Myasthenia Gravis: an autoimmune disease: A Cross-sectional Study of Its Risk Factors, prevalence and Complications in Tripoli, Libya

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الملخص:

الخلفية: مرض الوهن العضلي الشديد اشتق اسمه من ثلاثة مصطلحات لاتينية هي: العضلات, الضعف, الشدة. هو مرض مناعي ذاتي مزمن وقاتل ونادر يتميز بظهور اجسام مضادة ذاتية تهاجم امكنة التقاء العضلات بالأعصاب في الجهاز الهيكلي, وخصوصا مستقبلات الأستيل كولين, مما يؤدي الى ايقاف نقل المؤشرات العصبية الى العضلات. الوهن العضلي يزداد سوءا بالحركة والنشاط ويتحسن بالراحة. ويتراوح الوهن العضلي من ضعف متوسط الشدة في عضلات العيون الى ضعف عام حاد. **الهدف:** لدراسة مدى انتشار المرض وتشخيص عوامل خطورته مثل العمر, الجنس, الحالة الصحية , والادوية. وكذلك لتحديد نسبة المرضى اللذين تظهر عندهم المضاعفات متل استئصال الغدة الزعترية.

المواد وطرق البحث هذا البحث تم اجرائه في الفترة ما بين شهر يونيو 2023 ويناير 2024. تم اجراء الدراسة على خمسون مريض بعد موافقة المرضى تم تجميع المعلومات السريرية وفق ا للاستبيان المعد لذلك.

النتائج: 52٪ من المرضى كانوا اناث مقابل48 ٪ من الذكور, متوسط العمر 43 عاما, ومتوسط تاريخ التشخيص كان خمس سنوات. 54٪ من المرضى كان لديهم امراض جانبية بالإضافة الى وهن العضلات. بالنسبة للتحاليل الروتينية, كان هناك نقص في معدل فيتامين (د) و(ب 12) عن المعدل الطبيعي, مع ارتفاع في عدد خلايا الدم البيضاء. وبالنسبة للتحاليل المناعية, وجدنا ارتفاع في معدل الاجسام المضادة الذاتية ضد

مستقبلات الأستيل كولين, والاجسام المضادة للعضلات. بعض الاعراض كانت اكثر ارتباطا بالمرض مثل: تدلي الجفون, عسر البلع, الرؤية المزدوجة .تم اكتشاف علاقة احصائية مميزة بين عسر البلع والعمر.

الخلاصة: في هذه الدراسة تم تحديد عوامل الخطورة التي ترتبط بشدة المرض, وكان العمر اهم المؤشرات وخصوصا ان زيادة العمر تترافق مع ظهور المضاعفات مثل عسر البلع.

Abstract:

Background: The term myasthenia gravis (MG) is derived from the Greek terms my, asthenia, and gravis, which mean muscle, weakness, and severe, respectively. It is a rare and fatal chronic autoimmune disorder in which circulating autoantibodies attack components of the neuromuscular junction (NMJ) of skeletal muscle, most commonly the nicotinic acetylcholine receptor (AChR), blocking the resulting neuromuscular transmission. Muscle weakness usually worsens with continuous activity, and the patient improves with rest, while the severity ranges from mild eye muscle weakness to severe general muscle weakness. **Aims:** To determine the disease prevalence and to investigate its associated risk factors such as age, gender, health condition, and medications. Also, to determine the percentage of patients who have more complications, such as removal of the thymus gland. **Materials and methods:** This research was conducted on the period from June 2023 to January 2024. 50 MG patients were included in this study. After informed consent, patients' data were collected according to the previous provided survey. **Results:** 52% of the patients were females and 48% males, their average age was 43 years and the date of diagnosis was 5 years. 54% were suffering from other diseases in addition to GM disease. In terms of general laboratory parameters, there was a decrease in the levels of Vitamin D and Vit.B12, with an increase in the leukocytes count. In immunological analysis, an increase in both Anti-Acetylcholine Receptors and Anti Muscular Antibodies has been determined. Many symptoms associated with

the disease have appeared, including Ptosis, Dysphagia, and Double Vision. Significant relationship between age and disease complications age and dysphagia (P=0.014) .**Conclusion:** In summary, this study demonstrated that risk factors can contribute to myasthenia relapse. Age of onset is an important predictor, there was a weak, statistically significant direct relationship between age and dysphagia, meaning that the older the age, the greater the impairment of dysphagia.

