

# Hypothyroidism, the main thyroid dysfunction in Iranian patients with myasthenia gravis: A case serie

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## Keywords

Thyroid Disease; Myasthenia Gravis; AChR Ab

## Abstract

**Background:** Several concomitant disorders especially thyroid abnormalities have been reported in patients with myasthenia gravis (MG). We aimed to estimate the frequency and pattern of thyroid disorders in Iranian patients with MG.

**Methods:** All consecutive patients with MG referred to neurology clinic of Rasool-e-Akram Hospital during 2006-2007 were enrolled. All patients underwent clinical assessment of thyroid gland as well as thyroid function test. AChR Ab titer was measured as well. Nerve conduction study (NCS), Electromyography (EMG), and Repetitive Nerve Stimulation (RNS) was done by a same neurologist. The diagnosis of MG was made on the basis of clinical examinations, an edrophonium chloride test and electrophysiological studies. The diagnosis of thyroid disorders were based on clinical presentation as well as thyroid function tests.

**Results:** Fifty eight patients (mean age [SD]: 37.1 [16.9], range: 10-80; female: 65.5%) were enrolled in this 12-month study. Four patients (6.9%) had abnormal thyroid function tests (Hypothyroidism: 3 [5.2%]; 4 females; 3 with hypothyroidism and 1 with hyperthyroidism). The mean age (SD) in men and women were 41.4 (21.3) and 34.9 (13.8)

years (P: N.S.), respectively. In addition, once the MG patients are younger than 50, female gender is dominant while they are more than fifty, male is the dominant gender.

**Conclusion:** Our results show that Iranian patients with MG tend to be female and young. Before sixth decade of life, women are the most presenting patients thereafter, men are the predominant gender. About 7 percent of them may suffer from concomitant thyroid problem especially hypothyroidism.

## Introduction

Myasthenia Gravis (MG) has been considered as a disease once Thomas Willis described a woman with dysarthria in 1672, and is a prototype of both synaptic and autoimmune disorders. In most patients, auto-antibodies against the nicotinic acetylcholine receptor (AChR) are the cause and concentrate at the post-synaptic region of the neuromuscular junction [1].

Although MG is rare, epidemiological evidences suggest that frequency of MG is increasing over time, likely due to either improvements in diagnosis or a true increase of disease frequency. Recent prevalence rates for MG approach 20/ 100,000 [2]. Earlier point prevalence rates varied between 0.5 and 15 per 100,000 [3-5]. In western countries, a wide range of incidence has been reported with an estimate of about 2.0 to 10.4/million/year in Virginia to 21.27/million/year in Barcelona, Spain [6,7].

There has been proposed an interaction between MG and demographic features of the disease. Studies showed that the onset of MG is influenced by gender and age in a bimodal fashion. For instance in patients younger than 40, women gender predominates (female/male: 7/3). In the fifth decade, new cases of MG are evenly distributed between men and women. After age 50, new cases of MG are slightly more common in men with male/female ratio of 3/2 (8-10). It seems that future prevalence of the disease will be affected by the spontaneous remission rate (20%) and the fact that without treatment a further 20–30% will die within 10 years [4,5].

The thyroid gland is essential for normal human development and maintenance. In most situations, however, the presentations of thyroid disease are insidious, and include many neurological manifestations [11]. For the first time in 1908 Rennie G. described the association of Graves' disease, GD with MG [12]. Since then, this association has often been reported [11,13-17]. Although the pathogenic link between these two autoimmune diseases remains unclear, but an immunological cross-reactivity between neuromuscular junction and thyroid components was found in overlapping GD and MG [18].

Clinical and experimental findings from the 1970s showed that MG can be an autoimmune disease, the ideas that have been applied to other autoimmune disorders of the neuromuscular junction [19,20]. Patients with MG may have evidence of coexisting autoimmune thyroid disease (AITD) [12,21-24] as well as other autoimmune disorders like type 1 diabetes mellitus, primary hypogonadism, pernicious anemia, and adrenal insufficiency, generally referred as the polyglandular syndrome [26]. The rates of autoimmune diseases association with MG in a Norwegian and Danish studies were 22.9% and 9.4%, respectively [13,26]. The Danish study has also shown that AITDs such as Graves' disease and Hashimoto's thyroiditis are most frequently associated disease with MG [13]. Other epidemiological studies showed that AITD occur in approximately 5-10% of MG patients and GD is the commonest AITD associated with MG and both GD and MG are more common in females [27, 28]. In a series of consecutive Japanese patients with MG, associated autoimmune diseases were found in 19.7% of them, among which GD (7.7%) and Hashimoto's thyroiditis (4.2%) were predominant [25].

