

Incidence and clinical feature of Myasthenia gravis: A five-year data analysis in Ulaanbaatar, Mongolia

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Received: 4 July 2021; **Accepted:** 25 October 2021; **Published:** 30 November 2021

Edited by: Battuvshin Lkhagvasuren (Mongolian National University of Medical Sciences, Mongolia)

Reviewed by: Tuvshingerel Sandagdorj (National Cancer Center of Mongolia, Mongolia);

Goh Khean Jin (Universiti Malaya, Malaysia)

<https://doi.org/10.31117/neuroscirn.v4i3Suppl.96>

Abstract: Myasthenia gravis (MG) is a rare neuromuscular disorder. Till now, there are no studies on the prevalence and incidence of MG in Mongolia. The current study aimed to elucidate the incidence of MG in Ulaanbaatar, the age of onset, and the gender distribution of Mongolian patients with MG. We conducted a cross-sectional, hospital-based study involving MG patients (n=48) all around Ulaanbaatar from 1 January 2015 to 1 January 2020. The clinical diagnosis was assessed with the Myasthenia Gravis Foundation of America (MGFA) classification system. The disease severity was evaluated by using Osserman's classification. The diagnosis was confirmed with serological and electrophysiological tests. Statistical analysis was performed using SPSS software. A total of 30 patients with MG were registered for the last five years in Ulaanbaatar. The average annual incidence of MG in Ulaanbaatar was 0.65 per 100,000 populations (95%CI 0.26-1.34), 0.60 in males (95%CI 0.25-1.28), and 0.69 in females (95%CI 0.33-1.46). The cumulative incidence in the study period was 3.2 per 100,000 populations. The ratio of males to females was 1:1.3. The median age for onset of MG was 33 years (ranging from 27 to 46 years); 43.3% of patients had ocular and 56.7% generalized symptoms at the disease onset. Only 23.3% of patients remained with purely ocular symptoms (Osserman I stage). The average incidence of MG between 2015 and 2020 was 6.5 per 1,000,000 population, and the annual incidence was relatively stable. Although ocular and generalized symptoms were observed each in about half of the cases, only one-fourth remained with pure ocular signs at the end of the review period.

Keywords: Myasthenia gravis; annual incidence; early-onset myasthenia gravis; late-onset myasthenia gravis;

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1.0 INTRODUCTION

Myasthenia gravis (MG) is an autoimmune antibody-mediated chronic disorder affecting the postsynaptic membrane of neuromuscular junctions ([Gilhus et al., 2015](#); [Pakzad et al., 2011](#)). MG is characterized by fluctuating weakness and fatigability of voluntary

muscles improving with rest and worsening with repetitive usage ([Turner, 2007](#); [Vincent, 2008](#)). According to a survey of MG cases worldwide over the past 60 years, the incidence rate ranged from 1.7 to 21.3 cases per million person-years, and the prevalence rate ranged from 15-179 per million ([Carr et al., 2010](#)).

Studies demonstrating age and gender show that it is more common in young (20-40) women and older (50-70) men, and females are more commonly affected than males (about 1:1.5) ([Aarli, 1999](#); [Carr et al., 2010](#); [Lee et al., 2018](#)). Alshekhlee and colleagues studied a hospital-based study of 5,502 patients in the United States from 2000 to 2005 and found that the incidence was 2-3 times higher in women during the first five decades. In men, the incidence of admission was higher during the sixth, seventh, and eighth decades ([Alshekhlee et al., 2009](#)). In comparison, the incidence of MG has been steadily rising in Asian countries for the past 30 years ([Leeamornsiri et al., 2011](#); [Murai et al., 2011](#)). Japanese colleagues reported about decreasing incidence of early-onset Myasthenia gravis (EOMG) in 2005 compared with 1987, while the incidence of late-onset Myasthenia gravis (LOMG) was increased ([Murai et al., 2011](#)).

