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Original Research Article

Factors Leading to Delay in Diagnosis of Myasthenia Gravis

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Abstract: *Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disorder with variable presentations, often mimicking other conditions, which leads to delayed diagnosis. Early identification and management are critical to prevent morbidity and improve prognosis. In resource-limited settings like Pakistan, diagnostic delays may be influenced by clinical, systemic, or diagnostic limitations.* ***Objective:*** *To determine the factors contributing to delayed diagnosis of myasthenia gravis among patients presenting to the Department of Neurology at Jinnah Postgraduate Medical Centre, Karachi.* ***Methods:*** *This cross-sectional study was conducted in Ward 28, Department of Neurology, Jinnah Postgraduate Medical Centre (JPMC), Karachi, from December 12, 2024, to April 13, 2025. After obtaining ethical approval from the institutional review board, a total of 172 patients aged 18–72 years of both genders, diagnosed with myasthenia gravis, were recruited through non-probability consecutive sampling. Data on demographic characteristics, presenting symptoms, duration before diagnosis, and treatment modalities were collected using a structured proforma. The primary outcome was the duration of diagnostic delay (≤1 year vs. >1 year). Chi-square tests were used for categorical variables, and a p-value <0.05 was considered statistically significant.* ***Results:*** *Among 172 patients, 87 (51%) experienced a diagnostic delay of more than one year, while 85 (49%) were diagnosed within one year of symptom onset. The most frequent presenting symptom was ptosis (32%), followed by diplopia (24%), dysphagia (23%), and generalized fatigue or muscle weakness (15%). Anticholinesterase therapy was the most common treatment modality (29%), followed by immunosuppressants (25%), plasmapheresis (24%), and IVIG (22%). Notably, 58% of patients with delayed diagnosis had negative laboratory test results compared to 42% in those diagnosed earlier (p = 0.022), indicating a statistically significant association.* ***Conclusion:*** *A substantial proportion of myasthenia gravis patients experience diagnostic delays exceeding one year. Non-specific initial symptoms and negative laboratory findings are major contributors. Enhancing clinical suspicion and improving diagnostic protocols in tertiary care settings may facilitate timely diagnosis and reduce disease burden.*

Keywords: myasthenia gravis, delay, diagnosis, factors

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Introduction

Myasthenia Gravis (MG) is a chronic autoimmune neuromuscular disorder of weakened voluntary muscles that occur on account of a communications breakdown between nerves and muscles (1). However, because of how the condition can present with fluctuating symptoms, it is underdiagnosed, and its symptoms can be mistaken for those associated with other neurological or muscular conditions (2). The global incidence of MG is in the range of 15–20 cases per 100,000 populations, and incidence has been increasing as a result of improved diagnostic techniques, earlier diagnosis, and increased awareness (3). Despite this, delayed diagnosis remains a significant challenge, with prolonged morbidity and compromised quality of life resulting from delayed diagnosis (4). MG is a diverse disease with a clinical presentation ranging from ocular symptoms (ptosis, diplopia), to generalized muscle weakness and respiratory weakness in severe cases (5). Misdiagnosis is a main contributor to delayed diagnosis as studies show that 32.2% of MG patients were initially diagnosed with stroke, anxiety disorder or any other muscular disease (6). This misdiagnosis often results in delayed effective treatment which eventually allows the disease to progress. Further complicating the diagnostic process is a lack of fluctuation in symptoms and negative laboratory results. Diagnostic delays have a significant effect on patient outcomes, as highlighted in recent research. Myllynen et al. (2024) conducted a study that demonstrates that patients, whose diagnosis is delayed more than one year had significantly higher rates of crises episodes and intensive care interventions (7). Like Heldal et al. (2019), analysis of delayed diagnosis in myasthenia gravis found that patients with delayed diagnosis had less response to standard treatments such as anticholinesterase inhibitor and immunosuppressant (8). Pivotal role in this is also played by sociodemographic factors. Patients from rural areas or with lower educational attainment face greater diagnostic delays due to limited access to specialized neurology services. There have also been observed gender differences, namely, that females are more likely than males to be misdiagnosed while pregnant. Early recognition of MG is the key to improved patient outcomes (9). To address diagnostic challenges primary care physicians, need to be more aware, standardized diagnostic protocols have to be put into place and access to neurology services increased (10). It is important to understand what factors are causing delays so that we might reduce the burden of this debilitating disease. The objective of the present study is to determine the factors leading to delay in diagnosis of myasthenia gravis in patients presenting in department of neurology Jinnah Postgraduate Medical Centre.

