ARTICLE

# Depression and anxiety among Filipino myasthenia gravis patients seen in a public tertiary hospital in Metro Manila

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**ABSTRACT**

Anxiety and depression complicate treatment of Myasthenia Gravis (MG) as it overlaps with somatic symptoms related to the disease itself. While both are established factors for disease severity in developed countries, similar research in underdeveloped regions is lacking. This study aims to determine the prevalence of anxiety and depression in patients with MG in a tertiary hospital in the Philippines, and to identify the sociodemographic and illness related factors that affect both mental disorders. Locally validated Hospital Anxiety Depression Scale-Pilipino (HADS-P) questionnaires were administered to 59 consenting MG patients to screen for anxiety and depression. Those who scored more than 8 for each subset of HADS-P were presumed to have anxiety, depression or both. The prevalence of anxiety and depression was 50.9% and 15.3%, respectively. Among the factors analyzed, only the female sex had a significant association with anxiety (p=0.019). The total HADS-P score (p=0.009) and HADS-P score for anxiety (p=0.008) had significant positive correlation with MGFA class. The high prevalence of anxiety and depression in MG warrants proper screening and recognition to institute proper treatment and management. This will also prevent confusion with somatic symptoms associated with MG.

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## 1. INTRODUCTION

Depression and anxiety impose a great deal of disease burden and decrement in health. (1,2) In general population, the lifetime prevalence of depression is 7 to 17%. (3,4) However, numerous studies suggest that this prevalence was markedly and consistently higher among people with chronic illnesses such as cardiovascular diseases, diabetes mellitus, rheumatoid arthritis, cancer and osteoporosis. (5)

Myasthenia gravis (MG) is a life-long autoimmune disorder characterized by fluctuating muscular weakness, unpredictable course, and with disability prevalence of 6/100,000. (6)(7) Patients with this condition often face psychologic stress brought about by difficulties in maintaining daily activities and coping with severe fluctuating weakness, added to the constant

**KEYWORDS**

Myasthenia gravis, Depression, Anxiety, Hospital Anxiety and Depression Scale, Philippines

need to take medications. (8) Depression and anxiety have long been suggested to be common in patients with MG, and these psychiatric co-morbidities may complicate treatment, as some symptoms such as weakness and shortness of breath, may be mistaken as myasthenic symptoms. In addition, somatic symptoms of depression tend to overlap with medical ones which may lead to underdiagnosis. (9)

In developing countries, it is uncommon to refer patients with MG to a psychiatrist as part of routine evaluation. Anxiety and depression are often overlooked and often attributed to the disease itself leading to frequent hospital visits and persistent subjective complaints despite adjustment of medications. As a consequence, the prevalence of anxiety and depression, as well as socioeconomic and illness-related factors that may affect them, are unknown, and the burden of the condition is assumed non-existent. In contrast, the relationship of these mental disorders to MG in Western countries is well-known, hence, managed accordingly.

Therefore, we perceive the need to further study depression and anxiety among patients with MG. In this study, we aimed to determine the prevalence of anxiety and depression among adult patients with MG using the validated Filipino version of the hospital, and anxiety and depression scale (HADS-P)(10), and identified possible correlation with certain socio-demographic and health-related factors.

## 2. METHODOLOGY

### 2.1. Study design and settings

This was a prevalence-based research conducted in a public tertiary hospital in the Philippines from November 2018 to March 2019. The institution was equipped with health services (i.e. diagnostic and therapeutic modalities) which catered patients with MG.

### 2.2. Participants

#### 2.2.1. Recruitment

Confirmed MG patients determined from the daily patient censuses in the Department of Neurosciences of Philippine General Hospital were included. These patients were contacted via phone call and invited for screening and participation. Participants were also recruited via direct referral from their attending physician or neurologist during days of clinic visits and follow up. If the patient agreed to be screened using the predefined inclusion and exclusion criteria listed below, he or she was invited to participate in the study. Consent was obtained using a premade informed consent approved by the institutional ethics board. A data gathering tool containing details on demographic profile and the HADS-P questionnaire were subsequently administered. (Figure 1)

