Prevalence of Depression
Among Sudanese patients with Myasthenia Gravis

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ABSTRACT:
Myasthenia gravis, like all chronic diseases, may have psychiatric consequences i.e: psychiatric morbidity usually appears as anxiety disorder, such as panic disorder and generalized anxiety disorder, and as depressive disorder. **Objective:** to determine the prevalence of depression among Sudanese patients with myasthenia gravis seen in Elshaab Teaching Hospital. **Methodology:** This is a descriptive prospective, hospital based, cross sectional study. It was conducted in Al Shaab Teaching Hospital. Almost 33 patients with myasthenia gravis, referred or admitted to Al Shaab Hospital in the period from January 2009 to September 2009, were included in the study. Full detailed history & clinical examinations were performed for each patient in addition to list of investigations included Tensilon test, x-ray & CT. Chest. Depressive symptoms were evaluated using DSM1V-TR criteria. **Results:** we found that 45% of our patients had an evidence of depression, 30% of them had major depression, & 15% had minor depression. The prevalence rate of depression was found to be higher among females. Most of the cases with MG were seen from western Sudan. It was observed that most of our patients were house wives, with higher prevalence of depression among them. The frequency of depression was found to be higher early in the disease & decrease as duration increase. Most of our patients found to have depression (10 patients), showed no or mild response to treatment of MG. **Conclusion:** Patients with MG experience depression at a higher rate than the general population.

Key Word: Myesthenia Gravis, Sudanese, Depression

INTRODUCTION

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 generalised anxiety disorder, and as depressive disorders. 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-
recognised 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. Differentiation of the aetiology of these symptoms might alter the treatment choice and, therefore, affect the treatment success rate and patients' well-being. Psychiatric treatments must be carefully planned because of the risk of aggravating the underlying neurological disease. Even though there appears to be an intricate relationship between MG and psychiatric symptoms, there is very limited information on this subject. There is evidence that in MG patients, cholinergic transmission in the central nervous system (CNS) is also affected. This evidence includes observations of reduced REM sleep, electroencephalographic changes, and detection of Ach receptor antibodies in the cerebrospinal fluid of MG patients. Also, there are some studies on the mental status of MG patients. They manifest higher trait anxiety and greater suppression of anger, and nearly 20% of them were initially diagnosed as having a psychiatric disorder. They may show cognitive impairment as well. Acetylcholine is related to several mental disorders, including mood and cognitive disorders. It is reported that MG patients manifest higher levels of trait anxiety. They also may inhibit the expression of anger. A retrospective study of MG patients revealed that almost 20% of them had initially received a psychiatric diagnosis. Young women are at increased risk to receive a diagnosis in this way. Depression seems to be related to the dose of anticholinesterase treatment needed and the self-reported muscular weakness. Apart from "pure" psychiatric symptomatology, it seems that MG patients manifest lower Mini-Mental State Examination scores and also score lower in various memory tests. MG patients may suffer from a disorder of higher cognitive functioning that responds to therapeutic intervention. Between 20% and 30% of MG patients are initially misdiagnosed with a psychiatric illness. Perhaps even more clinically significant, symptoms of depression among individuals already diagnosed with MG may be dismissed as symptoms of the neurological disease, thus delaying appropriate treatment of the mood disturbance.

OBJECTIVE:

To determine the prevalence of depression among Sudanese patients with myasthenia gravis seen in Elshaab Teaching Hospital from January to September 2009.

METHODOLOGY:
This is a descriptive, prospective, hospital based, cross sectional study. It was conducted at El Shaab Teaching Hospital which is a tertiary hospital, located in the centre of Khartoum town. There are two neurological units with 43 beds and two neurosurgical units with 50 beds, there are three intensive care units, two neurology referred clinics and three neurosurgery referred clinics each week. A total number of 33 patients with myasthenia gravis were included in the study. The period of the study was from January 2009 to September 2009.

**Inclusion criteria:** All Sudanese patients with myasthenia gravis, their age above 18 years, admitted or referred to Elshaab Hospital during the period of the study were included. Exclusion criteria: Non Sudanese patients, those below 18 years of age, or those who refused to be included in the study, were excluded. The data was collected by the authors using structural questionnaire. The informers were either the patients or close relatives. A full detailed history was taken from each patient, the history included: Age, Sex, origin, symptoms of weakness, drooping of the eyelids, double vision, difficulty of swelling, nasal speech and related neurological and systemic symptoms (disturbance of high cerebral function, syncope, motor and sensory defect, sphincter defects, symptoms infavour of cranial nerve involvement). Also past medical history (similar illness, psychiatric illness, autoimmune disease, rheumatoid arthritis, hypertension and DM), drugs history, family history (similar illness, neurological illness, autoimmune disease) and social history were taken.

