

A Five-year Retrospective Study on the Clinical Profile of Myasthenia Gravis with Ocular Involvement in a Tertiary Hospital

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ABSTRACT

Introduction: Myasthenia Gravis (MG) with ocular involvement has an elusive diagnosis. Ptosis and Diplopia are the most common and early presenting features of MG. Acetylcholine receptor (AChR) antibody titre, Nerve conduction studies and chest imaging are important diagnostic tests for MG. A simple test like an ice pack test can help in differentiating MG from other causes of neurological ptosis and other symptoms.

Aim: To study the systemic presentation, the profile of ocular involvement, clinical and laboratory tests and treatment modalities used in patients diagnosed with MG in a tertiary hospital.

Materials and Methods: This was a hospital based five year retrospective study of 14 cases of MG, diagnosed and treated between January 2012 and December 2016. Analysis of presenting signs and symptoms of generalised and ocular MG was done. Profile of diagnostic clinical, laboratory, and radiological tests performed for each patient and their results were noted and analysed. Various treatment modalities used to manage the cases were noted. Permission from the Institutional

Ethics committee was taken prior to starting the study. SPSS software version 23 was used for data analysis.

Results: Mean age of presentation was found to be 40.2 years with a predilection for male gender; 81.71% of patients, who presented with Generalised MG, 14.2% had ocular involvement. Ptosis was found to be the most common ocular symptom in combination with diplopia (SD-0.554). Lateral rectus was most commonly involved muscle. Ice pack test, nerve conduction studies were specific in diagnosis of MG. Antibody titres were positive in 66.6% patients. About 30% patients underwent HRCT chest out of which 60% showed some Thymus involvement. Various forms of treatment were used including oral Pyridostigmine, oral steroids and oral immunosuppressants.

Conclusion: The pattern of involvement in MG in this study was slightly different. The mean age was lower, there was preponderance of male gender and lateral rectus muscle was most commonly involved muscle. A simple ice pack test is cheap and reliable test to diagnose MG with ocular involvement. We suggest HRCT to rule out thymic abnormalities.

Keywords: Ice pack test, Myogenic ptosis, Nerve conduction studies, Serology in myasthenia

INTRODUCTION

Myasthenia Gravis (MG) is an acquired autoimmune disease of the Neuromuscular Junction (NMJ). Antibodies are formed against the NMJ and the postsynaptic nicotinic Acetylcholine Receptors (AChR). The characteristic weakness present in MG is due to an antibody-mediated, T-cell dependent immunological attack which is aimed at proteins in the postsynaptic membrane of the NMJ (acetylcholine receptors and/or receptor-associated proteins). There are two forms of MG: the ocular form which is restricted to eyelids and the extraocular muscles, and secondly the generalised form which presents as a combination of bulbar involvement, respiratory and limb weakness. Most patients have ocular involvement first which later progresses to the generalised form. Most commonly encountered ocular symptoms are ptosis, double vision, restriction of ocular movements, and rarely visual loss. Abnormalities of the thymus gland are associated with MG. The diagnosis of myasthenia focuses on confirming the typical history and clinical examination by various tests.

The recommended laboratory tests are serological testing, chest imaging for thymoma, and electrophysiologic testing and they aid in early diagnosis and initiation of appropriate treatment. Diagnosis of MG can be elusive sometimes. A simple ice pack test can help in early and easy diagnosis of Ocular Myasthenia Gravis. The sensitivity of the test ranges from 80-100%. Not many studies have been done in this region of southern India to validate this test in terms of efficacy and ease of performing the test in an outpatient set-up.

The purpose was to study the clinical profile of MG especially the pattern of ocular involvement. To determine the tests performed routinely to diagnose the condition and to know the various modalities of treatment used in the hospital.

MATERIALS AND METHODS

This retrospective hospital-based study was carried out on patients who were diagnosed and treated for MG at our institution over a five year period (January 2012 to December 2016). Clearance from Institution's ethical committee was obtained. A search was made using the hospital electronic medical record system with ICD-10 XX and the files of patients were retrieved and analysed.

