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CLINICAL AND NEUROLOGICAL FEATURES OF MYASTHENIA GRAVIS DEPENDING ON THE AGE OF PATIENTS

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Abstract.
This article is devoted to investigate the clinical and neurological features of myasthenia gravis given the ages of patients. Myasthenia gravis is a multifactorial autoimmune disease in which ethnic factors, age, genetics, human leukocyte antibody (HLA) and environmental factors play an important role. The study included 107 patients with myasthenia gravis aged between 19 and 69 years. The patients were divided into two groups depending on their age: the first group included 50 patients with myasthenia gravis under 40 years of age, the second group consisted of 52 patients with myasthenia gravis after 40 years of age. According to the results obtained, myasthenia gravis, the pathogenesis of which is based on the formation of thymoma, is irreversible, which leads to a decrease in the effectiveness of therapy and worsening of the quality of treatment.
Keywords: Myasthenia gravis, thymus changes, clinic, treatment

Introduction. Myasthenia gravis is a chronic rapidly progressive autoimmune disease characterised by impaired neuromuscular transmission due to the formation of autoantibodies to various autoantigenic epitopes of the peripheral neuromuscular apparatus, clinically manifested by weakness and pathological muscle fatigue [1]. While myasthenia gravis used to be considered a rare disease with a prevalence of 0.5-5 cases per 100,000 people in the 1960s, the disease is now considered quite frequent with a prevalence of 4.8-5.0 to 17.5-20.3 per 100,000 people with an annual increase in the number of patients by 5-10% in all age groups [2,4,6]. Myasthenia gravis often impairs the ability to work and often leads to disability of patients, reduction in the quality of life, which determines the high medical and social significance of the problem. Identification of pathological mechanisms of myasthenia gravis development leads to the application of effective and safe

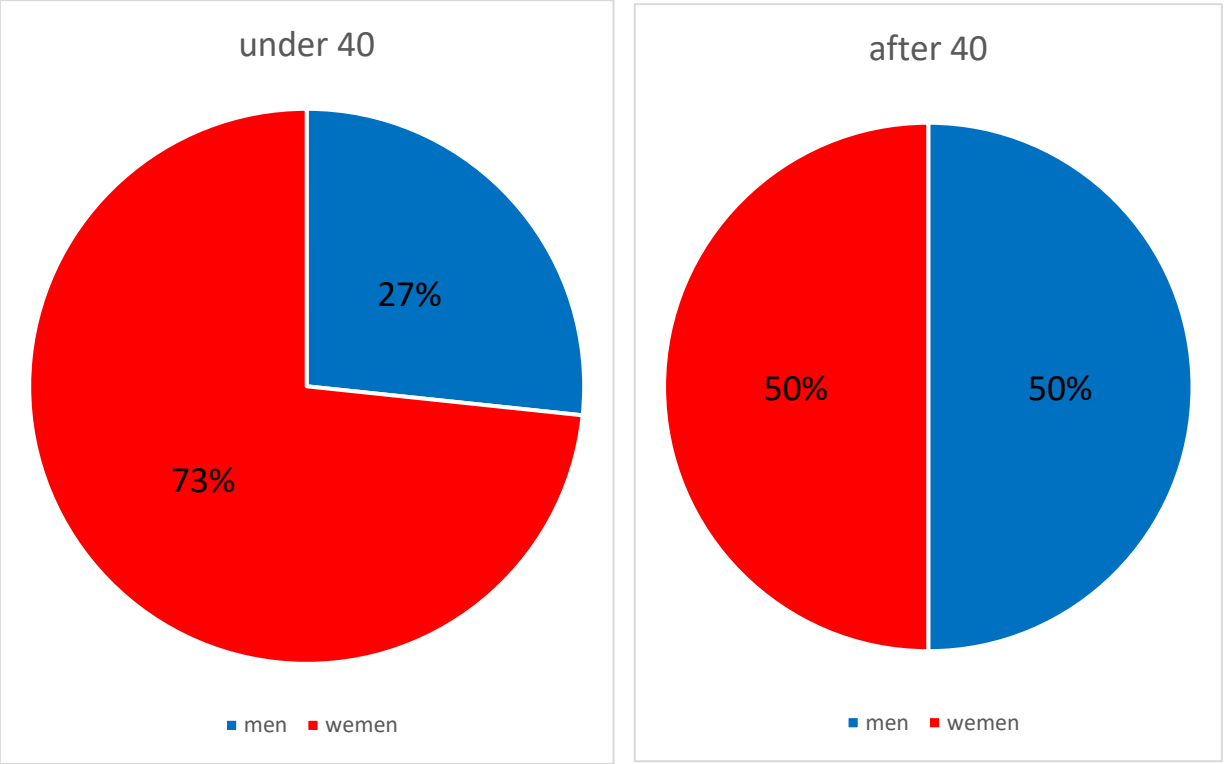
therapeutic measures. Myasthenia gravis is a multifactorial autoimmune disease in which ethnic factors, age, genetics, human leukocyte antibody (HLA) and environmental factors play an important role. Classification of myasthenia gravis: early onset, late onset, ocular and muscular forms. Early onset is seen before the age of 50 and is expressed by a high titre of antibody to AChR and thymus follicular hyperplasia. This form is more common in women [3, 4, 5]. Myasthenia gravis seen over 50 years of age is called late-onset, characterised by thymus atrophy, thymoma and autoantibodies. Ocular myasthenia gravis affects the extraocular muscles, eyelid raising muscles, and visual circle muscles and results in ptosis and diplopia [5,6]. Signs of the disease are observed for 2 years in patients with myasthenia gravis autoantibodies to agrin receptor, collagen Q, cortactin, ryanodine, and potassium channels are detected [1,6]. Some studies show that antibodies to AChR and MuSK are not detected in patients with myasthenia gravis.