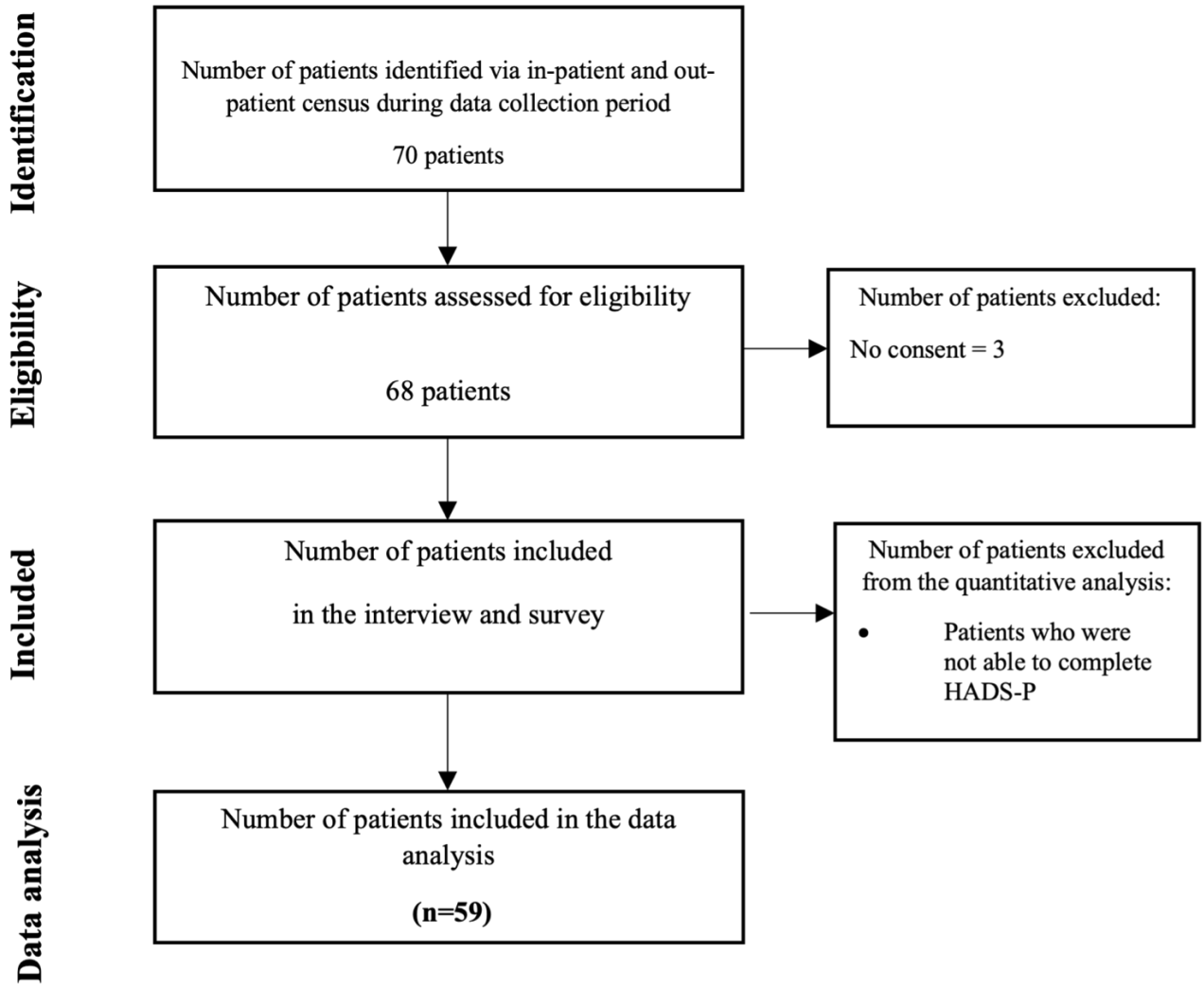


**Figure 1: Flow diagram of patient inclusion for this study**

#### 2.2.2. Inclusion and Exclusion criteria

Adult patients aged 19 years old and above being seen in the Neurology OPD clinic, who are diagnosed with myasthenia gravis by clinical, and/or via diagnostic methods, either through electrodiagnosis or serologic testing, and who can comprehend and respond with written and verbal questions, were invited to participate. Patients who were severely symptomatic (i.e. on oxygen support, dyspneic, severe weakness) and those who refused to participate, were excluded from the screening process. These criteria were predetermined to ensure that the participants would be able to answer the self-report questionnaire.

### 2.3. HADS-P questionnaire

Hospital anxiety and depression scale (HADS) was developed in 1983 as a practical, reliable, valid, and easy to use tool to identify and quantify symptoms of anxiety and depression. This tool is not primarily used to diagnose psychiatric disorder, rather, it is used to screen patients who need further psychiatric evaluation and treatment.(11) The presence of anxiety and depression was determined using a HADS-P screening tool, which is a 14-item, self-administered, Filipino-translated form of HADS. The tool was validated by De Guzman in 2013 among medically-ill Filipino patients. Participants who reached a score of > 8.0 points in the anxiety and/or depression arms were deemed to have significant anxiety and/or depressive symptoms. (12) Patients who only met the cut off for depression or anxiety alone will be grouped either in the depression or anxiety group respectively, while those who met the cut off score for both were referred to as having anxiety AND depression. Each participant who met the cut off scores using this screening tool was directed back to their primary attending physicians for them to be referred to the Psychiatry department for formal assessment.

### 2.4. Data sources and collection process

A data gathering tool containing demographic and basic clinical information was used in this study. The following information was obtained from the participants during the interview and medical record review: age, sex, civil status, educational attainment, occupational status, duration of disease, MGFA class, the status of thymoma, whether the patient underwent thymectomy, medications taken daily for MG, and other comorbidities. Codes were assigned for each patient to ensure anonymity. The consenting participants were invited individually inside a private cubicle inside the Neurology OPD clinic to answer the HADS-P questionnaire.(10) The filled-out questionnaires and data collection forms were first surveyed for completeness and was subsequently secured inside an envelope to ensure data privacy.