According to the Myasthenia Gravis Foundation of America (MGFA) classification, MG is clinically classified as an ocular and generalized form (mild, moderate, severe, and intubation needed to maintain the airway) ([Jaretzki et al., 2000](#)). The ocular symptoms are frequently the first manifestation signs of MG ([Ding et al., 2020](#)), tending to spread to the other parts of the body within two years of disease onset ([Bever Jr et al., 1983](#)). MG produces long-term disability and affects health-related quality of life. Patients with MG get disability approval from specialists in our country when the serological and electrophysiological tests are positive. The duration of disability benefits will be decided based on the clinical manifestations of the MG in Mongolia.

There are no studies known for this neuromuscular disease in Mongolia. According to an annual report from the National Statistical Office of Mongolia, neuromuscular diseases were not registered constantly and were often referred to as the classification of other diseases. No data are available on the MG prevalence and incidence in Mongolia, and there are also no guidelines for the diagnosis and treatment of MG.

Almost half of Mongolia's three million population lives in the capital city of Mongolia. The serological and electrophysiological diagnostic can confirm the diagnosis of MG but are available only in the capital city. Therefore, confirming the diagnosis of MG in rural areas is not available. The current study aims to elucidate the incidence of the MG in Ulaanbaatar city and analyze the age of disease onset, gender distribution, and clinical symptoms of patients with MG.

2.0 MATERIALS AND METHODS

The Ulaanbaatar city is officially divided into nine districts: Baganuur, Bagakhangai, Bayangol, Bayanzurkh, Chingeltei, Sukhbaatar, Songinokhairkhan, Khan-Uul and Nalaikh. The patients with suspected MG are first referred to a district neurologist for diagnostic and follow-up care. The data of all patients with MG (G70.0) attending the nine district hospitals as outpatient visits or in hospital admission data were collected in this study. In addition, the patients were selected based on a serological and electrophysiological test of MG, which was available only in two hospitals in Ulaanbaatar, Mongolia (The Reflex Neurological Clinic, and the Japan-Mongolia Teaching Hospital). Twenty-four patients from nine districts hospital, 42 patients from Reflex Neurological hospitals, and ten patients from Japan-Mongolia teaching hospitals were overlapped registered with a diagnosis of MG.

We conducted a cross-sectional, hospital-based study involving MG patients (n=48) diagnosed clinically and by serological and electrophysiological tests in Ulaanbaatar city from 1 January 2015 to 1 January 2020. The study inclusion criteria were: 1) citizenship of Ulaanbaatar city; 2) the clinical diagnosis of MG was confirmed by at least 1 serological or electrophysiological test. The exclusion criteria include living in rural areas, a childhood MG or Lambert-Eaton myasthenic syndrome. The clinical manifestation at the beginning of the MG is not specific for MG, leading to misdiagnosis or delayed diagnosis. This study only confirmed the diagnosis using the serological and electrophysiological test to prevent the misdiagnosis. There is no availability to confirm the diagnosis of MG in the rural areas due to a lack of diagnostic tools capacity. We only included the patients from Ulaanbaatar city to improve the accuracy of the study. We aimed to study the incidence of MG among adults in Mongolia, so patients below 18 years are excluded from this study. Lambert-Eaton myasthenic syndrome is similar to MG in terms of clinical manifestation, which could be misdiagnosed as MG. According to exclusion criteria, 18 people with MG were excluded, and the remaining 30 were identified for the review. The study was conducted accordingly to the Helsinki Declaration, and it was approved by the Medical Ethical Committee of the Mongolian National University of Medical Sciences (METc №2020/3-04).

We used the registration data of the total population of Ulaanbaatar in 2015-2020 by gender from The Ulaanbaatar Statistics Office (www.ubstat.mn), estimated the number of people over 18 years of age, and then calculated the average number of adults in the

last 5 years (**Table 1**). We divided the MG patients into the following two groups depending on the age of onset: 1) early-onset myasthenia gravis (EOMG) with age under 45 and 2) late-onset myasthenia gravis (LOMG) with age over 45 years. In addition, the population data from the Ulaanbaatar statistics office

between 2015 and 2020 were obtained and calculated the age-adjusted incidence rate by weighing the absolute numbers with the population of the corresponding age group (aged >45 and <45 years old) (**Table 2**).

