

# The Impact of the Coronavirus Disease-2019 Pandemic on the Psychological Status and Quality of Life of Myasthenia Gravis Patients

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## Abstract

**Objectives:** The coronavirus disease 2019 (COVID-19) is the largest pandemic of our times. We wanted to investigate the impact of COVID-19 pandemic on the psychological status, quality of life (QoL) and quality of sleep (QoS) of myasthenia gravis (MG) patients. **Methods:** Data on the epidemiological and clinical characteristics of MG were collected. We used a self-designed questionnaire (consisting of 12 questions), a revised 15-item Myasthenia Gravis Quality of Life Questionnaire (MGQOL15r), a 36-item health survey of the Medical Outcomes Study Short Form (SF36), Pittsburgh sleep quality index (PSQI), Hamilton scales for the assessment of anxiety (HAM-A), and depression (HAMD) were used. We reassessed patients who were tested three years ago using the same questionnaires. **Results:** The study included 64 MG patients. We noticed a statistically significant difference between the results obtained three years ago and the results from April 2020 in PSQI scores ( $P < 0.01$ ). MGQOL15r, SF36, and PSQI scores correlate with severe clinical manifestation, high scores on HAM-A and HAM-D ( $P < 0.01$ ). Higher scores on HAM-D and fear that MG symptoms will be worse if the patient gets an upper respiratory infection were independent predictors of the lower SF36 scores. Regarding MGQOL15r-independent predictors of the higher score were higher scores on HAM-D. **Conclusions:** There is a significant impact of the COVID-19 epidemic on the psychological status and especially on the quality of sleep of MG patients. Healthcare organizations need to provide professional therapeutic advice and psychosocial support for this population of patients during the pandemic.

**Keywords:** COVID-19, myasthenia gravis, quality of life, quality of sleep

## INTRODUCTION

The novel coronavirus disease (COVID-19) has spread worldwide, which caused widespread anxiety due to its rapid transmission and severe clinical symptoms.<sup>[1,2]</sup> Pandemics are severe stressors to vulnerable groups and this highly contagious disease exerts considerable impacts on mental health.<sup>[3,4]</sup> In the face of extreme life-threatening tension and fear, people tend to show some anxiety-related behaviors.<sup>[5]</sup> Since the COVID-19 outbreak, the Serbian government has taken several public health interventions, such as isolation, quarantine, and social distancing to control further transmission. Protective apparels and social isolation were used to reduce the risk of infection in pandemic outbreaks.<sup>[6,7]</sup> On the other hand, unethical media related false information's about COVID-19 is present worldwide, resulting in more emphasized stress related to the unknown illness of this pandemic.<sup>[8]</sup> In some previous cases, emotional distress was particularly neglected among those most severely affected by the pandemic, such as patients with chronic diseases. There is very little information regarding patients with chronic autoimmune diseases and the impact of the pandemic on their psychological status.

Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disease, which notably affects daily physical engagement, working ability, family functioning, sleeping, and overall Quality of Life (QoL).<sup>[9]</sup> Many MG patients have long-term immunosuppressive therapy (corticosteroids,

azathioprine, cyclosporine...) which may lead to an increased risk of infections.<sup>[10]</sup> Social isolation would bring great challenges to MG patients. It might be difficult for them to go back to the hospital to complete regular follow-up visits in time. Also, they would suffer from fear and uncertainty similar to the general population. Therefore, timely care to the MG patients during the COVID-19 outbreak is urgently required.

During 2017, we tested MG patients using questionnaires for QoL, Quality of Sleep (QoS), level of depression, and anxiety. We then wanted to evaluate the QoL and QoS in MG patients regarding the epidemiological and clinical factors of the disease.<sup>[11,12]</sup> In April 2020, we reassessed these patients to investigate the possible impact of the COVID-19 pandemic and the state of emergency and the police lockdown in Serbia on

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MG patients. We also wanted to compare these findings with our results obtained in 2017 on the same cohort of patients.

## METHODS

We performed a cross-sectional study via an online survey for a period of one month (April 2020), during Serbia's state of emergency during the COVID-19 pandemic. MG patients previously assessed during 2017 were invited to do the reassessment.

