



# Evaluation of Depression and Anxiety of Patients with Multiple Sclerosis During the COVID-19 Pandemic: A Comparison with the General Population

## COVID-19 Döneminde Multipl Sklerozlu Hastaların Anksiyete ve Depresyon Düzeylerinin Değerlendirilmesi: Genel Popülasyon ile Karşılaştırılması

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### Abstract

**Objective:** The coronavirus disease-2019 (COVID-19) pandemic can increase anxiety and depression in patients with multiple sclerosis (PwMS). This study aimed to evaluate the predictors of anxiety and depression in PwMS during the COVID-19 pandemic and compare it with the general population (GP).

**Materials and Methods:** The study was conducted in an MS clinic in Istanbul University Istanbul Faculty of Medicine. Data were collected online using a form including sociodemographics and questions on COVID-19-related knowledge and the hospital anxiety and depression scale.

**Results:** This study included 800 participants (GP: 421, MS: 379). Anxiety (42.3% vs. 32.2%,  $p=0.002$ ) and depression (53.9% vs. 39.6%,  $p<0.001$ ) were more common. COVID-19-related knowledge was lower ( $9.1\pm 1.5$  vs.  $9.9\pm 1.2$ ,  $p<0.001$ ), and rate of COVID-19 infection was higher (15.4% vs. 6.9%,  $p<0.001$ ) in the GP than PwMS. Among other factors, COVID-19-related knowledge was a common predictor of anxiety and depression in both GP and MS groups [odds ratio (OR): 0.8, 95% confidence interval (CI) 0.7-0.9,  $p=0.007$  and OR: 0.7, 95% CI 0.7-0.9,  $p=0.020$ , for anxiety; OR: 0.7, 95% CI 0.7-0.9,  $p=0.001$  and OR: 0.8, 95% CI 0.7-1.0,  $p=0.023$  for depression, respectively].

**Conclusion:** This study revealed that PwMS have less anxiety and depression than the GP. Our study shows the importance of COVID-19-related knowledge and the need for psychological support during the pandemic.

**Keywords:** Multiple sclerosis, COVID-19, anxiety, depression, COVID-19-related knowledge

### Öz

**Amaç:** Koronavirüs hastalığı-2019 (COVID-19) pandemisi multipl skleroz (MS) hastalarında anksiyete ve depresyonu artırabilir. Bu çalışmanın amacı COVID-19 pandemisi sürecinde MS hastalarında anksiyete ve depresyonu değerlendirmek, yordayıcılarını belirlemek ve genel popülasyon (GP) ile karşılaştırmaktır.

**Gereç ve Yöntem:** Çalışma İstanbul Üniversitesi İstanbul Tıp Fakültesi MS kliniğinde yürütüldü. Veriler, sosyodemografik özellikleri, COVID-19 bilgi düzeyini ve hastane anksiyete ve depresyon ölçeğine ilişkin soruları içeren bir form ile online olarak toplandı.

**Bulgular:** Çalışmaya 800 katılımcı (GP: 421, MS: 379) dahil edildi. Anksiyete (GP: %42,3 vs. MS: %32,2,  $p=0,002$ ) ve depresyon (GP: %53,9 vs. MS: %39,6,  $p<0,001$ ) MS hastalarında genel popülasyona kıyasla daha düşük bulundu. COVID-19 bilgisi ise daha yüksekti (GP:  $9,1\pm 1,5$ 'e vs. MS:  $9,9\pm 1,2$ ,  $p<0,001$ ). COVID-19 enfeksiyonu geçirme oranı daha düşüktü (GP: %15,4'e vs. %6,9,  $p<0,001$ ). Diğer faktörlerin yanı sıra, COVID-19 hakkında bilgi düzeyi hem GP hem de MS gruplarında anksiyete ve depresyonun ortak bir yordayıcısıdır [anksiyete için odds oranı (OR): 0,8, %95 güven aralığı (GA): 0,7-0,9,  $p=0,007$  ve OR: 0,7, %95 GA: 0,7-0,9,  $p=0,020$ , depresyon için; OR: 0,7, %95 GA: 0,7-0,9,  $p=0,001$  ve OR: 0,8, %95 GA: 0,7-1,0,  $p=0,023$ ].

**Sonuç:** Çalışmamız MS hastalarının GP'ye göre daha az anksiyete ve depresyona sahip olduğunu ortaya koydu. Bu çalışma pandemi sürecinde COVID-19'a ilişkin bilgi düzeyinin önemini ve psikolojik destek ihtiyacının gerekliliğini göstermektedir.

**Anahtar Kelimeler:** Multipl skleroz, COVID-19, anksiyete, depresyon, COVID-19 bilgi düzeyi

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## Introduction

Coronavirus disease-2019 (COVID-19) affected and killed millions of people in a short time after its emergence in China and the World Health Organization declaration as a pandemic (1). Turkey is among the most affected countries by COVID-19, with 6,987,494 cases and 62,745 deaths as of September 2021 (2). In our society, where the epidemic had got out of control, public health practices, such as individual measures, quarantine, lockdown, and remote work, became inevitable. The epidemic threatened society in terms of personal health, loss of close relatives, social and occupational life interruption, and economic burden. This threat had negative psychological impacts (fear, stress, insomnia, anxiety, and depression). These psychological impacts have been reported higher among populations with chronic diseases and high-risk groups (3).

Like other individuals with a chronic disease, patients with multiple sclerosis (PwMS) are known to be at risk for anxiety and depression (4). Additionally, the unknown course of immunosuppressed patients with COVID-19, isolation from daily life, and lack of social support due to the lockdown worsened the anxiety and depression of patients (4,5). The COVID-19 pandemic has become a severe stressor in PwMS due to insufficient information at the initial and misinformation in the later stages. Increasing the awareness and elimination of the misinformation may decrease the risks of patients' anxiety and depression.