Keywords: Myasthenia Gravis, *Risk Factors, Prevalence, Complications*

1. INTRODUCTION:

Myasthenia gravis (MG). is a chronic, rare, and fatal autoimmune disorder affecting the neuromuscular receptor and it is mediated by type II postsynaptic antibodies against nicotinic acetylcholine (nacho) receptors, that attack the neuromuscular junction (NMJ) leading to damage the postsynaptic membrane via complement fixation. This attack causes nerve cells to fail, resulting in neuromuscular failure or weakness without stiffness (**Breen E, 2014**). The annual prevalence of myasthenia gravis is relatively lower, as for every 100,000 people, 0.21-2 patients are affected (**Wendell L, 2011**). The age of male patients distributed between the ages of 60-89 years, while in females, it peaks between the ages of 30 and 50 years (**Carr AS, 2010**). Before the age of forty, women are affected, as the ratio of females to males at the beginning of myasthenia gravis is 3:1. While infection rates are equal between men and women in the fifth decade of life, after the age of fifty, the infection rate for men is higher than for women by a ratio of 2:3 (**Ciafaloni E, 2019**). The characteristic clinical symptom of myasthenia gravis is fluctuating muscle weakness that is activated by movement and improves with rest. The visual symptoms appear with or without general weakness in rates ranging from 50% to 85% of patients, which may lead to visual impairment in 50% to 60% of patients and develop general weakness either within

3 years from the onset of symptoms or 15% to 25% of patients remain visually impaired during the disorder course (**Strauss A, 1960**) and (**Patrick J & Lindstrom Jon, 1973**). Nearly 20% of MG patients suffer from persist bulbar symptoms with impairment of head extension and flexion. The weakness of the limbs is more proximal than distal. Myasthenia crisis is an auto immune disorder which associated with general muscle impairment that leads to respiratory failure and may require intubation and mechanical ventilation (**Jaretzki A, 2000**).

Myasthenia gravis is a rare neurological disorder, and it is even rarer in children. There are significant geographic differences in incidence and prevalence, but MG incidence is thought to have increased globally over the past seven decades. The prevalence of MG was estimated at 1 in 200,000 between 1915 and 1934, increasing to 1 in 20,000 in 1934 after the introduction of anticholinesterase drugs, and to 1 in 17,000 in 1969 after the discovery of acetylcholine receptor antibodies (Grob **D, 2008**). Prevalence rates range from 150 to 200 cases per million people and have increased steadily over the past 50 years, at least in part due to improvements in detection, diagnosis, treatment, and overall increases in life expectancy (**Phillips H, 2003**). Recent incidence studies in Europe indicate 4.1 to 30 cases per million person-years (**Somnier E, 2002**) and (**MacDonald K, 2000**). Myasthenia gravis affects all ages. The approximate age of onset is one year (**Seybold E, 1981**), while the oldest age of onset is 98 years (**Keesey JC, 2004**). There has been a continuous increase in the incidence of late-onset myasthenia gravis in Western and Asian countries over the past thirty years. The incidence of myasthenia gravis increased by 1.5-fold in those aged 50 years or older, while it showed a 2.3-fold increase in those aged 65 years or older (**Matsui N, 2009**) and (**Murai H, 2011**). The most common age of onset of myasthenia gravis is between 20 and 39 years in women and between 50 and 70 years in men (**Beghi E, 1991**).

Gender is an epidemiological risk factor for the development of many autoimmune diseases, because the immune system is the subject of sexual dimorphism (**Da Silva P, 1999**). Many autoimmune diseases, including myasthenia gravis, are more prevalent in women than in men (**Lopomo A, 2017**).

Acquired myasthenia gravis may first occur during pregnancy as pregnancy has a variable impact on the disease; 41% of patients experience an exacerbation, 29% experience remission, and 30% experience no change in course (**Avidan N, 2014**). Additionally, women often describe symptoms that worsen as progesterone levels decrease before menstruation (**Leker RR, 1998**).

