IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 22, Issue 12 Ver I. (Dec. 2023), PP 74-81
www.iosrjournals.org

Long Term outcome after Thymectomy for Myasthenia Gravis Patient

Dr. Mohammad Ata Ullah[1], Dr Heemel Saha[2], Dr. Sumaiya Mamun[3], Prof. Dr. Md. Abduz Zaher[4], Dr. Shahanara Akhter[5]

1. *Assistant Professor (Paediatric Cardiac Surgery), Department of Cardiac surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.*
2. *Associate Professor (Thoracic), Assistant Professor, Department of Cardiac surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.*
3. *Associate Professor, Institute of Nutrition and Food Science, University of Dhaka, Dhaka, Bangladesh.*
4. *Professor, Institute of Nutrition and Food Science, University of Dhaka, Dhaka, Bangladesh.*
5. *Assistant Registrar, Department of Gynecology, Noakhali 250 Bed General Hospital, Noakhali, Bangladesh.*

Corresponding author: Dr. Mohammad Ata Ullah, Assistant Professor (Paediatric Cardiac Surgery), Department of Cardiac surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. E-mail: atau998@gmail.com

ABSTRACT

Background: *Myasthenia gravis (MG) is an autoimmune disorder characterized by muscle weakness due to antibodies targeting acetylcholine receptors and other components like MuSK, Agrin, and LRP4 at the neuromuscular junction. Thymic abnormalities, such as thymoma and thymic hyperplasia, are common in MG patients. Treatments include anticholinesterase agents, immunosuppressants, plasmapheresis, and thymectomy.*

Aim of the study: *This study aims to evaluate the clinical outcomes and prognosis of MG patients following thymectomy.*

Methods: *This comparative cross-sectional study, conducted in the Department of Cardiac Surgery at Bangabandhu Sheikh Mujib Medical University, Dhaka, spanned from July 2015 to February 2017. It involved 23 patients with Myasthenia Gravis (MG), divided into two groups: Group A (15 patients) without plasmapheresis or immunoglobulin therapy and Group B (8 patients) with such therapies. All patients underwent extended thymectomy via standard median sternotomy. Preoperative evaluations included EMG and acetylcholine receptor antibodies. Postoperative follow-ups were conducted quarterly for 36 months. Statistical analysis was performed using SPSS, with significant p-values set at ≤0.05.*

Result: *The study included 23 subjects divided into Group A (N=15) and Group B (N=8). Group B had a younger cohort, with 75% aged 21-30, while Group A had a broader age range and a mean age of 32.67 years. Gender distribution skewed females in Group A (66.67%), while Group B was evenly split. Both groups had similar clinical presentations, with eyelid drooping and limb weakness being common. Group B had higher rates of generalized weakness and thyroid disorders. Electrophysiological studies and antibody positivity were more common in Group B. Treatment approaches were similar, with no significant differences in outcomes or complications. Group A had higher rates of complete remission.*

Conclusion: *Thymectomy significantly improves clinical outcomes in myasthenia gravis patients, especially those without preoperative plasmapheresis or immunoglobulin therapy. Group A showed better improvement and remission rates than Group B. Despite limitations like small sample size and short follow-up, the study supports thymectomy's benefits, indicating a need for further research.*

Keywords: *Thymectomy, myasthenia gravis and long-term outcome.*

I. INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disorder that results from the production of abnormal antibodies targeting acetylcholine receptors at the neuromuscular junction, leading to impaired neuromuscular transmission and function [1]. Initially, the autoimmune attack was believed to be directed solely at the acetylcholine receptor (AChR) on the postsynaptic membrane of the neuromuscular junction. However, in the past decade, other autoimmune targets have been identified, including muscle-specific tyrosine kinase (MuSK), Agrin, and lipoprotein receptor-related protein 4 (LRP4), all of which are crucial for maintaining neuromuscular junction integrity [2]. Clinically, MG is characterized by fluctuating muscle weakness, often starting with ocular muscles and progressing to generalized weakness and, in severe cases, respiratory failure [1,2]. The prevalence of MG is reported to range from 150 to 300 cases per million, with an annual incidence of more than 10 per million.

