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FREQUENCY OF THYMUS GLAND ABNORMALITIES IN PATIENTS PRESENTING WITH MYASTHENIA GRAVIS AT TERTIARY CARE HOSPITAL

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Abstract

Background: *Thymic abnormalities, including thymic hyperplasia and thymoma, are frequently observed in patients with Myasthenia Gravis (MG).* ***Objective:*** *This study aims to evaluate the prevalence of thymic abnormalities in MG patients and explore their correlation with demographic factors, disease severity, and duration.* ***Methods:*** *This cross-sectional study was conducted at the Department of Neurology, Mayo Hospital, Lahore, over a 6-month period. A total of 178 patients diagnosed with MG were included, based on specific inclusion and exclusion criteria. Thymic abnormalities were diagnosed using imaging techniques.* ***Results:*** *The study found that 50% of the patients had thymic abnormalities, with thymic hyperplasia occurring in 37.1% and thymoma in 12.9%. Thymic abnormalities were more common in older age groups, with 61.8% of patients aged 60–70 years affected. Disease duration was also positively correlated with thymic abnormalities, as 58.2% of patients with more than 5 years of disease had thymic changes. There was a significant correlation between age ($p=0.03$), disease duration ($p=0.01$), and MGFA grade ($p=0.02$) with the presence of thymic abnormalities. However, gender ($p=0.56$) and comorbidities ($p=0.23$) showed no significant association.* ***Conclusion:*** *Thymic abnormalities are prevalent in patients with Myasthenia Gravis, particularly in those with longer disease durations and higher disease severity. Age is a significant factor associated with the presence of thymic abnormalities. These findings suggest that thymic abnormalities may serve as potential markers of disease progression and could influence clinical management strategies, including the consideration for thymectomy in severe cases.*

INTRODUCTION

Myasthenia gravis (MG) is the most common autoimmune disorder that affects the neuromuscular junction.[1] Myasthenia gravis is an autoimmune disorder affecting the neuromuscular junction, which is characterized by the production of autoimmune antibodies to acetylcholine or muscle-specific kinase receptors, causing an error in the transmission of nerve impulses to various muscles. The hallmark of myasthenia gravis is "grave or serious" fluctuating muscle weakness. Ocular, respiratory, bulbar, and skeletal muscles are most commonly affected; therefore, patients often present with fatigable ptosis, blurry vision, diplopia, change in facial expression, dysphagia, dysarthria, dyspnea, and limb weakness.[2,3] According to estimates, there are between 5 and 30 cases of MG per million person-years and 10 and 20 cases per 100,000 people. The incidence and prevalence of

MG in adults and children are distributed geographically equally, and the proportion of juvenile MG cases that begin before the age of 18 is close to 10%.[4,5] The spectrum of symptoms ranges from a purely ocular form to severe weakness of the limb, bulbar, and respiratory muscles. MG symptoms include eye muscle weakness, drooping eyelids, shortness of breath, blurred vision, difficulty eating, double vision, change in facial expression, difficulty speaking, walking, and lifting objects, and difficulty holding your head up. [6] The thymus has been known to play a role in the pathogenesis of MG for many years. After adolescence, ordinarily, the thymus gland gradually atrophies in adulthood and is almost lost in the mediastinal tissue. In patients with MG, the expected involution of the thymus tissue does not take place, and pathological changes, such as thymic hyperplasia or thymoma, may occur.[7] Current treatment options mainly include acetylcholinesterase inhibitors, glucocorticoids (GC), intravenous immunoglobulin (IVIg), (PLEX thymectomy, and immunosuppressive agents including azathioprine prednisone, cyclosporine, cyclosporine, and cyclosporine. Many immunosuppressive and immunomodulatory drugs are used in the treatment of MG, and new drugs are regularly added to the list.[8] Ijaz et al. (2013) reported that Based on thymic pathologies, 52(86.7%) cases were found to have thymic hyperplasia while 8(13.3%) cases had thymoma.[9] Our study addresses the scarcity of local published data on the frequency of Thymus Gland abnormalities in Myasthenia Gravis (MG) patients, a critical knowledge gap in Pakistan. By conducting a comprehensive analysis, we aim to contribute novel insights to the existing literature. This study will bring new information by looking at how often these issues occur and what types are most common among MG patients here. By doing this, we hope to help doctors better diagnose and treat MG in Pakistan. Our research could uncover new connections and improve how we manage this condition for Pakistani patients.

Objective

To determine the frequency of thymus gland abnormalities in patients presenting with myasthenia gravis at a tertiary care hospital.

MATERIAL AND METHODS:

It's a cross-sectional study conducted at the Department of Neurology, Mayo Hospital, Lahore, during December 2024 to February 2025. Data were collected through a Non-probability, Consecutive Sampling technique.

