Clinical features and outcomes of patients with myasthenia gravis

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ABSTRACT

الأهداف: أبلغت هذه الدراسة عن المظاهر السريرية والمخبرية ومقاييس النتائج في مرضى الوهن العضلي (MG) من مركز واحد في المملكة العربية السعودية.

الطريقة: راجعنا بأثر رجعي الملفات الطبية للمرضى الذين لديهم MG (تم توثيق البيانات حول مقاييس النتائج بأثر مستقبلي) الذين قاموا بالمتابعة في عيادتنا العصبية والعضلية بين 1 أغسطس 2014 و 31 يناير 2019.

النتائج: في المجموع تم تضمين 95 مريضاً (55 امرأة، 40 رجل). كان العمر بداية المرض 40.5±18.1 سنة لدى الرجال و 31.3±15 سنة لدى النساء. كان متوسط فترة المتابعة في عيادتنا 34.7±14.1 شهرًا، وكان متوسط المدة منذ بداية المرض 8.0±7.2 عامًا. من جميع المرضى، كان لدى 92.6% وهن عضلي عام، 82.1% لديهم أجسام مضادة (AChR)، 4.2% لديهم أجسام مضادة من MuSK، 78.9% لديهم بداية المرض مبكرة مع عدم وجود ذروة ثانية بعد 50 سنة، 22.1% عانو من أزمة الوهن العضلي (crisis)، 12.6% لديهم وهن عضلي مقاوم للعلاج، كان 31.6% لديهم فرط تنسج في الغدة التوتة، و 10.5% لديهم ورم التوتة، و61.1% كانوا بحاجة إلى أكثر من علاج مثبط للمناعة. في المتابعة الأخيرة، جميع المرضى باستثناء اثنين قد حققوا أفضل النتائج (تصنيف مؤسسة MG الأمريكية لـ ≥ II). بالنسبة المرضى الذين لايوجد لديهم اجسام مضادة لا يوجد عند اي منهم ورم الغدة الزعترية أو احتاج دواء رتوكسماب أو القلوبيولين المناعي .

الخاتمة: بالمقارنة مع المجموعات العرقية الأخرى، تفتقر مجموعة المرضى هنا إلى ذروة ثانية من بداية MG، وتؤكد النتيجة الإيجابية لغالبية المرضى.

Objectives: To report clinical and laboratory features and outcomes of patients with autoimmune myasthenia gravis (MG) recruited from a single center in Saudi Arabia.

Methods: We retrospectively reviewed prospectively collected data obtained from MG patients who have undergone examination and follow-up at our neuromuscular clinic between August 1, 2014 and January 31, 2019.

Results: Ninety-five patients (55 females) were included. The mean age of onset of MG was 40.5±18.1 years in males and 31.3±15 years in females (p=0.009). The mean duration of follow-up at our clinic was 34.7±14.1 months, while the mean duration since MG onset was 8.0±7.2 years. Of all patients, 92.6% had generalized MG, 82.1% had acetylcholine receptor (AChR) antibodies, 4.2% had muscle-specific tyrosine kinase (MuSK) antibodies, 78.9% had early-onset MG with no second peak after age of 50 years, 22.1% had myasthenia crisis, 12.6% had refractory MG, 31.6% had thymic hyperplasia, 10.5% had thymoma, and 61.1% required ≥2 immunosuppressive therapies. At the last follow-up, 93 patients had achieved an optimal outcome (MG Foundation of America classification ≤ II). No patient with double-seronegative (dSN)-MG had thymoma, needed rituximab or intravenous immunoglobulin maintenance therapy, or was classified as refractory MG.

Conclusion: Contrary to other studies, we did not observe a second-peak of MG onset. Clinical outcomes were favorable in the majority of our patients.