Table 1: Gender-specific annual population in Ulaanbaatar.

Year	Total		Female		Male	
	Population	>18 years	Population	>18 years	Population	>18 years
2015	1,345,500	892,942	694,521	473,182	650,979	419,760
2016	1,380,792	921,857	718,892	493,775	661,900	428,082
2017	1,417,396	941,517	737,838	503,721	679,558	437,796
2018	1,394,363	941,198	721,420	500,112	672,943	441,086
2019	1,466,125	938,505	755,670	498,024	710,455	440,481
Average	1,400,835	927,203	725,668	493,763	675,167	433,441

Table 2: Age-specific annual adult population in Ulaanbaatar.

Year	Total Population	>18 years	EOMG (<45 years)	LOMG (>45 years)
2015	1,345,500	892,942	635,388	257,554
2016	1,380,792	921,857	652,375	269,482
2017	1,417,396	941,517	658,819	282,698
2018	1,394,363	941,198	645,830	295,368
2019	1,466,125	938,505	629,223	309,282
Average	1,400,835	927,203	644,327	282,876

We followed the Myasthenia Gravis Foundation of America (MGFA) Clinical Classification to assess the clinical manifestation at the onset of the disease (**Table 3**) ([Jaretzki et al., 2000](#)) and also used Osserman's classification for evaluating the severity of the disease (**Table 4**). The statistical analysis was performed using SPSS version 27.0 software. Continuous variables were

presented as means with standard deviations (SD), and median values were reported for variables with nonparametric distributions, whereas categorical variables were reported as numbers with proportions. The Mid-P exact test was used to estimate the incidence of MG. A two-sided statistical significance was set at $p < 0.05$ for all tests.

Table 3: Myasthenia Gravis Foundation of America (MGFA) clinical classification.

Grade	Clinical symptoms
I	Ocular MG
IIa	Mild generalized MG, predominant limb or axial muscles involvement
IIb	Mild generalized MG, predominant bulbar or respiratory muscles involvement
IIIa	Moderate generalized MG, predominant limb or axial muscles involvement
IIIb	Moderate generalized MG, predominant bulbar or respiratory muscles involvement
IVa	Severe generalized MG, predominant limb or axial muscles involvement
IVb	Severe generalized MG, predominant bulbar or respiratory muscles involvement
V	MG cases requiring intubation

Table 4: Osserman's grading (maximum disease severity).

Stage	Clinical symptoms
I	Ocular myasthenia gravis: involvement of extraocular muscle with diplopia and ptosis
IIa	Mild generalized myasthenia gravis: ocular symptoms are associated with slow involvement of bulbar (dysphagia and dysarthria) and skeletal muscles (generalized weakness). Respiratory muscles are spared.
IIb	Moderately generalized myasthenia gravis: progressive onset of symptoms with significant manifestation of weakness. Respiratory muscles are spared.
III	Acute myasthenia gravis: rapid onset (within 6 months) of severe bulbar and skeletal muscles involvement with important weakness. Respiratory muscles are involved.
IV	Severe late myasthenia gravis: progressive in severity for 2 or more years.

3.0 RESULTS

We reviewed a total of 30 patients' medical records with confirmed MG in Ulaanbaatar from 2015 to 2020.