Both prevalence and incidence increase with age, and AChR-associated MG exhibits a bimodal incidence pattern, peaking in young adults around the age of 30 and increasing again after age 50 [1-3]. The earlier onset is more common in women, reflecting a typical pattern seen in many autoimmune diseases, while late-onset MG occurs more frequently in men [2,3]. Thymic abnormalities are closely associated with MG. Thymoma occurs in 10-20% of patients, and 65-70% of MG patients present with thymic hyperplasia. Conversely, 20-47% of thymoma patients develop MG [2,4]. Standard medical treatment includes anticholinesterase agents, immunosuppressants, plasmapheresis, corticosteroids, and gamma globulin, with up to 15% of patients achieving clinical remission [1-4]. Thymectomy, first successfully performed by Blalock et al., in a 26-year-old woman with MG and a thymic cyst, has become a recognized treatment option [1,2,4,5]. Numerous studies support the use of thymectomy in patients with generalized MG, particularly in milder forms, showing clinical improvement in 70-80% of cases and remission in 33-38% [2,5-7]. While thymectomy has long been performed in both thymomatous and non-thymomatous MG patients, its effectiveness in non-thymomatous MG was debated until the landmark MGTX trial in 2016. This trial demonstrated that extended transsternal thymectomy, compared with medical therapy alone, led to improved MG symptoms, reduced hospitalizations, and lower steroid requirements after three years of follow-up in patients with AChR-Ab-positive non-thymomatous MG under 65 years old [8]. Moreover, a smaller subset of patients in the MGTX extension study maintained these benefits over five years [9]. Over the past three decades, thymectomy has become an evidence-based treatment for MG, showing long-term, sustained benefits [3,5,7,10]. Most patients undergoing thymectomy experience better symptom control and reduced medication needs compared to those managed solely with medical therapy. However, ongoing debate remains regarding patient selection, the optimal surgical approach, and the extent of mediastinal dissection required [1,2,5,7,10]. This study aims to evaluate the clinical outcomes and prognosis of MG patients following thymectomy.

II. METHODOLOGY & MATERIALS

This comparative cross-sectional study was carried out in the Department of Cardiac Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka. It lasted two years, from July 2015 to February 2017. Patients diagnosed with Myasthenia Gravis admitted to the Department of Cardiac Surgery, BSMMU, were selected for the study. Prior to the commencement of this study, the proposed protocol was approved by the Institutional Review Board (I.R.B) of BSMMU. All the patients presenting to the study place during the study period with symptoms suggestive of myasthenia gravis were evaluated by detailed history and examination. The patients who were clinically diagnosed as MG were admitted. A total of 23 patients were enrolled and analyzed into two groups.

Group A (N=15): Patients without plasmapheresis or immunoglobulin therapy.

Group B (N=8): Patients with plasmapheresis or immunoglobulin therapy or with both plasmapheresis and immunoglobulin therapy (both Preoperative and Post-Operative).

Inclusion criteria

All the patients fulfilling the diagnostic criteria of MG were enrolled in the study.

Exclusion criteria

- Bronchial asthma, pseudocholinesterase deficiency. Congenital myasthenic syndrome, progressive restricted myopathies, steroid and inflammatory myopathies, motor neuron disease.
- Multiple sclerosis, variants of Guillain-Barre syndrome (e.g., Miller-Fisher syndrome).
- Eaton-Lambert syndrome.
- Stroke.
- Drug-causing myasthenia like- neuromuscular blocking agents, aminoglycosides, penicillamine, antimalarial drugs, colistin, streptomycin, polymyxin B, tetracycline, organophosphate toxicity.
- Hypokalemia; hypophosphatemia.

Extended thymectomy was performed in all cases. A standard median sternotomy was done. The thymus was identified. Phrenic nerves and innominate veins were identified and preserved. Blunt dissection of overlying mediastinal pleura done. Thymectomy has been done along with the removal of the peri glandular, peri pericardial, peripheral and peri diaphragmatic pad of fat. The excised thymus was sent for histological study just after the operation, using formalin preservative.

All the patients presenting to the study place during the study period with symptoms suggestive of myasthenia gravis were evaluated by detailed history and examination. The patients who were clinically diagnosed as MG were admitted. Later, a preoperative evaluation was done. EMG and antibodies to acetylcholine receptors were assessed. Patients who fulfilled the diagnostic criteria were enrolled in the study. A thymectomy was

performed. Post-operative four follow-ups were done 3 monthly for 36 months to assess the outcome of the study population.