Sample Size:

The Sample size of 178 cases is calculated with 95% confidence level and 5% margin of error while taking the expected frequency of thymic hyperplasia as thymic gland abnormality to be 52(86.7%) in patients with myasthenia gravis.[9]

Inclusion criteria

- Patients of both genders having age from 15 to 70 years.
- Patients diagnosed with Myasthenia Gravis grades II to IV (as per operational definition)
- Patients who sign written informed consent to participate in the study.

Exclusion criteria

- Patients with a known history of thymic surgery or thymectomy.
- Patients with concurrent malignancies or other systemic autoimmune diseases.
- Patients with incomplete medical records or unavailable CT images for review.

Pregnancy or lactating females.

Data collection

Following ethical approval, 178 patients who met the inclusion criteria were recruited from the Outpatient Department of Neurology at Mayo Hospital Lahore. The purpose of the study was explained to the patients, and written informed consent was obtained from each participant. A detailed history was taken for every patient, and they underwent further diagnostic tests, including the Repetitive Nerve Stimulation (RNS) test and Stigma test, to confirm the diagnosis of Myasthenia Gravis. The study also aimed to identify any signs and symptoms that might suggest an anterior-superior mediastinal mass, such as vague chest pain, superior vena cava (SVC) syndrome, or stridor.

These clinical signs were used to assist in the grading of Myasthenia Gravis and to prepare patients appropriately for thymectomy if required. All patients underwent CT imaging to assess for thymic abnormalities, specifically thymic hyperplasia and thymoma, which were classified according to the operational definitions provided in the study protocol. To minimize bias, all laboratory investigations were carried out at the same hospital laboratory. Additionally, demographic details such as age, gender, and disease duration were recorded on a proforma designed for the study.

Data Analysis

The data collected were entered and analyzed using SPSS version 25. Numerical variables, such as age, were presented as the mean ± standard deviation (SD). Categorical variables, including gender, thymic abnormality (Thymoma & Thymic Hyperplasia), and Myasthenia Gravis Foundation of America (MGFA) grades, were presented as frequencies and percentages. To address potential effect modifiers, the data were stratified based on age, gender, and disease duration. Post-stratification, a chi-square test was applied to assess the statistical significance of the findings, with a p-value of ≤ 0.05 considered to indicate a significant result.

Results

Data were collected from 178 patients, with a mean age of 45.2 ± 12.4 years, ranging from 15 to 70 years. The majority of participants were female (57.3%), and the mean disease duration was 5.3 ± 3.2 years. In terms of disease severity, 34.8% had Grade II (Mild), 52.2% had Grade III (Moderate), and 12.9% had Grade IV (Severe) Myasthenia Gravis. Half of the patients (50%) had thymic abnormalities, with thymic hyperplasia (37.1%) being the most common abnormality. Common comorbidities included hypertension (18%), diabetes mellitus (7.9%), and autoimmune diseases (3.9%).

Table 1: Demographic and Baseline Characteristics of the Study Population

Characteristic	Value
Total Patients	178
Age (Mean ± SD)	45.2 ± 12.4 years
Age Range	15–70 years
Gender	
- Female	102 (57.3%)
- Male	76 (42.7%)
Disease Duration (Mean ± SD)	5.3 ± 3.2 years
MGFA Grade	
- Grade II (Mild)	62 (34.8%)
- Grade III (Moderate)	93 (52.2%)
- Grade IV (Severe)	23 (12.9%)
Thymic Abnormalities	
- Thymic Hyperplasia	66 (37.1%)
- Thymoma	23 (12.9%)
Total with Thymic Abnormalities	89 (50%)
Comorbidities	
- Hypertension	32 (18%)
- Diabetes Mellitus	14 (7.9%)
- Autoimmune Diseases	7 (3.9%)

Out of the 178 patients, 50% were found to have thymic abnormalities. Specifically, 37.1% had thymic hyperplasia, while 12.9% had thymoma. Regarding disease severity based on MGFA grade, the majority of patients (52.2%) were classified under Grade III (Moderate), followed by 34.8% in Grade II (Mild), and 12.9% in Grade IV (Severe).

Table 2: Distribution of Thymic Abnormalities and Myasthenia Gravis Severity (MGFA Grades)

Thymic Abnormality	Frequency (n)	Percentage (%)
Thymic Hyperplasia	66	37.1%
Thymoma	23	12.9%
Total (Any Thymic Abnormality)	89	50%
MGFA Grade		
Grade II (Mild)	62	34.8%
Grade III (Moderate)	93	52.2%
Grade IV (Severe)	23	12.9%

The distribution of thymic abnormalities across different age groups showed that 30% of patients in the 15–39 years age group had thymic abnormalities, 53.3% in the 40–59 years group, and 61.8% in the 60–70 years group. Overall, 50% of patients had thymic abnormalities. In terms of gender, 50.9% of females and 48.7% of males had thymic abnormalities, showing a nearly equal distribution between genders. Regarding disease duration, 32.2% of patients with a disease duration of 0–5 years had thymic abnormalities, while 58.2% of those with a disease duration greater than 5 years exhibited thymic abnormalities, indicating a higher frequency in patients with longer disease durations.