### 2.5. Sampling method and sample size calculation

A non-probability convenience sampling design in enrolling patients with MG was utilized. The null hypothesis was set such that the prevalence of anxiety and depression in MG patients was the same as that of the general population. The alpha was set at 0.05, the power at 0.8, and the proportion of MG with anxiety and depression at 22% and that of the general population at 7%.(13) The sample size was calculated using the Exact Agresti-Coull method for two-tailed test, yielding a sample size of 40. The drop out was accounted for, thus, an additional 20% of the computed sample size was included, yielding a total sample size of 48.

### 2.6. Statistical analysis

The analysis was conducted using the JMP® Software, Version *14* (SAS Institute Inc., Cary, NC, 1989-2019). Mean and standard deviation for continuous variables and frequency and proportions for the categorical variables were used. One-sample proportion test to compare the proportion of MG patients with anxiety and depression with that of the general population was done. The Pearson's correlation was employed to determine the possible correlation of age, MGFA class, and duration of illness to HADS-P scores. Two-sample proportions test and chi square test to compare the proportion of MG patients with anxiety and depression among the groups in terms of the following factors: sociodemographic (sex, employment status, civil status and educational attainment), presence of comorbid illnesses, thymoma and thymectomy status, MGFA class and medications. The level of significance for all analyses was set at p-value < 0.05 using two-tailed comparisons.

## 3. RESULTS

### 3.1. Clinical Profile

A total of 59 participants were recruited. All the 59 participants completed the data collection tool and questionnaire. The mean age was 42.8 years (range: 21 to 70) with higher proportion of female (86%). Most reached tertiary education (college level, both graduate and undergraduate, 64%), were married (40.7%) and were unemployed (79.6%). The mean duration of illness was 7.98 years, with most taking pyridostigmine only for their symptoms (30.5%). Majority of the recruited participants were MGFA IIb (37.3%). Other comorbid illnesses, such as hypertension and diabetes mellitus, were reported in 28.8% of patients. Most participants were non-thymomatous (49.2%) and had not undergone thymectomy (61%). The mean HADS-P score for depression was 4.7, that of anxiety was 8.6, while the mean total score was 13.1. The baseline characteristics of the participants were summarized in Table 1.

### 3.2. Prevalence of anxiety and depression

Out of the 59 participants who took the HADS-P questionnaire, 9 (15.2%) of them had a score of more than 8 in the depression subset, and 30 (50.8%) had a score of more than 8 in the anxiety subset. There were 8 (13.6%) participants who had scores of more than 8 in both anxiety and depression subsets.

### 3.3. Anxiety

The comparison of proportion of anxiety among MG patients in terms of the various factors analyzed in this study was summarized in Table 2. The proportion of patients with anxiety among female participants (54.9%) was significantly higher (p= 0.019) than that of males (12.5%).

No significant differences were found among other factors analyzed in this study. Nevertheless, higher proportions of anxiety were seen in patients who reached secondary education (52.9%), widowed/widower (60.0%) and employed (50.0%). Higher proportions were also noted among those without other co-morbid illnesses (52.9%), non-thymomatous (55.2%), those who did not have thymectomy (50.0%), and those taking pyridostigmine, prednisone and azathioprine in combination (54.6%). In terms of the MGFA class, there was also no significant difference in proportion seen. However, note that there was only one patient recruited in this study which was classified as MGFA IIIb (100%), who also met the HADS-P score cut off.

An inverse correlation was found between age and duration, and HADS-P score for anxiety, but this was not statistically significant. In contrast, a direct statistically significant correlation was seen between HADS-P score and increasing MGFA class (r=0.34, p=0.008).

### 3.4. Depression

The proportion of depression who met the cut off HADS-P score was higher in the following groups: female patients (15.7%); those reaching secondary education (29.4%); widowed/widower

(20.0%); employed status (33.3%); those without other co-morbid illness (16.7%), those without thymoma (17.2%); who did not undergo thymectomy (19.4%); MGFA class IIb; and those taking pyridostigmine alone (22.2%). None of these factors reached statistical significance in terms of difference in proportion for each category.

Linear correlation analysis done for age, duration of illness and MGFA, plotted against HADS-P score for depression subset, showed that there was a tendency towards direct correlation, but the correlation was not significant. The results were summarized in Table 2.

### 3.5. Subset analysis for Anxiety and Depression

A separate subset analysis was done for those patients who met the cut off scores for both anxiety and depression. The proportion of all factors in this study showed no difference among the groups, as shown in Table 2. The proportions were seen to be higher among the following categories: female (13.7%); secondary education (23.5%); widow/widower (20.0%); employed (25.0%); without other co-morbidities (14.3%); non-thymomatous (55.2%); did not undergo thymectomy (16.7%); MGFA class IIb; and those taking pyridostigmine alone (22.2%).

Linear correlations tests between the total HADS-P score and age, illness duration, and MGFA classes, showed a direct relationship, but only MGFA class yielded a statistically significant correlation (r=0.34,p=0.009).

