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MYASTHENIA GRAVIS;

FREQUENCY OF DIFFERENT CLINICAL FEATURES IN PATIENTS PRESENTING TO A TERTIARY CARE HOSPITAL, KARACHI

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ABSTRACT… Objectives: To determine the frequency of different clinical features of myasthenia gravis in patients presenting to a tertiary care hospital, Karachi. **Study Design:** Cross sectional study. **Setting:** Neurology ward, JPMC, Karachi. **Period:** 23rd January 2013 to 22nd July 2013. **Patients and Methods:** A total of 71 diagnosed patients of Myasthenia Gravis (MG) between the age 15 and 70 years were recruited. Structured questionnaire was used to collect the data regarding most common clinical manifestations of MG. Data were entered and analyzed in SPSS version 17. Chi-Square test was used as test of significance. **Results**: Mean age ± S.D of patients was 34.11 ± 10.42 years. The mean ± SD of duration of symptoms among these patients was 5.23 ± 3.52 months. Most of the patients (21%) belong to age between 21 to 30 years. Regarding clinical features in these patients of myasthenia gravis it was noted that ptosis and diplopia were most common symptoms, 62% and 54.9%, respectively. **Conclusion:** Myasthenia gravis, a chronic neuromuscular disorder leads to various degrees of neurologic dysfunction which manifest as different clinical features. The current study found that ocular symptoms are commonest presenting features.

Key words: Myasthenia gravis, ocular symptoms, ptosis, generalized weakness, dysphagia.

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INTRODUCTION

Myasthenia gravis (MG) is the commonest disorder affecting neuromuscular junction. Annual incidence is 2 to 4 per million. MG is autoimmune disease characterized auto antibodies against components of the postsynaptic neuromuscular junction.[1,2] When the overall numbers of acetylcholine receptors (AChR) decreases it will ultimately causes decreased in muscle strength.[3] The incidence rate of MG is subjective to sex and age: it is estimated that women are three time more prone to MG than males during their early adulthood before the age of 40 years.[4,5]

Thymus has been implicated as having central role in pathogenesis of MG & thymic abnormalities such as thymic hyperplasia & thymoma. Thymic abnormalities are found in 75% of patients, germinal hyperplasia 85% & thymic tumors in 15%.[6]

Regarding age at onset of myasthenia, Singhal BS, et al., (2008) found that in male patients 22.58% were in sixth decade while in 22.09% of patients peak age was seventh decade.[7]

Female (29.77%) developed myasthenia gravis earlier with a peak age at onset was in third decade. Patients may present with wide range of neurological symptoms but usually develop ptosis and / or diplopia at some point in their illness. The presenting symptoms are ocular in 50% (diplopia in 25%, Ptosis in 25%) followed by generalized weakness in 10%, bulbar weakness in 10%, leg weakness in 10%. In 7% of patients only presenting feature was weakness of ocular muscles.[8] In the patients who were above 50 years of age dyspnoea was frequent as diplopia (25%). However diagnosis is not straight in all the cases and delayed or missed diagnosis frequently occurs. Currently the diagnosis is based on presence of antiAChR antibodies in serum which are found in 85% of patients with generalized myasthenia and 50%–60% with ocular myasthenia

gravis. The antiAChR antibodies negative patients are called serum negative myasthenia and in the presence of antibodies to muscle specific Kinase (MuSK) receptors are mainstay of diagnosis.[1,9,10] MG is treated by cholinesterase inhibitors, corticosteroids, immune suppressants like azathioprine, and cyclophosphamide which has steroid sparing agent effect as well, Plasmapheresis, transfusion of immunoglobulin and in selected of thymectomy.[11-13] That is why this study has been conducted to determine the most common clinical manifestation of patients diagnosed with Myasthenia gravis.

PATIENTS AND METHODS

The study design was descriptive case based study and conducted through cross sectional sampling technique for the duration of six months in the in the department of Neurology, Jinnah Postgraduate Medical Centre (JPMC), Karachi.

We examined 71 patients through non-probability sampling technique those who were admitted in the Neurology ward as a diagnosed case of Myasthenia Gravis between the ages of 15 - 70 years of either sex.

The following diseases were excluded after proper clinical history, examination, and relevant investigation i.e. CSF examination, Imaging studies, electrophysiological studies, metabolic profile where suggested by history and examination findings.