The study procedures were conducted with approval from the local clinical research ethics committee and all participants provided written informed consent. Procedures were conducted by the committee's guidelines and regulations, including the Basics of Good Clinical Practice, the Declaration of Helsinki, and the Law on Health Care of the Republic of Serbia.

Data on the epidemiological and clinical characteristics of the disease were collected (gender, current age, disease duration, place of residence, marital status, number of children, profession and employment status, addiction history) from the structured interview and previous medical documentation. The actual severity of the clinical manifestation was estimated using MG activities of daily life (MGADL).<sup>[13]</sup> Patients were then classified according to the type and severity of clinical complaints using the system proposed by the Myasthenia Gravis Foundation of America—MGFA classification, based on neurological findings from the last visit to our department before COVID-19 outbreak (all visits were maintained from January until March 2020).

We excluded patients on artificial ventilation that belong to group V, according to the MGFA classification system. Patients with other chronic diseases that could affect the QoL (diabetes, asthma, malignancy—with an exception of malignant thymoma, arterial hypertension, heart failure, renal, and hepatic insufficiency) were also excluded.

For the investigation of the psychological status, emotional response, MG-related problems during the COVID-19 pandemic, we used a self-designed questionnaire, consisting of 12 questions. In addition, we used a revised 15-item Myasthenia Gravis Quality of Life Questionnaire (MGQOL15r), a 36-item health survey of the Medical Outcomes Study Short Form (SF36), Pittsburgh sleep quality index (PSQI), Hamilton scales for the assessment of anxiety (HAM-A) and depression (HAM-D).

The MGQOL15r questionnaire consists of 15 questions, each ranging from 0 to 4.<sup>[14]</sup> The maximum score is 60 and it represents the biggest impact on the QoL in these patients. MGQOL15r was translated and cross-culturally adapted using the standard recognized methodology for use in the Serbian language.<sup>[11]</sup>

SF36 measures eight general health dimensions: physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF),

role-emotional (RE), and mental health (MH). A total score was also measured. The scores for each of the eight domains and the total score were converted to a 0-100 scale, with a higher score representing better health.

PSQI questionnaire consists of 19 self-rated questions. Components of the questionnaire measure self-perceived quality, duration, latency, common efficacy of sleep, and functionality during the day. These 19 questions are grouped into seven groups, each scored from 0-3. The obtained global PSQI score is from 0 to 21, where higher scores indicate lower QoS. A total score of more than 5 indicates poor QoS. It has been the most used QoS questionnaire so far, which was translated and standardized in the Serbian language.<sup>[15]</sup>

HAM-D measures the intensity of depression, and the values are interpreted as follows: 0-9 (without depression), 10-13 (mild depression), 14-17 (mild to moderate depression), and 18 or more (moderate to severe depression).<sup>[16]</sup> HAM-A measures the intensity of anxiety, where the ultimate values below 17 indicate the absence or mild anxiety, values between 18 and 24 mild to moderate anxiety, and values 25 and 30 moderate to severe anxiety.<sup>[17]</sup>

All data were statistically processed by IBM SPSS statistical software (version 21) for Windows Operative System. Numerical data are presented as medians and interquartile range (IQR) for nonparametric data and as mean  $\pm$  standard deviation (SD) for parametric data. The Mann-Whitney test was used to compare continuous variables between two groups, and the Kruskal-Wallis test was used to compare more than two groups. Correlations were assessed using Pearson's correlation coefficients or Spearman's correlation coefficients. Factors that significantly correlated with higher scores on used questionnaires were included in the multiple linear regression analysis (stepwise method). Stepwise criteria were as follows: the probability of F to enter variable was  $\leq 0.05$ , and the probability to remove variable  $\geq 0.10$ .

## RESULTS

The study included 64 adult MG patients ( $\geq 18$  years), whose socio-demographic characteristics are listed in Table 1.

In the self-designed part of the questionnaire, the first two questions were concerned with the patient's knowledge of infection routes and what the main source of information for MG patients was. Only 3.5% of patients did not have any knowledge about the infection routes, 40.0% reported that they know all about the infection routes, 31.6% were very familiar with and 24.9% were not very familiar with the knowledge of the ways for COVID-19 transmission. Television was the main source of information for MG patients (47.4%).