**Table 1: Clinical features of the included participants with myasthenia gravis (MG)**

| | | | | | |
|---|---|---|---|---|---|
| **Sample size**, N | 59 | | **Current medications for MG**, n (%) | | |
| **Age**, mean (SD) | 42.8 | (13.3) | Pyridostigmine | 18 | (30.5) |
| **Sex**, n (%) | | | Pyridostigmine & prednisone | 13 | (22.0) |
| Male | 8 | (13.6) | Pyridostigmine + azathioprine | 17 | (28.8) |
| Female | 51 | (86.4) | Pyridostigmine, prednisone & azathioprine | 11 | (18.6) |
| **Educational attainment**, n (%) | | | | | |
| Primary | 4 | (6.8) | **Comorbidities**, n (%) | | |
| Secondary | 17 | (28.8) | Absent | 42 | (71.2) |
| Tertiary | 38 | (64.4) | Present | 17 | (28.8) |
| **Civil status**, n (%) | | | **Thymoma status**, n (%) | | |
| Single | 21 | (35.6) | Thymomatous | 22 | (37.3) |
| Married | 24 | (40.7) | Non-thymomatous | 29 | (49.2) |
| Separated | 4 | (6.8) | Unknown | 8 | (13.6) |
| Widow/Widower | 10 | (17.0) | | | |
| | | | **Thymectomy status**, n (%) | | |
| **Employment status**, n (%) | | | No | 36 | (61.0) |
| Unemployed | 47 | (79.7) | Yes | 23 | (39.0) |
| Employed | 12 | (20.3) | | | |
| | | | **HADS-P* scores**, mean (SD) | | |
| **Duration of illness**, mean (SD) | 8.0 | (6.9) | Depression | 4.8 | (3.0) |
| | | | Anxiety | 8.6 | (3.9) |
| | | | Total | 13.1 | (5.8) |
| **MGFA class**, n (%) | | | | | |
| I | 14 | (23.7) | **HADS-P* > 8**, n (%) | | |
| IIa | 15 | (25.4) | Depression | 9 | (15.2) |
| IIb | 22 | (37.3) | Anxiety | 30 | (50.8) |
| IIIa | 1 | (1.7) | Anxiety & depression | 8 | (13.6) |
| IIIb | 5 | (8.5) | | | |
| IVb | 2 | (3.4) | | | |

*HADS-P, Hospital and Anxiety and Depression (Pilipino) scale.

**Table 2: Comparison of proportions of anxiety and depression among subgroups of factors**

| Factors | Category | Anxiety | | | Depression | | | Anxiety and depression | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Proportion (%) | Chi-square | P-value | Proportion (%) | Chi-square | P-value | Proportion (%) | Chi-square | P-value |
| **Sex** | Male | 12.5 | 5.536 | **0.019*** | 12.5 | 0.057 | 0.812 | 12.5 | 0.009 | 0.924 |
| | Female | 54.9 | | | 15.7 | | | 13.7 | | |
| **Educational attainment** | Primary | 25.0 | 1.042 | 0.594 | 0.0 | 4.013 | 0.134 | 0.0 | 2.367 | 0.306 |
| | Secondary | 52.9 | | | 29.4 | | | 23.5 | | |
| | Tertiary | 50.0 | | | 10.5 | | | 10.5 | | |
| **Civil status** | Single | 57.1 | 2.479 | 0.479 | 19.0 | 1.269 | 0.737 | 19.0 | 0.208 | 0.556 |
| | Married | 41.7 | | | 12.5 | | | 8.3 | | |
| | Separated | 25.0 | | | 0.0 | | | 0.0 | | |
| | Widow/widower | 60.0 | | | 20.0 | | | 20.0 | | |
| **Employment** | Employed | 50.0 | 0.004 | 0.947 | 33.3 | 3.265 | 0.071 | 25.0 | 1.481 | 0.224 |
| | Unemployed | 48.9 | | | 10.6 | | | 10.6 | | |
| **Comorbidities** | Present | 47.6 | 0.137 | 0.711 | 11.8 | 0.235 | 0.628 | 11.8 | 0.067 | 0.795 |
| | Absent | 52.9 | | | 16.7 | | | 14.3 | | |
| **Thymoma status** | Thymomatous | 45.4 | 0.975 | 0.614 | 13.6 | 0.180 | 0.914 | 13.6 | 0.009 | 0.995 |
| | Non-thymomatous | 55.2 | | | 17.2 | | | 13.8 | | |
| | Unknown | 37.5 | | | 12.5 | | | 12.5 | | |
| **Thymectomy status** | Yes | 47.8 | 0.027 | 0.871 | 8.7 | 1.339 | 0.247 | 8.7 | 0.802 | 0.371 |
| | No | 50.0 | | | 19.4 | | | 16.7 | | |
| **MGFA* class** | I | 28.6 | 4.550 | 0.473 | 7.1 | 2.333 | 0.801 | 7.1 | 3.325 | 0.650 |
| | IIa | 46.7 | | | 13.3 | | | 6.7 | | |
| | IIb | 59.1 | | | 22.7 | | | 22.7 | | |
| | IIIa | 100.0 | | | 0.0 | | | 0.0 | | |
| | IIIb | 60.0 | | | 20.0 | | | 20.0 | | |
| | IVb | 50.0 | | | 0.0 | | | 0.0 | | |
| **Medications** | Pyridostigmine | 50.0 | 0.680 | 0.878 | 22.2 | 1.160 | 0.763 | 22.2 | 2.232 | 0.526 |
| | Pyridostigmine & prednisone | 53.8 | | | 15.4 | | | 15.4 | | |
| | Pyridostigmine & azathioprine | 41.2 | | | 11.8 | | | 5.9 | | |
| | Pyridostigmine, prednisone, & azathioprine | 54.6 | | | 9.1 | | | 9.1 | | |