Statistical analysis:

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 22.0 for Windows (SPSS, Illinois, USA). Categorical variables were presented in the form of frequency and percentage, and quantitative data was presented in the form of mean and standard deviation. The results were presented in tables and figures. An unpaired t-test was used to compare quantitative variables, and Fisher's exact test and chi-square test were used to analyze the categorical variables, shown with cross-tabulation. p values ≤ 0.05 are considered statistically significant.

III. RESULT

The study population of 23 subjects was divided into two groups: Group A (N=15) and Group B (N=8). Table 1 shows the age distribution showed that Group B had a younger cohort, with 75% of the patients aged between 21-30 years, compared to 33.33% in Group A. Group A exhibited a broader age range, with patients in age groups ≤ 20, 31-40, 41-50, and ≥ 50 years, resulting in a slightly higher mean age of 32.67±11.13 years compared to 27.88±5.62 years in Group B. However, this difference was not statistically significant (P=0.271). Gender distribution was skewed towards females in Group A (66.67%) but was evenly split in Group B (50.00% male, 50.00% female), with no significant difference between groups (P=0.435). Disease duration was also comparable between the groups, with 66.67% of Group A and 50.00% of Group B having the disease for ≤1 year (P=0.435). Clinically, both groups shared similar presentations. Drooping of the eyelid was the most prevalent symptom in both groups (93.33% in Group A and 87.50% in Group B), followed by upper limb weakness (73.33% and 87.50%, respectively). Symptoms like difficulty swallowing, double vision, and generalized weakness occurred with comparable frequency in both groups. Group B, however, showed a higher prevalence of weakness in chewing (75.00% vs. 46.67% in Group A) and generalized weakness and fatigue (75.00% in Group B vs. 40.00% in Group A). However, these differences did not reach statistical significance (Table 2). Regarding associated co-morbidities, thyroid disorders were found in 25.00% of Group B but absent in Group A, though the difference was not statistically significant (P=0.161). Other co-morbidities, such as hypertension and diabetes, were rare and mostly observed in Group A (6.67%) Table 3). Investigatory findings in Table 4 showed that a higher proportion of Group B patients (100.00%) tested positive for AchR antibodies compared to Group A (80.00%), though this difference was not significant (P=0.421). Electrophysiological studies were more frequently positive in Group B (75.00%) compared to Group A (26.67%), with a trend toward significance (P=0.079). Imaging results revealed that mediastinal masses were more frequently detected in Group A (73.33%) than in Group B (87.50%), though this was not statistically significant (P=0.126). Chest X-rays were mostly normal in both groups, with 60.00% of Group A and 87.50% of Group B showing no abnormalities (P=0.373). Treatment approaches were similar between the two groups. Almost all patients in both groups received Pyridostigmine Bromide (93.33% in Group A and 100.00% in Group B, P=0.455) and Neostigmine Bromide (86.67% in Group A, 100.00% in Group B, P=0.625). Corticosteroid use was slightly higher in Group B (75.00%) compared to Group A (66.67%). In comparison, immunosuppressant use was more common in Group A (93.33%) than in Group B (75.00%), but neither difference was statistically significant (Table 5). Figure 1 illustrates the percentage distribution of two groups, Group A and Group B, based on histopathological findings: normal, hyperplasia, and thymoma. Group A has 20.00% normal findings, 20.00% hyperplasia, and 53.33% thymoma cases. In contrast, Group B has no normal findings (0.00%), a higher percentage of hyperplasia at 37.50%, and 50.00% of subjects showing thymoma. Figure 2 shows the distribution of post-operative morbidity and mortality among two groups of patients (Group A and Group B) following surgery. The categories assessed include Myasthenic crisis, other complications, mortality, and cases with no complications. Group A has a 0% incidence of Myasthenic crisis and mortality, with 13.33% experiencing other complications and 86.67% reporting no complications. In Group B, 12.5% experienced a Myasthenic crisis, 25% had other complications, while no cases of mortality were reported, and 62.5% had no complications. Table 6 summarizes the outcomes of study subjects. A higher percentage of subjects in Group A (93.33%) experienced clinical changes compared to Group B (75%), though the difference was not statistically significant (p=0.192). Regarding improvement levels, most subjects in Group A (73.33%) showed significant improvement, while only 37.50% in Group B did. In contrast, Group B had more subjects with mild (25%) or moderate (12.50%) improvement than Group A. A statistically significant difference (p=0.031) was found in complete remission, where 73.33% of Group A achieved remission, compared to 37.50% in Group B.

