Psychiatric Morbidities among Myasthenia Gravis' Patients

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LIST OF ABBREVIATIONS

Ab	Antibody
AChR	Acetyle choline receptor
Anti-SM	Anti–striated muscle
CNS	Central nervous system
DSM-III	Diagnostic and Statistical Manual of Mental Disorders Third Edition
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders Fourth Edition- Text Revision
ECT	Electro-convulsive therapy
EEG	Electroencephalogram
EPSs	Extra pyramidal side effects
GHQ	General health questionnaire
ICU	Intensive care unit
IVIg	Intravenous immuneglobulin
MDD	Major depressive disorder
MG	Myasthenia Gravis
MINI	Mini-international neuropsychiatric interview
MuSK	Muscle-specific receptor tyrosine kinase
NMJ	Neuromuscular Junction
PP	Plasmapheresis
QoL	Quality of life
REM	Rapid eye movement

RNS	Repetitive nerve stimulation
SCID-IV	Structured clinical interview for DSM IV-tr
SD	Standard deviation
SFEMG	Single-Fiber electromyography

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INTRODUCTION

The coincidence of a psychiatric and a neurological disorder in the same patient may be an especially challenging and common clinical situation **(Rüegga *et al.*,2007)**.

That fact was clarified many times in different studies, in one of them; two psychiatric screening instruments, the Mini-Mental State (MMS) and the General Health Questionnaire (GHQ), were administered to 197 neurological inpatients. The results suggest a high rate of psychiatric disturbance. The highest rate of cognitive disturbance was found in patients with Parkinson's disease. And for emotional disturbance were found in patients with myasthenia Gravis and multiple sclerosis **(Raymond *et al.*, 2009)**.

Myasthenia Gravis (MG) is a chronic, autoimmune disease involving neuromuscular junctions. It is frequently associated with symptoms such as loss of muscle strength, difficulty in respiration and swallowing, diplopia and ptosis **(*Grob et al.*, 2008)**.

All chronic diseases, including MG, may have psychiatric consequences in terms of coping and adaptation. Psychiatric morbidity usually appears as anxiety disorders, such as panic

disorder and generalized anxiety disorder, as well as depressive disorders **(Kulaksizoglu, 2007).**

In a study about Psychiatric disturbances associated with myasthenia Gravis, Seventy-four myasthenic patients (54 females, 20 males; mean age 49.6 years) were evaluated using the diagnostic criteria of the DSM-III in order to investigate the prevalence of psychiatric disturbances. Psychiatric disturbances were observed in 38 subjects (51%), in particular, adjustment disorders with depressed mood (19%), affective disorders (13.5%) and personality disorders (18%) **(Magni *et al*., 2007)**

In cooperation with the German Myasthenia Association, 2,150 patients with confirmed MG were studied in relation to socio-demographic data, impairments, therapeutic course, and use of complementary therapies, illness-related costs, and quality of life. About one-third of the patients suffered from co-morbid diseases such as depression. Depression, walking problems, and metabolic disorders had a negative influence on mental health, whereas stability of MG showed a positive association with mental health **(Sabine *et al.*, 2010).**

When psychiatric and neurological disorder exist in the same patient the diagnosis of myasthenia Gravis (MG) risks to be missed when additional factors complicating the clinical picture are present **(Rüegga *et al.*, 2007).**

The interaction between MG and psychiatric disorders needs to be appreciated, especially in the primary care setting, since the symptoms may overlap. MG may be under-recognized initially because the psychiatric symptoms may coincide with those of the actual disease, such as fatigue, lack of energy and shortness of breath. On the other hand, co-morbid psychiatric symptoms that appear during the course of the illness may be misdiagnosed as true myasthenic symptoms; thus, leading to unnecessary drug treatment **(Kulaksizoglu, 2007).**

Even though there appears to be an intricate relationship between MG and psychiatric symptoms, there is very limited information on this subject. As such, prospective, randomized, controlled pharmaco/psychotherapy studies are needed to better direct the management of patients and, thus, improve quality of life during the course of the illness (**Calarge*et al.*, 2004).**

Rational of the study:

Myasthenia Gravis is commonly associated with psychiatric consequences to the extent that it may mask the diagnosis or negatively affect the prognosis. Hence, it is very important to throw the light on this situation, as up to our knowledge there is no available studies in Egypt to describe or explain that correlation.