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Acquired myasthenia gravis (MG) is a neuromuscular junction (NMJ) disorder resulting from an autoimmune attack of postsynaptic structures. Most of the patients with MG (85%) test positive for

acetylcholine receptor (AChR) antibodies, while 4% to 6% patients test positive for muscle-specific tyrosine kinase (MuSK) antibodies.[1] Between 7% and 32.7% of patients with double-seronegative-(dSN) MG test positive for low-density lipoprotein receptor-related protein (LRP4) antibodies.[2] The ensuing impairment in synaptic transmission at the NMJ, as a result of these autoantibodies, clinically manifests in fatigable weakness including ptosis, diplopia, dysarthria, dysphagia, and weakness in the neck, proximal limb, and respiratory muscles. In a majority of patients (85%), MG has an ocular onset that subsequently generalizes.[3] The remaining patients are classified into localized ocular, ocular and bulbar, or ocular and peripheral MG.[3]

Contrary to international studies that report a second peak of onset of MG after 50 years of age,[3,4] Al-Moallem et al[5] studied a cohort of patients with MG in Saudi Arabia and observed a peak age of onset in the second and third decades in females and third and fourth decades in males. Nonetheless, the rates of remission and clinical profiles were comparable with those reported in other racial groups.[5] A study from Libya reported a higher incidence of MG in young females and older males.[6] In general, MG has not been extensively studied in Saudi Arabia and other Arab countries, with the study by Al-Moallem et al. being the only other study conducted locally.[5] Unfortunately, that study did not employ rigorous measurement of MG-specific outcome measures. In this study, we aimed to retrospectively analyze prospectively collected data related to clinical, laboratory, and MG-specific outcome measures of a cohort of patients with MG who were registered and managed at our neuromuscular clinic.

Methods. The Neuromuscular Clinic at King Saud University Medical City, Riyadh, Kingdom of Saudi Arabia was established in August 2014. The clinic protocol involves examination and follow-up by the author at least twice a year, in addition to close monitoring and documentation of MG-specific outcome measures in every visit to the clinic. This study was a retrospective chart review of prospectively collected data from patients who underwent examination and follow-up care at our Neuromuscular Clinic between August 1, 2014 and January 31, 2019. Patient demographics, clinical characteristics, disease-related history, type of MG antibodies, therapy, and MG-specific outcome measures were prospectively documented during each visit to the neuromuscular clinic. For patients who had been diagnosed with MG prior to the establishment of our clinic, we reviewed their medical charts and transferred the available data into our clinic records. The study was approved by the King Saud University College of Medicine Institutional Review Board, and informed consent was waived. We included Arab patients who were at least 14 years of age and were diagnosed with MG by a neuromuscular specialist. The diagnosis of MG was based on the presence of suggestive clinical features of MG, and either elevated antibodies (AChR or MuSK antibodies) or abnormal electrodiagnostic studies (≥ 10% decrement on repetitive nerve stimulation or increased jitter and blocking on single-fiber electromyography). Patients who had made a minimum of 2 visits to our Neuromuscular Clinic, with the last visit being not more than 6 months (the maximum follow-up period allowed in our clinic) prior to the time of data collection were included in the study.

Study variables. We collected demographic data and data related to the age at onset of MG, disease duration from the time of onset, duration of follow-up at our clinic, type of MG (ocular or generalized), type of MG antibodies (AChR, MuSK, or dSN), thymectomy status, thymus histopathology, current MG therapy, previous use of intravenous immunoglobulin (IVIg) or plasma exchange (PLEX), number of MG crises (defined as severe respiratory distress requiring admission to an intensive care unit [ICU]) or exacerbations (defined as worsening of MG symptoms requiring hospitalization, rescue therapy with IVIg or PLEX, or escalation of steroid dose), number of intubations due to MG, number of patients who were classified as having refractory MG, and presence of a coexisting autoimmune disease. Refractory MG was defined as: (a) failure to respond adequately to appropriate doses and durations of conventional immunosuppressive therapies; (b) occurrence of severe or intolerable side effects of MG therapies; (c) requirement of high doses of potentially harmful therapies; (d) presence of comorbidities that prevent the use of conventional therapies; or (e) requirement of repeated rescue therapy with IVIg or PLEX.[7]

Outcome measures. We collected the following MG-specific outcome measures from our documentation of the last visit to the clinic: MG composite score (MGCS; total score ranges from 0 to 50),[8] MG-manual muscle test (MG-MMT) score (total score ranges from 0 to 120),[9] MG quality-of-life revised Arabic version (MG-QOL15R-A) score (total score ranges form 0-30),[10] and MG-activity of daily living Arabic version (MG-ADL-A) score (total score ranges

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Table 1 - Demographic information, MG-related history, therapy, and outcomes in the most recent follow-up visit in male and female patients.