There are several sub classifications of MG, as follows:

1. Early myasthenia gravis: This begins at the age of less than 50 years. It is characterized by enlargement of the thymus gland, usually in females.
2. Late-onset myasthenia gravis: beginning at age >50 years. It is characterized by atrophy 4 of the thymus gland, especially in males.
3. Myasthenia associated with thymoma (10%-15%).
4. MG with anti- Muscle-specific tyrosine kinase (MUSK) antibodies.
5. Optic Myasthenia (OMG): The symptoms affect the muscles outside the eye only.
6. MG with no anti-AChR antibodies and muscle-specific tyrosine kinase (MUSK) antibodies (**Gilhus E, 2011**).

Myasthenia gravis cases with thymoma usually show sensible anti-AChR antibodies in serum. MG associated with thymoma may also contain fresh MG-associated antibodies (e.g., anti-voltage-gated K+ and Ca++ channels, anti-Hu protein, anti-di-hydropyrimidinase associated protein 5, and anti-glutamic acid decarboxylase antibodies) (**Leite M, 2010)** and (**Meriggioli N, 2009**). About 15% of cases with generalized myasthenia gravis don't have anti-AChR antibodies on

current laboratory assays. In 40% of this group, antibodies to MUSK and another postsynaptic neuromuscular junction (NMJ) protein were set up. They've atypical clinical features similar as picky weakness of the facial, bulbar, neck or respiratory muscles with occasionally marked muscle atrophy with relative sparing of the optical muscles. Respiratory heads are more common when muscle groups similar as the Para spinal muscles and upper esophageal muscles are affected. Increased perceptivity, non-response, or indeed clinical deterioration to anticholinesterase medicines has also been reported. The complaint has an early onset with a womanish ascendance and thymic towel is generally normal (**Vernino S, 2004**). Serum MG warrants both anti-AChR and anti-MUSK antibodies and constitutes a clinically miscellaneous group with purely optical, mild generalized or severe generalized complaint. Some cases may have low- affinity anti-AChR antibodies, which cannot be detected by current tests. They're basically indistinguishable from cases with anti-AChR antibodies in terms of clinical instantiations, response to medicine remedy, and maybe indeed thymic abnormalities (**Leite M, 2005**) and (**Vincent A, 2004**). Thymomas are constantly associated with autoimmunity. Neoplastic epithelial cells in thymomas express multitudinous tone- suchlike antigens including AChR- such like, titin- such like, and ryanodine- receptor- such like epitopes ((**Morgenthaler T, 1993**). These antibodies reply with epitopes on the muscle proteins titin and ryanodine receptor, are set up substantially in association with thymoma and late- onset myasthenia gravis, and may relate with myasthenia gravis inflexibility. These striational antibodies are basically detected only in the sera of cases with MG and infrequently set up in AChR antibody-negative MG. The frequentness of striational antibodies in thymoma- associated MG cases are high. Antititin antibodies are detected in 49 – 95 of thymic-associated MG, antiryanodine receptor antibodies in 70 – 80, and anti- KV1.4

(VGKC) in 40 – 70 of the cases (**Romi F, 2005**). Since the presence of striational autoantibodies is associated with a more severe complaint in all MG groups, these antibodies can thus be used as prognostic determinants in MG cases (**Romi F, 2000**).

To establish the diagnosis of MG, necessary investigations include—acetylcholine receptor AChR antibodies, muscle specific kinase MUSK antibodies, and Computerized Tomography/ Magnetic Resonance Imaging CT/MRI of anterior mediastinum for thymoma or thymic hyperplasia. Neurophysiological examination with repetitive nerve stimulation and jitter measurements are important in establishing the initial diagnosis, especially in patients without detectable antibodies (**Sathasivam S, 2008**). The primary hallmark of myasthenia gravis is fatigue and fluctuating weakness that worsens with repetitive activity and improves with rest. The weakness is exacerbated by exposure to heat, infection and stress (**Grob D, 2008**). The feature that distinguishes myasthenia gravis from other disorders is the fluctuating weakness that presents with similar weakness. The weakness involves some of the skeletal muscles. It is generally distributed to the extremities, including the eyes, bulbar, proximal, and neck, and rarely includes the muscles of the respiratory system. In some patients, weakness is either mild in 26%, moderate in 36%, or severe in 39%, with an association with dysphagia, depressed cough, and decreased vital capacity .The most common initial symptom of myasthenia gravis is eye muscle weakness, affecting 85% of patients. Generalized progression will develop in 50% of these patients within 2 years. Symptoms appear with fluctuating ptosis, blurry vision, or occasional diplopia. Myasthenia weakness is detected by inducing

