

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ABSTRACT

Background: Myasthenia gravis (MG) is the most common autoimmune neuromuscular disease that may occur in any age. Regarding to the controversies about the epidemiology of MG and lack of sufficient data about MG status in Iran, the present study was performed on patients referred to Shafa hospital, in Kerman, between 1998-2003 in order to determine clinical manifestations, accompanying diseases, complications, and thymus pathologies in patients with MG.

Methods: It was a descriptive study including 102 patients with MG. Initial data about sex, age of disease onset, disease severity according to Osserman classification, respiratory crisis, thymus pathology, and accompanying diseases were recorded. Chi-square and independent t-test were used for statistical analysis.

Results: The study population included 69(68%) females and 33(32%) males. For patients aged >40 years, female to male (F/M) ratio was 1:1. Disease manifestations were commenced before 20 and 40 years of old in 15.8% and 76.2% of patients respectively. Follicular hyperplasia of thymus was reported in 61.5%, whereas in 23% the pathology was normal or atrophy and in 15.4% was thymoma. Ocular involvement was found in 20.6% of patients. Based on Osserman classification, severity of IIA, IIB, III and IV were reported in 43.1, 21.6, 10.8, and 3.9% of the subjects, respectively.

Conclusion: F/M ratio, age of disease onset, pathology of thymus, disease severity, and accompanying diseases have shown slight differences with prior studies. Epidemiological studies in other parts of the country are suggested.

Key words: Myasthenia gravis, Kerman, Thymus pathology, Osserman classification, Accompanying diseases

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Myasthenia gravis (MG) is an autoimmune neuromuscular disease occurring at any age¹. The most common age of onset is between 20 and 40, and 60% of the patients at this period are women, while in patients with the age of disease onset (ADO) over 40, the female/male(F/M) ratio is 1:1²⁻⁵.

Thymic tumors have been observed in 10-15% of myasthenic patients whereas lymphofollicular hyperplasia of thymus has been observed in 60% of them. The association of MG with some autoimmune diseases such as thyrotoxicosis, systemic lupus erythematosus, rheu-

matoid arthritis, and sjorgen syndrome has been reported. One of the most important and serious complications of this disease is respiratory crisis that may lead to death. A rapid deterioration of the myasthenia itself, termed myasthenia crisis, can bring the patient to the brink of respiratory failure and quadriplegia¹.

This study was performed to investigate the clinical manifestations, complications, thymus pathology, and accompanying diseases in myasthenic patients referring to Shafa Hospital (Kerman, Iran). Since Shafa hospital is the only

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referral center for MG patients, the results of study show the condition of all MG patients in province.

Subjects and Methods

In this descriptive study, records of 102 patients with MG referring to Shafa Hospital during 1998-2003 were reviewed. The patients were examined by two neurologists, then the Tensilon test and electromyographic studies (including repetitive nerve stimulation) were used for diagnosis. Chest CT scan was a diagnostic test for evaluation of thymus in new cases. Data including sex, ADO, disease severity, crisis and its etiology, pathology of thymus, and accompanying diseases were collected via a questionnaire. Disease severity was determined based on clinical manifestation in the active phase. Osserman classification was used for the disease grading as follows:

I. Ocular myasthenia

II.A. Mild generalized myasthenia with slow progression; no crisis; drug-responsive,

B. Moderately severe generalized myasthenia; severe involvement of skeletal and bulbar muscles but no crisis; drug response less than satisfactory,

III. Acute fulminating myasthenia; rapid progression of severe symptoms with respiratory crises and poor drug response; high incidence of thymoma; high mortality,

IV. Late onset severe myasthenia; symptoms same as class III, but resulting from steady progression over 2 years from class one to class two¹.

Data analysis was done through using Chi-square test, independent t-test and Fisher Exact test.

Results

69 subjects (68%) of 102 were females and remaining patients (33 subjects) were males (32%). The F/M ratio was 2.1:1 in the whole population and 1:1 in patients over 40 years old.

Mean ADO in the whole population was 33.9 ± 15.3 years, while it was 39.97 ± 19.6 in male patients and 30.87 ± 11.89 in females.

There was a significant difference between male and female in ADO ($P < 0.05$). In 15.8% of patients, the ADO was under 20 and in 76.2%, it was under 40. 82.4% of females and 63.6% of males were under 40 years old that shows a significant difference ($P < 0.038$).

Table 1 shows the frequency of disease stages based on Osserman classification in both sexes which shows no significant difference.