Variables	Total (n=95)	Males (n=40)	Females (n=55)	*P*-value
	Mean±SD or n(%)			
Current age (years)	42.7±17.6	47.1±19.4	39.5±15.6	0.037
Age at onset (years)	35.2±16.9	40.5±18.1	31.3±15.0	0.009
Disease duration (years)	8.0±7.2	6.6±6.6	9.0±7.6	0.10
Follow-up duration (months)	34.7±14.1	33.7±13.4	35.4±14.6	0.55
History of autoimmune disorder	26 (27.4)	2 (5.0)	24 (43.6)	<0.001
MG type				
Ocular	7 (7.4)	4 (10.0)	3 (5.5)	0.45
Generalized	88 (92.6)	36 (90.0)	52 (94.5)	
Antibody status				
AChR	78 (82.1)	33 (82.5)	45 (81.8)	
MuSK	4 (4.2)	0	4 (7.3)	0.12
Double negative	13 (13.7)	7 (17.5)	6 (10.9)	
MG-QOL15R-A, M±SD	5.2±6.0	4.4±5.0	6.0±6.6	0.19
MG-ADL-A, M±SD	1.7±2.4	1.0±1.9	2.3±2.5	0.005
MGCS, M±SD	1.6±2.7	0.8±1.9	2.2±3.0	0.005
MG-MMT, M±SD	2.2±4.7	0.6±1.8	3.3±5.8	0.002
MGFA				
CSR	5 (5.3)	2 (5.0)	3 (5.5)	
PR	51 (53.7)	29 (72.5)	22 (40)	
MGFA I	10 (10.5)	3 (7.5)	7 (12.7)	0.004
MGFA II	27 (28.4)	6 (15.0)	21 (38.2)	
MGFA III	2 (2.1)	0	2 (3.6)	
MG crisis	21 (22.1)	11 (27.5)	10 (18.2)	0.28
MG exacerbation	37 (38.9)	17 (42.5)	20 (36.4)	0.55
Refractory MG	12 (12.6)	3 (7.5)	9 (16.4)	0.20
Thymectomy*	61 (64.2)	21 (52.5)	40 (72.7)	0.04
Thymoma	10 (10.5)	8 (20.0)	2 (3.6)	0.02
Thymic hyperplasia	30 (31.6)	11 (27.5)	19 (34.5)	0.47
Therapy at last follow-up†				
Prednisolone	77 (81.1)	34 (85.0)	43 (78.2)	0.40
Pyridostigmine	59 (62.1)	24 (60.0)	35 (36.6)	0.72
Azathioprine	45 (47.4)	22 (55.0)	23 (42.6)	0.23
Mycophenolate	14 (14.7)	8 (20.0)	6 (10.9)	0.22
Maintenance IVIg	16 (16.8)	4 (10.0)	12 (21.8)	0.13
Rituximab	11 (11.6)	3 (7.5)	8 (14.5)	0.35
Previous IVIg	51 (53.7)	24 (60.0)	27 (49.1)	0.29
Previous plasma exchange	10 (10.5)	6 (15.0)	4 (7.3)	0.23

AchR - acetylcholine receptor antibodies, CSR - complete stable remission, IVIg - intravenous immunoglobulin, M - mean, MG - myasthenia gravis, MG-ADL-A - Arabic version of the MG-activity of daily living scale, MG-MMT - MG-manual muscle test score, MGCS - MG composite score, MGFA - MG foundation of America classification, MGFA I - ocular MG, MGFA II - mild generalized MG, MGFA III - moderate generalized MG, MG-QOL15R-A - Arabic version of the MG quality-of-life revised questionnaire, MuSK - muscle specific tyrosine kinase antibodies, PR - pharmacologic remission, SD - standard deviation. Percentages (%) are derived from the total number of patients in the respective columns. All MG-specific outcome measures were derived from the last follow-up clinic visit.* Histopathology results were normal in 10 patients and missing in 11 patients. †Therapy at last follow-up: represent total number (%) of each therapy use whether single or combined

Table 2 - MG therapy combinations at last follow-up.