Then, we wanted to find out how much our patients were concerned about the COVID-19 pandemic and what the main cause of this state was. Regarding the information that they received from media, we found that 14.4% of patients were very concerned, 36.8% somewhat generally concerned,

40.4% not very concerned, and 8.8% were not concerned at all. Furthermore, regarding the concerns about the impact of the COVID-19 pandemic on their health or the health of their relatives and friends, 21.4% of patients were very concerned, 31.6% somewhat generally concerned, 38.6% not very concerned, and 8.8% were not concerned at all. We further investigated the reasons why they were scared of the COVID-19 outbreak. The main reason for concern was that some patient's relatives or friends could be infected with COVID-19 (82.5%), that someone they know could die due to the infection (29.8%), and the lack of specific treatment options (15.8%). Other causes were noted in less than 10% of our patients (for instance, high mortality rates in the world, high contagiousness and changes in the lifestyle after the pandemic, changes in incomes after the pandemic, etc.). Daily activities of 13.4% of patients were very influenced by the pandemic and the police lockdown and the state of emergency, whereas 45.7% were influenced to some extent, and 40.9% of the patients did not experience any changes in their daily activities.

Regarding the status of MG, during the COVID-19 outbreak, 1.8% of patients thought they had an improvement, 71.8% of patients reported feeling no change, 21.1% of patients reported their condition got worse, and 5.3% had new symptoms never experienced before. The main concern about the MG status was that their disease would be worse if they got an upper respiratory infection (34.7%), that they would experience some difficulties in drug availability (65.6%), that they could not go to the hospital as usual (56.1%). All other causes were noted in less than 15%. Nearly 65% of patients would try to get in contact with their medical doctors if their diseases got worse, 19.3% would try to get in contact with a nearby hospital or a physician by phone, 10.5% would try to find information on the internet, and 5.3% of patients would make some changes in drugs self-initiative. Patients who would not go to the hospital and try to find their doctor stated the fear of getting infected as the main reason (80.5%). Assuming that their medications at home were running out, 77.2% patients reported they would go to a nearby pharmacy to buy drugs according to the former therapeutic plan 8.8%, patients would reduce the drug dosage to keep taking drugs every day, and 14% of patients would take drugs as usual and then stop immediately.

The results obtained by other questionnaires and the clinical characteristics of MG patients are presented in Table 2. We noticed a statistically significant difference between the results obtained three years ago and the results from April 2020 only in PSQI scores, which indicates worse QoS in MG patients during the COVID-19 pandemic than in regular circumstances ( $P < 0.01$ ). PSQI score was worse in 56.1% of patients than it was in 2017, the same in 22.8% of patients, and better in 22.1% of patients. In addition, we asked patients in a self-designed questionnaire how they were sleeping compared to the time before the pandemic outbreak, and 63.1% of patients answered that they were sleeping worse. Nevertheless, the scores on MGQOL15r, SF36 (including

**Table 1: Demographic features of the patients with myasthenia gravis (n=64)**

Variables	Value
Female gender (%)	61.4
Current age (years) (Mean±SD*)	54.1±16.4
Disease duration (years) (Mean±SD)	7.1±4.9
Occupation (%)	
Physical work	21.1
Intellectual work	17.5
Unemployed	25.8
Retired	35.6
First symptoms <50 years (%)	54.4
Partner status- married or cohabitant (%)	78.9
Smokers (%)	61.4
Alcohol (%)	8.8
Number of children (%)	
Zero	24.6
One	43.9
Two or more	31.6
Area of living	
Town >100.000 inhabitants	47.7
Town <100.000 inhabitants	38.6
Village	14.0
Current oral medication used (%)	
Pyridostigmine	79.6
Oral corticosteroids	62.7
Azathioprine	22.5
Cyclosporine A	2.1
None	11.3