diplopia by having the patient look sideways for 20-30 seconds, which causes eye muscle fatigue. (Grob **D, 1987**).

Management of myasthenia gravis depends on the characteristics of the patient and the severity of the disease. There are two ways to manage myasthenia gravis, based on the pathophysiology of the disease. The first is by using an acetyl cholinesterase inhibitor agent in order to increase the amount of acetylcholine available to bind to the postsynaptic receptor, while the second is by using immunosuppressive drugs where the binding of acetylcholine receptors to antibodies is reduced. To treat myasthenia gravis, there are four basic treatments: (1) Treat symptoms with acetyl cholinesterase inhibitors (**Drachmann D, 1994**).

(2) Short-term rapid immunotherapy with plasmapheresis and intravenous immunoglobulin (**Batocchi A, 2000**) and (**Samuelsson A, 2001**).

(3) Long-term chronic immunotherapy with glucocorticoids and other immunosuppressive drugs (Pascuzzi R, 1984).

(4) Surgical treatment "Thymectomy" (Lavrnic **D, 2005**).

2. MATERIAL AND METHODS:

2.1. Population study:

This descriptive cross-sectional study was conducted from June 2023 to January 2024. Fifty cases diagnosed with myasthenia gravis, aged 19-74 years, were collected.

2.2 Study design:

Samples were collected from Central Medical University Hospital and the archive records of Ali Omar Asker Hospital, Tripoli, Libya.

2.3 Methods of diagnosis:

Patients were diagnosed using radiological imaging (MRI, X-ray, CT, and EMG). Different biochemical blood tests such as Vitamin D level, Vitamin B 12 level,

and complete blood count were performed. Additionally, some immunological analysis such as detection of Acetylcholine receptors antibodies and anti- Muscle-specific tyrosine kinase (MUSK) antibodies were also done.

2.4 Statistical analysis:

Statistical analysis was performed using SPSS version 26. The Chi-Square test and Pearson correlation coefficient was used for significant difference and $P < 0.05$ was considered as statistically significant.

3. RESULTS*:*

3.1 Classification of patients based on demographic data:

This research was conducted on the period from June 2023 to January 2024. 50 MG patients were included in this study. After informed consent, patients' data were collected according to the previous provided survey. Most patients were females (52%). the mean age of patients was 43.4 years, while the mean of the period of disease was 5.7 years.

Table 1. Distribution of the patient's demographic data

Variables	Total N (%)	Male N (%)	Female N (%)
Gender	50 (100%)	24 (48%)	26 (52%)
Age			
19-29 Y	10 (20%)	5 (21%)	5 (19%)
30-39 Y	9 (18%)	4 (17%)	5 (19%)
40-49 Y	14 (28%)	2 (8%)	12 (46%)
50-59 Y	12 (24%)	8 (33%)	4 (15%)
60-69 Y	3 (6%)	3 (13%)	0 (0%)
More than 70Y	2 (4%)	2 (8%)	0 (0%)
Mean ± SD	43.4 ± 13.9	47.0 ± 16.7	40.0 ± 9.9
Period of disease			
1-5 Y	28 (56%)	12 (50%)	16 (62%)
6-10 Y	15 (30)	10 (42%)	5 (19%)

11-15 Y	5 (10%)	1 (4%)	4 (15%)
16-19 Y	2 (4%)	1 (4%)	1 (4%)
Mean ± SD	5.7 ± 4.1	5.4 ± 3.8	6.0 ± 4.4

3.2 Classification of patients based on medical history:

Our study showed that 54% were suffering from other diseases, and their percentage was higher among males (71%) than females (39%). Among these diseases, 20% were diabetes, 20% blood pressure, 8% were gout, 2% were heart disease, asthma, goiter, and kidney failure, and 6% were Cohn's disease. Only a significant relationship between diabetes (0.029) and hypertension (0.004) with the MG. was detected.