This study aimed to assess the predictors of anxiety and depression during the COVID-19 pandemic and the effect of COVID-19 awareness on the psychological state of patients compared to the general population (GP).

## Material and Methods

### Research Design, Sample, and Setting

This case-control study was performed in PwMS who were followed up in the outpatient MS clinic at the Istanbul University, Istanbul Faculty of Medicine. Our study included 379 patients who are older than 18 years without a relapse in the last month. The control group consisted of 421 healthy individuals.

### Data Collection

The data were collected using an online survey (Google forms) between October 2020 and February 2021. Participants were asked to complete the questionnaire, which took approximately 15 min, via e-mail or other communication applications. A snowball sampling strategy was used to access the healthy controls.

### Data Collection Tools

An online questionnaire and hospital anxiety and depression scale (HADS) were employed. The questionnaire included sociodemographic and clinical characteristics (duration of diagnosis, drugs used, etc.), questions regarding COVID-19 infection status, and lifestyle changes (medication use, occupation, daily physical activities, sleep, nutrition, etc.). Participants were also assessed for COVID-19-related knowledge (transmission route, protection, etc.). This part of the questionnaire was prepared in line with the COVID-19 Guidelines of the Ministry of Health. Each correct answer was evaluated as one point, and each incorrect or blank answer was evaluated as zero. The total score of the test was calculated by summing the item scores.

The HADS was developed by Zigmond and Snaith (6) and adapted to Turkish by Aydemir et al. (7) This is a 14-item self-assessment four-points Likert scale that evaluates anxiety and depression. The scores range between 0 and 21. The cut-off score is 10 for anxiety and 7 for depression in the Turkish population.

### Ethical Aspect of the Study

The ethical principle compliance was evaluated by the ethics committee of the institution where the study was conducted, and the Ethics Committee approval was obtained (Istanbul University, Istanbul Faculty of Medicine, Department of Neurology, Istanbul, Turkey, file number: 2020/1095, no: 29624016-050.99- 1215). Consent to participate was obtained using online forms.

### Statistical Analysis

The Statistical Package for the Social Sciences (v 21.0, IBM) software was used for statistical data analysis. Data were analyzed for normality distribution using the Kolmogorov-Smirnov test and expressed as mean ( $\pm$  standard deviation) for continuous variables or frequencies (n, %) for categorical variables. Independent samples t-test and One-Way analysis of variance test were used to compare continuous variables between the groups and chi-square test to compare the categorical variables. The Pearson correlation analysis was used to correlate continuous variables and multivariate logistic regression analysis to determine the associated factors with anxiety and depression. The analysis of covariance (ANCOVA) was used to adjust for group differences based on covariates.

## Results

A total of 800 individuals (MS: 379, controls: 421) participated in the study. The mean age of patients was  $35.8 \pm 9.9$  [minimum-maximum (min-max): 18-67] years, 67.5% (n=256) were female, 50.9% (n=193) were married, and 70.4% (n=267) had a university degree. The mean age of the controls was  $28.6 \pm 8.5$  (min-max: 16-65) years, 37.8% (n=159) were female, 40.4% (n=170) were married, and 62% (n=261) had a university degree (Table 1).

The mean disease duration was  $8.2 \pm 6.6$  (min-max: 1-34) years. During the COVID-19 pandemic, 21.4% (n=81) of the patients reported an attack, 47.5% (n=180) were admitted to the hospital due to MS, 13.7% (n=52) reported worsening in motor function, and 4.7% (n=18) reported starting antidepressants. Interestingly, 13.7% (n=52) of the patients thought to discontinue their disease-modifying therapies (DMT) and 12.9% (n=49) discontinued their DMT due to fear of getting COVID-19.

More individuals reported changes in their working conditions in the MS group compared to the GP (46.6% vs. 24.9%,  $p < 0.001$ ). The rate of starting smoking during the pandemic was higher in the controls compared to patients (5.9% vs. 2.9%,  $p = 0.039$ ). The number of COVID-19 infected individuals in the GP was higher than in the PwMS (15.4% vs. 6.9%,  $p = 0.039$ ). The rate of COVID-19 deaths among relatives was higher in the GP than in PwMS (24.7% vs. 11.9%,  $p < 0.001$ ). In both groups, during the COVID-19 pandemic, at least half of the individuals reported changes in their sleeping and eating habits, physical activity, and body weight. The most affected habit was physical activity in both groups. Furthermore, compared to PwMS, insomnia ( $p < 0.001$ ), eating habits ( $p < 0.001$ ), weight gain ( $p < 0.001$ ), and decreased physical activity ( $p = 0.015$ ) were more frequent in the GP (Table 2).