\* standard deviation

**Table 2: Clinical features of the patients with myasthenia gravis and scores on obtained tests (n=64)**

Variables	Results from 2017	Results from april 2020
MGFA <sup>†</sup> classification (%)		
I	21.1	24.8
II (IIa+IIb)	29.8	35.8
III (IIIa+IIIb)	31.6	26.6
IV (IVa+IVb)	17.5	12.8
MGADL <sup>‡</sup> (Mean±standard deviation)	5.1±3.6	4.5±3.6
MGQOL15r § (Mean±standard deviation)	23.2±12.0	25.1±11.4
SF36 <sup>  </sup> (Mean±standard deviation)	56.9±24.1	53.2±24.0
PSQI <sup>¶</sup> (Mean±standard deviation)**	11.4±3.5	12.9±3.2
HAM-D <sup>**</sup> (Mean±standard deviation)	10.2±6.2	11.4±5.6
HAM-A <sup>**</sup> (Mean±standard deviation)	9.4±7.3	10.6±6.7

$P < 0.05^*$ ,  $P < 0.01^{**}$ ; <sup>†</sup>Myasthenia Gravis Foundation of America;

<sup>‡</sup>Myasthenia gravis activities of daily living; <sup>§</sup>Questionnaire of Life

Quality Specific for Myasthenia Gravis - 15 items revised version;

<sup>||</sup>36-item health survey of the Medical Outcomes Study Short Form;

<sup>¶</sup>Pittsburgh sleep quality index ; <sup>\*\*</sup>Hamilton depression scale; <sup>\*\*</sup>Hamilton anxiety scale

all the sub-scores with an exception of the sub-score for bodily pain which was slightly better), HAM-A and HAM-D were worse than three years ago but without any statistically significant difference.

Statistically significant correlations between the scores on PSQI, SF36, and MGQOL15r and other variables are presented in Table 3. Other epidemiological or clinical factors did not significantly correlate with the scores from the obtained questionnaires. Patients who experience fear that their disease would get worse if they got a respiratory infection had higher scores on SF36 ( $P < 0.05$ ). Patients who were more concerned about the impact of the COVID-19 pandemic on their health or the health of their relatives, and who feared that they would be infected with COVID-19 which would negatively affect their MG status had higher scores on MGQOL15r ( $P < 0.05$ ). Multiple linear regression analysis showed that higher scores on HAM-D (beta = -0.79,  $P < 0.01$ ) and the fear that the disease would be worse if the patient got an upper respiratory infection (beta = 0.21;  $P < 0.05$ ) were independent predictors of the lower SF36 scores (adjusted  $R^2 = 0.52$ ,  $P < 0.01$  for the overall model). Regarding MGQOL15r scores, independent predictors of the higher scores were higher scores on HAM-D (beta = 0.63,  $P < 0.01$ ) and higher MGADL scores (beta 0.47,  $P < 0.05$ ); (adjusted  $R^2 = 0.74$ ,  $P < 0.01$  for overall model).

## DISCUSSION

MG patients were very well informed about COVID-19 infection routes, and they mainly used television for information about the pandemic. We found that adult MG patients had different degrees of fear of this novel contagious disease. More than 50% of our patients were concerned regarding the information from media and the impact of COVID-19 on their health or the health of their relatives. The main reason for fear was that some patient's relatives or friends could be infected with COVID-19 and that someone they know could die due to the infection. The main concern about MG status was that their disease would be worse if they got an upper respiratory infection, that they would experience some difficulties in drug availability and that they could not go to the hospital as usual. The majority of patients (if they get worse) would try to get to their physician, and patients who would not go to the hospital and try to find their doctor,

stated the fear of getting infected as the main reason. Previous studies have found that public health emergencies have a significant impact on QoL and the psychological status of the population.<sup>[18,19]</sup> In a nationwide survey of psychological distress in Chinese people during the COVID-19 outbreak, it was found that 35% of the general population experienced psychological distress.<sup>[20]</sup> Also, another study of the influence of the COVID-19 pandemic showed significantly higher levels of depression and alcohol use the Hubei province residents (the epicenter of the COVID-19 epidemic) than in other provinces in China.<sup>[21]</sup> Groups affected psychologically the most by the COVID-19 pandemic are women, individuals with previous psychiatric illnesses, individuals living in urban areas and those with an accompanying chronic disease.<sup>[22]</sup> Because MG patients are suffering from a chronic autoimmune disease, it is expected from them to have more issues with the outbreak of COVID-19 than the general population. Unfortunately, there is no data about the influence of the pandemic on MG patients' psychological status in the literature available.