Demographic details of patients including age and gender were noted. MG was classified based upon the clinical presentations. The diagnostic criteria of MG were based on the typical history and the presenting symptoms and signs which were confirmed by clinical and serologic tests (AChR antibody titer), and electrophysiological studies (repetitive nerve stimulation studies-RNS). Also, High-Resolution Computerised Tomography (HRCT) of the chest was done to rule out thymic abnormalities. Ice pack test was carried out on patients with ocular involvement and who were referred to the ophthalmology OPD. Although patients who had no or severe ptosis were excluded from this test as it would give false results. In our study, we classified the patients into three categories: those patients with a clinical presentation involving only the eye i.e., ophthalmic symptoms, those with only systemic and those with an overlap of both systemic and ocular manifestations.

All the patient's records were analysed for the above tests and their results were noted. Various treatment modalities used viz., oral Pyridostigmine, steroids, and immunosuppressants were noted. The outcome of treatment could not be analysed due to the lack in follow-up by most patients. Only two patients came for follow-up after discharge, with improvement in symptoms.

STATISTICAL ANALYSIS

After data collection, an analysis was done using SPSS software version 23. Analysed data is presented in the form of text, tables, and graphs.

RESULTS

This study consisted of 11 males (78.17%) and 3 females (21.43%) who were diagnosed with MG and underwent treatment. The mean age of presentation was found to be 40.21 years (range 10 years to 61 years, SD-16.31). However, a maximum number of cases were seen in the age group 31 to 41 years (six cases).

In the present study, 81.71% of patients had generalised MG, 14.2% had only ocular MG, and 7.14% had both generalised and ocular MG. The generalised presentation had a combination of bulbar symptoms like dysarthria, slurring of speech, restrictive myopathy symptoms like respiratory muscles weakness and proximal weakness in the body especially neck extension. A total of 60% of patients presented with fatigue and dysarthria, 40% presented with dysphagia and proximal weakness.

The most frequently occurring symptom was ptosis (71.4%) followed by diplopia which was 28.6%, also 17.1% had involvement of extraocular muscles. Lateral Rectus was most commonly involved (21.4%) muscle, Superior Rectus and Medial Rectus muscles were involved in 7.1% patients, and Medial and Lateral rectus together in 7.1% patients.

AChR antibody titer was carried out in six patients, out of which four had positive results and two patients were found to be seronegative. Mean of AChR antibody titer was found to be 11.46 nmol/L (SD-8.64). The minimum titer noted was 4.47 nmol/L and the maximum was 24.2 nmol/L. Ice pack test was performed on 42.9% patients six and all had positive results. 31.71% of patients underwent Nerve Conduction Study with positive results for MG. Five patients underwent HRCT chest, out of which three had Thymoma. Patients with Thymoma were advised Thymectomy but no follow-up records were available. Neostigmine test was performed on one patient with positive results. [Table/Fig-1].

	Performed (n)	Not performed (n)	Positive (n)	Negative (n)
Ice pack test	6	8	6	0
Neostigmine test	1	13	1	NA
Edrophonium test	0	14	NA	NA
HRCT chest	5	9	3	2
AChR antibody test	6	8	4	2
Antibody titre-high	--	--	NA	NA
Antibody titre-low	4	--	--	--

[Table/Fig-1]: List of tests performed on patients diagnosed with MG.

DISCUSSION

Early onset MG before 10 years of age has a female preponderance but there is no gender bias in later years and is supported by studies, however, a late presentation after 60 years is characterised by male preponderance [1,2]. This study showed a male preponderance at an early age which was consistent with few other studies [1-5]. Studies done in Asian and Indian populations observed an overall female preponderance [6-8].

In this study, 71.4% of the patients presented with a combination of ptosis and diplopia both. It was 64% in the study done by Kupersmith MJ et al., [9]. Few other studies have noted a low occurrence of only diplopia as a presentation [9,10].

The high percentage of involvement of extraocular muscles is probably due to the fact that extraocular muscles are different from skeletal muscles, having higher firing frequencies, tonic muscle fibers, and a different AChR pattern. These properties predispose the extraocular muscles to neuromuscular blockade [11]. extraocular muscles involvement occurs usually within one year of onset of the disease [12]. In this study, only 10% of the patients with ocular MG had restricted ocular movements, in contrast to 69% observed by Sommer N et al., [13]. Lateral Rectus was the most commonly involved muscle in our study (21.4%). Other studies have shown superior rectus and inferior oblique combination to be the most commonly involved muscles [14,15].