| Table 1. Sociodemographic characteristics of participants (n=800) |                |         |                |         |          |         |
|---|----------------|---------|----------------|---------|----------|---------|
| Characteristics   | Control        |         | PwMS           |         | $\chi^2$ | p       |
|   | n              | %       | n              | %       |          |         |
| <b>Age</b><br>(Mean $\pm$ SD), (min-max)                          | 28.6 $\pm$ 8.5 | (16-65) | 35.8 $\pm$ 9.9 | (18-67) | 11.1     | <0.001* |
| <b>Gender</b>   |                |         |                |         |          |         |
| Female  | 159            | 37.8    | 256            | 67.5    | 70.8     | <0.001  |
| Male  | 262            | 62.2    | 123            | 32.5    |          |         |
| <b>Education</b>  |                |         |                |         |          |         |
| Primary/secondary education                                       | 32             | 7.6     | 32             | 8.4     | 9.0      | 0.011   |
| High school   | 128            | 30.4    | 80             | 21.1    |          |         |
| University  | 261            | 62.0    | 267            | 70.4    |          |         |
| <b>Income</b>   |                |         |                |         |          |         |
| Less than expenses  | 143            | 34.0    | 86             | 23.1    | 29.4     | <0.001  |
| Equal to expenses   | 218            | 51.8    | 262            | 70.6    |          |         |
| More than expenses  | 60             | 14.3    | 31             | 8.4     |          |         |
| <b>Marital status</b>   |                |         |                |         |          |         |
| Married   | 170            | 40.4    | 193            | 50.9    | 41.8     | <0.001  |
| Single  | 246            | 58.4    | 153            | 40.4    |          |         |
| Divorced/widow  | 5              | 1.2     | 33             | 8.8     |          |         |
| <b>Children</b>   |                |         |                |         |          |         |
| Yes   | 130            | 30.9    | 167            | 44.1    | 14.8     | <0.001  |
| No  | 291            | 69.1    | 212            | 55.9    |          |         |
| <b>Smoking</b>  |                |         |                |         |          |         |
| Yes   | 154            | 36.6    | 100            | 26.5    | 9.4      | 0.002   |
| No  | 267            | 63.4    | 279            | 73.5    |          |         |
| <b>Antidepressant use</b>   |                |         |                |         |          |         |
| Yes   | 15             | 3.6     | 84             | 22.2    | 63.6     | <0.001  |
| No  | 406            | 96.4    | 295            | 77.8    |          |         |

\*Independent samples t-test, SD: Standard deviation, PwMS: Patients with multiple sclerosis, min: Minimum, max: Maximum

The mean score of COVID-19-related knowledge was higher in patients than in the GP (9.9 $\pm$ 1.2 vs. 9.1 $\pm$ 1.5,  $p$ <0.001). Patients had better knowledge, especially on questions regarding transmission routes, whereas their knowledge on protective measures was comparable (Table 3).

Interestingly, the rate of anxiety and depression, when some confounders (age, gender, education, marital status, antidepressant use, COVID-19-related knowledge, and COVID-19 infection status) were adjusted using the ANCOVA, were higher in the GP compared to the patients (42.3% vs. 32.2% for anxiety,  $p$ =0.002; 53.9% vs. 39.6% for depression,  $p$ <0.001) (Figure 1). In line with this observation, anxiety, and depression scores were higher in the controls than PwMS (8.5 $\pm$ 4.5 vs. 7.7 $\pm$ 4.5 for anxiety,  $p$ =0.005; 7.7 $\pm$ 4.0 vs. 6.4 $\pm$ 3.9 for depression,  $p$ <0.001). Additionally, when correlations among anxiety, depression, and COVID-19-related knowledge were assessed, a significant positive correlation was found between the anxiety and depression scores ( $r$ =0.63,  $p$ <0.001) and weak negative correlations between anxiety, depression, and knowledge scores (Figure 2). The anxiety and depression scores of participants are shown in Table 4.

The relationship between the patients' clinical features, anxiety, and depression scores revealed no significant correlations between

the disease duration, anxiety ( $r$ =0.81,  $p$ =0.099), and depression ( $r$ =0.01;  $p$ =0.781). As expected, the anxiety scores of individuals who started using antidepressants during the pandemic period were higher than those who did not use antidepressants (10.2 $\pm$ 5.5 vs. 7.5 $\pm$ 4.4,  $p$ =0.013). No significant difference was found in anxiety and depression scores between the patients according to hospital admission status due to worsening MS (7.4 $\pm$ 4.5 vs. 7.9 $\pm$ 4.5,  $p$ =0.271 and 6.6 $\pm$ 3.9 vs. 6.3 $\pm$ 3.9,  $p$ =0.377, respectively). Anxiety and depression scores of patients with relapse were higher than those on remission (9.1 $\pm$ 4.6 vs. 7.3 $\pm$ 4.4,  $p$ =0.028 and 8.1 $\pm$ 3.9 vs. 6.0 $\pm$ 3.8,  $p$ <0.001, respectively). The anxiety and depression scores did not differ according to the state of planning to discontinue the DMT (8.7 $\pm$ 4.2 vs. 7.5 $\pm$ 4.5,  $p$ =0.065 and 6.4 $\pm$ 3.3 vs. 6.5 $\pm$ 4.0,  $p$ =0.855, respectively).

A multivariate logistic regression analysis was performed to determine the predictive factors of anxiety and depression. The model included age, gender, education, marital status, child status, antidepressant use, COVID-19 infection status, loss of relative due to COVID-19, and COVID-19-related knowledge as covariates. The predictors of anxiety include gender (being female) [odds ratio (OR): 1.7, 95% confidence interval (CI): 1.1-2.7,  $p$ =0.015] and knowledge about COVID-19 in the GP (OR: 0.8, 95% CI: 0.7-0.9,