The association of MG and hyperthyroidism has been reported by many authors [11,12,25,29-37]. Various estimates place the incidence of hyperthyroidism at from 3 to 8 % in cases of MG [38]. It is generally believed that hyperthyroidism is far more commonly associated with MG than is hypothyroidism. However, no clear explanation has been offered to account for this difference. In present study we aimed to assess concomitant thyroid disorders in Iranian patients with MG as well understand the pattern of thyroid abnormality in our patients

## Materials and Methods

All the subjects of present observational, descriptive, cross-sectional study were recruited consecutively from Rasool-e-Akram hospital affiliated to Tehran University of Medical Sciences. All patients with MG referred to neurology clinic during 2006-2007 were enrolled and detailed questionnaire including age, gender, thyroid disease and MG presentation were filled out for each subject. All of them underwent clinical assessment of thyroid gland as well as thyroid function test (Thyroid Stimulating Hormone, TSH; Free thyroxine, FT4; triiodothyronine, T3). AChR-Ab titer was measured in all the patients at screening. Nerve conduction study (NCS), Electromyography (EMG), and Repetitive Nerve Stimulation (RNS) was done by a same neurologist. The study was approved by ethical committee of Tehran University of Medical Sciences and all patients were informed of the study and provided their written consent before participating in the study.

The diagnosis of MG was made on the basis of clinical examinations, an edrophonium chloride test where necessary, and electrophysiological studies. The diagnoses of thyroid disorder were based on clinical presentation as well as thyroid function tests.

Quantitative variables were expressed as mean (SD). Chi-Square test and t-test were used for qualitative and quantitative data, respectively. Non parametric tests were used where appropriate. A P value of less than 0.05 was considered significant. All calculations were performed with the SPSS Version 16.0 for Windows (SPSS Inc., Chicago, Illinois, USA).

## Results

Fifty eight patients with mean age (SD) of 37.1 (16.9) years were enrolled in this twelve- month study. Thirty eight of them were women (65.5%). The clinical and paraclinical findings of the enrolled patients are depicted in table 1. Four patients (6.9 %) had abnormal thyroid function test among whom, 3 cases had hypothyroidism (5.2%). All patients who had abnormal thyroid function tests were female and the only one who had hyperthyroidism was a 37 year old female.

The mean age (SD) of men and women were 41.4 (21.3) and 34.9 (13.8) years (P: N.S.), respectively. Distribution of patients' gender regarding age classification is depicted in figure 1. There was a trend of positive RNS findings as the ages increased (less than 20: 71.4%, 20-30: 94.1%, 30-40: 93.3%, 40-50: 100%, 50-60: 100%, 60-70: 80%,  $\geq 70$ : 33.3%; P value: 0.04). There was no clinical or paraclinical presentation differences among MG patients with and without thyroid function abnormality. There was no age difference among patients with and without clinical presentations such as ocular, bulbar, extremities, respiratory system involvement.

**Table 1.** The clinical and paraclinical findings of study subjects.

	Number	Percent
Thyroid Problem	4	6.9
Clinic, Involvement		
Ocular	54	93.1
Bulbar	50	86.2
Extremities	50	86.2
Respiratory system	32	55.2
Paraclinic		
EMG positive finding	38	65.5
RNS positive finding	51	87.9
NCS positive finding	0	0
AchR- Ab	55	94.8

### Discussion

Present study showed that mean age of the recruited MG patients was 37 years and women were the predominant gender. The frequency of thyroid dysfunction was 6.9% among MG patients. Moreover, hypothyroidism was the most frequent thyroid dysfunction. Moreover, female gender was the predominant one among those who suffer from both MG and Thyroid diseases. In addition, the predominance of gender in ages less and more than sixty was female and male, respectively.

Once MG disease was reported by an Oxford physician in 1672 [1], several other case reports or series mentioned a wide variety of concomitant disorders [11-17, 21-38]. Since 1970s, it has been proposed that MG has some autoimmune origin [10, 24, 26-28]. Thereafter, several studies reported concomitant diseases with autoimmune pathophysiology in MG patients with a rate of 5 to 23% (26-28). Among them, the two prototypes of hypo- and hyper-thyroidism, Hashimoto and Graves' disease, has been reported as the most common concomitant disorder with MG [11,12,25,29-37].