Table 1: Demographic profile of study population (N=23).

Variables	Group A (N=15)		Group B (N=8)		P-value
	N	%	N	%	
Age (years)					
≤20	2	13.33	0	0.00	0.271
21-30	5	33.33	6	75.00	
31-40	5	33.33	2	25.00	
41-50	1	6.67	0	0.00	
≥50	2	13.33	0	0.00	
Mean±SD	32.67±11.13		27.88±5.62		
Gender					
Male	5	33.33	4	50.00	0.435
Female	10	66.67	4	50.00	
Duration of disease					
≤1 year	10	66.67	4	50.00	0.435
>1 year	5	33.33	4	50.00	

Table 2: Distribution of the patients according to clinical presentation in two groups (N=23).

Clinical presentation	Group A (N=15)		Group B (N=8)		P-value
	N	%	N	%	
Symptoms					
Drooping of eyelid	14	93.33	7	87.50	0.636
Double Vision	8	53.33	3	37.50	0.496
Weakness in chewing	7	46.67	6	75.00	0.192
Difficulty in swallowing	7	46.67	4	50.00	0.879
Slurring of speech	5	33.33	2	25.00	0.679
Weakness in upper limbs	11	73.33	7	87.50	0.433
Weakness in lower limbs	4	26.67	2	25.00	0.931
Generalized weakness and fatigue	6	40.00	6	75.00	0.11
Diurnal variation	11	73.33	5	62.50	0.591
Sign					
Ptosis	14	93.33	7	87.50	0.636
Weakness of facial muscle	6	40.00	4	50.00	0.645
Weakness of neck muscle	1	6.67	0	0.00	0.455
Voice change	1	6.67	2	25.00	0.268
Proximal weakness of limb muscle	11	73.33	8	100.00	0.108

Table 3: Distribution of the patients according to associated co-morbid conditions (N=23).

Associated disease	Group A (N=15)		Group B (N=8)		P-value
	N	%	N	%	
Thyroid disorders	0	0.00	2	25.00	0.161
Hypertension	1	6.67	0	0.00	0.455
Diabetes mellitus	1	6.67	0	0.00	0.455

Table 4: Distribution of the study subjects according to investigatory findings (N=23).

Investigations	Group A (N=15)		Group B (N=8)		P-value
	N	%	N	%	
AchR antibody					
Positive	12	80.00	8	100.00	0.421
Negative	1	6.67	0	0.00	
Not done	2	13.33	0	0.00	
Electrophysiological study (RNS, SFEMG, NCS, EMG)					
Positive	4	26.67	6	75.00	0.079
Negative	1	6.67	0	0.00	
Not done	10	66.67	2	25.00	
Chest X-ray (CXR)					

Normal	9	60.00	7	87.50	0.373
Mediastinal mass	5	33.33	1	12.50	
Hilar lymphadenopathy	1	6.67	0	0.00	
Chest CT scan					
Normal	4	26.67	0	0.00	0.126
Mediastinal mass	11	73.33	7	87.50	
Hilar lymphadenopathy	0	0.00	1	12.50	

Table 5: Distribution of the patients according to treatment (N=23).