MG therapy	Number (%)
Prednisolone and azathioprine	28 (29.5)
Prednisolone alone	19 (20.0)
Prednisolone and Mycophenolate	10 (10.5)
Pyridostigmine alone	8 (8.4)
Prednisolone, azathioprine and IVIg	7 (7.4)
Azathioprine alone	4 (4.2)
Prednisolone and Rituximab	3 (3.2)
Prednisolone, azathioprine, IVIg and Rituximab	3 (3.2)
Prednisolone, azathioprine and Rituximab	2 (2.1)
Prednisolone, Mycophenolate, IVIg, and Rituximab	2 (2.1)
Prednisolone, Rituximab, and IVIg	1 (1.1)
Prednisolone, Mycophenolate, and IVIg	1(1.1)
Azathioprine, Mycophenolate, and IVIg	1 (1.1)
Prednisolone and IVIg	1 (1.1)
No current therapy	5 (5.3)
≥ 2 immunosuppressive therapies	58 (61.1)

MG - myasthenia gravis, IVIg - intravenous immunoglobulin

from 0 to 24).[11] Higher scores on the aforementioned scales indicate greater levels of MG symptom severity. In addition, the severity of MG was determined according to the Myasthenia Gravis Foundation of America classification (MGFA I, ocular MG; MGFA II, mild generalized MG; MGFA III, moderate generalized MG; MGFA IV, severe generalized MG; and MGFA V, intubation).[12] Patients who had no weakness (except mild weakness related to eyelid closure) were classified into either "pharmacologic remission (PR)," if they still required MG-specific therapy, or "complete stable remission (CSR)," if they did not require MG-specific therapy for at least one year.

Analysis. Data related to demographics, MG-related history, clinical characteristics, MG therapies, and MG-specific outcome measures have been reported as mean±SD or number (%), as appropriate. Patients were categorized into groups based on sex, age at onset (early-onset: EOMG, <50 years; late-onset: LOMG, ≥50 years), MG-antibody status, and thymectomy status. Differences in categorical variables between patient subgroups were assessed using the Chi-square, Fisher's exact, or Kruskal–Wallis tests, as appropriate. Mann–Whitney U tests with Bonferroni corrections were employed for post-hoc comparisons. Differences in continuous variables between patient subgroups were evaluated by nonparametric tests or analysis of variance (ANOVA), as appropriate. Results with two-tailed *p*-values less than 0.05 were considered statistically significant. Data analysis was performed using SPSS 23.0 (IBM, Armonk, New York).

Results. In total, 95 patients were included (40 males; 55 females; M/F ratio- 1:1.4) in the study. We excluded 4 patients: 2 patients died due to reasons other than MG (brain metastasis and Middle East respiratory syndrome coronavirus) and lost 2 patients to follow-up (both had AChR-positive generalized MG with an MGFA of II). The demographic and clinical characteristics of the study cohort are detailed in **Table 1**. Of all participants, 82.1%, 4.2%, and 13.7% patients tested positive for AChR, MuSK, and dSN antibodies, respectively. AChR antibodies were observed in 84.1% and 57.1% of patients with generalized and ocular MG, respectively. The age at onset of autoimmune MG ranged from 4 to 80 years, with a mean of 35.2±16.9 years; female patients were significantly younger than male patients at onset of MG (p=0.009; **Table 1**). The duration since the onset of MG ranged from 1 to 31 years, with a mean of 8.0±7.2 years. The disease duration exceeded 2 years in 82.1% of the patients in our sample. The mean follow-up duration at our clinic was 34.7±14.1 months. The proportion of female patients with a comorbid autoimmune disease was significantly higher than that of male patients. The most prevalent comorbid autoimmune disease was hypothyroidism (n=14), followed by systemic lupus erythematosus (n=5). Thymectomy was performed more frequently in females, while thymoma was more frequently observed in males. Disease severity was milder in males than in females in all the MG-specific outcome measures, except one (**Table 1**). Myasthenic crises requiring ICU admission occurred in 21 (22.1%) patients (6 patients had >1 crises) and 8 patients required intubation. Twelve (12.6%) patients met the criteria for refractory MG. We did not observe a significant difference (p=0.13) in the age at MG onset between patients with refractory MG (29.3±14.2 years) and those with non-refractory MG (36.0±17.2 years).