*MGFA, Myasthenia Gravis Foundation of America

**Table 3: Correlational analysis of age, duration of illness and MGFA class with HADS-P* scores.**

| Factors | Anxiety score | | Depression score | | Total score | |
|---|---|---|---|---|---|---|
| | Correlation coefficient | P-value | Correlation coefficient | P-value | Correlation coefficient | P-value |
| **Age** | -0.030 | 0.819 | 0.209 | 0.112 | 0.109 | 0.414 |
| **Duration of illness** | -0.001 | 0.995 | 0.19 | 0.885 | 0.005 | 0.937 |
| **MGFA† class** | 0.343 | **0.008*** | 0.158 | 0.233 | 0.34 | **0.009*** |

*HADS-P, Hospital and Anxiety and Depression (Pilipino) scale.
†MGFA, Myasthenia Gravis Foundation of America

## 4. DISCUSSION

The screening of anxiety and depression in MG patients in a tertiary hospital yielded a prevalence of 50.8% and 15.2%, respectively. Among the various sociodemographic factors that have been analyzed, female sex and the presence of anxiety were found to have significant association. Likewise, a significant, positive correlation was seen in terms of the HADS-P score for anxiety and the total score, as well as the MGFA class, which roughly correlates with the severity of the symptoms. In contrast, the duration of illness, presence of co-morbidities, medications being taken, thymoma and thymectomy status, did not seem to correlate with the presence of anxiety and depression.

Depression has a lifetime prevalence of 7 to 17% in the general population. (3,4) In the Philippines, the incidence of depression is 5.3% per year, as per the Department of Health (DOH) data. On the other hand, large population-based surveys showed that the prevalence of anxiety disorder is 28.8%.(14) Philippine data on the proportion of anxiety in the population is not well documented. However, the prevalence of anxiety found in the present study is generally comparable to similar studies in the past. Specifically, Lundeen (2004), in her report of 69 patents using Beck Anxiety Inventory (BAI) questionnaire, found the prevalence to be 55%. (15) Meanwhile, in a study of 161 patients which utilized the Hamilton Anxiety Rating (HAM-A) scale, the prevalence was found to be 45.3%. (16) Using the HADS questionnaire in a recent survey of 80 patients, Braz (2018) identified anxiety to be present in 43.75% of these patients. (17)

Compared to similar studies in the past, the prevalence of depression in our study was lower. In a study comparing 36 patients with 20 controls using the National Institutes of Health Diagnostic Schedule (DIS), the prevalence was found to be 42%. (18) Another report, which utilized Beck Depression Inventory (BDI) scale and Hamilton Depression Rating (HAM-D) scale, involving 42 patients showed a prevalence of 52.4% and 40.5%, respectively. (19) HAM-D was also used by Qiu (2010) in similar patients, which showed the prevalence to be 58.3%. (16) In contrast to the studies mentioned, Braz (2018) utilizing HADS, obtained a lower prevalence of 27.5%.(17) Despite the varying numbers, the published reports consistently showed that patients with MG had a higher prevalence of depression compared to the general population. Our data shows that the prevalence of depression in Filipino patients with MG is comparable to the lifetime prevalence in the general population. The reason for the lower prevalence seen in our study may be attributed to the tool used to screen for depression. As the presence of somatic symptoms tend to be misleading since it may overlap with symptoms of MG itself, screening tools such as BDI, HAM-A, HAM-D, Multiscale Depression Inventory (MDI) and Chicago Multiscale Depression Inventory (CMDI), may not be able to delineate a patient's medical state from psychological state leading to overestimation of the prevalence. (18,20) This is the advantage of using the HADS questionnaire as this scale only includes psychological symptoms and omits somatic components attributable to physical symptoms.(21)

The significant association with anxiety and female sex category is consistent with previous studies using various screening instruments.(19,22,23) Anxiety disorders are generally more prevalent in females than in males, and this has been proven in large epidemiologic studies, hence can be a cofounder. (24) Specifically, the lifetime male:female prevalence ratio was found to be 1.1:1.7.(24) Female predisposition to develop anxiety more than males can be explained by social factors such that women experience more stressors, and they have coping and cognitive styles more prone to worry and rumination. In addition, biological influences also contribute by having anxiety sensitivity and hormonal fluctuations. (25) Moreover, MG has been known to be more common in women below the age of 50, beyond which, men and women are equally affected.(26) This is important as majority of the recruited participants in our study were females and the mean age was 42.8 years old. On the other hand, the occurrence of depression had not been shown in our study to be significantly different between males and females. Two previous studies had similar findings. (19,22) The study of Parada (2014), however, showed significant sex difference in the HADS score for depression. (23)