3.1 Incidence

The average annual incidence of MG in Ulaanbaatar was 0.65 per 100,000 populations (0.26-1.34 with 95% CI (Confidence Interval)), 0.60 for males (0.25-1.28 with 95% CI), and 0.69 for females (0.33-1.46 with 95% CI). The annual incidence was relatively stable (**Table 5**). The cumulative incidence was 3.2 (2.22-4.56 with 95% CI) per 100,000 populations. The average annual incidence of EOMG was 0.56 per 100,000 populations (0.25-1.12 with 95% CI) and for LOMG was 0.84 per 100,000 populations (0.39-1.97 with 95% CI) (**Table 6**). Surveyed by area of the residence, there were 7 cases from Bayanzurkh district, 6 cases from Khan-Uul district, 5 cases from Chingeltei district, 4 cases from Sukhbaatar district, 4 cases from Songinokhairkhan district, 3 cases from Bayangol district, and 1 case from Baganuur district. However, no cases were reported from Nalaikh and Bagakhangai districts in those years. The number of cases was calculated per 100,000 population due to the

different population numbers in each district. The highest number of cases was reported in Khan-Uul district (5.53 per 100,000), and the lowest number of cases was reported in Songinokhairkhan district (1.92 per 100,000). The number of cases for the remaining districts was counted as follows: Baganuur district (5.23 per 100,000), Chingeltei district (4.82 per 100,000), Sukhbaatar district (4.27 per 100,000), Bayanzurkh district (3.14 per 100,000), and Bayangol district (2.07 per 100,000).

3.2 Age and sex distribution

The median age at onset was 33 years (interquartile range 27–46 years), and the mean age at onset was 37.27 ± 13.83 years (19–72 years). Among all probands, 43.3% (n=13) were male, and 56.7% (n=17) were female. The gender ratio of males to females was 1: 1.3. The peak age of MG in both genders was 31–40 years (**Figure 1**). Assessing the relationship between incidence and age group, the number of cases of LOMG has decreased in the last two years, while the number of cases of EOMG has increased rapidly (**Figure 2**).

Table 5: Gender-specific annual incidence (per 100,000 persons) of Myasthenia gravis with intervals among adults in Ulaanbaatar.

Year	Total		Female		Male	
	N*	Incidence (CI**)	N*	Incidence (CI**)	N*	Incidence (CI**)
2015	3	0.33 (0.09-0.91)	2	0.42 (0.07-1.40)	1	0.24 (0.01-1.17)
2016	7	0.76 (0.33-1.50)	3	0.61 (0.15-1.65)	4	0.93 (0.30-2.25)
2017	6	0.64 (0.26-1.32)	4	0.79 (0.25-1.92)	2	0.46 (0.07-1.51)
2018	7	0.74 (0.33-1.47)	5	0.99 (0.37-2.22)	2	0.45 (0.07-1.5)
2019	7	0.75 (0.33-1.37)	3	0.60 (0.15-1.64)	3	0.45 (0.08-1.50)
Average	6	0.65 (0.26-1.34)	3.4	0.69 (0.33-1.46)	2.6	0.60 (0.25-1.28)

N*-Number of new cases; CI**-95% Confidence Interval

Table 6. Age-specific annual incidence (per 100,000 persons) of Myasthenia gravis with intervals among adults in Ulaanbaatar.

Year	Total		EOMG		LOMG	
	N*	Incidence (CI**)	N*	Incidence (CI**)	N*	Incidence (CI**)
2015	3	0.33 (0.09-0.91)	3	0.47 (0.12-1.29)	4	0.16 (0.12-1.29)
2016	7	0.76 (0.33-1.50)	3	0.46 (0.12-1.25)	4	0.15 (0.05-0.39)
2017	6	0.64 (0.26-1.32)	2	0.46 (0.12-1.24)	3	0.11 (0.03-0.29)
2018	7	0.74 (0.33-1.47)	4	0.62 (0.20-1.49)	1	0.34 (0.07-1.5)
2019	7	0.75 (0.33-1.37)	6	0.95 (0.39-2.12)	-	-
Average	6	0.65 (0.26-1.34)	3.6	0.56 (0.25-1.12)	2.4	0.84 (0.39-1.97)