Purpose of the study. Determination of peculiarities of clinical and neurological symptoms depending on the age of myasthenia gravis in patients with myasthenia gravis.

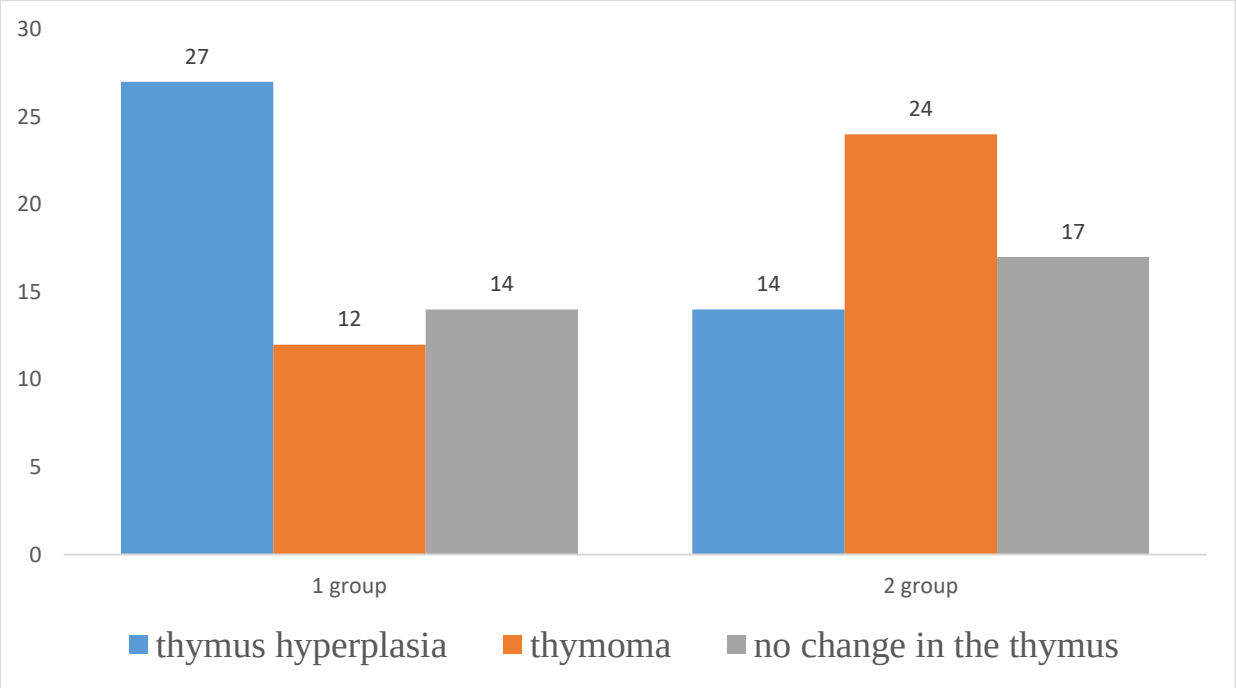
Materials and methods. The study collected data from 107 patients treated in the the clinical hospital No. 7 of Tashkent city with myasthenia gravis aged from 19 to 69 years were included in the study. Patients were divided into 2 groups. Group 1 - patients with myasthenia gravis unrelated to thymoma.Group 2 - patients with myasthenia gravis associated with thymoma.