In this study 52 patients underwent thymectomy. Those patients with MG class II or higher who were between puberty and 55 years of age⁸, candidated for thymectomy. Table 2 shows the frequency of three forms of pathologies that were found in MG patients.

Considering the accompanying diseases, hyperthyroidism showed the highest prevalence (7%). Hypothyroidism (2%), systemic lupus erythematosus, rheumatoid arthritis, Guillan-Barre syndrome, chronic inflammatory demyelinating polyneuropathy, diabetes, pituitary microadenoma (each in one patient) were other findings in our subjects.

There were 17 MG patients with history of respiratory crisis. Infection (respiratory source) was the most frequent cause (7 cases). After that, emergency surgeries (5 cases), natural course of disease (3 cases), drug withdrawal, sedative use, thymectomy, and cholinergic crisis (each one had 1 case) were found. 5 cases were reported with unknown etiology. Some of the patients had more than one crisis.

Discussion

According to the results of the present study, the mean ADO was lower in women than men. In this study, F/M ratio in all subjects was 2.1:1, while in those with ADO over 40, it was 1:1. Some texts have reported a F/M ratio of 2-3:1³. In other reports, the F/M ratio was 2-3:1 for ADO under 40, and the reverse ratio and a higher prevalence in men have been reported at ADO over 40⁶. In a study by Aarli et al, 47.8% of patients showed ADO less than 40 with F/M ratio of 2.4:1; while in those with ADO over 40, the F/M ratio was 1:1.1⁷. In a study done in Sweden, the mean age of disease

onset has been reported 40.2 in all subjects, 34.9 in women, and 48.5 in men ⁸.

Table 1. Frequency of disease stages based on Osserman classification.

Disease stage	Female	Male	Total
I	17 (21%)	4 (12.1%)	21 (20.6%)
IIA	30 (43.5%)	14 (42.4%)	44 (43.1%)
IIB	14 (20.3%)	8 (24.2%)	22 (21.6%)
III	6 (8.7%)	5 (15.2%)	11 (10.8%)
IV	2 (2.9%)	2 (6.1%)	4 (3.9%)
Total	69 (100%)	33 (100%)	102 (100%)

Table 2. Frequency of Thymus Pathology in MG patients.

Sex	Pathology		
	Hyperplasia	Normal	Thymoma
Male	13 (40%)	2 (17%)	6 (75%)
Female	19 (60%)	10 (83%)	2 (25%)
Total	32 (61.5%)	12 (23%)	8 (15.4%)

In the present study, 19.4% of subjects were in the ocular stage and this stage was more prevalent in females. Some texts have reported the rate of 15-20% for ocular stage ¹. In a study done in Sweden, the ocular stage was seen in 8% of the whole, 14% of males, and 7% of females which differ from our results ⁸. In a study by Mantegazza et al, the rate of ocular myasthenia has been reported 39.3% ⁹. In our study, the rate of class IIA was 43.1% and that of class III was 10.8%.

In this study, 52 patients underwent thymectomy (Table2). In the study done in Sweden, 57% of the patients underwent thymectomy of which 64% had follicular hyperplasia, 14% had thymoma, and 20% had normal pathology ⁸.

In our study, the most common causes of crisis were respiratory infection and surgery; comparing to the previous study in which infections and decrease in dosage of the drug

were the main causes of it ¹⁰. In a study carried out by Togha et al on myasthenic patients hospitalized in Imam Khomeini and Sina hospitals (Tehran) during 10 years, all cases of myasthenic crisis were investigated. The most common causes of crises were thymectomy, incorrect drug use and infection ¹¹.

In the present study, the most common accompanying autoimmune disease was hyperthyroidism (7%). Almost all accompanying autoimmune disease were found in females; The exception was one case of hypothyroidism in a male, which shows the higher prevalence of accompanying diseases in female patients with MG. In our study, 17% of female patients and 3% of male patients had autoimmune diseases. This difference was seen mostly in patients under 40 years old and 90% of the observed autoimmune diseases were seen in females. In a study done on 132 myasthenic patients in Mexico in 2003, 5% had connective tissue diseases of whom 5 patients had rheumatoid arthritis and one had systemic lupus erythematosus. The mean age of patients was 28.5 years and all were female ¹².

According to the results, F/M ratio, disease severity, age of disease onset, thymus pathology, and accompanying diseases have shown slight differences with prior studies. Epidemiological study in other parts of the country is suggested. The interesting point in this study is the absence of a late onset peak after the age of 50. This discrepancy can be explained considering two points, one is that mean life expectancy in Kerman seems to be low, especially in men, and the other point is that old people may not consider their symptoms and refer, therefore remain undiagnosed.

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