Table 2. Lifestyle changes due to the COVID-19 pandemic

| Characteristics                                 | Control |      | PwMS |      | $\chi^2$ | p       |
|---|---------|------|------|------|----------|---------|
|   | n       | %    | n    | %    |          |         |
| <b>COVID-19 diagnosis</b>                       |         |      |      |      |          |         |
| Yes   | 65      | 15.4 | 26   | 6.9  | 14.5     | <0.001* |
| No  | 356     | 84.6 | 353  | 93.1 |          |         |
| <b>Place of COVID-19 treatment</b>              |         |      |      |      |          |         |
| Home  | 46      | 10.9 | 25   | 6.6  | 20.2     | <0.001* |
| Hospitalized                                    | 19      | 4.5  | 1    | 0.3  |          |         |
| <b>Death of close relatives due to COVID-19</b> |         |      |      |      |          |         |
| Yes   | 104     | 24.7 | 45   | 11.9 | 21.6     | <0.001* |
| No  | 317     | 75.3 | 334  | 88.1 |          |         |
| <b>Concern about COVID-19</b>                   |         |      |      |      |          |         |
| None  | 71      | 16.9 | 35   | 9.2  | 83.7     | <0.001* |
| Mild  | 99      | 23.5 | 82   | 21.6 |          |         |
| Moderate  | 199     | 47.3 | 112  | 29.6 |          |         |
| High  | 52      | 12.4 | 150  | 39.6 |          |         |
| <b>Following the COVID-19 chart</b>             |         |      |      |      |          |         |
| Never   | 30      | 7.1  | 15   | 4.0  | 17.7     | <0.001* |
| Sometimes                                       | 191     | 45.4 | 129  | 34.0 |          |         |
| Always  | 200     | 47.5 | 235  | 62.0 |          |         |
| <b>Change in working conditions</b>             |         |      |      |      |          |         |
| Yes   | 69      | 24.9 | 173  | 46.6 | 31.9     | <0.001* |
| No  | 208     | 75.1 | 198  | 53.4 |          |         |
| <b>Start smoking</b>                            |         |      |      |      |          |         |
| Yes   | 25      | 5.9  | 11   | 2.9  | 4.3      | 0.039   |
| No  | 396     | 94.1 | 368  | 97.1 |          |         |
| <b>Change in sleep</b>                          |         |      |      |      |          |         |
| None  | 124     | 29.5 | 183  | 48.3 | 39.7     | <0.001* |
| Medium disruption                               | 204     | 48.5 | 160  | 42.2 |          |         |
| High disruption                                 | 93      | 22.1 | 36   | 9.5  |          |         |
| <b>Change in eating habits</b>                  |         |      |      |      |          |         |
| None  | 158     | 37.5 | 203  | 53.6 | 21.8     | <0.001* |
| Medium disruption                               | 185     | 43.9 | 132  | 34.8 |          |         |
| High disruption                                 | 78      | 18.5 | 44   | 11.6 |          |         |
| <b>Change in body weight</b>                    |         |      |      |      |          |         |
| Decreased                                       | 59      | 14.0 | 83   | 21.9 | 19.1     | <0.001* |
| Not changed                                     | 164     | 39.0 | 172  | 45.4 |          |         |
| Increased                                       | 198     | 47.0 | 124  | 32.7 |          |         |
| <b>Change in physical activity</b>              |         |      |      |      |          |         |
| Decreased                                       | 284     | 67.5 | 231  | 60.9 | 8.4      | 0.015   |
| Not changed                                     | 113     | 26.8 | 106  | 28.0 |          |         |
| Increased                                       | 24      | 5.7  | 42   | 11.1 |          |         |

\*The significance was evaluated as  $p < 0.003$  with the Bonferroni correction. COVID-19: Coronavirus disease-2019, PwMS: Patients with multiple sclerosis

$p = 0.007$ ), and they were age (OR: 0.9 95% CI: 0.9-1.0,  $p = 0.010$ ), education (OR: 0.3, 95% CI: 0.1-0.9,  $p = 0.025$ ), antidepressant use (OR: 2.2, 95% CI: 1.3-3.8,  $p = 0.004$ ), and COVID-19-related knowledge (OR: 0.7, 95% CI: 0.7-0.9,  $p = 0.020$ ) in PwMS (Table 5).

The predictors of depression include loss of relatives due to COVID-19 (OR: 1.8, 95% CI 0.9-1.0,  $p = 0.010$ ) and COVID-19-

related knowledge (OR: 1.7, 95% CI 0.7-0.9,  $p = 0.001$ ) in the GP, whereas education (higher education) (OR: 0.3, 95% CI: 0.1-0.7,  $p = 0.005$ ), marital status (being divorced or widowed) (OR: 2.7, 95% CI: 1.1-7.1,  $p = 0.033$ ), antidepressant use (OR: 2.8, 95% CI: 1.7-4.8,  $p < 0.001$ ), and knowledge on COVID-19 (OR: 0.8, 95% CI 0.7-1.0,  $p = 0.023$ ) (Table 6) in the PwMS.