The most commonly used therapy was prednisolone, followed by pyridostigmine. Maintenance IVIg and rituximab were used in 16.8% and 11.6% of cases, respectively (**Table 1**). The most commonly used combination immunosuppressive therapy consisted of prednisolone and azathioprine (**Table 2**).

A majority of patients (78.9%) had an EOMG. The proportion of males was higher in the LOMG group (F/M ratio- 1:3), whereas that of females was higher in the EOMG group (F/M ratio- 2:1) (**Table 3 and Figure 1**).

There were no significant differences between the early and late onset groups of MG patients in most of the outcome measures or therapy, except that the EOMG group had a higher mean MG-QOL15R-A score than the LOMG group.

Table 4 shows the results of the comparison between patient groups categorized based on antibody status. Of the 4 MuSK-positive patients with MG, one patient was not on therapy (CSR), one worsened with pyridostigmine, and 2 showed no response to it. **Table 5** outlines the results of the comparisons between patient groups categorized based on their thymectomy status. The mean duration between thymectomy and the last follow-up visit was 7.36±6.5 years (range: 1-29 years). After excluding patients with MuSK-MG and those who had thymoma, our analysis revealed no significant differences in MG-specific outcome measures between patients who underwent thymectomy and those who did not undergo the surgery. Thymus histopathology results revealed hyperplasia (n=30), thymoma (n=10), and normal or atrophic (n=10) thymus. We did not have access to data from 11 patients who had undergone the surgery more than a decade prior to the study.

Discussion. Similar to the findings of other international studies,[3] our study reports that Saudi Arabian female patients with MG showed onset of symptoms at a significantly younger age (peak: 20-29 years) than male patients with MG (peak: 30-39 age). In agreement with previous findings,[13] we also observed a sex-related bias in our study, in that female patients outnumbered male patients. A majority of patients from both sexes had an EOMG; in the LOMG group, male patients outnumbered female patients, which is in line with the report by Al-Moallem et al.[5] However, contrary to previous studies from the United States, Europe, and South Africa, and studies performed on Dutch and Norwegian patients that have consistently shown a bimodal peak of onset for females and a late single peak for males,[14] we did not observe a second peak of MG onset after 50 years of age in males or females in our cohort. This may be attributed either to environmental factors or to differences in ethnicity and racial composition.

In this study, a majority of patients was diagnosed with generalized MG; no patient had a pure bulbar or peripheral MG. The frequency of detection of AChR antibodies among patients was within the range reported worldwide (62-90%).[15] On the other hand, the frequency of detection of MuSK antibodies among AChR-negative patients was 23.5%, which is lower than the reported mean rate worldwide (36-37%).[15,16] The proportion of MuSK-positive patients who had experienced an MG crisis or exacerbation was higher than that of patients with AChR-positive or dSN-MG; however, this result was not statistically significant, likely due to the small number of MuSK-positive patients in our sample. The MG-specific outcome measures at the last follow-up visit were similar among the 3 antibody groups. It has been reported that MuSK-positive patients experience more severe weakness at maximum disease severity than other antibody-group patients; however, the likelihood of attaining an optimal outcome was not different among the 3 antibody group patients.[17,18] Our findings support these reports. In addition, the findings from the MuSK-positive patient subgroup in our study confirm the previously reported predominance among females, intolerance or poor response to pyridostigmine, and improvement with immunosuppressive medications including rituximab in such patients.[18] Notably, no patient with dSN-MG had thymoma, needed rituximab or IVIg maintenance therapy, or was classified as refractory MG. However, these patients were not tested for LRP4 antibodies or low-affinity antibodies. While these results were not statistically significant, they suggest that the dSN-MG group may have better outcomes than the other MG-antibody groups. As data on MG-specific outcome measures were not collected for patients in whom the onset of MG was before the establishment of our clinic, it remains possible that patients with dSN-MG have milder symptoms from the outset.