EOMG (≤ 45 years); LOMG (>45 years); N*-Number of new cases; CI**-95% Confidence Interval

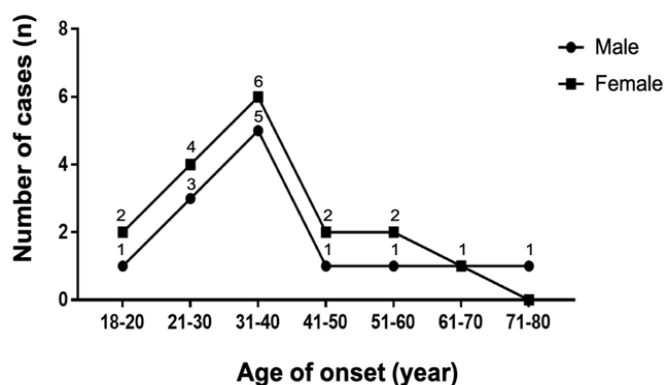


Figure 1: Age group at onset of disease in 2015-2020. The peak age was from 31 to 40 years in both genders.

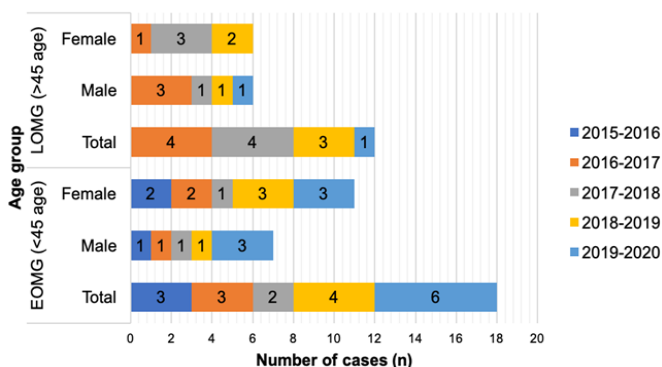


Figure 2: Annual number of cases of MG in 2015-2020 in Ulaanbaatar (by age group).

3.3 Clinical features of MG in Ulaanbaatar

The initial presenting symptoms were classified into seven categories: ocular symptoms, bulbar symptoms, lower extremity weakness, upper extremity weakness, facial weakness, neck flexor weakness, and respiratory failure. The most common initial presenting symptoms were ocular and bulbar symptoms in 56.6% (n=17) and 40.0% (n=12) of patients, respectively. Besides, 20.0%

(n=6) of patients presented with lower extremity weakness, 13.3% (n=4) with upper extremity weakness, 10.0% (n=3) with facial weakness, 3.3% (n=1) of patients had neck flexors weakness, and no one showed respiratory failure. **Figure 3** shows the frequency of initial presenting symptoms as reported by the patients with MG. The clinical manifestation at the onset of the disease was assessed according to the MGFA classification. At the onset of the MG 43.3% and 56.7% were ocular and generalized MG forms, respectively (**Figure 4**). Among the patients with generalized MG 36.7% (n=11) of patients were classified with grade II, 20% (n=6) with grade III. No patients have presented with grade IV or V. 46.2% of patients with initial ocular presentation shifted to generalized symptoms. The average period of shifting ocular to generalized symptoms was 23 months (1-140 months). The maximum disease severity was evaluated using Osserman's classification. At the end of the review period, only 23.3% of patients remained with purely ocular symptoms (stage I). In comparison, 76.7% of patients continued to have generalized MG, among them 43.3% with Osserman stage IIa, 20% with stage IIb, 6.7% with stage III and 6.7% with stage IV (**Figure 5**).