Hypothesis:

The thesis was designed to verify the following hypotheses:

- Myasthenia Gravis is a stressful chronic debilitating disease. That commonly associated with psychiatric morbidities.
- The psychiatric comorbidities with Myasthenia Gravis are mainly related to disease characteristics more than to patient socio-demographic or familial variables.

Aim of the study

The aim of this study is to:

1. In the theoretical part:

   - To highlight theoretical considerations of Myasthenia Gravis; definition, etiology, pathology, diagnosis and management modalities and its relations to psychopathology of psychiatric disorders.

2. In the practical part:

   - To recognize the occurrence of psychiatric morbidity among Myasthenia Gravis' patients.
   - To assess the socio-demographic variations of Myasthenia Gravis' patients and assess its relevance.

CHAPTER I

CLINICAL CHARACTERISTICS OF MYASTHENIA GRAVIS AND ASSOCIATED PSYCHIATRIC DISORDERS

A. Myasthenia Gravis :

Myasthenia Gravis (MG) is an autoimmune disease of the skeletal neuromuscular junction. The clinical symptoms of MG are caused by autoantibodies which in most cases attack the postsynaptic nicotinic acetylcholine receptor (AChR) of the muscle endplate. In other cases, non-AChR components of the postsynaptic endplate, such as the muscle-specific receptor tyrosine kinase (MuSK), might be attacked by autoantibodies **(*Meriggioli,* 2009)**.

The presentation and progression of myasthenia Gravis (MG) vary. The usual initial complaint is a specific muscle weakness rather than generalized muscle weakness. The severity of the weakness typically fluctuates over hours being least severe in the morning and worse as the day progresses; it is increased by exertion and alleviated by rest. The degree of weakness also varies over the course of weeks or months, with exacerbations and remissions **(*Keesey,* 2004)**.

Extra ocular muscle weakness or ptosis is present initially in 50% of patients and occurs during the course of illness in 90%.

Bulbar muscle weakness is also common, along with weakness of head extension and flexion **(*Engel,* 1999)**.

Patients progress from mild to more severe disease over weeks to months. About 87% of patients have generalized disease within 13 months after onset. In patients with generalized disease, the interval from onset to maximal weakness is less than 36 months in 83% of patients **(*Grob et al.,* 2008)**.

In addition, exposure to bright sunlight, surgery, immunization, ***emotional stress***, menstruation, and physical factors might trigger or worsen exacerbations. Spontaneous remissions are rare. Long and complete remissions are even less common. Most remissions with treatment occur during the first 3 years of disease **(*Drachman,* 1994)**.

Myasthenia Gravis crisis occurs when myasthenia Gravis weakness is severe enough to require mechanical ventilation. A number of factors have been identified as precipitants of a myasthenia Gravis crisis: *Infections, Stress, Recent surgery, trauma, Botulinum toxin administration and Medications: Antibiotics – Antiarrythmics – Analgesics - Muscle relaxants – Neuropsychiatric drugs like phenytoin, lithium, barbiturates and chlorpromazine* (***Bershad et al.,* 2008)**.

Myasthenia Gravis can mimic other diagnoses that may be misdiagnosed as MG and vice versa. Examples of such pathology include diagnoses such as *congestive heart failure, pulmonary embolism, compressive lesions of cranial nerves and depression* **(*Qureshi et al.,* 2004)**.

The anti–acetylcholine receptor (AChR) antibody test is reliable for diagnosing autoimmune myasthenia Gravis . It is highly specific as high as 100%. Results are positive in as many as 90% of patients who have generalized MG but in only 50-70% of those who have only ocular MG; thus false negatives are common in cases of purely ocular MG ***(Padua et al.,* 2000*).***

The anti–striated muscle (SM) antibody test is also important in patients with MG. Anti-SM Ab. is present in about 84% of patients with thymoma who are younger than 40 years and less often in those without thymoma ***(Sanders et al.,* 2003*).***

About half of the patients with negative results for anti-acetyl choline receptors antibodies (seronegative MG) may have positive test results for antibody to muscle-specific kinase (MuSK), a receptor tyrosine kinase that is essential for neuromuscular junction development ***(Hoch et al.,* 2001, *Martignago et al.,* 2009*)***.