| Table 3. COVID-19-related knowledge of patients with MS and the general population   |                 |        |                 |        |          |          |
|--|-----------------|--------|-----------------|--------|----------|----------|
| Characteristics  | Control         |        | PwMS            |        | $\chi^2$ | P        |
|  | n               | %      | n               | %      |          |          |
| <b>COVID-19 is transmitted by the coughing or sneezing of the infected person</b>  |                 |        |                 |        |          |          |
| *Yes   | 335             | 79.6   | 319             | 84.2   | 2.8      | 0.093    |
| No   | 86              | 20.4   | 60              | 15.8   |          |          |
| <b>COVID-19 is transmitted through contact with the mouth, nose, and eyes</b>  |                 |        |                 |        |          |          |
| *Yes   | 266             | 63.2   | 365             | 96.3   | 131.3    | <0.001   |
| No   | 155             | 36.8   | 14              | 3.7    |          |          |
| <b>COVID-19 is transmitted by the contact of the hands with the mouth, nose, and eyes after touching the surface where the droplets adhere</b> |                 |        |                 |        |          |          |
| *Yes   | 373             | 88.6   | 352             | 92.9   | 4.3      | 0.038    |
| No   | 48              | 11.4   | 27              | 7.1    |          |          |
| <b>The mask is necessary to protect against COVID-19</b>   |                 |        |                 |        |          |          |
| *Yes   | 419             | 99.5   | 376             | 99.2   | 0.3      | 0.906    |
| No   | 2               | 0.5    | 3               | 0.8    |          |          |
| <b>Hand washing is necessary to protect against COVID-19</b>   |                 |        |                 |        |          |          |
| *Yes   | 396             | 94.1   | 361             | 95.3   | 0.5      | 0.457    |
| No   | 25              | 5.9    | 18              | 4.7    |          |          |
| <b>Social distancing is required to protect from COVID-19</b>  |                 |        |                 |        |          |          |
| *Yes   | 421             | 100    | 379             | 10     | -        | 1.00     |
| No   | -               | -      | -               | -      |          |          |
| <b>COVID-19 is transmitted from domestic animals</b>   |                 |        |                 |        |          |          |
| Yes  | 142             | 33.7   | 90              | 23.7   | 9.6      | 0.002    |
| *No  | 279             | 63.3   | 289             | 76.3   |          |          |
| <b>Washing the nose with salty water prevents COVID-19</b>   |                 |        |                 |        |          |          |
| Yes  | 84              | 20.0   | 82              | 21.7   | 0.4      | 0.545    |
| *No  | 337             | 80.0   | 297             | 78.3   |          |          |
| <b>Using alcohol prevents COVID-19</b>   |                 |        |                 |        |          |          |
| Yes  | 67              | 15.9   | 21              | 5.5    | 21.9     | <0.001   |
| *No  | 354             | 84.1   | 358             | 94.5   |          |          |
| <b>COVID-19 is transmitted by mosquitoes</b>   |                 |        |                 |        |          |          |
| Yes  | 124             | 29.5   | 59              | 15.6   | 21.8     | <0.001   |
| *No  | 297             | 70.5   | 320             | 84.4   |          |          |
| <b>The flu vaccine protects from COVID-19</b>  |                 |        |                 |        |          |          |
| Yes  | 68              | 16.2   | 62              | 16.4   | 0.006    | 0.937    |
| *No  | 353             | 83.8   | 317             | 83.6   |          |          |
| <b>No. of correct answers mean <math>\pm</math> SD (min-max)</b>   |                 |        |                 |        |          |          |
|  | 9.10 $\pm$ 1.50 | (4-11) | 9.85 $\pm$ 1.21 | (4-11) | 7.813    | <0.001** |

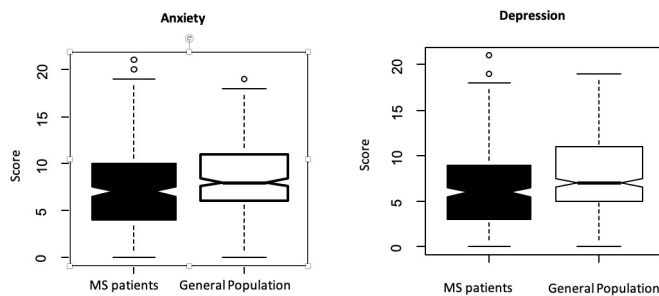
\*Correct answer option, \*\*Independent samples t-test, COVID-19: Coronavirus disease-2019, PwMS: Patients with multiple sclerosis, SD: Standard deviation, min: Minimum, max: Maximum

## Discussion

The COVID-19 pandemic continues to be a burden on public health worldwide. The insufficient known effective treatment at the beginning of the pandemic, the anxiety of getting the virus, and the uncertainties of the disease caused panic in society. Additionally, social and economic issues arose due to inevitable

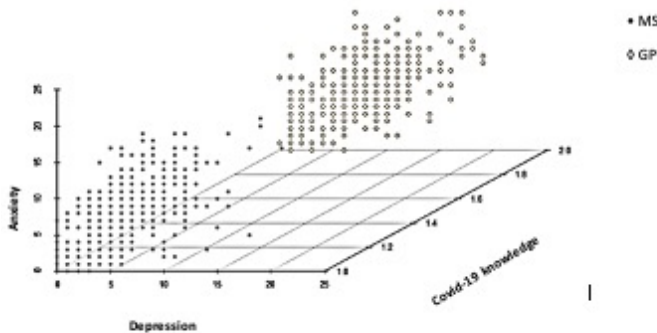
measures, such as social distancing and lockdown, that further affected the public mental health. This study was carried out during the second wave of the pandemic in Turkey to compare the anxiety and depression levels of PwMS with the GP and evaluate some related factors, including COVID-19-related knowledge.

Studies conducted during the COVID-19 period draw attention to the detrimental psychological effects of the pandemic (8,9,10).



**Figure 1.** Comparison of the means of anxiety and depression scale scores between patients with MS and controls

MS: Multiple sclerosis



**Figure 2.** Scatterplot of anxiety and depression scores with COVID-19 knowledge scores

COVID-19: Coronavirus disease-2019, MS: Multiple sclerosis, GP: General population

A study conducted in China at the beginning of the epidemic revealed that 54% of the society was psychologically affected, 17% experienced moderate-severe depression, and 29% had moderate-severe anxiety symptoms, whereas, in Turkey, 24% complained of depression, and 45% of anxiety (9,11). The pandemic caused additional unfavorable psychological effects in individuals with chronic diseases, including MS (4,8). Since the psychological status may alter the immune system, knowledge of the emotional changes of PwMS during the pandemic is critical (12).