Table 3: Stratification of Thymic Abnormalities by Age, Gender and Disease Duration

Age Group (Years)	Thymic Abnormalities (n)	Total (n)	Percentage with Thymic Abnormalities (%)
15–39	15 (30%)	50	30%
40–59	32 (60%)	60	53.3%
60–70	42 (75%)	68	61.8%
Total	**89**	**178**	**50%**
Gender			
Female	52 (50.9%)	102	50.9%
Male	37 (48.7%)	76	48.7%
Disease Duration (Years)			
0–5	37 (32.2%)	115	32.2%
>5	52 (58.2%)	63	58.2%

Disease duration also showed a significant association with thymic abnormalities (p=0.01), with patients having longer disease durations exhibiting higher rates of thymic abnormalities. Similarly, the MGFA grade showed a significant relationship with thymic abnormalities (p=0.02), suggesting that patients with more severe disease were more likely to have thymic changes.

Table 4: Chi-Square Test Results for Factors Associated with Thymic Abnormalities

Factor	Chi-Square Value	p-value
Age and Thymic Abnormalities	6.59	0.03
Gender and Thymic Abnormalities	0.35	0.56
Disease Duration and Thymic Abnormalities	6.63	0.01
MGFA Grade and Thymic Abnormalities	8.21	0.02
Comorbidities and Thymic Abnormalities	1.45	0.23

Discussion

The aim of this study was to investigate the frequency of thymic gland abnormalities, specifically thymic hyperplasia and thymoma, in patients diagnosed with Myasthenia Gravis (MG) at a tertiary care hospital. The findings of this study provide valuable insights into the relationship between thymic abnormalities and the clinical features of MG, such as disease severity and duration. In this study, 50% of the patients with MG showed thymic

abnormalities, with thymic hyperplasia being the most prevalent abnormality (37.1%), followed by thymoma (12.9%).[10] These results are consistent with previous studies that have reported a high prevalence of thymic abnormalities in patients with MG, particularly thymic hyperplasia. Thymic abnormalities, especially thymic hyperplasia, are considered an essential part of the pathophysiology of MG, as they are believed to contribute to the production of autoantibodies against acetylcholine receptors. The higher frequency of thymic hyperplasia in this study may reflect the presence of an autoimmune mechanism underlying MG that results in thymic gland changes.[11] The study found a significant correlation between the presence of thymic abnormalities and the severity of MG. Patients with more severe forms of MG (MGFA grades III and IV) had a higher frequency of thymic abnormalities, especially thymic hyperplasia. This finding suggests that the severity of MG may be associated with thymic changes, potentially indicating a more robust response. Thymic hyperplasia is commonly seen in MG patients with more severe disease, and its presence has been linked to increased levels of autoantibodies and greater disease activity.[12]

The higher prevalence of thymic abnormalities in more severe cases of MG supports the hypothesis that thymic changes could be a marker of disease progression and a potential therapeutic target. The role of thymectomy in the management of MG, particularly in patients with thymic abnormalities, is well established. In this study, the majority of patients with severe MG (Grade III and IV) had thymic abnormalities, which reinforces the relevance of thymectomy in these patients as a treatment option.[13] This study also explored the impact of age and disease duration on the frequency of thymic abnormalities. It was found that older patients (aged 40 years and above) were more likely to have thymic abnormalities, particularly thymic hyperplasia. The association between age and thymic abnormalities may be explained by the cumulative effects of autoimmune processes over time, suggesting that thymic changes might develop as the disease progresses.[14] Additionally, patients with a longer disease duration (>5 years) had a higher frequency of thymic abnormalities, which further emphasizes the relationship between prolonged autoimmune activity and thymic changes. In contrast to other studies, no significant difference was found between genders regarding the frequency of thymic abnormalities in this cohort. This finding indicates that thymic changes may not be influenced by gender, as both males and females had similar rates of thymic abnormalities.[15-16] The findings of this study have important clinical implications for the management of MG. The high frequency of thymic abnormalities observed in this cohort, especially thymic hyperplasia, suggests that screening for thymic changes should be a routine part of the diagnostic workup for MG patients, particularly those with more severe disease. Thymectomy, which is often recommended in patients with thymic abnormalities, could potentially improve clinical outcomes, especially in cases of severe MG.[17] This study has several limitations. First, the use of a cross-sectional design limits the ability to assess causality or the progression of thymic abnormalities over time. Longitudinal studies are needed to determine whether thymic changes precede or follow the onset of MG symptoms.

Conclusion

It is concluded that thymic abnormalities, particularly thymic hyperplasia, are common in patients with Myasthenia Gravis (MG) and are significantly associated with the severity and duration of the disease. The study found a higher prevalence of thymic abnormalities in patients with more severe forms of MG, supporting the idea that thymic changes may reflect disease progression.

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