Treatment	Group A (N=15)		Group B (N=8)		P-value
	N	%	N	%	
Pyridostigmine Bromide					
Taken	14	93.33	8	100.00	0.455
Not taken	1	6.67	0	0.00	
Neostigmine Bromide					
Taken	13	86.67	8	100.00	0.625
Not taken	2	13.33	0	0.00	
Conticosteroid					
Taken	10	66.67	6	75.00	0.304
Not taken	5	33.33	2	25.00	
Immunosuppressant drugs					
Taken	14	93.33	6	75.00	0.214
Not taken	1	6.67	2	25.00	

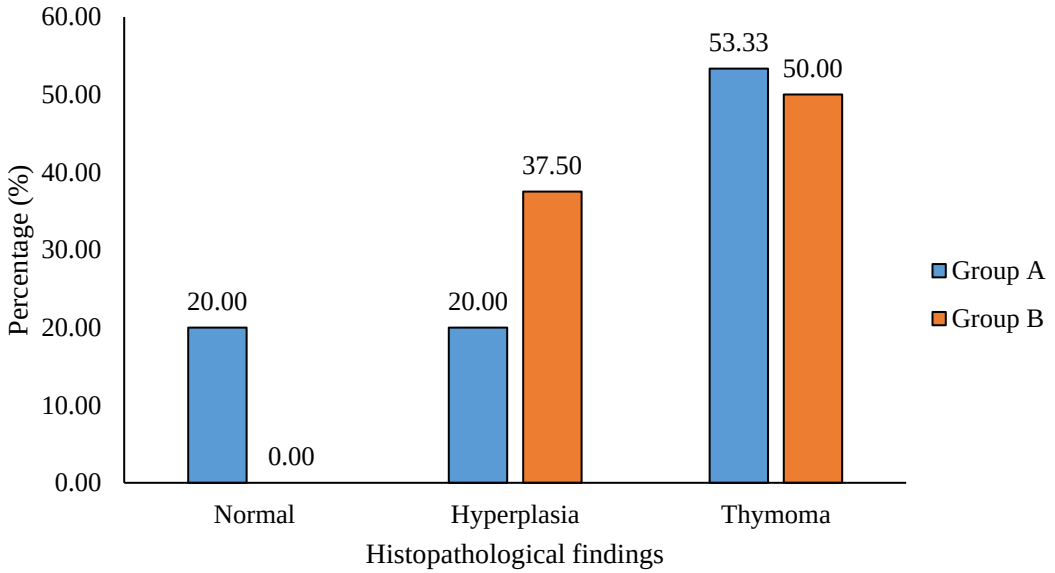

Figure 1: Distribution of the study subjects according to histopathological findings (N=23).

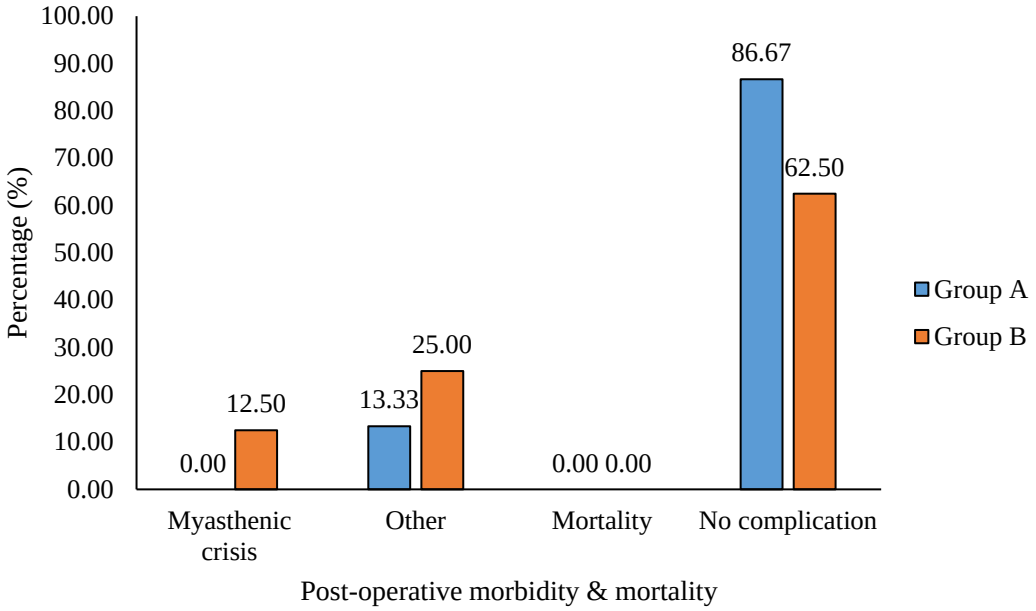

Figure 2: Distribution of the patients according to post-operative complications (N=23).