We assessed QoL and QoS of MG patients using MGQOL15r, SF36 and PSQI. In our study, only the PSQI score was significantly higher during the pandemic than it had been three years ago. Nevertheless, all other scores obtained from questionnaires were worse but without any clinical significance, despite that the disease severity was slightly better than (MGADL score  $5.1 \pm 3.6$  vs.  $4.5 \pm 3.6$ ). Previous studies reported diminished QoL in MG patients compared to the healthy control groups.<sup>[23]</sup> Studies conducted in two large population MG cohorts found the same QoL levels across time (despite more MG treatment options becoming available over the time).<sup>[24,25]</sup> These mild changes in scores obtained on QoL questionnaires could be related to the relatively mild course of the COVID-19 pandemic in Serbia compared to other countries. Prolonged monitoring of MG patients after the COVID-19 pandemic is necessary for a better understanding of the influence of the COVID-19 pandemic on MG patients QoL and the overall psychological status.

Our previous findings from the same cohort showed that patients with severe clinical manifestations as well as those with anxiety and depression have poorer QoL.<sup>[11]</sup> We confirmed these results during the COVID-19 pandemic, but now we did not find a correlation between poor QoL and the disease duration or the employment status. Previous studies have shown a link between the severity of the disease and the impact on the QoL of those affected, especially on the physical aspects.<sup>[26]</sup> Basta *et al.* showed a correlation between the estimated anxiety and depression with the QoL.<sup>[27]</sup> The relationship between depression and sleep disorders with poor QoL was also recorded in a study conducted by Happe *et al.* which is similar to our results.<sup>[28]</sup> Depression and anxiety symptoms usually develop as comorbidity during MG disease.<sup>[29]</sup> Mental health must be a clinical focus during the treatment of somatic symptoms during MG, especially during the pandemic. The results related to the influence of other socio-demographic and clinical factors on QoL of MG patients

**Table 3: Clinical and epidemiological variables which correlate with the obtained scores from questionnaires (n=64)**

	MGQOL15r <sup>§</sup>	SF36 <sup>  </sup>	PSQI <sup>¶</sup>
MGFA <sup>†</sup>	0.35*	-0.11	0.27*
MGADL <sup>‡</sup>	0.60**	-0.26*	0.48**
HAM-D <sup>**</sup>	0.70**	-0.72**	0.69**
HAM-A <sup>**</sup>	0.84**	-0.88**	0.71**
PSQI <sup>¶</sup>	0.60**	-0.27*	/

\*  $P < 0.05$ ; \*\*  $P < 0.01$ ; <sup>†</sup>Myasthenia Gravis Foundation of America;

<sup>‡</sup>Myasthenia gravis activities of daily living; <sup>§</sup>Questionnaire of Life Quality Specific for Myasthenia Gravis - 15 items revised version;

<sup>||</sup>36-item health survey of the Medical Outcomes Study Short Form;

<sup>¶</sup>Pittsburgh sleep quality index ; <sup>\*\*</sup>Hamilton depression scale; <sup>\*\*</sup>Hamilton anxiety scale

are ambiguous.<sup>[25,30]</sup> In this study, we did not find any significant role of the gender, age, place of residence, marital status, the number of children, the professional and employment status, and the addiction history on QoL of MG patients.

Although the current study presents many innovative findings, the results should be evaluated in the context of several limitations. First of all, we had a relatively small sample. Longer longitudinal follow-up is needed to examine the sub-acute and long-term psychological complications, such as posttraumatic stress disorder on MG patients.

The COVID-19 epidemic has a significant impact on psychological status and especially on QoS in MG patients. Our findings raise the awareness that professional advice for those people with chronic autoimmune diseases who require long-term immunosuppressive therapy is needed as soon as the serious public health emergencies occur, so it is important to provide professional therapeutic advice and psychosocial support for this population of MG patients during the pandemic. Support has a positive effect on the level of psychological stress that a person suffers. In this regard, help could alleviate the stress caused by the pandemic. It would help these patients maintain the control of their disease better and it would assist them in managing emotional distress and improving the QoL.

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### Conflicts of interest

There are no conflicts of interest.

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