Our study revealed that PwMS had increased levels of anxiety (32%) and depression (40%) compared to the pre-pandemic period (13). Additionally, we observed that anxiety and depression are related to the sociodemographic and clinical characteristics of patients. Similar to the literature, our study revealed that young age (14), low educational level (15), low income (16), being divorced/widowed (17), smoking (15), motor disability (16), frequent relapses (18), and antidepressant use (19) were all associated with increased levels of anxiety and depression. The regression models of patients revealed that young age, low educational level, and antidepressant use are predictors of anxiety, whereas low educational level, being divorced/widowed, and antidepressant use for depression. A study (20) revealed that 51% of patients discontinued their treatments because of anxiety, and this rate was 13% in our study. Another study reported that 26% of PwMS stopped their DMT and 13% decreased their dose without the permission of their health care providers (21).

Our study revealed that 42% of the general Turkish population had anxiety and 54% had depression. A previous Turkish study,

conducted at the onset of the pandemic, reported that 45% of the GP had anxiety and 24% had depression (9). Another study reported mild to moderate depression in 48% of patients (22). A meta-analysis reported that the prevalence of anxiety was 32%, and the prevalence of depression was 34% during the COVID-19 period (23). During the pandemic, various studies reported that some sociodemographic characteristics might affect anxiety and depression (11,22). Consistent with previous studies, our study revealed that female gender (9), unemployment (24), low educational level (11), and low income (25) were associated with anxiety and depression. As expected, many studies reported that having COVID-19 and the death of a close relative due to COVID-19 caused worsening in anxiety and depression levels (11,26). Likewise, our study also showed that the female gender was a predictor of anxiety, and the death of a close relative was a predictor of depression.

Contrary to the literature, the anxiety and depression levels of the GP were higher than PwMS when sociodemographic characteristics were adjusted using ANCOVA (21,27) due to acquired adaptability to unexpected conditions in chronic patients and active use of social media. The use of social media has been reported as an effective method in coping with depression in PwMS (28). Additionally, PwMS usually had easier access to their health care providers (i.e., physicians and nurses) during the pandemic, which might positively affect their anxiety and depression. Moreover, the GP's higher levels of anxiety and depression might have been caused by the high rate of unemployment, being single, antidepressant use, COVID-19 infection, and death of close relatives in the GP. It is worth mentioning that the majority of the GP was composed of young male individuals and a significant proportion was unemployed. Considering the gender roles of males in our patriarchal society, we can postulate that the endangered employment status of males might have been perceived as a higher stress factor that cause increased levels of anxiety and depression in the GP.

Another important feature that affects anxiety and depression is COVID-19-related knowledge. As the understanding increases, anxiety and depression are expected to decrease. The COVID-19-related knowledge was discovered as a predictor of anxiety and depression in all individuals. As in the literature, the knowledge level of the GP was lower than PwMS in our study (29). Hence, this low-level knowledge may explain the high levels of anxiety and depression in the GP.

The literature reported that the prevalence of COVID-19 was similar in MS and the GP (30). However, our study revealed more COVID-19 cases in the control than in the MS group. Interestingly, the fear of being infected by COVID-19 was lower in PwMS. PwMS have a lower perceived risk of COVID-19 due to their high level protection and isolation compared to controls.

### Study Limitations

Our study has some limitations. First, the groups differ in terms of sociodemographic characteristics. Second, this study was conducted online, thus most participants were young individuals who actively used the technology. Individuals who did not have internet access were excluded from the study. Third, our study shows a momentary status in the constantly changing COVID-19 pandemic. Our study might have underestimated the COVID-19 prevalence because the participation rate of participants with active COVID-19 infection might have been low.

Table 4. Comparison of anxiety and depression scores of participants according to sociodemographic features and COVID-19 related changes in lifestyle