Table 6: Distribution of the study subjects according to final outcome (N=23).

Outcome	Group A (N=15)		Group B (N=8)		P-value
	N	%	N	%	
Clinically changed					
Yes	14	93.33	6	75.00	0.192
No	1	6.67	2	25.00	
Improvement					
Mild improvement	1	6.67	2	25.00	0.134
Moderate improvement	2	13.33	1	12.50	
Significant improvement	11	73.33	3	37.50	
Complete remission					
Yes	11	73.33	3	37.50	0.031
No	4	26.67	5	62.50	

IV. DISCUSSION

In the present study, the mean age of the patients was 32.67 ± 11.13 years, with 39.13% being male and 60.87% female. This aligns closely with the findings of Muhammed et al. (2016), who reported a mean patient age of 25.6 ± 11.8 years [11]. Similarly, Grob et al. (2008) observed that the majority of patients were over 20 years old, with a mean age of 44 years [12]. In terms of disease duration, 60.87% of patients in this study had been diagnosed for less than one year. Takanami et al. (2009) found comparable results, with 77.8% of patients having a disease duration of ≤24 months and 22.2% with a duration exceeding 24 months [13]. Kim et al. (2007) also reported similar outcomes, with 75% of patients having the disease for ≤1 year and 25% for more than a year [14]. Most patients in this study presented with symptoms such as ptosis, diurnal variation in muscle strength, weakness in the upper limbs, diplopia, generalized weakness, difficulty chewing, and dysphagia. These findings are consistent with those reported by Grob et al. (2008) [12]. Muhammed et al. (2016) similarly noted that the most common symptoms were limb weakness (87.5%) and ptosis (81.3%), with additional symptoms like dysphagia (75%), diplopia (43.8%), respiratory crises (25%), dysphonia (18.8%), and chest pain (6.3%) [11]. In this study, two patients (8.69%) had hyperthyroidism, while one patient each had hypertension (4.35%) and diabetes mellitus (4.35%). Notash et al. (2009) reported that 18% of patients had a history of autoimmune diseases, with 9.8% of all myasthenia gravis (MG) cases involving hyperthyroidism, and 3.2% involving diabetes mellitus, findings that are consistent with the present study [15]. Elevated acetylcholine receptor (AchR) antibody titers were detected in most patients, which parallels the results of Kagotani et al. (1985), who found that raised AchR antibodies were a common feature and served as a prognostic indicator for post-thymectomy therapy [16]. However, in this study, postoperative AchR antibody testing was not performed due to cost constraints. Preoperative chest X-rays revealed mediastinal masses in 33.33% of patients, while chest CT scans identified mediastinal masses in 78.26%. These findings align with those of Howard (2013) [17]. Vachlas et al. (2012) also reported that thymoma is present in

20-65% of MG cases, with many thymomas being incidentally discovered during preoperative imaging [18], which is comparable with the current study. The majority of patients were treated with Pyridostigmine Bromide and Neostigmine Bromide, and 69.56% were receiving corticosteroids, while 86.96% were on immunosuppressants. Nieto et al. (1999) similarly highlighted the effectiveness of anticholinesterase agents, corticosteroids, and immunosuppressants in improving neuromuscular transmission and reducing antibody concentrations, findings that are consistent with the present study [19]. All patients in this study underwent extended thymectomy, and histopathological examination revealed thymic hyperplasia in 20.00% of group A patients and 37.50% of group B patients, thymoma in 53.33% of group A and 50.00% of group B, and normal thymus in 20.00% of group A. El-Medany et al. (2003) also found that thymectomy outcomes were correlated with histology, with thymic hyperplasia associated with higher rates of improvement [20], which is consistent with the findings of this study. Postoperative complications in this study included myasthenic crisis in one patient (12.50%), cholinergic crisis in another, and hoarseness in one patient. There was no postoperative mortality. These results are consistent with those reported by Bedlack (2002) [21]. Muhammed et al. (2016) similarly found that 10.9% of patients developed postoperative myasthenic crisis [11]. Patients were followed for 36 months, with clinical improvement observed in 93.33% of group A and 75.00% of group B. Mild improvement was noted in 6.7% of group A and 25.00% of group B, moderate improvement in 13.33% of group A and 12.50% of group B, and significant improvement in 73.33% of group A and 37.50% of group B. Complete remission was achieved in 73.33% of group A and 37.50% of group B. These results were statistically significant, with group A showing greater improvement than group B ($p=0.031$). These findings are consistent with the studies by Gajdos et al. (2008) and Yeh and Chiu (1999) [22, 23]. Similarly, Muhammed et al. (2016) reported that 38.7% of patients had significant improvement, as determined by reduced medication needs [11]. At the 36-month follow-up, 60.87% of patients had achieved complete remission. Muhammed et al. (2016) also found that 38.7% of patients achieved complete remission [11], while Kim et al. (2007) reported a 75% complete remission rate in a five-year follow-up study [14].