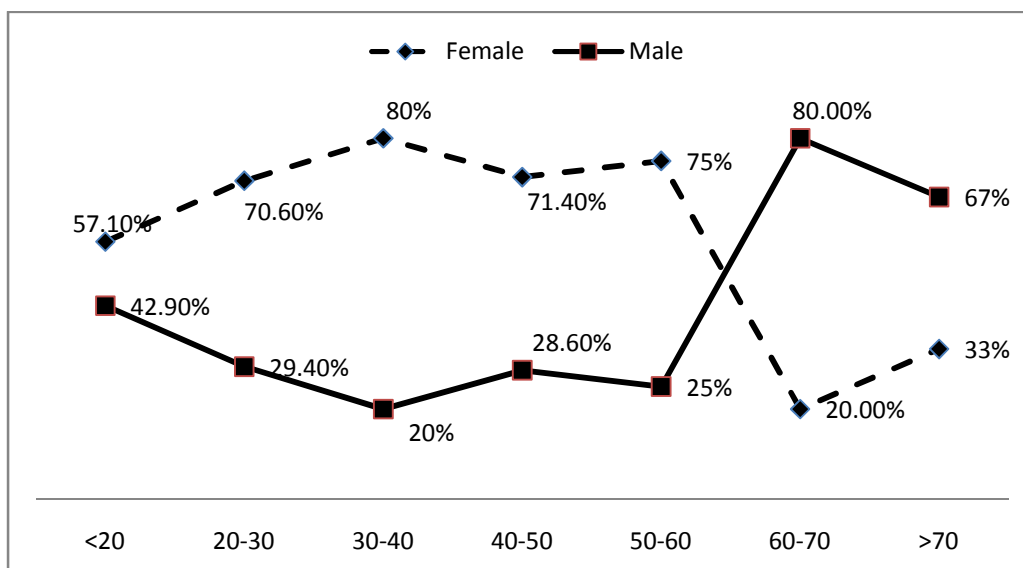
Interestingly, Hypothyroidism was the most frequent thyroid problem among our patients. This finding is not in

accordance with all studies [25,27-37] but with some [38]. In Iran legislation of salt iodization was established in 1994, however goiter and urinary iodine concentration remained elevated in many provinces of Iran. In 2006, Aminorroaya et al performed a population-based study to assess the prevalence of hypothyroidism in Isfahan, Iran. They found that hypothyroidism was common (12.8% of women and 4.7% of men) and probably due to autoimmunity with no correlation to iodine intake [39]. It seems that the higher frequency of concomitant hypothyroidism may be due to endemy of hypothyroidism in our country. However, whether this difference is due to geographic distribution of thyroid problems or genetic or environmental difference of MG among nations should be elucidated in well structured ecologic studies.

Present study confirmed previous reports in which female gender was described as the most frequent one among patients with MG [11,24,27,28,40]. In our study, the mean age of women with MG was lower than men [35 vs. 41], however, was not statistically significant. Our study did not show gender difference in ages less than 20, however, till 60 years of age, female gender was the most frequent one among patients and thereafter, men were the most common presenting gender, figure 1. These findings are in accordance with previous studies [8,9,11,41,42]. Since 20-50 years is the reproductive period of women and before climacteric period, we hypothesize that the specific hormonal balance may have a role in presentation of clinical features of MG patients possibly as an exacerbating factor.

Our study did not show any clinical presentation difference among MG patients with and without thyroid problem as well no paraclinical assessment (EMG, RNS, AchR-Ab) difference was found between these two groups.

Whether these findings are pure clinical finding or a consequent of not having enough study subjects remain to



**Figure 1.** Distribution of patients' gender regarding their age range

be elucidated by future studies with more patients.

In summary, Iranian patients with MG tend to be female and young. Up to six decade of life, women are the most presenting patients. Thereafter, men are the predominant gender. About 7 percent of MG patients may suffer from concomitant thyroid problem especially hypothyroidism.

This estimate can warn our neurologist to think of concomitant thyroid disease in diagnosis and management of patients suspicious to MG. The higher frequency of hypothyroidism may be a clue to elucidate more the interaction of thyroid disorders with MG.

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