The present study suggests that the severity of the symptoms possibly correlates with the occurrence of anxiety. A retrospective study done in 2018 of 103 patients showed that the incidence of psychiatric symptoms was exacerbated with progression of MG. (27) A study done in 1999 comparing the development of psychiatric symptoms between MG patients who had history of respiratory failure compared to those who did not, showed a significant difference in the proportion of both anxiety and depressive symptoms. The high rate of psychiatric co-morbidities in these patients was attributed to life-threatening aspect of unexpected respiratory stress and mechanical ventilation. (28) History of myasthenic crisis or respiratory failure, however, was not accounted for in our study. Our analysis that an increasing HADS-P score is associated with increasing the MGFA class or severity, may be reasonable. The small sample size could have affected the lack of association seen when the MGFA class were taken as a categorical variable. Other factors that may be worth stating are the use of steroid and thymectomy status. Steroid use has been argued by previous studies to be one of the factors associated with depression in MG.(29) In fact, the reported incidence of mental health issues following steroid use in general is 2% to 60%.(30) However, this association has not been found consistently in all studies. In the study of Yamamoto et al. in 2018, it was shown that the initiation of steroid therapy or increases in its dosage did not exacerbate psychiatric disorders in patients with MG. Instead, they found

that disease state of MG was associated with psychiatric disorders. Furthermore, they have found that psychiatric disorders were less frequent in patients with concurrent myositis who were treated with chronic oral steroids.(31) Our study, likewise failed to demonstrate this association. Thymectomy, on the other hand, has been regarded as one of the standards of treatment in thymomatous and nonthymomatous anti-AChR positive MG, to reduce medication requirement and disease severity overtime. (32) The expected improvement usually begins at 6 to 12 months after thymectomy, and gradually over years. MG patients with a history of thymectomy has been shown to have a lower prevalence of depression in the study of Gavrilov et al. in 2019. (33) Our study failed to find this association. It is possible that the findings of the present study may be partly due to the failure to account for the period of time thymectomy has been performed. The authors also hypothesize that the interplay of these several factors that could have affected the overall disease status of the patients could render analysis of each of these factors as independent variables, be more complicated than it seems to be.

Our study showed that it is not uncommon for patients with MG to have concurrent psychiatric morbidities, particularly anxiety and depression, which may be confused with physical manifestations of the disease. HADS-P is a useful screening tool that has been validated and by which cut off score of 8 has been found to have a sensitivity of 91%, specificity of 59%, and a positive predictive value of 61%. (34) The high sensitivity of this cut off score allows clinicians to screen and institute proper referral and treatment to these patients. It is important to note that, although effective in detecting patients with anxiety and depression, this tool is not valid for diagnosis.(23) Proper referral of these patients to psychiatry is warranted to address these symptoms and institute appropriate treatment so as not to confound with the neurologic manifestations of MG itself.

Our study has several limitations. First is the small sample size. Some variables warrant replication in larger number of participants. The recruited samples were underrepresented in terms of individuals with higher MGFA class, who were likely to have more severe disease, and thus, more prone to developing depressive and anxiety symptoms. This lack of diversity accounts for the lack of association between the anxiety and depressive states with increasing severity of illness. Increasing the sample size and recruitment of more participants on a wider perspective, such as interhospital participation, as well as more extensive identification and screening of not just ambulatory, but also hospitalized patients, could address this issue. Secondly, it must be noted that HADS-P is only a screening tool and should not replace proper physician evaluation using clinical assessments and well accepted diagnostic criteria such as DSM 5, in the diagnosis of anxiety and depressive disorders. The identification of anxiety and depressive disorders with formal psychiatric assessment is out of the scope of this study. Taking this into consideration for future studies, formal and structured assessment by mental health specialists would greatly increase the accuracy of determination of the prevalence of these mental disorders in MG. Moreover, there may also be a value in adding validated instruments and tools in assessing the quality of life (i.e. MG QOL) and activities of daily living (i.e. MG-ADL.) Another limitation is the lack of inclusion of assessment of family and social systems as possible factors associated with development of anxiety and depressive symptoms. For instance, a previous study had shown that there was an association between family dysfunction and depression.(35) This, and other factors are important determinants that future studies may want to look into, to better understand the development of these mental health disorders in chronic diseases. Other social factors that could have affected the development of psychiatric disturbances in MG such as monthly income, financial burden, social support and disadvantages, may also be worthy of being analyzed in the future.

Our study has several implications in clinical practice. Given the relatively high prevalence of anxiety symptom in patients with MG, which is likewise correlated with the disease severity, it is reasonable to recommend early screening of anxiety, as well as, depressive symptoms during the course of treatment of these patients. Early recognition and referral could positively affect the course of the disease, and with proper psychotherapy, improve the debilitating symptoms. With overlapping symptoms being difficult to clearly delineate, addressing underlying medical and psychiatric comorbidities would greatly affect the overall status of the patient. This, likewise, alleviate the burden on attending neurologists in continuously titrating medications that does not seem to effectively address the symptoms, only to find out the patient is also in need of psychological intervention.