Methodology

After the ethical approval from the institutional review board, this crossectional study was conducted at Ward 28, Department of Neurology Jinnah Postgraduate Medical Centre (JPMC) Karachi, from from 12 December 2024 till 13 April 2025. Through non-probability consecutive sampling 172 patients aged 18-72 years, both gender, with myasthenia gravis were included in the present study. Patients who require intubation and who are not willing to participate in the study were excluded from the present study. A written informed consent for the study was obtained from the patient who fulfilled the inclusion criteria. Detailed demographic details of each patient including gender, age, residence, educational status and employment status was obtained. Each patient will be inquired about

current clinical symptoms and treatment. On the basis of clinical symptoms, type of myasthenia gravis was confirmed. Each patient was inquired about time of first symptom onset and time of myasthenia gravis diagnosis in order to confirm delay in diagnosis. Each patient was inquired about absence of fluctuation, negative laboratory testing, delay in visiting neurology department and other diagnosis. All results were collected and filled in proforma accordingly by the researcher. After collection of data the analyses was conducted by using Statistical Package for Social Science (SPSS) software, Version 25.

Mean and standard deviation was calculated for quantitative variables like age (years) and duration of delay (years). Frequency and percentages was calculated for categorical variables like gender, age in groups, residence, educational status, employment status, sign and symptoms, treatment, type of myasthenia gravis, delay in diagnosis (≤ 1 year or > 1 year), absence of fluctuation, negative laboratory testing, delay in visiting neurology department and other diagnosis. Effect modifiers like gender, age in groups, residence, educational status, employment status, type of myasthenia gravis, absence of fluctuation, negative laboratory testing, delay in visiting neurology department and other diagnosis was controlled by stratification with delay in diagnosis (≤ 1 year or > 1 year). Post-stratification chi-square test was applied by taking p value ≤ 0.05 as significant.

Results

A total of 172 patients were included in the study. The mean age of participants was 42.6±15.04 years. Among them, 95 (55%) were male, and 77 (45%) were female. The majority of patients resided in urban areas, accounting for 89 (52%), while 83 (48%) came from rural settings. Regarding education, 39 (23%) of the patients had completed matriculation, and an equal proportion (23%) had attained graduation or higher levels of education. Intermediate-level education was reported in 35 (20%), while 30 (17%) and 29 (16%) were educated at the primary level or were illiterate, respectively. Employment status was almost evenly distributed, with 87 (51%) employed and 85 (49%) unemployed. A delay in diagnosis of more than one year was reported in 87 (51%) of patients, while 85 (49%) were diagnosed within one year (Table 1)

In terms of clinical symptoms, drooping eyelids were the most common, observed in 55 (32%) patients, followed by double vision in 41 (24%) patients, difficulty swallowing in 40 (23%), and fatigue or muscle weakness in 26 (15%). Treatment modalities showed that 50 (29%) of the patients were receiving anticholinesterase therapy, 43 (25%) were on immunosuppressants, 41 (24%) had undergone plasmapheresis, and 38 (22%) were treated with intravenous immunoglobulin (IVIG) (Table 2) .

The distribution of myasthenia gravis types revealed that 90 (52%) patients had generalized MG, while 82 (48%) had ocular MG. Absence of fluctuation in symptoms was noted in 91 (53%) of the patients, negative laboratory testing in 100 (58%), delay in visiting a neurology department in 82 (47%), and a prior misdiagnosis in 79 (46%)(Table 3).

Stratification based on delay in diagnosis revealed no significant association with age, gender, residence, education, employment status, type of myasthenia gravis, absence of fluctuation, or delay in visiting the neurology department ($p > 0.05$). However, negative laboratory testing was significantly more common in patients with a delay of more than one year (58% vs. 42%, $p = 0.022$). These findings highlight the role of diagnostic challenges in delayed identification of MG (Table 4).