Depressive symptoms were evaluated, a full detailed history was taken from each patient in semistructural interview using DSM1V-TR criteria for depressive disorder asked about depressed mood most of the time, diminished interest in all
activities, decrease or increase in appetite, weight loss or gain, fatigue, in appropriate guilt, diminished ability to concentrate, recurrent thought of death, impaired in social and occupational function, duration of the above symptoms. Proper systemic and neurological examination was performed to each patient by the authors including cardiovascular, respiratory, abdomen, musculoskeletal, CNS (including high cerebral function, cranial nerves, motor and sensory systems). The following investigations done for each patient: Urine analysis, Hemoglobin, TWBC, Tensilon Test, Chest X-Rays, CT scan chest. Post brandial blood sugar, Rheumatoid Factor, T3 T4 TSH were done if needed. The data was introduced in the computer from a master sheet recording using software program, the data was analyzed and the results were expressed into figures, tables, graphs using statistical package for social science (SPSS).

Limitations of the study:
The explanatory power of the study was limited by its small sample size. A further limitation related to the duration of the study which was short (The period of the study was from January 2009 to September 2009).

Results:
Regarding sex distribution among our studied group, females represent 70% & males 30%. It was found that 12 females had depression while 3 males had depression. Among age group (18-27) we found 7 females & 3 males, age group (28-37) 3 females and 2 males, age group (38-47) 5 females & 3 males, while age group (48-57) we have 2 females & 2 males, & age group ≥58 there were 6 females but no male. Those belong to age group (18-37) : 5 patients of them had depression &10 had no depression, while age (38-57) 8 had depression and 4 had no depression. Regarding age ≥58, 2 of them had depression while 4 had no depression. Out of 33 patients with MG, 12 patients were from Khartoum state, 13 from western Sudan, 6 from central Sudan, 2 from north while no one from east or south. It was found that 6 patients from
Khartoum had depression, 5 from western Sudan had depression while 4 patients from central Sudan had depression. There was no depression among patients from northern Sudan. It was found that 15 patients with MG were housewives, 10 students, 5 officers & 3 workers. It was found that 8 of housewives had depression, 3 students had depression, 3 officers had depression while 1 worker had depression. Regarding duration of symptoms of MG it was found that 12 patients had duration of ≤1 year, while those who had duration ≤2 years were 6 patients, those who had duration ≤3 years were 6, those who had duration ≤4 years were 4, those who had duration ≤5 were 2 & those who had duration ≥5 years were 3 patients. Among those who had duration ≤1 year we found that 9 had depression & 3 had no depression. Among those who had duration ≤2 years 2 had depression & 4 had no depression. Those who had duration ≤3 years 3 of them had depression & 3 had no depression. Those who had duration ≤4 years had no depression. Among those who had duration ≤5 years one had depression & 2 had no depression. Drooping of eyelids was found in 31 patients, diplopia in 28, slurred speech in 4, dysphagia in 5, nasal regurgitation in 4, while proximal weakness was observed in 14 patients. Expressionless face was found in 14 patients, ptosis in 31, ophthalmoplegia in 19, nasal speech in 5, dysarthria in 4 & proximal myopathy in 14 patients. Our study showed that 10 patients with generalized MG had depression & 5 of them had no depression, while those with ocular type, 5 of them had depression & 13 had no depression. It did appeared that 4 of patients with MG showed no response to treatment, 10 showed mild response, 8 moderate response & 11 patients showed marked response. Those patients who showed no response to treatment, 3 of them had depression. Regarding patients with mild response: 7 had depression. Among those who had moderate response 4 had depression. While those with marked response, only 1 patient had depression & 10 had no depression. Out of 33 patients with MG 6 had DM, one patient had hyperthyroidism, one had hypothyroidism & 2 of them had thymoma. It was found that 2 of patients with DM and MG had depression, the one with hyperthyroidism had depression, while that with hypothyroidism had no depression. One of the patients with thymoma had depression. Depressed mood was found in 16 patients, anhedonia in 13, sleep disturbance in 14, appetite and weight change in 15, decrease energy in 13, ↑ or ↓ psychomotor activity in 7, decrease concentration in 7, guilt or feeling of worthlessness in 9, while no one had suicidal ideation. The results showed that 45% of patients with MG had depression, 30% of them had major depression while 15% had minor form & no one showed dysthymia.