Ice pack test was found to be a sensitive test for the diagnosis of MG. Our study showed positive results in all patients on whom the test was performed which are consistent with other studies showing 80% positive results [16]. The cooling effect on the affected muscle improves the muscle function by inhibiting acetylcholine esterase function. Ice pack test is a safe, fast, easily administrable test with high sensitivity and specificity [16]. In the present study, the ice pack test was carried out in all six patients who were referred to ophthalmology OPD, as all the patients included in the study were treated under Department of Neurology, primarily.

Nerve conduction studies were found to be highly specific for MG. In our study, all patients of MG had positive tests. Farrugia ME et al., found 13 out of 21 patients to have positive results [3]. Other studies have found a high percentage of positive results among patients with MG [16].

In this study, five patients underwent HRCT chest. three out of five patients who underwent HRCT had positive results and belonged to an age group ranging from 10 years to 18 years. Other studies have observed Thymus involvement after 40 years of age and seen in 10-20% of patients with MG [17]. In a study done by Huang D et al., 66.4% had Thymic Hyperplasia as the most common finding, while 14.8% had Thymoma [17]. In MG the muscular abnormalities take place by an antibody-mediated process which originates in the Thymus gland. About 71% of patients with MG display thymic abnormalities, hence carrying out HRCT chest may prove beneficial as studies have shown significant improvement in MG after thymectomy [18]. HRCT chest was advised to all patients but was not done due to financial constraints.

AChR antibody titer is a specific but expensive test. The sensitivity of this test is approximately 81% for generalised MG and 10% for ocular MG [19]. Antibody titers do not correlate with the severity of the disease. In the present study, 66.6% of patients had positive AChR antibody. All patients with positive titers were males. Other studies have shown an 87.6% of patients to have positive results [3,7]. In contrast, Sommer N et al., found low or absent titers [13]. Affordability may be an issue in limited resource conditions.

Treatment of MG is aimed at relieving the patient of general and ocular symptoms. In the present study, the most common treatment strategy was a combination of oral Prednisolone, Pyridostigmine, and Azathioprine. Others were treated with intravenous Methylprednisolone and Plasmapheresis. Studies show that patients with diplopia respond to initiation of corticosteroids [8,9,12]. Other studies have shown no difference in treatment outcomes of steroids and immunosuppressants when given alone [8]. The various forms of treatment all patients underwent are given in [Table/Fig-2]. Patients with Thymus abnormalities on HRCT were referred to cardiothoracic surgeon and surgery was advised. Studies have found Thymectomy to be beneficial in the prevention of disease progression [18,19].

[Table/Fig-3] shows a comparison in the presentation of MG as observed in studies in the last 10 years against the present study [4,7,10,20].

Type of Treatment	Number of patients underwent the treatment
Combination therapy of oral Pyridostigmine, steroid and Azathioprine	6
Injectable Neostigmine	1
Intravenous Methylprednisolone+oral Pyridostigmine	1
Oral Pyridostigmine	3
Injection Neostigmine+oral Pyridostigmine+oral steroids	1
Plasmapheresis+oral steroids	1
Combination therapy of oral Pyridostigmine, steroid and Azathioprine+intravenous immunoglobulin	1

[Table/Fig-2]: Treatment administered to the patients.

Studies	Ocular MG	Generalised MG
Singhal BS et al., [4]	26.31%	73.68%
Casetta I et al., [7]	47.00%	13.00%
Huang X et al., [10]	82.00%	18.00%
Murai H et al., [20]	31.70%	64.30%
Present study	14.20%	81.71%

[Table/Fig-3]: Distribution of ocular vs generalised MG in different studies in past 10 years [4,7,10,20].

LIMITATION

The study has its drawbacks of a retrospective one. There was a lack of uniformity in the number of patients undergoing each test. Due to the lack of follow-up, we cannot comment on the improvement after treatment, yet two patients who followed up had improvement in symptoms.

CONCLUSION

The mean age group of the participants was 40.21 years which was lesser in comparison to studies done in other regions. A male preponderance was seen contrary to the common female preponderance in MG. Lateral rectus muscle was found to be the commonest muscle to be involved. Ice pack test was found to be positive in all patients who underwent the test. Most patients who underwent HRCT chest had thymus abnormalities.

It can be recommended that Ice pack test should be carried out in all suspected cases of ocular involvement of MG. Wherever, possible HRCT must be done to look for thymus abnormalities. All cases of suspected MG would benefit from timely ophthalmic screening.

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