4.0 DISCUSSION

Our study is the first study of the incidence of MG in Ulaanbaatar (Mongolia). Myasthenia gravis is well investigated in other countries. Spain has the highest annual incidence among European countries in the last 10 years (2.1 per 100,000), while Norway (0.04 per 100,000) has the lowest number of cases ([Boldingh et al., 2015](#)). Among Asian countries, the annual incidence rate was similar in Japan (0.69-0.87 per 100,000), Korea (0.69 per 100,000), and China (0.68 per 100,000) ([Chen et al., 2020](#); [Lee et al., 2016](#); [Matsui et al., 2009](#)). Our estimated average annual incidence rate during the period 2015-2020 among the population in Ulaanbaatar

(0.65 per 100,000) had no significant difference compared to other Asian countries.

Several studies have shown that the incidence of the disease tends to increase every year due to improved MG diagnostic capacity ([Casetta et al., 2010](#); [Matsuda et al., 2005](#)). In our study, the annual incidence was relatively stable, although we found that the incidence of EOMG has increased, and the incidence of LOMG has slightly decreased in the last two years. The decrease in the number of LOMG may be explained by a lack of correct diagnostic of muscle weakness due to confusing clinical interpretation in the elderly. If we look to the age-adjusted incidence of MG was approximately 2.5-3 times higher in the younger (≤ 45) compared with, the older (>45) age group.

Although the MG can affect people of all ages, there is a bimodal distribution of onset age for females and males. In the female population, [Wing et al. \(2003\)](#) observed two peaks between 40-49 years and 60-69 years. [Lavrnić et al. \(1999\)](#) reported about two peaks between 20-40 years and 70-80 years. However, [Mantegazza et al. \(2003\)](#) and [Singhal et al. \(2008\)](#) reported a single peak in the females in the third decade. In the male patients, [Mantegazza et al. \(2003\)](#) observed a bimodal onset with peaks in the third and sixth decade. However, [Singhal et al. \(2008\)](#) and [Poulas et al. \(2001\)](#) reported single peaks in the sixth to a seventh decade in males. In our study, the onset of MG was observed at a single peak (31-40 years) in males and females, which can depend on the pure diagnostic capacity in elderly patients in our country. Most studies in Europe have shown that MG is predominant in females. For example, the MG male to female gender ratio was 1:1.41 in Greece ([Poulas et al., 2001](#)) and 1:1.94 in Italy ([Mantegazza et al., 2003](#)). Studies in most Asian countries showed that MG was predominant in females: Singapore 1:1,6, Hong Kong 1:2,1 ([Wing et al., 2003](#); [Yu et al., 1992](#)). On the contrary, a study from India showed MG predominancy in males ([Singhal et al., 2008](#)). Our study showed a female preponderance among the people with MG, corroborating the outcome of other studies.

As in most studies, we observed ocular and bulbar signs as the most common initial presenting symptoms. However, compared with studies in Singapore and Nigeria, ocular symptoms were less pronounced, while bulbar symptoms were more pronounced ([Wing et al., 2003](#); [Oparah & Ibanga, 2020](#)).

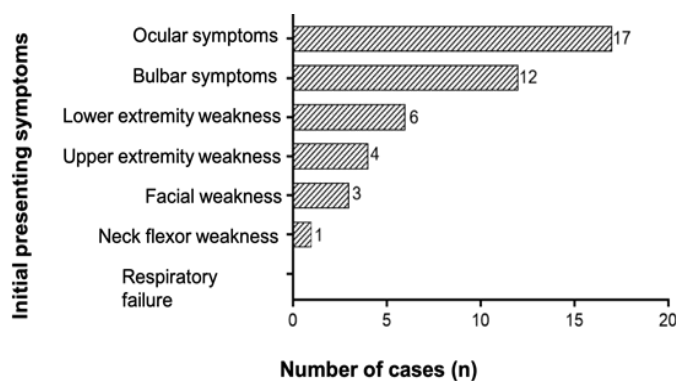


Figure 3: Initial presenting symptoms of Myasthenia gravis.