| Characteristics                    | Control          |                  | PwMS             |                  |
|------------------------------------|------------------|------------------|------------------|------------------|
|                                    | Anxiety          | Depression       | Anxiety          | Depression       |
| <b>Age</b>                         | -0.056           | -0.058           | -0.102           | 0.035            |
| (r, p)                             | 0.249            | 0.234            | <b>0.047</b>     | 0.500            |
| <b>Gender</b>                      |                  |                  |                  |                  |
| Male                               | 8.2±4.0          | 7.5±3.8          | 7.3±4.0          | 6.3±4.0          |
| Female                             | 9.0±4.2          | 7.8±4.2          | 7.8±4.6          | 6.4±3.8          |
| p                                  | <b>0.049</b>     | 0.388            | 0.290            | 0.825            |
| <b>Education</b>                   |                  |                  |                  |                  |
| Primary/secondary education        | 8.0±3.9          | 6.5±3.3          | 10.0±4.4         | 8.9±4.4          |
| High school                        | 8.2±4.0          | 7.9±3.9          | 8.2±4.7          | 7.5±4.2          |
| University                         | 8.7±4.2          | 7.6±4.1          | 7.1±4.3          | 5.8±3.5          |
| p                                  | 0.435            | 0.209            | <b>0.001</b>     | <b>&lt;0.001</b> |
| <b>Income</b>                      |                  |                  |                  |                  |
| Less than expenses                 | 9.6±4.59         | 8.7±4.2          | 10.0±4.4         | 8.5±4.2          |
| Equal to expenses                  | 7.8±3.82         | 6.8±3.8          | 6.9±4.3          | 5.9±3.5          |
| More than expenses                 | 8.3±3.6          | 8.0±3.7          | 6.9±4.1          | 4.6±3.2          |
| p                                  | <b>0.001</b>     | <b>&lt;0.001</b> | <b>&lt;0.001</b> | <b>&lt;0.001</b> |
| <b>Marital status</b>              |                  |                  |                  |                  |
| Married                            | 8.3±3.7          | 7.2±3.9          | 7.5±4.3          | 6.3±3.9          |
| Single                             | 8.6±4.4          | 7.9±4.1          | 7.5±4.5          | 6.1±3.5          |
| Divorced/widow                     | 8.6±2.9          | 8.8±3.3          | 8.5±4.9          | 8.1±4.5          |
| p                                  | 0.738            | 0.196            | 0.500            | <b>0.027</b>     |
| <b>Smoking</b>                     |                  |                  |                  |                  |
| Yes                                | 8.7±4.0          | 8.1±3.8          | 8.5±4.7          | 7.3±4.2          |
| No                                 | 8.3±4.2          | 7.3±4.1          | 7.3±4.3          | 6.0±3.7          |
| p                                  | 0.333            | <b>0.045</b>     | <b>0.024</b>     | 0.004            |
| <b>Antidepressant use</b>          |                  |                  |                  |                  |
| Yes                                | 9.5±2.9          | 8.7±3.9          | 9.1±5.1          | 7.9±4.5          |
| No                                 | 8.4±4.1          | 7.6±4.0          | 7.2±4.2          | 6.0±3.5          |
| p                                  | 0.340            | 0.295            | <b>0.003</b>     | <0.001           |
| <b>COVID-19 diagnosis</b>          |                  |                  |                  |                  |
| Yes                                | 8.2±4.68         | 7.0±4.0          | 9.5±5.4          | 6.5±4.1          |
| No                                 | 7.2±4.33         | 6.0±3.7          | 7.5±4.4          | 6.4±3.8          |
| p                                  | <b>0.037</b>     | <b>0.014</b>     | <b>0.028</b>     | 0.85             |
| <b>Concerns about COVID-19</b>     |                  |                  |                  |                  |
| None                               | 6.8±4.4          | 6.8±4.4          | 7.1±4.47         | 5.7 ± 3.4        |
| Mild level                         | 7.6±3.5          | 6.9±3.5          | 7.4±4.64         | 6.4 ± 4.0        |
| Moderate level                     | 8.9±4.0          | 7.7±4.0          | 7.6±4.35         | 6.2 ± 3.6        |
| High level                         | 10.7±4.0         | 9.6±3.8          | 7.9±4.57         | 6.7 ± 4.1        |
| p                                  | <b>&lt;0.001</b> | <b>&lt;0.001</b> | 0.749            | 0.533            |
| <b>Change in physical activity</b> |                  |                  |                  |                  |
| Worse                              | 9.2 ± 4.1        | 8.0 ± 4.1        | 8.1±4.6          | 7.1±3.9          |
| None                               | 7.1 ± 3.9        | 6.5 ± 3.6        | 6.9±4.5          | 5.7±3.8          |
| Better                             | 7.4 ± 4.0        | 7.9 ± 3.8        | 6.9±3.9          | 4.6±2.6          |
| p                                  | <b>&lt;0.001</b> | <b>0.002</b>     | <b>0.052</b>     | <b>&lt;0.001</b> |
| <b>Change in sleep</b>             |                  |                  |                  |                  |
| None                               | 6.3 ± 3.6        | 5.8 ± 3.7        | 5.4 ± 3.7        | 5.1±3.4          |
| Medium disruption                  | 8.8 ± 3.7        | 7.8 ± 3.7        | 9.5 ± 4.0        | 7.4±3.6          |
| High disruption                    | 10.7 ± 4.3       | 9.5 ± 4.0        | 10.3 ± 4.9       | 8.2±4.9          |
| p                                  | <b>&lt;0.001</b> | <b>&lt;0.001</b> | <b>&lt;0.001</b> | <b>&lt;0.001</b> |

**Table 4. continued**

|                                | Control  |         | PwMS     |         |
|--------------------------------|----------|---------|----------|---------|
| <b>Change in eating habits</b> |          |         |          |         |
| None                           | 6.7±3.7  | 6.2±3.8 | 5.9±3.8  | 5.2±3.6 |
| Medium disruption              | 9.0±3.9  | 7.9±3.6 | 9.3±4.2  | 7.4±3.3 |
| High disruption                | 10.9±3.8 | 9.7±4.0 | 10.4±4.6 | 8.7±4.6 |
| p                              | <0.001   | <0.001  | <0.001   | <0.001  |
| <b>Change in body weight</b>   |          |         |          |         |
| Decreased                      | 9.1±3.9  | 8.4±4.3 | 7.8±4.4  | 6.9±4.1 |
| Not changed                    | 7.3±3.8  | 6.7±3.6 | 6.8±4.3  | 5.6±3.6 |
| Increased                      | 9.3±4.2  | 8.1±4.1 | 8.5±4.5  | 7.2±3.9 |
| p                              | <0.001   | 0.001   | 0.005    | 0.001   |

