Association of Severity of Myasthenia Gravis with Complement C3 Level

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INTRODUCTION

- Myasthenia gravis is a neuromuscular junction disorder characterized by weakness and fatigability of skeletal muscles.
- It is an autoimmune disease mediated by autoantibodies against the nicotinic acetylcholine receptor (AchR) at the neuromuscular junction (NMJ).
- Exacerbation of myasthenic symptoms can cause difficulty in chewing, swallowing impairment, respiratory failure or death. So, it is important to detect immunological factors that can assess reliably the variation in severity of myasthenia gravis and with the help of these factors patient can receive timely and adequate treatment to avoid exacerbations or myasthenic crisis.

- Aberrant activation of complement is important in autoimmune disease.
- There are very few studies regarding correlation of severity of myasthenia gravis with complement level. Although there are about 30 proteins in the complement system, there are three complement activation pathways, classical, alternative and lectin, which converge at the assembly of C3 convertases.
- C3 is an appropriate component. In this study, we monitor C3 concentration by nephelometry and severity of MG by the quantitative myasthenia gravis score (QMGS).

RATIONALE

- Timely diagnosis of myasthenia gravis (MG) is of utmost importance.
- Certain medications, surgical procedures and anesthesia, may lead to the respiratory crisis and increase risk of mortality, in the case of non-recognition.
- Myasthenic crisis a life threating complication of MG.
- However, AchRab titre does not predict the severity of disease in individual patient and is not a consistent marker of overall response to therapy.

As complement C3 is the the common by product of all the complement pathway, complement mediated injury is best assessed by complement C3. Several studies have been done in abroad about the association of severity of MG with complement C3 but less published data is available in our country. If this association is found C3 the maybe useful to see the prognosis of MG and optimized the treatment accordingly. And C3 inhibitor may be used in the treatment of MG.

RESEARCH QUESTION

Is there any association between complement C3 level and severity of myasthenia gravis?