Table 2. Relationship between MG with other diseases

Variables	Total N (%)	Male N (%)	Female N (%)	P-Value
Infection with other diseases Yes	27 (54%)	17 (71%)	10 (39%)	0.491
No	23 (46%)	7 (29%)	16 (61%)	
Diabetes mellitus Yes	10 (20%)	6 (25%)	4 (15%)	0.029
No	40 (80%)	18 (75%)	22 (85%)	
Hypertension Yes	10 (20%)	7 (29%)	3 (12%)	0.004
No	40 (80%)	17 (71%)	23 (88%)	
Gout Yes	4 (8%)	3 (12%)	1 (4%)	0.328
No	46 (92%)	21 (88%)	25 (96%)	
Heart disease Yes	1 (2%)	1 (4%)	0 (0%)	0.223
No	49 (98%)	23 (96%)	26 (100%)	
Asthma Yes	1 (2%)	1 (4%)	0 (0%)	0.432
No	49 (98%)	23 (96%)	26 (100%)	
Cohn's Disease Yes	3 (6%)	2 (8%)	1 (4%)	0.162

No	47 (94%)	22 (92%)	25 (96%)	
Enlargement of the thyroid gland Yes	1 (2%)	0 (0%)	1 (4%)	0.344
No	49 (98%)	24 (100%)	25 (96%)	
Renal failure Yes	1 (2%)	2 (8%)	0 (0%)	0.132
No	49 (98%)	22 (92%)	26 (100%)	

3.3 Evaluation of general laboratory parameters:

58% of patients showed decreased levels of Vitamin D and Vitamin B12 (52%), while 82% had an increase in leukocytes count .The red blood cell counts were within normal levels in 66% of them. No significant impact of patient's gender on the laboratory parameters.

Table 3. Evaluation of General laboratory parameters

Variables	Total N (%)	Male N (%)	Female N (%)	
Vitamin D Low	29 (58%)	15 (63%)	14 (54%)	0.814
High	0 (0%)	0 (0%)	0 (0%)	
Normal	21 (42%)	9 (37%)	12 (46%)	
White blood cells Low	2 (4%)	1 (4%)	1 (4%)	0.539
High	41 (82%)	20 (83%)	21 (81%)	
Normal	7 (14%)	3 (13%)	4 (15%)	
Red blood cells Low	18 (34%)	9 (38%)	9 (35%)	0.898
High	0 (0%)	0 (0%)	0 (0%)	
Normal	32 (66%)	15 (62%)	17 (65%)	
Vitamin B12 Low	30 (52%)	15 (62%)	15 (57%)	0.689
High	1 (2%)	0 (0%)	1 (4%)	
Normal	19 (46%)	9 (38%)	10 (39%)	

3.4 Evaluation of Immunological Test:

88 % of patients had high concentrations of acetylcholine receptors autoantibodies , most of them were females (92%) compared to males (83%), whereas levels of anti Muscle-specific tyrosine kinase (MUSK) antibodies were high in 66% of patients with higher levels in males (71%) compared to females (62%). patient's gender showed significant impact on the acetylcholine receptors autoantibodies(P=0.043).

Table 4. Evaluation of Immunological analysis

Variables	Total N (%)	Male N (%)	Female N (%)	P-Value
Anti-Acetylcholine Receptors	1 (2%)	0 (0%)	1 (4%)	0.043
Low				
High	44 (88%)	20 (83%)	24 (92%)	
Normal	5 (10%)	4 (17%)	1 (4%)	
Anti (Musk)	2 (4%)	1 (4%)	1 (4%)	0.426
Low				
High	33 (66%)	17 (71%)	16 (62%)	
Normal	15 (30%)	6 (25%)	9 (34%)	

3.5 Classification of examination methods:

Different radiological methods were used for the detection of the thymus carcinoma (thymoma). Thymectomy was performed for 12 patients (24%), 7 males (29%) and 5 females (19%). No significant differences between males and females in the thymoma detection.