- Probable Myasthenia Gravis i.e. having clinical features like MG but not meeting laboratory criterion for diagnosis, congenital myasthenic syndrome, progressive restricted myopathies, steroid and inflammatory myopathies, motor neuron disease, multiple sclerosis, Gullain Barre syndrome, organophosphate toxicity, botulism, back widow spider venom, Eaton-lambert syndrome, stroke, medications such as neuromuscular blocking agents, amino glycosides, pencillamine, antimalarial drugs, streptomycin, tetracycline, hypokalemia, and hypophosphatem.

Before taking a detailed history consent was taken and thorough examination was performed regarding neurological manifestation the focus was on presence of different common clinical features. These were as present or absent were recorded.

DATA ANALYSIS

The data were analyzed on SPSS version 16.0. The clinical features were presented by their frequencies along with percentages. The age of the patients were presented by their mean ± SD values. Stratification was done with regards to age, gender, and durations of disease to see the effect of these on the outcome variables. Similarly clinical features were classified according to gender (male and female) to know any association with particular sex group. Chi Square test was applied taking P value of <0.05 as significant.

RESULTS

The mean ± SD age of patients was 34.11 ± 10.42 years with range of 1860 years. The mean ± SD of duration of symptoms among these patients was 5.23 ± 3.52 months (Range: 112 months) Table-I.

Statistics (n = 71)	
AGE - Years	
Mean	34.1
Standard Deviation	10.42
Minimum	18
Maximum	60
DURATION OF SYMPTOMS - Months	
Mean	5.23
Standard Deviation	3.52
Range	1 – 2

Table-I. Baseline characteristics of study subjects:

Females were in majority i.e. 59.2% (n = 42), while males were 40.8% (n = 29) Figure-1. Eight patients (11.3%) were under the age of 20 years. Other 31% (n= 22) were of age 2130 years, 29.6% (n = 21) were of age 3140 years, 19.7% (n = 14) aged between 4150 years while in age category 5160 years there were 8.5% (n = 6).

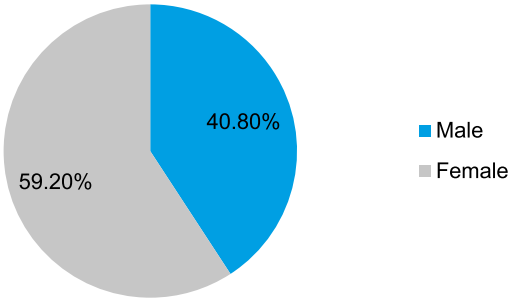

Figure-1. Gender wise distribution of study participants:

Regarding clinical features in these patients of myasthenia gravis it was noted that ptosis and diplopia were most common symptoms, 62% and 54.9%, respectively. These were followed by generalized weakness of body (43.7%) and weakness of leg muscles or low power (26.8%). Dysphagia was present in 14.1%, dysarthria in 12.7% while dyspnoea was found in 16.9% patients Figure-2.

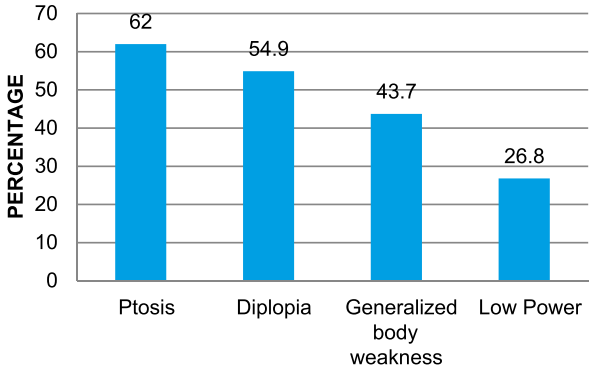

Figure-2. Common clinical symptoms of patients with myasthenia gravis

Stratified analysis was done to see the effect modification of frequency of different clinical features (like ptosis, generalized weakness etc).

A miscellaneous picture was seen in which age, gender and duration of disease were found to be effect modifier for the different clinical features (like ptosis, generalized weakness etc). All of these findings were not significant (i.e. p value >0.005).