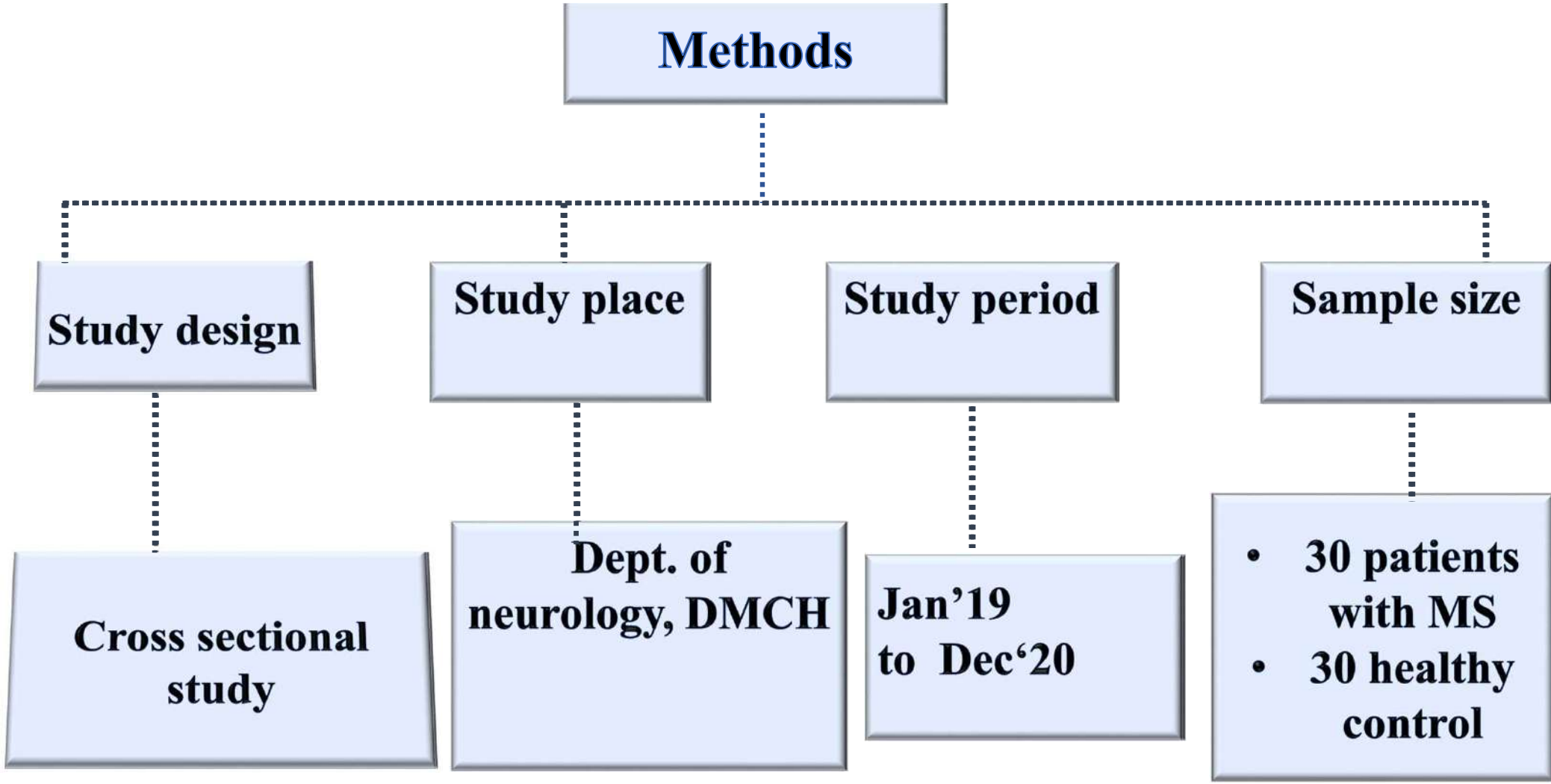
OBJECTIVES

- **General Objective:** To assess the association of complement C3 with severity of disease in patients with myasthenia gravis.

- **Specific objectives:**

1. To estimate the complement C3 level in myasthenia gravis patients and healthy control
2. To assess quantitative myasthenia gravis (QMG) score in myasthenia gravis patients
3. To estimate the complement C3 level in healthy adult subjects for comparison.

METHODS


Methods
Study design
Study place
Study period
Sample size
Cross sectional study
Dept. of neurology, DMCH
Jan'19 to Dec'20
• 30 patients with MS
• 30 healthy control

Sampling method

Non-Randomized purposive sampling

Selection criteria

Inclusion criteria

- Patient diagnosed as generalized myasthenia gravis by history, clinical examination and relevant investigation presence or absence of acetylcholine receptor antibody and or positive repetitive nerve stimulation (RNS) test.