## 5. CONCLUSION

The prevalence of anxiety and depression in myasthenia gravis using the HADS-P questionnaire was 50.9% and 15.3%, respectively. The proportion of female patients with anxiety was significantly higher compared to males. The total HADS-P score and subset score for anxiety was positively correlated with the severity of MG. This study did not find a significant association between anxiety and depression with sociodemographic factors namely, age, civil status, employment status, and educational attainment; and illness related factors such as comorbid illness, medications, thymoma and thymectomy status. The high prevalence of these psychiatric symptoms in these patients suggests that there is a need for the clinicians to recognize and screen for these conditions, and subsequently, institute proper referral and therapy.

## 6. REFERENCES


1. Baxter AJ, Vos T, Scott KM, Ferrari AJ, Whiteford HA. The global burden of anxiety disorders in 2010. Psychol Med. 2014 Aug 22;44(11):2363–74.

2. Moussavi S, Chatterji S, Verdes E, Tandon A, Patel V, Ustun B. Depression, chronic diseases, and decrements in health: results from the World Health Surveys. The Lancet. 2007 Sep;370(9590):851–8.

3. Blazer DG, Kessler RC, McGonagle KA SM. The prevalence and distribution of major depression in a national community sample: the National Comorbidity Survey. American Journal of Psychiatry. 1994 Jul;151(7):979–86.

4. Wells K, Golding J BM. Psychiatric disorder in a sample of the general population with and without chronic medical conditions. American Journal of Psychiatry. 1988 Aug;145(8):976–81.

5. Clarke DM, Currie KC. Depression, anxiety and their relationship with chronic diseases: a review of the epidemiology, risk and treatment evidence. Medical Journal of Australia. 2009 Apr 6;190(S7).

6. Chu HT, Tseng CC, Liang CS, Yeh TC, Hu LY, Yang AC, et al. Risk of Depressive Disorders Following Myasthenia Gravis: A Nationwide Population-Based Retrospective Cohort Study. Front Psychiatry. 2019 Jul 9;10.

7. Keesey JC. Does myasthenia gravis affect the brain? J Neurol Sci. 1999 Nov;170(2):77–89.

8. Suzuki Y, Utsugisawa K, Suzuki S, Nagane Y, Masuda M, Kabasawa C, et al. Factors associated with depressive state in patients with myasthenia gravis: a multicentre cross-sectional study. BMJ Open. 2011 Dec 19;1(2):e000313–e000313.

9. Cherukupally KR, Kodjo K, Ogunsakin O, Olayinka O, Fouron P. Comorbid Depressive and Anxiety Symptoms in a Patient with Myasthenia Gravis. Case Rep Psychiatry. 2020 Jan 8;2020:1–3.

10. Lourdes M, Guzman RE De. The Validation of the Hospital Anxiety and Depression Scale ( HADS-P ) among the1. Lourdes M, Guzman RE De. The Validation of the Hospital Anxiety and Depression Scale ( HADS-P ) among the medically-ill Filipino patients in Philippine General Hospital A V. 2016;(January 2014).

11. Michopoulos I, Douzenis A, Kalkavoura C, Christodoulou C, Michalopoulou P, Kalemi G, et al. Hospital Anxiety and Depression Scale (HADS): validation in a Greek general hospital sample. Ann Gen Psychiatry. 2008 Dec 6;7(1):4.

12. Lourdes M, Guzman RE De. The Validation of the Hospital Anxiety and Depression Scale ( HADS-P ) among the1. Lourdes M, Guzman RE De. The Validation of the Hospital Anxiety and Depression Scale ( HADS-P ) among the medically-ill Filipino patients in Philippine General Hospital A V. 2016;(January 2014).

13. Chu HT, Tseng CC, Liang CS, Yeh TC, Hu LY, Yang AC, et al. Risk of Depressive Disorders Following Myasthenia Gravis: A Nationwide Population-Based Retrospective Cohort Study. Front Psychiatry. 2019 Jul 9;10.

14. Devane CL, Chiao E, Franklin M KE. Anxiety disorders in the 21st century: status, challenges, opportunities, and comorbidity with depression. Am J Manag Care. 2005;11(12):S344-S353.

15. Lundeen J, Fisher J, Kothari MJ. Frequency of Anxiety in Myasthenia Gravis. J Clin Neuromuscul Dis. 2004 Sep;6(1):9–12.

16. Qiu L, Feng H yu, Huang X, Mo R, Ou C yi, Luo C ming, et al. Study of incidence and correlation factors of depression, anxiety and insomnia in patients with myasthenia gravis. Zhonghua Yi Xue Za Zhi. 2010 Dec 7;90(45):3176–9.

17. Braz NFT, Rocha NP, Vieira ÉLM, Barbosa IG, Gomez RS, Kakehasi AM, et al. Muscle strength and psychiatric symptoms influence health-related quality of life in patients with myasthenia gravis. Journal of Clinical Neuroscience. 2018 Apr;50:41–4.