**DISCUSSION**

It did appear that 45% of our patients had an evidence of depression, this is similar to what was mentioned by Robert H. Paul, Ronald A et al inspite of using different
methodology to assess depression among their studied group (CMDI; Chicago Multiscale Depression Inventory: vegetative scale was used in this study to assess symptoms of depression). Our study was differed from what was reported by Fisher, Justin et al where they found that 33% of their patients with MG were depressed. Also it was differed from study done by Magnei et al where they found that 32% of their patients were depressed. The difference is due to the fact that Magnei study was analyzed by psychiatrist. It was found that 30% of our patients had major depression, & 15% had minor depression, these findings were not consistent with what was reported by other researchers. The differences were due to the fact that the occurrence of depression among our studied group was due to other factors rather than MG itself ie: availability & cost of the drugs, compliance, level of education, cultural & environmental factors. Also variation in depression rate may be due to the use of different measures of depression, or depression measures that confound symptoms of disease activity with common features of depression (e.g., fatigue). The other possibility is the fact that the previous studies may be limited by small sample sizes. Like what was mentioned in literature females were affected with MG more than males. The study showed that the prevalence rate of depression was higher among females which is keeping with what was mentioned in the literature. Similar to what was reported by Andreas Hinz et al, our study showed that the age group (18-27) was more affected with MG, while the prevalence of depression was found to be higher among the age group (38-57). In spite of the fact that the study was conducted in Khartoum, most of patients with MG were seen from western Sudan, this raises the need for genetic, environmental studies. However the prevalence rate of depression among those from western Sudan appeared to be less than among those from Khartoum, this may reflect true variation in the determinants of depression related to environmental, cultural, nutritional, racial or genetic factors. It was observed that most of our patients were housewives, with the prevalence of depression was higher among them, this may raise the possibility that job satisfaction can play a role in minimization of occurrence of depression. The frequency of depression was found to be higher early in the disease & decrease as duration increase, this unlike what was mentioned by Robert H. Paul et al. This may be due to the fact that Sudanese patients face a lot of problems concerning the use of drugs, compliance, cost & availability of drugs, also incorporation between psychiatrist & neurologist may contribute to that. In addition, social stigma of chronic diseases in our society may raise the prevalence rate of depression. Like what was mentioned in the literature higher prevalence of depression was found among those with generalized type of MG, 10 patients as compared with 5 patients with ocular type. This may reflect the fact that patients with generalized MG facing complications like dysphagia and respiratory muscles
Our study found that, associated diseases with MG, don’t affect the prevalence of depression, this unlike what was reported by other researchers and can be explained by the fact that our study was limited by small size sample. The study showed that out of 33 patients with MG two had thymoma, only one had depression & from this it seems that the number of patients with thymoma is few to a degree that it cannot be used in the analysis to support the idea that the presence of thymoma increase the chance of depression among patients with MG. Most of our patients found to have depression (10 patients), showed no or mild response to treatment of MG, while 4 showed moderate response & only 1 patient showed marked response (following thymectomy). This may reflect the effect of depression on the course & outcome of MG (as one of chronic illnesses), this is similar to what was reported by Wells et al where they found that patients with a recent diagnosis of depression perceived their general health as poorer than subjects without a psychiatric disorder, even when controlling for the presence of chronic illness. Depression was also associated with significant limitation in physical functioning. The role of Ach in higher cognitive function is well studied and established. However, this is not so concerning a possible role for Ach in the pathogenesis of depression. The Ach role in depression (if any) is not well studied. The inhibition of behavior produced by some agents (e.g., phystostigmine) that are known to increase central Ach activity suggests that an Ach-norepinephrine imbalance is central in the pathogenesis of depression. However, other authors propose a relationship only to personality traits. It has also been suggested that the simultaneous increase reported in the activity of catecholamines and in measurements that reflect the hypothalamus-pituitary-adrenal axis in depressed patients indicates, in fact, an increase of Ach activity. The increase of the central cholinergic basal activity after the administration of centrally active agents like phystostigmine, arecholine, and oxotremorine usually triggers or worsens the behavioral analogs of depression. Many authors suggest that pharmacologically induced changes in Ach activity could lead to the development of a model of depression by influencing other transmitter systems (e.g., GABA, serotonin, dopamine, or norepinephrine).

**Conclusion:** Patients with MG experience depression at a higher rate than the general population.

**Recommendations:** Further studies - with larger sample size – are needed to assess the rate of depression among patients with MG.

**References:**

3. Scherer K, Bedlack RS, Simel DL. "Does this patient have myasthenia gravis?". JAMA (2005); 293 (15): 1906–14.
7. Leite MI, Jacob S, Viegas S. "IgG1 antibodies to acetylcholine receptors in 'seronegative' myasthenia gravis". Brain 131 (July 2008); (Pt 7): 1940–52.
27. Dunlop, BW, Nemeroff, CB. The role of dopamine in the pathophysiology of depression. Arch Gen Psychiatry 2007; 64:327.
29. Sapolsky, RM. Glucocorticoids and hippocampal atrophy in neuropsychiatric disorders. Arch Gen Psychiatry 2000; 57:925.
37. 17-http://www.emedicine.com\MED\topic523.htm


59. Nyenhuis DL, Luchetta T, Yamamoto C: The development, standardization, and initial validation of the Chicago Multiscale Depression Inventory 1998; 70:386–401


62. Murphy, JM, Laird, NM, Monson, RR. A 40-year perspective on the prevalence of depression: the Stirling County Study. Arch Gen Psychiatry 2000; 57:209

64. Fisher, Justin MD; Parkinson, Kari; Kothari, Milind J. DO. Self-reported Depressive Symptoms in Myasthenia Gravis. Journal of Clinical Neuromuscular Disease:March 2003 ;( 4 ) 105-108