Patients in both groups were similar in clinical and paraclinical parameters. The total duration of treatment was 14-30 days.Pyristostigmine bromide, methylprednisolone were administered as the main treatment in myasthenia gravis. Plasmapheresis was performed in 30 patients with generalised form of myasthenia gravis. Plasmapheresis was performed on MCS + ‘Haemonetics’ (USA) apparatus in protocol mode PPP (receiving plasma with reduced number of leukocytes). Each patient underwent 3-4 procedures with an interval of 1-3 days.

Results.

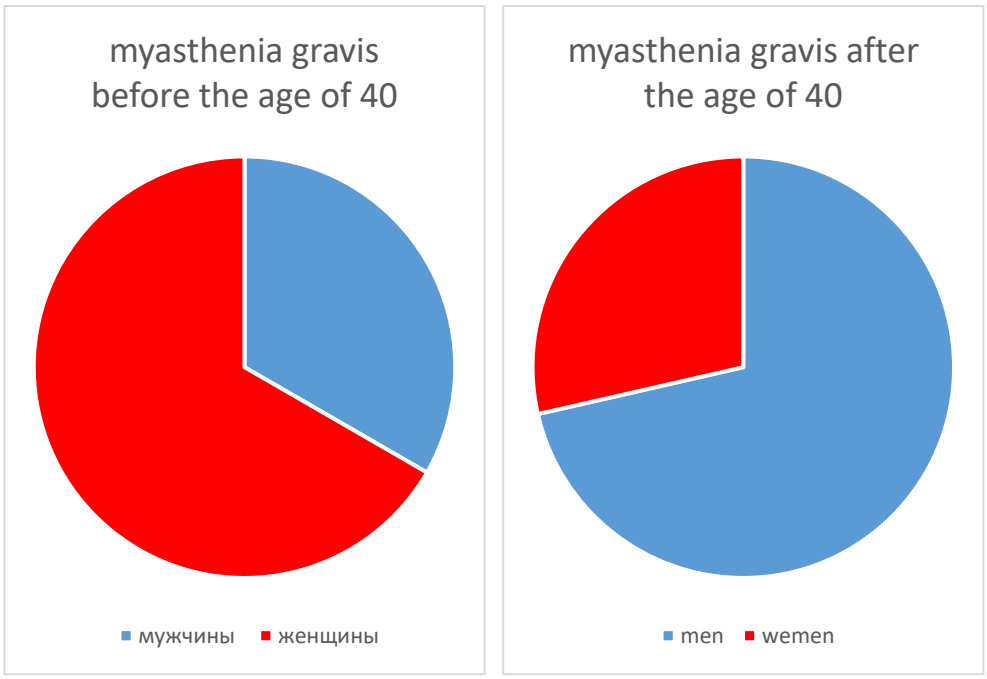


In determining the sex ratio in each group of the study, the first group was dominated by females (73%) compared to the second group, while in the second group, males and females constituted the same percentage (50%).



The second significant factor was the nature of thymus changes. In the first group, thymus changes were detected in 52% of patients. Thymus hyperplasia was found in more than half of patients (2.5 times more often than thymomas). In the

second group, thymus changes were detected only in 25% of patients, with thymoma occurring twice as often as thymic hyperplasia.



When considering the sex ratio of patients with thymoma in the first group, there were more women in the first group, while in the second group, myasthenia gravis associated with thymoma was more common in men (71.4%).Analysis of the presented data suggests that at a young age, myasthenia gravis associated with thymoma is less common in men and the risk of this disease increases with age, while in women these changes regress with age.In diagnosis, this may serve as an etiological factor in myasthenia gravis.