18. Stewart SB, Robertson KR, Johnson KM, Howard JF. The Prevalence of Depression in Myasthenia Gravis. 2007;

19. Aysal F, Karamustafalioğlu O, Özçelik B, Yilmaz M, Karamustafalioğlu N, Yumrukçal H, et al. The Relationship of Symptoms of Anxiety and Depression with Disease Severity and Treatment Modality in Myasthenia Gravis: A Cross-sectional Study. Noro Psikiyatr Ars. 2013 Dec;50(4):295–300.

20. Paul RH, Cohen RA, Goldstein JM, Gilchrist JM. Severity of Mood, Self-Evaluative, and Vegetative Symptoms of Depression in Myasthenia Gravis. J Neuropsychiatry Clin Neurosci. 2000 Nov;12(4):499–501.

21. Aherrera JM, Abrahan L, Racaza G, Train C, Jara R. APSC2015-1178 Depression and Anxiety in Adult Filipinos With Congenital Heart Disease Using the Validated Filipino Version of the Hospital Anxiety and Depression Score (HADS). Glob Heart. 2015 Jun;10(2):e8.

22. Güleç Uyaroğlu F, Bilgin Ş, Keleş EH, Zorlu Y. Anxiety And Depression Symptoms In Patients With Generalized Myasthenia Gravis. The Journal of Tepecik Education and Research Hospital. 2016;

23. Parada P, Oliva M, Lázaro E, Amayra I, López JF, Martínez O, et al. Anxiety , Depression and Self-Efficacy in Patients with Myasthenia Gravis. 2014;105–13.

24. McLean CP, Asnaani A, Litz BT, Hofmann SG. Gender differences in anxiety disorders: Prevalence, course of illness, comorbidity and burden of illness. J Psychiatr Res. 2011 Aug;45(8):1027–35.

25. Hantsoo L, Epperson CN. Anxiety Disorders Among Women: A Female Lifespan Approach. Focus (Madison). 2017 Apr;15(2):162–72.

26. Kincaid A. Myasthenia Gravis. In: xPharm: The Comprehensive Pharmacology Reference. Elsevier; 2007. p. 1–5.

27. Yamamoto A, Kimura T, Watanabe S, Yoshikawa H. Clinical characteristics of patients with myasthenia gravis accompanied by psychiatric disorders. Neurol Clin Neurosci. 2019 Mar;7(2):65–70.

28. Kulaksizoglu IB. Mood and Anxiety Disorders in Patients with Myasthenia Gravis Aetiology , Diagnosis and Treatment. 2007;21(6):473–81.

29. Suzuki Y, Utsugisawa K, Suzuki S, Nagane Y, Masuda M, Kabasawa C, et al. Factors associated with depressive state in patients with myasthenia gravis : a multicentre cross-sectional study. 2011;

30. West S, Kenedi C. Strategies to prevent the neuropsychiatric side-effects of corticosteroids. Curr Opin Organ Transplant. 2014 Apr;19(2):201–8.

31. Yamamoto A, Kimura T, Watanabe S, Yoshikawa H. Clinical characteristics of patients with myasthenia gravis accompanied by psychiatric disorders. Neurol Clin Neurosci [Internet]. 2019 Mar;7(2):65–70. Available from: http://doi.wiley.com/10.1111/ncn3.12267

32. AL-Bulushi A, Al Salmi I, Al Rahbi F, Farsi A Al, Hannawi S. The role of thymectomy in myasthenia gravis: A programmatic approach to thymectomy and perioperative management of myasthenia gravis. Asian J Surg. 2021 Jun;44(6):819–28.

33. Gavrilov Y V., Alekseeva TM, Kreis OA, Valko PO, Weber KP, Valko Y. Depression in myasthenia gravis: a heterogeneous and intriguing entity. J Neurol. 2020 Jun 5;267(6):1802–11.

34. Lourdes M, Guzman RE De. The Validation of the Hospital Anxiety and Depression Scale ( HADS-P ) among the1. Lourdes M, Guzman RE De. The Validation of the Hospital Anxiety and Depression Scale ( HADS-P ) among the

medically-ill Filipino patients in Philippine General Hospital A V. 2016;(January 2014).

35. Guerrero-Muñoz D, Salazar D, Constain V, Perez A, Pineda-Cañar CA, García-Perdomo HA. Association between Family Functionality and Depression: A Systematic Review and Meta-Analysis. Korean J Fam Med. 2021 Mar 20;42(2):172–80.

## ETHICAL CONSIDERATIONS

This research adhered with the Philippine National Ethical Guidelines for Health and Health-related Research (NEGHHRR) 2017. The protocol was approved by the Research Ethics Board of the institution where the study was conducted.

## AUTHORS CONTRIBUTIONS

KJA: conceptualization, investigation, methodology, project administration, resources, writing original draft, writing review and editing; MBP: data curation, formal analysis, supervision, writing review and editing; AIE: conceptualization, methodology, writing review and editing.