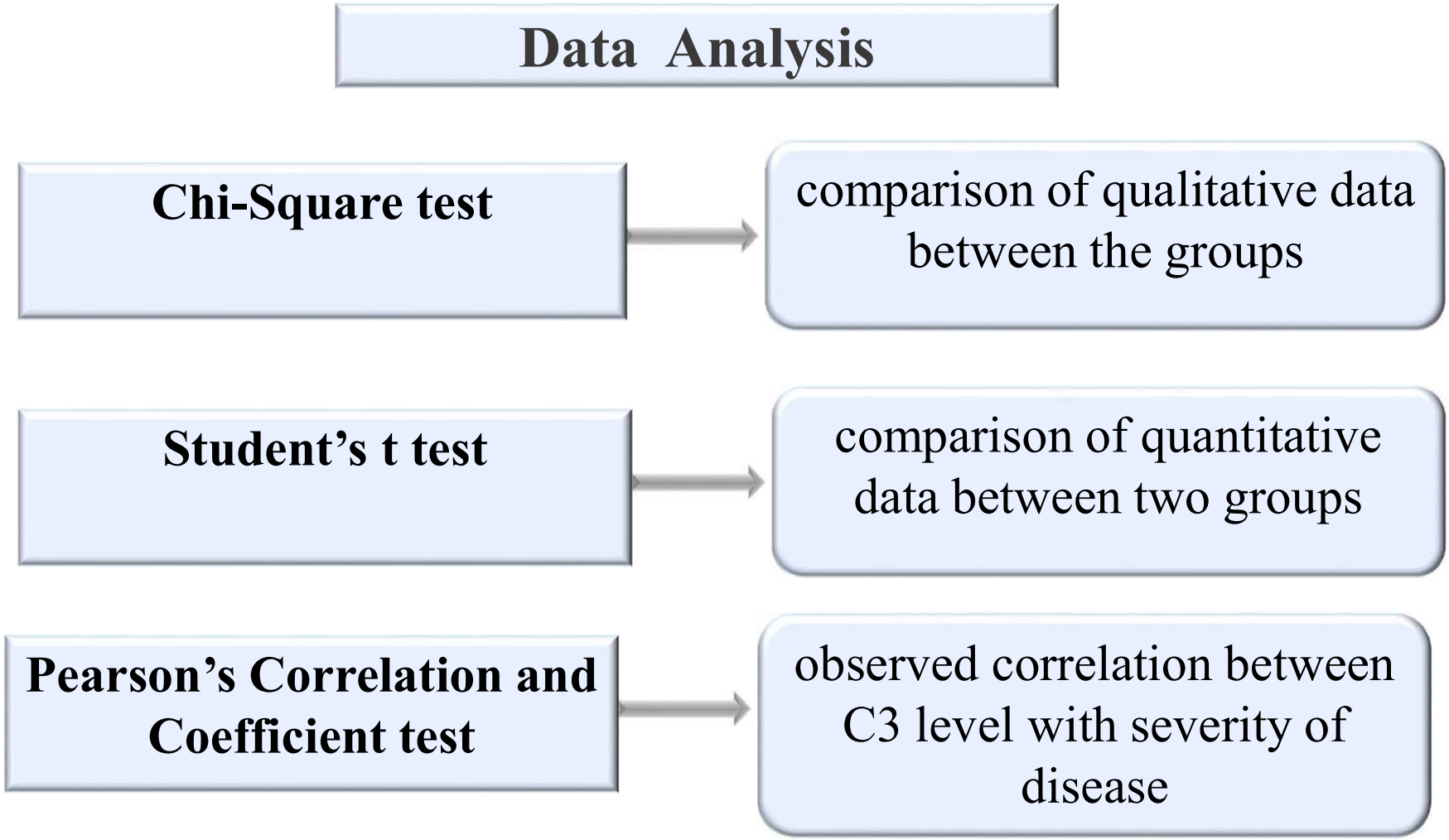
Exclusion criteria

Study group

- Drug induced myasthenic syndrome
- Presence of other autoimmune disease (eg. rehematoid arthiritis systemic lupus erythematous graves thyrotoxicosis)
- Not willing to participate

Control group

- Acute or chronic inflammation
- Malignancy
- Malnutrition
- Hepatic dysfunction
- Not willing to participate



p value <0.05 was considered as the level of significance

Quantitative Myasthenia Gravis Score (QMGS)

Test item grade	0	1	2	3
Double vision lateral gaze right or left (circle one)	61 sec	11-60 sec	1-10 sec	spontaneous
Ptosis (upwardgaze)	61 sec	11-60 sec	1-10 sec	spontaneous
Facial muscles	Normal lid	Complete, weak, some resistance	Complete, without resistance	Incomplete
Swallowing 4 oz water (1/2 cup)	Normal	Minimal coughing of throat clearing	Severe coughing/choking or nasal regurgitation	Cannot swallow (test not attempted)
Speech following counting aloud from 1 to 50 (onset of dysarthria)	None at #50	Dysarthria at #30-49	Dysarthria at #10-29	Dysarthria at #9
Right arm outstretched (90 sitting)	240 sec	90-239 sec	10-89 sec	0-9 sec
Left arm outstretched (90 sitting)	240 sec	90-239 sec	10-89 sec	0-9 sec
Vital capacity (% predicted)	≥80%	65-79%	50-64%	<50%

Right-handed grip (KgW)				
Male	≥45	15-44	5-14	0-4
Female	≥30	10-29	5-9	0-4
Right-handed grip (KgW)				
Male	≥35	15-34	5-14	0-4
Female	≥25	10-24	5-9	0-4
Head, lifted (45 supine)	120 sec	30-119 sec	1-29 sec	0 sec
Right leg outstretched (45 supine)	100 sec	31-99 sec	1-30sec	0 sec
Leftt leg outstretched (45 supine)	100 sec	31-99 sec	1-30sec	0 sec
Total score				