The rates of MG crises and refractory MG in our study are comparable to those reported elsewhere.[19] Of the 95 patients analyzed in this study, 93 patients had mild disease severity (MGFA ≤ II) at the last follow-up, reflecting the favorable prognosis of MG overall. This may be attributed to the aggressive treatment options used in our clinic: 61.1% of the patients were treated with two or more immunosuppressive therapies. However, given the fluctuating nature of MG and because the MG-specific outcome measures were derived from the last follow-up visit, one should acknowledge that the good outcomes reported here do not reflect long-term stability of the disease in our cohort. However, most of the patients in this study had previously participated in the study validating the Arabic versions of the MG-QOL15R and MG-ADL,[10,11] which involved collecting MG-specific outcome measure data at different times than data collected for this study. As these studies also report milder disease symptoms among the patients (MG-QOL15R-A: 84.6%; MG-ADL-A: 89.7%), we can consider that the overall prognosis of patients in our cohort is good.

Table 3 - Demographic information, MG-related history, therapy, and outcomes in the most recent follow-up among patients with early and late onset MG.

Variables	Early onset MG (<50 years, n=75)	Late onset (≥50 years, n=20)	*P*-value
	Mean±SD or n (%)		
Gender			0.001
Male	25 (62.5)	15 (37.5)	
Female	50 (90.9)	5 (9.1)	
Disease duration (years)	8.3±7.2	6.9±7.7	0.45
Follow-up duration (months)	34.7±14.5	34.7±12.8	1.00
History of autoimmune disorder	23 (30.7)	3 (15.0)	0.16
MG type at last follow-up visit			0.16
Ocular	4 (5.3)	3 (15.0)	
Generalized	71 (94.7)	17 (85.0)	
MG-QOL15R-A	5.7±6.0	3.5±5.9	0.04
MG-ADL-A	1.9±2.4	1.2±2.3	0.10
MGCS	1.9±2.8	0.7±1.7	0.07
MG-MMT	2.5±5.1	1.1±2.6	0.14
MGFA			0.34
CSR	5 (6.7)	0	
PR	36 (48.0)	15 (75.0)	
MGFA I	10 (13.3)	0	
MGFA II	22 (29.3)	5 (25.0)	
MGFA III	2 (2.7)	0	
MG crisis	15 (20.0)	6 (30.0)	0.37
MG exacerbation	28 (37.3)	9 (45.0)	0.53
Refractory MG	11 (14.7)	1 (5.0)	0.25
Therapy at last follow-up			
Prednisolone	60 (80.0)	17 (85.0)	0.76
Pyridostigmine	43 (57.3)	16 (80.0)	0.06
Azathioprine	33 (44.6)	12 (60.0)	0.22
Mycophenolate	13 (17.3)	1 (5.0)	0.17
Maintenance IVIg	12 (16.0)	4 (20.0)	0.74
Rituximab	11 (14.7)	0	0.06
Previous IVIg	40 (53.3)	11 (55.0)	0.89
Previous plasma exchange	8 (10.7)	2 (10.0)	0.93

AchR - acetylcholine receptor antibodies, CSR - complete stable remission, IVIg - intravenous immunoglobulin, M - mean, MG - myasthenia gravis, MG-ADL-A - Arabic version of the MG-activity of daily living scale, MG-MMT - MG-manual muscle test score, MGCS - MG composite score, MGFA - MG foundation of America classification, MGFA I - ocular MG, MGFA II - mild generalized MG, MGFA III - moderate generalized MG, MG-QOL15R-A - Arabic version of the MG quality-of-life revised questionnaire, MuSK - muscle specific tyrosine kinase antibodies, PR - pharmacologic remission SD - standard deviation. Percentages (%) are derived from the total number of patients in the respective columns. All MG-specific outcome measures were derived from the last follow-up clinic visit.

We observed that 61 patients from our sample had undergone thymectomy. The most common histopathological finding was thymic hyperplasia, which is supported by a previous study conducted in Saudi Arabia.[5] Thymoma occurred in 10.5% of the patients in our cohort and was more common in male patients than in females. In patients with generalized non-thymomatous AChR-positive MG, thymectomy has proven beneficial in improving clinical outcomes and in reducing immunosuppressive therapy and exacerbations.[20] In contrast, we did not observe differences in MG-specific outcome measures, number of MG crises or exacerbations, or the need for immunosuppressive therapy, between patients who had undergone thymectomy and those who had not undergone thymectomy. When we included

Table 4 - Demographic information, MG-related history, therapy, and outcomes in the most recent follow-up among patients with seronegative and AchR-positive MG.