Further analysis revealed that frequency of ptosis gradually increased from 50% in youngest age group (<20 years) up to 66.7% in middle age group (3140 years) and then it decreased up to 50% in eldest age group (5160 years) (P value = 0.893). On the other hand, frequency of generalized weakness increased gradually with increasing age from 37.5% (among those of below 20 years age) to 66.67% (among age group of 5060 years) (P value = 0.828). Similarly, gender was an effect modifier for frequency of ptosis & generalized weakness among patients of myasthenia gravis. Frequency of ptosis was much higher among males (72.4%) than females (54.8%) (P value = 0.104). The frequency of generalized weakness was slightly more in females than in males (41.4% versus 45.2% respectively) (P value = 0.469). The study also assessed the effect of duration of symptoms over frequency of ptosis & generalized weakness. It was nonsignificantly found that the frequency of both, ptosis and generalized weakness, decreased with increased duration of the disease (P value = 0.786 & P value = 0.308, respectively).

DISCUSSION

Myasthenia gravis (MG) is an autoimmune disease characterized by a fluctuating pathological weakness with remissions and exacerbations involving one or several skeletal muscle groups. MG does not affect involuntary muscles such as the heart, smooth muscles of the gut and blood vessels.[14,15]

We found in our study that ocular symptoms were most common clinical features. About two thirds of all patients (62%) in this study presented with ptosis while those complaining diplopia were about 55%. These findings were in strong concordance with other studies. A study from china reported that the ocular motor disturbance symptoms ocular symptoms ranged from 5090%. The external ocular muscles are affected initially in about 50% and eventually in 90% of cases. Ptosis (weakness of levator palpabrae) that is often partial and may be unilateral is a common presenting feature. It is often fluctuating in nature.

The progression of weakness in myasthenia gravis usually occurs in a craniocaudal direction: Ocular facial lower bulbar truncal limb muscles.

Ocular features include ptosis and diplopia which are discussed above while facial features include, dysphagia, dyarthria etc. the prevalence of involvement of bulbar muscles can be seen in 30% of the patients.[16,17] In the current study it was seen that these symptoms were not very common. Dysphagia and dysarthria were 14.1% & 12.7% respectively in our patients.

In current study we found that dyspnoea was not a very common clinical feature. It was mentioned by only 16.9% patients. With difference in variety of MG there is a documented difference in frequency of dyspnoea in such patients. Studies found that frequency of dyspnoea was ranging from 11% to 36%. Myasthenia can occur at any age. It can be congenital or acquired. In current study the mean ± SD age of patients was 34.11 ± 10.42 years. Other studies have found a different age patterns of MG patients which is due to demographic variability as well as difference in selection criteria.[18]

The patients which were included in our study had a relatively shorter history of the duration of myasthenia gravis. Contrary to many other studies, the mean ± SD duration of symptoms among our patients was 5.23 ± 3.52 months which ranged within 1 month to 1 year only. Studies documented this duration to be between 3 years to 23 years. Further the current study found that frequency of the certain clinical features (ptosis) reached to peak in age of middle age group (3140 years) and was lower in younger as well as elder age groups while the frequency of generalized weakness increased with increasing age and was highest in eldest age group patients. Although both these findings were nonsignificant yet we think this phenomenon was due to age factor. Majority of our patients were females. It is commonly known that female gender is more affected with MG.[7,19-21]

In females, generalized weakness was slightly more while other symptoms like ptosis were more frequent in males. (P value = 0.469). This phenomenon of gender differences was not understandable and needs to further exploration.

CONCLUSION

Myasthenia gravis, a chronic neuromuscular disorder leads to various degrees of neurologic dysfunction which manifest as different clinical features. The current study found that ocular symptoms are commonest presenting features. A rehabilitation program in combination with other forms of medical treatment can help relieve symptoms and improve function in MG.

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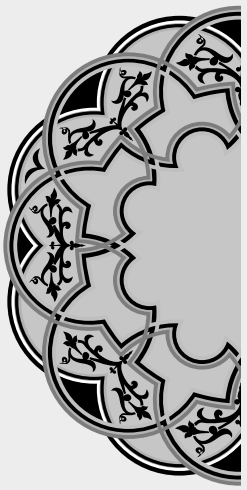

"Take the first step in faith.
You don't have to see the whole staircase,
just take the first step."

Martin Luther King Jr.

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
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2	Dr. Sunil Kumar	Initial writing and drafting	
3	Dr. Awais	Initial writing and drafting	
4	Dr. Atif Sitwat Hayat	Final proof reading	