Limitations of the study: The sample size of 23 patients is relatively small, which may affect the generalizability of the findings. The short duration of the study limited the ability to observe long-term complications and mortality outcomes. Furthermore, the absence of postoperative AchR antibody testing due to cost constraints limited the ability to assess biochemical remission. Lastly, the lack of a control group not undergoing thymectomy makes it difficult to compare the outcomes directly with non-surgical management.

V. CONCLUSION AND RECOMMENDATIONS

In conclusion, thymectomy significantly improves clinical outcomes in myasthenia gravis (MG) patients, particularly those without preoperative plasmapheresis or immunoglobulin therapy. Group A patients showed higher rates of significant improvement and complete remission compared to Group B. These findings align with previous studies, reinforcing the benefits of thymectomy in MG management. However, the study's limitations, including a small sample size and short follow-up duration, suggest the need for further research with larger cohorts and extended follow-ups to understand long-term outcomes better and refine patient selection criteria. Overall, thymectomy remains a valuable treatment for enhancing MG patients' quality of life.

Funding: *No funding sources*
Conflict of interest: *None declared*
Ethical approval: *The study was approved by the Institutional Ethics Committee.*

REFERENCES

[1]. Siwachat S, Tantraworasin A, Lapisatepun W, Ruengorn C, Taioli E, Saeteng S. Comparative clinical outcomes after thymectomy for myasthenia gravis: Thoracoscopic versus trans-sternal approach. Asian journal of surgery. 2018 Jan 1;41(1):77-85.
[2]. Green JD, Barohn RJ, Bartoccion E, Benatar M, Blackmore D, Chaudhry V, Chopra M, Corse A, Dimachkie MM, Evoli A, Florence J. Epidemiological evidence for a hereditary contribution to myasthenia gravis: a retrospective cohort study of patients from North America. Bmj Open. 2020 Sep 1;10(9):e037909.
[3]. Narayanaswami P, Sanders DB, Wolfe G, Benatar M, Cea G, Evoli A, Gilhus NE, Illa I, Kuntz NL, Massey J, Melms A. International consensus guidance for management of myasthenia gravis: 2020 update. Neurology. 2021 Jan 19;96(3):114-22.
[4]. Elnasr MM, El-Guindy DM, Al-Malt AM, Taha AH. Thymectomy in non thymomatous myasthenia gravis: Impact of pathology on outcome and role of survivin in pathogenesis. Journal of the Egyptian Society of Cardio-Thoracic Surgery. 2016 Dec 1;24(4):316-23.
[5]. Aydin Y, Ulas AB, Mutlu V, Colak A, Eroglu A. Thymectomy in myasthenia gravis. The Eurasian journal of medicine. 2017 Feb;49(1):48.
[6]. Zieliński M, Kużdżał J, Szlubowski A, Soja J. Comparison of late results of basic transsternal and extended transsternal thymectomies in the treatment of myasthenia gravis. The Annals of thoracic surgery. 2004 Jul 1;78(1):253-8.
[7]. Meacci E, Cesario A, Margaritora S, Porziella V, Tessitore A, Cusumano G, Evoli A, Granone P. Thymectomy in myasthenia gravis via original video-assisted infra-mammary cosmetic incision and median sternotomy: long-term results in 180 patients. European journal of cardio-thoracic surgery. 2009 Jun 1;35(6):1063-9.
[8]. Wolfe GI, Kaminski HJ, Aban IB, Minisman G, Kuo HC, Marx A, Ströbel P, Mazia C, Oger J, Cea JG, Heckmann JM. Randomized