Table 5. Diagnosis of thymoma based on different radiography

Variables	Total N (%)	Male N (%)	Female N (%)	P-Value
X-ray				
Not-done	0 (0%)	0 (0%)	2 (8%)	0.162
Thymoma	47 (94%)	24 (100%)	23 (88%)	
Normal	3 (6%)	0 (0%)	3 (4%)	
CTs	29 (58%)	13 (54%)	16 (62%)	
Not-done				0.295
Thymoma	9 (18%)	4 (17%)	5 (19%)	

Normal	12 (24%)	7 (29%)	5 (19%)	
EMG Not-done Thymoma Normal	 15 (30%) 31 (62%) 4 (8%)	 7 (29%) 14 (58%) 3 (13%)	 8 (31%) 17 (65%) 1 (4%)	0.604
MRI Not-done Thymoma Normal	 44 (88%) 1 (2%) 5 (10%)	 20 (83%) 1 (4%) 3 (13%)	 24 (84%) 2 (8%) 2 (8%)	0.423

CT=Computed Tomography; **EMG**=Electromyography; **MRI**= Magnetic Resonance Imaging

3.6 Classification of Clinical symptoms and complications:

Different symptoms and complications such as: Dysphagia (84%), Ptosis (94%), Eye deviation from its course (82%), and Double Vision (84%) were determined. Significant correlation between MG with dysphagia was detected (P=0.043).

Table 6. General clinical symptoms and complications

Variables	Total N (%)	Male N (%)	Female N (%)	P-Value
Dysphagia Yes No	42 (84%) 8 (16%)	18 (75%) 6 (25%)	24 (92%) 2 (8%)	0.043
Muscle Weakness Yes No	 43 (14%) 7 (86%)	 21 (88%) 3 (12%)	 22 (85%) 4 (15%)	0.664
Ptosis Yes No	47 (94%) 3 (6%)	23 (96%) 1 (4%)	24 (92%) 2 (8%)	0.575
Double Vision Yes No	42 (84%) 8 (16%)	20 (83%) 4 (17%)	22 (85%) 4 (15%)	1.00
Proximal myopathy Yes No	17 (34%) 33 (66%)	7 (29%) 17 (71%)	10 (39%) 16 (61%)	0.364
Weight loss Yes No	21 (42%) 29 (58%)	9 (38%) 15 (62%)	12 (46%) 14 (54%)	0.604

Vision Impairment Yes	7 (14%)	2 (8%)	5 (19%)	0.185
No	43 (86%)	22 (92%)	21 (81%)	
Weakness of movement Yes	22 (36%)	7 (29%)	15 (58%)	0.213
No	28 (64%)	17 (71%)	11 (42%)	
Cartilage damage Yes	1 (2%)	0 (0%)	1 (4%)	0.328
No	49 (98%)	24 (100%)	25 (96%)	
Eye deviation Yes	9 (82%)	6 (25%)	3 (12%)	0.185
No	41 (18%)	18 (75%)	23 (88%)	
Weight gain Yes	1 (2%)	0 (0%)	1 (4%)	0.328
No	49 (98%)	24 (100%)	25 (96%)	

3.7. Classification of patients based on therapy:

This study showed that most widely used therapy for the disease was acetylcholinesterase inhibitor (Mestinon); 96%, followed by immunosuppressive (Imuran); 62% and Cortisone (40%). A significant relationship between Mestinon with the disease was determined (P=0.049)

Table7. Classification of patients based on therapy

Variables	Total N (%)	Male N (%)	Female N (%)	P-Value
Mestinon Used	48 (96%)	23 (96%)	25 (96%)	0.049
Not Used	2 (4%)	1 (4%)	1 (4%)	
Imuran Used	31 (62%)	16 (67%)	15 (58%)	0.788
Not Used	19 (38%)	8 (33%)	11 (42%)	
Cortisone Used	20 (40%)	11 (46%)	9 (35%)	0.539
Not Used	30 (60%)	13 (54%)	17 (65%)	
Gupisone Used	2 (4%)	1 (4%)	1 (4%)	1.000
Not Used	48 (96%)	23 (96%)	25 (96%)	
Rituximab IV Used	3(6%)	0 (0%)	3 (12%)	0.162
Not Used	47 (94%)	24 (100%)	23 (88%)	