Table 1

Analysis of clinical, neurological and laboratory data of myasthenia gravis

Indicatirs	**1 group**	**2 group**
Ocular form %	35,8	18,8
Bulbar form %	50	31,2
Generalised form %	14,2	50
Muscle disorders (QMGS)	57,1	68,7

Severity of illness	Mild	21,4	18,7
	Moderate severity	42,8	37,5
	Severe	35,8	43,8
Average.AChR antibody titre (nmol/L)		13,7	14,8

The number of patients with ocular form of myasthenia gravis in group 1 was 35.8.5 %, in group 2 -18.8 %. With regard to the generalised form of the disease, there were differences between the groups in terms of the maximum severity of myasthenia gravis manifestations. Group 1 is a lighter group in terms of the severity of the course of the disease. Mild and moderately severe forms of the disease predominate in it (64.2 %). In accordance with the presented table, when analysing myasthenia gravis depending on clinical and immunological characteristics, significant differences ($p < 0.001$) were revealed (method used: Pearson's Chi-square). The severity of bulbar symptoms in the clusters also differed significantly. Thus, in the first group, clinically significant bulbar symptoms were observed in 50% of patients, in the second group, in 31.2%. The groups also differed significantly in the nature of muscle symptoms and the clinically significant QMGS (QMGS). The dominant specific weight belongs to ocular, bulbar and skeletal symptoms. In the second group, the proportion of debits manifesting generalised symptoms is significantly higher. Rare variants of debut symptoms, such as myasthenic crisis, sudden falls, isolated respiratory disorders and neck muscle weakness, are significantly more frequent in the second group. As a result of comparing both groups according to the severity of the disease, we found statistically significant differences ($p < 0.001$) (method used: Pearson Chi-square .

Pyridostigmine bromide, methylprednisolone was administered as the main treatment for myasthenia gravis. In both groups, the standard treatment of Myasthenia gravis was applied. However, for full effect and good result in

generalised forms, plasmapheresis method was used in addition to anticholinesterase and corticosteroids. Proserin was prescribed in hospital at the stage of establishing the final diagnosis Then, as a rule, the use of pyridostigmine bromide was recommended.The dose of pyridostigmine bromide was titrated from 15 mg once a day to a tablet 2-3 1 (60 mg) 3-4 . times or more per day The dose of the drug depended on the form and severity of clinical manifestations Simultaneously prescribed potassium 2-3 g daily If the patient's condition continued to worsen muscle weakness and generalisation of the process was added methylprednisolone at a rate of , 1- 1.5 mg kg body weight daily patients B / (12). Subsequently, the dose of glucocorticoids was very slowly reduced to the maintenance dose When the patient's condition improved and the pathological process stabilised, methylprednisolone was gradually withdrawn. In case of deterioration of the condition we returned to the initial dose of methylprednisolone followed by a very slow decrease by 0.25-0.5 mg per day In 10-15 . case of myasthenic crisis patients were hospitalised in the intensive care unit for ventilator Simultaneously performed plasmapheresis and pulse therapy with methylprednisolone 1 000 mg daily intravenous drip once / 3-5 per course with subsequent administration of prednisolone at a dose of 1.0-1.5 mg kg body weight per day with a gradual reduction in dose. Plasmapheresis was carried out in patients course 18 - my sessions with plasma exchange from 4-5 20-30 ml kg body weight.Duration of the positive effect of plasmapheresis was 2-5 months.

According to the results of the data, the study suggests a significant feature: almost all patients in both groups who had myasthenia gravis without changes in the thymus noted improvement of the condition (81.3%). Also the use of plasmapharesis in therapy increased the specific weight of positive effect (84,7%).Based on the data of the conducted treatment it was found that in the complex recovery of patients with myasthenia gravis improvement of the condition is observed only in those patients who do not have thymoma.

Conclusion: Myasthenia gravis before 40 years of age is characterised by the following features: female gender; thymus hyperplasia; more often with general skeletal weakness; milder benign course; lower representation of bulbar disorders and frequency of ocular myasthenia gravis; average titres of antibodies to AChR; lower probability of malignant progressive course; higher number of favourable treatment outcomes and achievement of remission. Myasthenia gravis with onset after 40 years of age has smoothed gender peculiarities, thymus changes are found in one third of patients, with thymus hyperplasia characteristic of men; onset of the disease most often with ocular and bulbar symptoms; dominance of bulbar disorders in the majority of patients; high antibody titres; often progressive, rather severe course; in many cases insufficient effectiveness of therapy. Through the analysis of the results obtained, it was found that with complex rehabilitation of patients with myasthenia gravis, improvement of the condition is observed only in those patients who do not have thymoma. This is confirmed by instrumental studies. According to the results obtained, myasthenia gravis, the pathogenesis of which is based on thymoma formation, proceeds irreversibly, which leads to a decrease in the effectiveness of therapy and deterioration of the quality of treatment. This mechanism may be related to the fact that pools of T-cell vasoactive cells adapting to neurons of the nervous system are formed under the influence of specific antibodies of IgG3 type.

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