RESULTS

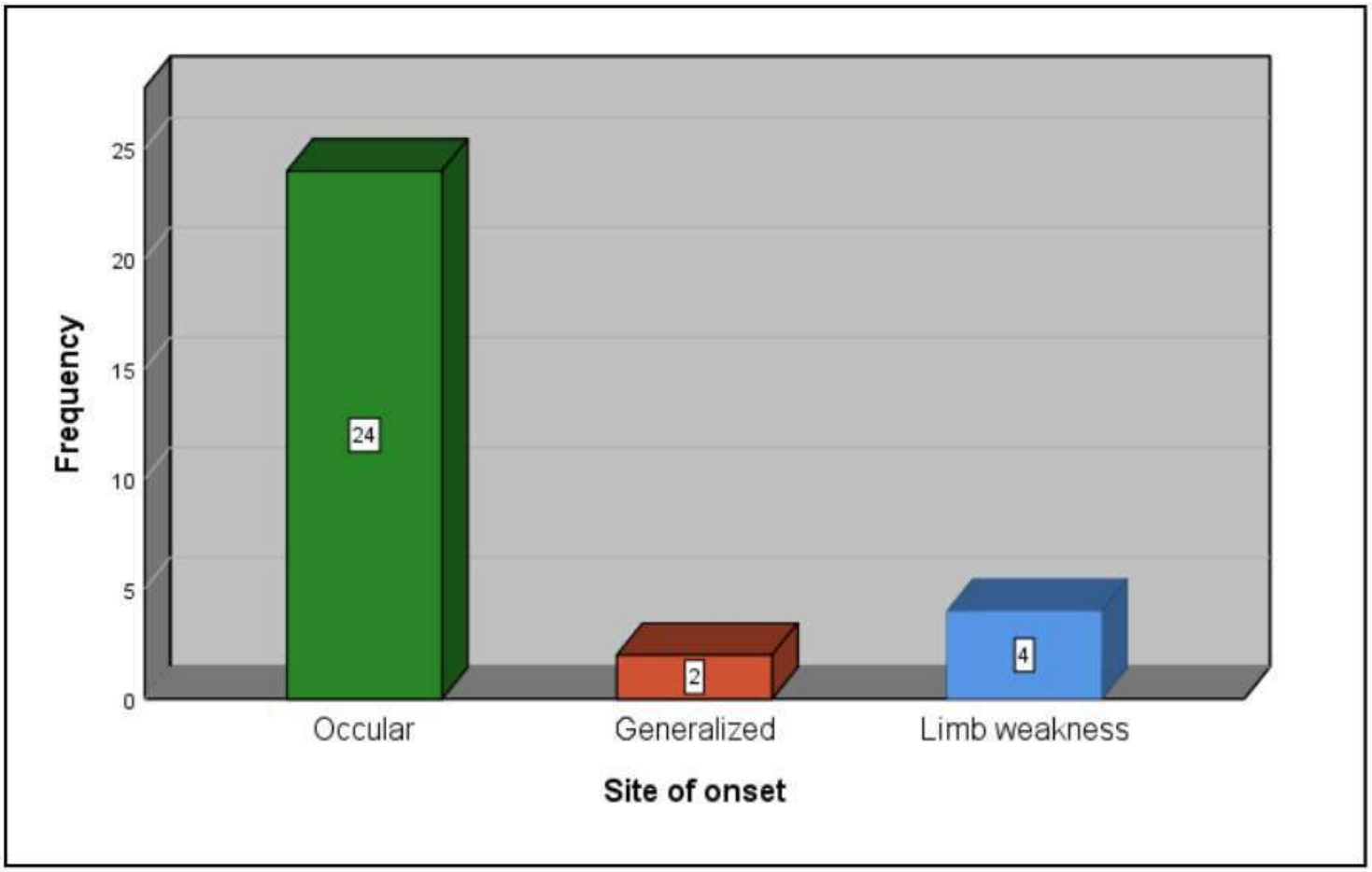


Figure-1: Distribution of study subjects (group A) according to site of onset (N=60)