Prednisolone Used Not Used	10 (20%) 40 (80%)	4 (17%) 20 (83%)	6 (23%) 20 (77%)	0.714
Cellcept Used Not Used	2 (4%) 48 (96%)	0 (0%) 24 (100%)	2 (8%) 24 (92%)	0.162

3.8 Correlation between patient's age and disease complications:

Pearson's correlation coefficient between age and disease complications showed a moderate positive relationship between age and Dysphagia (r=0.344), with a statistical significance of P=0.014. While some symptoms of Ptosis and Proximal Myopathy showed a postural defect (r= 0.135 and 0.228) and were not statistically significant (p= 0.348 and 0.111). Other tests, Muscle Weakness and Double Vision, showed a strong inverse relationship (r= -0.71, -0.42) and it was not statistically significant (p= 0.624, 0.773).

Table 8. The relationship between age and disease complication

Disease Complication	r	P value
Dysphagia	0.344*	0.014
Muscle Weakness	-0.71	0.624
Ptosis	0.135	0.348
Double Vision	-0.42	0.773

3.9 Correlation between patients' gender and disease complications:

The Pearson correlation coefficient between gender and disease complications showed a weak positive relationship for the following symptoms: Dysphagia, Double Vision, and Proximal Myopathy, and it was not statistically significant $P < 0.05$.

Other tests, Muscle Weakness, and Ptosis, showed a weak inverse relationship and it was not statistically significant $P < 0.05$.

Table 9. The relationship between gender and disease complications

Disease Complication	r	P value
Dysphagia	0.263	0.099

Muscle Weakness	-0.042	0.775
Ptosis	-0.074	0.609
Double Vision	0.017	0.904
Proximal Myopathy	0.098	0.498

3.10 Correlation between patient's age and immunological tests:

Pearson correlation coefficient between age and immunological analysis showed a weak positive correlation and was not statistically significant $P < 0.05$.

Table 10. The relationship between age and immunological tests

Disease Complication	r	P value
Anti-acetylcholine receptors antibodies	0.023	0.875
Anti -Musk antibodies	0.181	0.207

3.11 Correlation between patients' gender and immunological tests:

Pearson's correlation coefficient between age and immunological tests showed a weak positive relationship for the test (Acetylcholine Receptors) and was not statistically significant $P < 0.05$. The test (Anti-Musk) had a weak inverse relationship and was not statistically significant, $P < 0.05$.

Table 11. The relationship between gender and immunological tests

Disease Complication	r	P value
Anti-acetylcholine receptors antibodies	-0.247	0.084
Anti –Musk antibodies	0.095	0.511

4. DISSCUSSION:

The current study, which was conducted on 50 patients, showed that the disease appeared in (48%) of males and (52%) of females, and that the average age of patients with myasthenia gravis was 43.4 years. The average age of males was 47 years, the average age of females was 40 years, and the average date of diagnosis was 5.7 years. ± 4.1 years and (54%) suffer from chronic diseases accompanying the underlying disease, including (71%) males. And

(39%) are female. These findings were similar results to the previous study that showed that the average age was 48 years; in males it was 53 years and in females it was 34 years, as the duration of diagnosis ranged from one to eight years (Singhal**, B. S, 2008**).

With statistical significance (P = 0.029), the most common chronic diseases in this study were diabetes (20%) and hypertension (20%). Among the non-autoimmune comorbidities, type 2 diabetes and hypertension were more common in male patients with myasthenia gravis, which may be related to advanced age (Lee **I, 2018).**

Previous study in a Saudi (**Alanazy, M. H, 2019**) showed that the number of females outnumbered males with the infection, and that the symptoms appeared at a younger age in females compared to males, which is consistent with previous studies that showed that the disease is more prevalent in males than in females, and this may be due to This is either due to environmental factors or differences in race and ethnic composition **(Carr AS, 2010),** (**Al-Moallem MA, 2008**).