trial of thymectomy in myasthenia gravis. New England Journal of Medicine. 2016 Aug 11;375(6):511-22.
[9]. Wolfe GI, Kaminski HJ, Aban IB, Minisman G, Kuo HC, Marx A, Ströbel P, Mazia C, Oger J, Cea JG, Heckmann JM. Long-term effect of thymectomy in patients with non-thymomatous myasthenia gravis treated with prednisone: 2-year extension of the MGTX randomised trial. The Lancet. Neurology. 2019 Mar;18(3):259.
[10]. Ahmed AB, Al Salmi I, Al Rahbi F, Al Farsi A, Hannawi S. The role of thymectomy in myasthenia gravis: A programmatic approach to thymectomy and perioperative management of myasthenia gravis. Asian Journal of Surgery. 2021 Jun 1;44(6):819-28.
[11]. Muhammed J, Chen CY, Hitam WH, Ghazali MZ. Thymectomy for myasthenia gravis: A 10-year review of cases at the Hospital Universiti Sains Malaysia. The Malaysian Journal of Medical Sciences: MJMS. 2016 Jul;23(4):71.
[12]. Grob D, Brunner N, Namba T, Pagala M. Lifetime course of myasthenia gravis. Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine. 2008 Feb;37(2):141-9.
[13]. Takanami I, Abiko T, Koizumi S. Therapeutic outcomes in thymectomied patients with myasthenia gravis. Ann Thorac Cardiovasc Surg. 2009 Dec 1;15(6):373-7.
[14]. Kim HK, Park MS, Choi YS, Kim K, Shim YM, Han J, Kim BJ, Kim J. Neurologic outcomes of thymectomy in myasthenia gravis: comparative analysis of the effect of thymoma. The Journal of Thoracic and Cardiovascular Surgery. 2007 Sep 1;134(3):601-7.
[15]. Notash AY, Salimi J, Ramezanali F, Sheikhvatan M, Habibi G. Clinical features, diagnostic approach, and therapeutic outcome in myasthenia gravis patients with thymectomy. Acta Neurol Taiwan. 2009 Mar 1;18(1):21-5.
[16]. Kagotani K, Monden Y, Nakahara K, Fujii Y, Seike Y, Kitamura S, Masaoka A, Kawashima Y. Anti-acetylcholine receptor antibody titer with extended thymectomy in myasthenia gravis. The Journal of Thoracic and Cardiovascular Surgery. 1985 Jul 1;90(1):7-12.
[17]. Howard JF. Electrodiagnosis of disorders of neuromuscular transmission. Physical Medicine and Rehabilitation Clinics. 2013 Feb 1;24(1):169-92.
[18]. Vachlas K, Zisis C, Rontogianni D, Tavernarakis A, Psevdi A, Bellenis I. Thymoma and myasthenia gravis: clinical aspects and prognosis. Asian Cardiovascular and Thoracic Annals. 2012 Feb;20(1):48-52.
[19]. Nieto IP, Robledo JP, Pajuelo MC, Montes JA, Giron JG, Alonso JG, Sancho LG. Prognostic factors for myasthenia gravis treated by thymectomy: review of 61 cases. The Annals of thoracic surgery. 1999 Jun 1;67(6):1568-71.
[20]. El-Medany Y, Hajjar W, Essa M, Al-Kattan K, Hariri Z, Ashour M. Predictors of outcome for myasthenia gravis after thymectomy. Asian Cardiovascular and Thoracic Annals. 2003 Dec;11(4):323-7.
[21]. Bedlack RS, Sanders DB. On the concept of myasthenic crisis. Journal of clinical neuromuscular disease. 2002 Sep 1;4(1):40-2.
[22]. Gajdos P, Chevret S, Clair B, Tranchant C, Chastang C, Myasthenia Gravis Clinical Study Group. Clinical trial of plasma exchange and high-dose intravenous immunoglobulin in myasthenia gravis. Annals of neurology. 1997 Jun;41(6):789-96.
[23]. Yeh JH, Chiu HC. Plasmapheresis in myasthenia gravis: A comparative study of daily versus alternately daily schedule. Acta neurologica scandinavica. 1999 Mar;99(3):147-51.