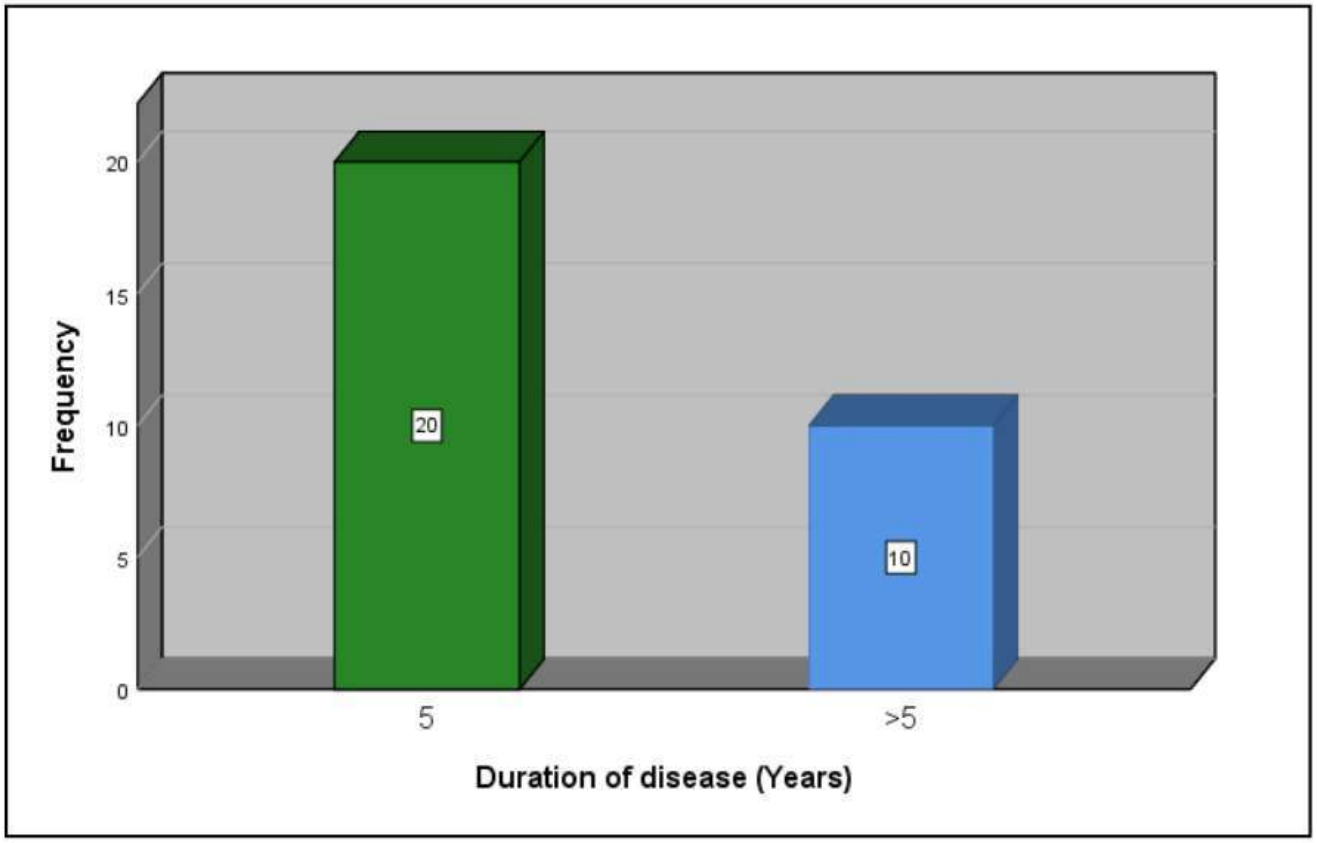


Figure-2: Distribution of study subjects (group A) according to duration of disease (n=30)

Figure-3: Distribution of study subjects (group A) according to age of onset of disease (n=30)

Table-IV: Distribution of study subjects (group A) according to clinical presentation (n=30)

Variable	Frequency	%
Dysarthria	15	50.0
Dyspnea	15	50.0
Dropping eye lid	23	76.7
Headache	10	33.3
Nasal voice	9	30.0
Restricted eye movement	9	30.0
Unilateral	7	23.3
Bilateral	2	6.7
Dysphagia	19	63.3
Limb weakness	28	93.3

Data were expressed as frequency and percentage. n= no. of subjects in each group, A= patients with

Table-V: Distribution of study subjects (group A) according to clinical sign (n=30)

Sign	Frequency	%
Ocular Sign		
Ocular movement		
Restricted	9	30.0
Not restricted	21	70.0
Sustained upgas test		
Positive	27	90.0
Negative	3	10.0
Ptosis		
Present	18	60.0
Absent	12	40.0
Ptosis time (sec)		
<10	2	6.7
10 to 60	25	83.3
>60	3	10.0
Abduction test		
<60 sec	26	86.7
>60 sec	4	13.3

Table-VI: Mean Quantitative Myasthenia Gravis Score (QMGS) of study subjects (Group A) (n=30)

Variable	Range	Mean ± SD
QMGS	2.00-27.00	11.33±6.50

Table-VII: Mean serum C3 (complement) level of the study population (N=60)

Serum C3 level (g/L)	Groups		Mean difference	95% CI	p value
	A (n=30)	B (n=30)			
Mean±SD	1.14±0.19	1.34±0.05	0.20	-0.277 to-0.131	<0.001

Table-VIII: Distribution of study subjects (group A) according to laboratory parameters (n=30)

Variable		r	p value
QMGS with	C3	-0.839	<0.001

Pearson's correlation coefficient test was performed and $p<0.05$ was accepted as level of significant.

DISCUSSION

- In present study, mean QMGS was 11.33±6.50 in patient with myasthenia gravis. The minimum score was 2.00 and the maximum score was 27.00.
- Almost similar findings were found by Oliveira et al. (2017). They found mean QMGS was 11.40±5.70 in patient with myasthenia gravis.
- Barnett et al. (2012) suggested that QMGS is a valid marker for disease severity as supporting the use of the QMGS as a primary outcome measure in clinical trials of MG.

- In present study, mean serum C3 level was 1.14±0.19 g/L in patients with myasthenia gravis which was significantly lower in myasthenia patients than healthy control.
- Aguirre et al. (2020) found that the levels of mean serum C3 was 1.25mg/ml.

THANK YOU