Variables	AchR (n=78)	Double seronegative (n=13)	Anti-MuSK (n=4)	*P*-value
		Mean±SD or n (%)		
Current age (years)	43.4±17.1	39.7±17.4	38.5±29.7	0.69
Age at onset (years)	35.3±16.3	35.2±16.1	32.5±32.9	0.95
Disease duration (years)	8.5±7.4	5.5±5.2	6.6±8.2	0.38
Follow-up duration (months)	36.1±13.4	27.8±15.4	29.5±17.5	0.11
History of autoimmune disorder	22 (28.2)	3 (23.1)	1 (25.0)	0.92
MG type				0.23
Ocular	4 (5.1)	2 (15.4)	1 (25.0)	
Generalized	74 (94.9)	11 (84.6)	3 (75.0)	
MG-QOL15R-A	5.1±5.9	3.8±5.0	11.3±8.7	0.25
MG-ADL-A	1.76±2.4	0.9±1.4	3.3±2.2	0.13
MGCS	1.7±2.8	1.2±1.7	1.7±1.5	0.79
MG-MMT	2.3±5.0	1.4±1.8	0.7±1.2	0.87
MGFA				0.61
CSR	4 (5.1)	0	1 (25.0)	
PR	43 (55.1)	6 (46.2)	2 (50.0)	
MGFA I	5 (6.4)	5 (38.5)	0	
MGFA II	24 (30.8)	2 (15.4)	1 (25.0)	
MGFA III	2 (2.6)	0	0	
MG crisis	17 (21.8)	2 (15.4)	2 (50.0)	0.35
MG exacerbation	32 (41.0)	2 (15.4)	3 (75.0)	0.07
Refractory MG	10 (12.8)	0	2 (50.0)	0.03*
Thymectomy	58 (74.4)	2 (15.4)	1 (25.0)	<0.001†
Thymoma	10 (12.8)	0	0	1.00
Thymic hyperplasia	28 (35.9)	1 (7.7)	1 (25.0)	1.00
Therapy at last follow-up				
Prednisolone	65 (83.3)	9 (69.2)	3 (75.0)	0.47
Pyridostigmine	52 (66.7)	7 (53.8)	0	0.02‡
Azathioprine	38 (49.4)	5 (38.5)	2 (50.0)	0.77
Mycophenolate	14 (17.9)	0	0	0.17
Maintenance IVIg	15 (19.2)	0	1 (25.0)	0.21
Rituximab	9 (11.5)	0	2 (50.0)	0.03*
Previous IVIg	45 (57.7)	4 (30.8)	2 (50.0)	0.19
Previous plasma exchange	9 (11.5)	0	1 (25.0)	0.29

AchR - acetylcholine receptor antibodies, CSR - complete stable remission, IVIg - intravenous immunoglobulin, M - mean, MG - myasthenia gravis, MG-ADL-A - Arabic version of the MG-activity of daily living scale, MG-MMT - MG-manual muscle test score, MGCS - MG composite score, MGFA - MG foundation of America classification, MGFA I - ocular MG, MGFA II - mild generalized MG, MGFA III - moderate generalized MG, MG-QOL15R-A - Arabic version of the MG quality-of-life revised questionnaire, MuSK - muscle specific tyrosine kinase antibodies, PR - pharmacologic remission, SD - standard deviation. Percentages (%) are derived from the total number of patients in the respective columns. All MG-specific outcome measures were derived from the last follow-up clinic visit. *p=0.008 for comparisons between patients who tested positive for MuSK antibodies and double seronegative patients. †p<0.001 for comparisons between patients who tested positive for AchR antibodies and double seronegative patients. ‡p=0.007 for comparisons between patients who tested positive for AchR antibodies and those who tested positive for MuSK antibodies.

only the subgroup of patients with generalized non-thymomatous AChR-positive MG in the analysis, we found that a significantly higher (p=0.04) proportion of patients (72.2%) in the "no thymectomy" group required azathioprine than that in the "thymectomy" group (43.5%); we observed no significant differences in other variables between the 2 groups (data not shown). In addition to the small sample size and lack of randomization in our study, this lack of difference between the 2 groups is probably due to a bias introduced by cultural factors as observed by the author, in that patients with mild generalized MG (MGFA II)

Table 5 - Demographic information, MG-related history, therapy, and outcomes in the most recent follow-up based on thymectomy status (patients with thymoma and anti-MuSK antibodies were excluded).