Table 1: Demographic Variables

Variables	Mean and Frequency
Age (years)	42.6±15.04
Gender	
Male	95 (55%)
Female	77 (45%)
Residence	
Urban	89 (52%)
Rural	83 (48%)
Education	
Illiterate	29 (16%)
Primary	30 (17%)
Matriculation	39 (23%)
Intermediate	35 (20%)
Graduation and Above	39 (23%)
Employment Status	
Employed	87 (51%)
Unemployed	85 (49%)
Delay in Diagnosis	
≤1 Year	85 (49%)
> 1 year	87 (51%)

Table 2: Clinical Symptoms and Treatment profile

Clinical Symptoms	
Difficulty in Swallowing	40 (23%)
Double Vision	41 (24%)
Fatigue, Muscle Weakness	26 (15%)
Drooping Eyelids	55 (32%)
Treatment	
Immunosuppressant	43 (25%)
Anticholinesterase	50 (29%)
IVOG	38 (22%)
Plasmapheresis	41 (24%)

Table 3: Other disease factors

Types of Myasthenia Gravis	Frequency (%)
Ocular	82 (48%)
Generalized	90 (52%)
Absence of Fluctuation	91 (53%)
Negative Laboratory Testing	100 (58%)
Delay in Visiting Neurology Department	82 (47%)
Other Diagnosis	79 (46%)

Table 4: Stratification of the variables based on delay in diagnosis

Variables	Delay in Diagnosis		P Value
	≤1 Year	> 1 year	
Age (years)			0.541
<40 years	40	45	
> 40 years	45	42	
Gender			0.747
Male	48	47	
Female	37	40	
Residence			0.224
Urban	40	49	
Rural	45	38	

Education			0.058
Illiterate	13	16	
Primary	16	14	
Matriculation	26	13	
Intermediate	17	18	
Graduation and Above	13	26	
Employment Status			0.759
Employed	44	43	
Unemployed	41	44	
Types of Myasthenia Gravis			0.6
Ocular	47	35	
Generalized	48	42	
Absence of Fluctuation			0.355
Yes	48	43	
No	37	44	
Negative Laboratory Testing			0.022
Yes	42	58	
No	43	29	
Delay in Visiting Neurology Department			0.288
Yes	44	38	
No	41	49	

Discussion

Delayed diagnosis of myasthenia gravis (MG) in this study is highlighted by various clinical and sociodemographic factors associated. The mean age of participants was 42.6±15.04 years, similar to previous studies with similar ages reflecting the predominant age affected by MG (11). This study found that male patients preponderated slightly over female patients, compared to previous findings that female patients have a greater prevalence than male patients under 50 years (12). With a slight urban predominance (52%), the distribution of provinces by urban and rural distribution reflects better access to healthcare facilities in urban areas and likely a greater problem of urban access to timely medical care (13). Here, identical to those reported in a systematic literature review conducted by Vakrakou et al. (2023) drooping eyelids (32%), double vision (24%), and difficulty swallowing (23%), which were also the most common presenting symptom, are consistent with well-established MG presentations (14). Fatigue and muscle weakness, reported in 15 per cent of patients, were likely under recognised, because such symptoms can be confused with other conditions and delay diagnosis. 59 (58%) of the 80 patients with delayed diagnosis had negative laboratory findings, consistent with previous research, and confirming that standard tests, such as the acetylcholine receptor antibody, may be of limited sensitivity in ocular MG cases (15). Consistent with the global trend, misdiagnosis rates are high because of overlapping symptoms with other neurological disorders, and 51% of patients experienced more than one year of diagnostic delay, as found. Stratification also revealed a striking association with delayed diagnosis and negative laboratory test ($p = 0.022$), underscoring the importance of more advanced diagnostic measures, including single fiber electromyography or newer antibody assays.

Conclusion

This study concluded with the reinforcement that timely MG diagnosis remains challenging because of a high proportion of negative laboratory results and nonspecific symptoms. Future efforts should be directed toward improving diagnostic accuracy with more clinical awareness and utilizing new diagnostic technologies that will reduce delay of diagnosis and associated morbidity.

Declarations

Data Availability statement
All data generated or analysed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department concerned. (IRBEC-JPMC-24)
Consent for publication
Approved
Funding
Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

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Manuscript drafting, Study Design,
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N (PG Trainee)
Study Design, manuscript review, critical input.
FGM (PG Trainee)
Manuscript drafting, Study Design,
LD (PG Trainee)
Review of Literature, Data entry, Data analysis, and drafting article.

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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