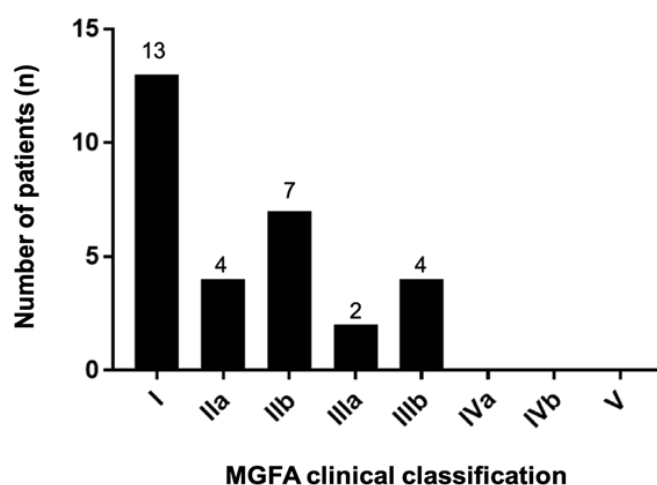


Figure 4: MGFA clinical classification of myasthenia gravis at the onset of disease.

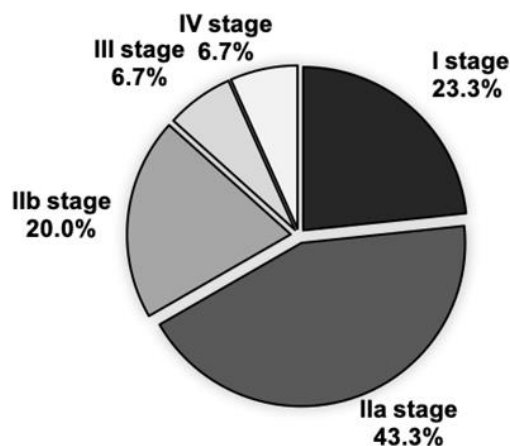


Figure 5: Osserman's classification of maximum disease severity.

The classification of MGFA described in studies reported by Asian countries has been determined that the ocular MG (MGFA I grade) rate was 26.3% (India), 32.7% (Hong Kong), and 55% (Singapore) ([Wing et al., 2003](#); [Singhal et al., 2008](#); [Yu et al., 1992](#)). Ocular signs as the initial symptoms of MG occurred in Mongolia more often (43.3%) than in India or Hong Kong. Respiratory failure can be a severe presenting feature of myasthenia gravis. In the studies reported by Mantegazza *et al.* ([2003](#)); [Singhal et al. \(2008\)](#) 0.8% and 1.32% presented with respiratory symptoms. No one in our study was presented with respiratory failure.

At the end of the survey, only one-fourth of patients remained with purely ocular symptoms, and the rest progressed to the generalized MG. The average duration of disease progression was 23 months (1-140 months). Robertson's study reported, 10-20% of the MG tend to be pure ocular MG, and the remaining of the myasthenia gravis will turn into generalized MG in two years ([Kupersmith et al., 2003](#)).

We conducted the first study of MG in Mongolia, defining the incidence and the clinical features of the disease in our country. The data of this study can be used as primary research data of this disease in the

future and will encourage the caregivers to improve MG diagnostic possibilities. This study was limited to only citizens of Ulaanbaatar. In future, we need to extend our study including patients from the rural areas of the country, more differentiated serological data, and treatment results.

5.0 CONCLUSIONS

The average incidence of MG between 2015 and 2020 was 6 per 1.000.000 population. The annual incidence was relatively stable. Myasthenia gravis in our study was more common in females (M: F of 1:1.3).

Acknowledgements: The authors acknowledge and thank the study team and the Mongolian National University of Medical Sciences for their support, as well as all the study participants. We also thank an anonymous reviewer for their excellent critique of the manuscript and for helping us better our work.

Author Contributions: B.D, O.Ch, S.J, and MR conceived and designed the study; O.Ch and MR collected data; O.Ch and BD analyzed the data; BD and O.Ch wrote the paper; SJ and BD reviewed and edited the paper.

Conflicts of Interest: The authors declare no conflict of interest.

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