Variables	Thymectomy (n=50)*	No thymectomy (n=31)	*P*-value
	Mean±SD or n (%)		
Current age (years)	37.7±13.3	50.4±19.7	0.003
Age at onset (years)	28.6±10.2	44.6±18.2	<0.001
Disease duration (years)	9.9±7.7	5.7±5.9	0.002
Follow-up duration (months)	38.3±11.9	30.5±16.1	0.05
MG type			0.07
Ocular	1 (2.0)	4 (12.9)	
Generalized	49 (98.0)	27 (87.1)	
MG-QOL15R-A	6.1±6.3	3.6±4.6	0.08
MG-ADL-A	2.0±2.5	1.4±2.2	0.19
MGCS	2.1±3.1	1.1±2.1	0.15
MG-MMT	3.2±5.9	1.0±2.3	0.12
MGFA			0.23
CSR	4 (8.0)	0	
PR	21 (42.0)	20 (64.5)	
MGFA I	5 (10.0)	5 (16.1)	
MGFA II	18 (36.0)	6 (19.4)	
MGFA III	2 (4.0)	0	
MG crisis	11 (22.0)	4 (12.9)	0.31
MG exacerbation	16 (32.0)	12 (38.7)	0.54
Refractory MG	9 (18.0)	1 (3.2)	0.08
Therapy at last follow-up			
Prednisolone	40 (80.0)	26 (83.9)	0.66
Pyridostigmine	32 (64.0)	19 (63.3)	0.81
Azathioprine	21 (42.0)	18 (58.1)	0.19
Mycophenolate	9 (18.0)	1 (3.2)	0.08
Maintenance IVIg	8 (16.0)	5 (16.1)	1.00
Rituximab	7 (14.0)	0	0.04
Previous IVIg	28 (56.0)	13 (41.9)	0.22
Previous plasma exchange	6 (12.0)	0	0.08

AchR - acetylcholine receptor antibodies, CSR - complete stable remission, IVIg - intravenous immunoglobulin, M - mean, MG - myasthenia gravis, MG-ADL-A - Arabic version of the MG-activity of daily living scale, MG-MMT - MG-manual muscle test score, MGCS - MG composite score, MGFA - MG foundation of America classification, MGFA I - ocular MG, MGFA II - mild generalized MG, MGFA III - moderate generalized MG, MG-QOL15R-A - Arabic version of the MG quality-of-life revised questionnaire, MuSK - muscle specific tyrosine kinase antibodies, PR - pharmacologic remission, SD - standard deviation. Percentages (%) are derived from the total number of patients in the respective columns. All MG-specific outcome measures were derived from the last follow-up clinic visit. *one of the 4 patients with anti-Musk had thymectomy before knowing Musk status

who are deemed good candidates for thymectomy tend to decline it and patients with moderate to severe MG tend to accept it.

Limitations of this study include bias introduced by referrals to a tertiary hospital and its retrospective design that included patients with missing data as they were diagnosed more than a decade prior to the study. However, it is noteworthy that the MG-specific outcome measures were prospectively documented in patient charts as it is a routine practice in our clinic and a strength of our study. In addition, the exclusion of patients who were lost to follow-up before the establishment of the neuromuscular clinic may have resulted in the exclusion of patients who have been in remission and those who relocated or died. Five of the 17 patients who were diagnosed with MG before 2006 had been followed in the institution where a similar study was conducted and published by Al-Moallem et al.[5] We cannot exclude the possibility that those 5 patients

were also included by Al-Moallem et al[5] resulting in a possible duplication of their data in our study.

In conclusion, the demographic data, clinical characteristics, antibody profile, requirement for immunosuppressive therapy, and clinical outcomes in our cohort of patients with MG are comparable to those reported in other ethnic groups. An exception to this conformance is the absence of a second peak of MG onset after 50 years of age in our cohort. Our study also confirms that the outcome is favorable for a majority of the patients with MG. Compared to other MG antibody-groups, patients with dSN-MG may have milder disease symptoms and/or better prognosis. A nation-wide multi-center study is warranted to validate our findings.

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