COVID-19: Coronavirus disease-2019, PwMS: Patients with multiple sclerosis

**Table 5. Multivariate logistic regression analysis to determine the predictors of anxiety**

| Variables                         | Control |                      |       | PwMS |                      |              |
|-----------------------------------|---------|----------------------|-------|------|----------------------|--------------|
|                                   | OR      | 95% CI (lower-upper) | P     | OR   | 95% CI (lower-upper) | P            |
| Age                               | 0.9     | 1.0-1.0              | 0.823 | 0.9  | 0.9-0.9              | 0.010        |
| Gender (female)                   | 1.7     | 1.1-2.6              | 0.015 | 1.0  | 0.6-1.7              | 0.833        |
| <b>Education</b>                  |         |                      |       |      |                      |              |
| Primary school                    | -       | -                    | 0.200 | -    | -                    | <b>0.009</b> |
| High school                       | 0.8     | 0.3-1.9              | 0.627 | 0.3  | 0.1-0.8              | 0.025        |
| University                        | 1.2     | 0.5-2.7              | 0.581 | 0.2  | 0.1-0.6              | 0.002        |
| <b>Marital status</b>             |         |                      |       |      |                      |              |
| Married                           | -       | -                    | 0.800 | -    | -                    | 0.220        |
| Single                            | 0.8     | 0.1-6.4              | 0.907 | 1.8  | 0.7-4.8              | 0.229        |
| Divorced/widow                    | 0.7     | 0.4-1.6              | 0.504 | 0.8  | 0.4-1.7              | 0.600        |
| Having children                   | 1.3     | 0.6-3.0              | 0.400 | 1.4  | 0.7-2.9              | 0.301        |
| Antidepressant use                | 1.0     | 0.3-3.1              | 0.949 | 2.2  | 1.3-3.8              | 0.004        |
| COVID-19 diagnosis                | 1.6     | 0.9-2.9              | 0.059 | 2.9  | 0.9-5.4              | 0.085        |
| Loss of relatives due to COVID-19 | 1.1     | 0.7-1.8              | 0.524 | 1.6  | 0.8-3.2              | 0.160        |
| Knowledge of COVID-19             | 0.8     | 0.7-0.9              | 0.007 | 0.7  | 0.6-1.0              | 0.020        |

COVID-19: Coronavirus disease-2019, PwMS: Patients with multiple sclerosis, OR: Odds ratio, CI: Confidence interval

**Table 6. Multivariate logistic regression analysis to determine the predictors of depression**

| Variables                         | Control |                      |       | PwMS |                      |              |
|-----------------------------------|---------|----------------------|-------|------|----------------------|--------------|
|                                   | OR      | 95% CI (lower-upper) | P     | OR   | 95% CI (lower-upper) | P            |
| Age                               | 1.0     | 0.9-1.0              | 0.780 | 0.9  | 0.9-1.0              | 0.269        |
| Gender (female)                   | 1.4     | 0.9-2.1              | 0.109 | 0.7  | 0.4-1.1              | 0.200        |
| <b>Education</b>                  |         |                      |       |      |                      |              |
| Primary school                    | -       | -                    | 0.549 | -    | -                    | <b>0.015</b> |
| High school                       | 1.1     | 0.4-2.6              | 0.742 | 0.4  | 0.1-1.0              | 0.071        |
| University                        | 1.3     | 0.6-3.0              | 0.395 | 0.3  | 0.1-0.7              | <b>0.005</b> |
| <b>Marital status</b>             |         |                      |       |      |                      |              |
| Single                            | -       | -                    | 0.601 | -    | -                    | 0.103        |
| Married                           | 1.0     | 0.5-2.0              | 0.919 | 1.3  | 0.6-2.5              | 0.387        |
| Divorced/widow                    | 0.3     | 0.1-2.1              | 0.332 | 2.7  | 1.1-7.1              | <b>0.033</b> |
| Having children                   | 0.7     | 0.3-1.5              | 0.423 | 0.8  | 0.4-1.5              | 0.504        |
| Antidepressant use                | 1.6     | 0.5-5.0              | 0.406 | 2.8  | 1.6-4.8              | <0.001       |
| COVID-19 diagnosis                | 1.1     | 0.6-1.9              | 0.724 | 0.7  | 0.3-1.9              | 0.565        |
| Loss of relatives due to COVID-19 | 1.8     | 1.1-2.9              | 0.010 | 1.3  | 0.7-2.6              | 0.346        |
| Knowledge of COVID-19             | 0.7     | 0.7-0.9              | 0.001 | 0.8  | 0.7-1.0              | 0.023        |

COVID-19: Coronavirus disease-2019, PwMS: Patients with multiple sclerosis, OR: Odds ratio, CI: Confidence interval



## Conclusion

In conclusion, our study revealed that the COVID-19 pandemic had a significant effect on the anxiety and depression levels of the GP and PwMS. Additionally, the GP had higher levels of anxiety and depression compared to PwMS. Anxiety and depression levels were also determined to be associated with various sociodemographic and clinical characteristics of patients. The female gender was related to anxiety, the death of a close relative due to COVID-19 to depression, and COVID-19-related knowledge to both anxiety and depression in the GP. In PwMS, age was related to anxiety, being single to depression, and low education level, antidepressant use, and COVID-19-related knowledge to both anxiety and depression. Our study emphasizes the importance of psychological support to the GP and PwMS during the pandemic.

## Ethics

**Ethics Committee Approval:** The ethical principle compliance was evaluated by the ethics committee of the institution where the study was conducted, and the Ethics Committee approval was obtained (Istanbul University, Istanbul Faculty of Medicine, Department of Neurology, Istanbul, Turkey, file number: 2020/1095, no: 29624016-050.99- 1215).

**Informed Consent:** Consent to participate was obtained using online forms.

**Peer-review:** Externally peer-reviewed.

## Authorship Contributions

Concept: G.Y.Y., C.P.D., Z.T., M.K., M.E., Design: G.Y.Y., C.P.D., Z.T., M.K. Data Collection or Processing: G.Y.Y., C.P.D., Analysis or Interpretation: G.Y.Y., C.P.D., Z.T., Literature Search: G.Y.Y., C.P.D., Writing: G.Y.Y., C.P.D.

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