The patients' chemical investigations showed decreased levels of vitamin D and this was similar to the results obtained by **(Askmark H, 2012).** Additionally, the deficiency of vitamin B12 was observed as previously published (**Khademolhosseini S, 2021**). Our results found high white blood cell counts in contrast to the study conducted by (**Fritze D, 1975**) that found that the leukocyte counts did not change significantly during the disease. Our findings had observed that 66% of patients had normal red blood cell counts, whereas 34% of them had low counts, these results were compatible with the results of (**Sekiguchi K, 2022**) who with other researchers had found that 40% of the MG patients in their study had anemia, whereas had the rest of them normal

counts. Their study was conducted only on female MG patients. Immunological analysis showed high levels of Acetylcholine Receptors (AChR) in 44(88%) of the patients; 5 (10%) were seronegative. similar to the findings by (**Huang Y, 1999**), (Suh **J, 2013**). 33(66%) of the patients had high concentrations of anti-MUSK antibodies, similar to the results of (**Rivner M, 2019**) who indicated that MUSK antibodies were found in 40% MG patients and were associated with specific clinical phenotypes. As shown in the study of (Suh **J, 2013**)11 patients (10 %) had high anti-MUSK antibodies, 82 (71 %) had anti-AChR antibodies, and 22 (19 %) were seronegative for both. Studies have found that patients with myasthenia gravis who have antibodies to MUSK have a response to conventional immunotherapy. This requires higher corticosteroid doses to manage symptoms, but have lower cure rates than those with anti-AChR antibodies(**Evoli A**, **2008**), (**Guptill JT,2010**).No significant impact of age and gender on the levels of auto-antibodies was determined.

The results of this study showed that myasthenia gravis was prevalent among patients under 50 years of age. The results of the study conducted by (**Mantegazza R, 2018**). Prevalence rates and factors associated with disease complications risk were gender (females), age<40 years, and thymectomy.

Studies have shown that patients whose disease began before the age of fifty are more likely to resist treatment than older patients; this has been supported by previous studies (Suh **J, 2013**).

Previous studies showed no impact of gender on the disease outcome (Andersen **JB, 2016**), (**Mao Z, 2010**), but this study showed higher rates in females compared to males. Relapse cases occurred as a result of thymus gland enlargement, as administration of prednisolone or thymectomy leads to a decrease in the relapse rate in patients with myasthenia gravis (**Wakata N,**

2003). The most common symptoms in patients with myasthenia gravis were ptosis (94%), dysphagia (84%), and double vision (84%). A significant number of patients reported various visual symptoms such as muscle weakness (86%) and proximal myopathy (34%), whereas, the study of(**Roh, H, 2011**)showed that the most common symptoms seen in patients with myasthenia gravis were diplopia (93%) and ptosis (87%). In our results, dysphagia was significantly correlated with younger age. Myasthenia gravis may be more severe in females than in males, perhaps because myasthenia symptoms can be influenced by menstruation, pregnancy, and postpartum hormonal changes (**Boldingh MI, 2016**), (**Leker RR, 1998**).

Also in the current study, thymoma was detected in 5(19%) of female patients, compared to, 7(29%) of males. This is similar to a study conducted in China by (Dong **D, 2020**). Our cross-sectional study had observed that mestinon (Pyridostigmine) was the most used MG therapy as it is the first drug of choice for this disease (**Andersen J B, 2010**).

5. CONCLUSION:

Myasthenia gravis (MG) is the most common autoimmune neuromuscular disorder and is mediated by autoantibodies to acetylcholine receptors or muscle –specific tyrosine kinase. It affects different ages and affects females more than males.

In summary, this study evaluated the disease prevalence and its risk factors that can contributed to myasthenia relapse. Age of onset was an important predictor, in additions to other factors such as female gender, thymus enlargement (thymoma), ptosis, or diplopia with early generalization of myasthenia gravis. There was a statistically significant relationship between age and Dysphagia, meaning that the older the age, the greater the impairment

of Dysphagia. The most medication that used acetyl cholinesterase inhibitor that inhibits the destruction of acetylcholine and to improve the muscle functions.

The small sample size of patients and only two-center analysis were the most limitations of this study.

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