

# Mood disorders after COVID-19 infection: a single-center experience

Fatih Uzer<sup>1\*</sup>, Aykut Cilli<sup>1</sup>, Sukriye Oner<sup>1</sup>, Mestan Emek<sup>2</sup>, Ata Nevzat Yalcin<sup>3</sup>

1. Department of Respiratory Medicine, Akdeniz University School of Medicine, Antalya, Turkey

2. Department of Public Health, Akdeniz University School of Medicine, Antalya, Turkey

3. Department of Infectious Disease, Akdeniz University School of Medicine, Antalya, Turkey

\*Corresponding Author: Fatih Uzer; Email: uzerfatih@gmail.com

## Abstract

### Objectives

The present study aimed to examine mood disorders in patients discharged from the hospital due to Coronavirus Disease-19 (COVID-19).

### Methods

The study included patients who were admitted to Akdeniz University with the diagnosis of COVID-19. Post-Traumatic Stress Disorder (PTSD) Checklist - Civilian Version (PCL-5), and Beck Anxiety and Depression Inventories were administered to the patients at least 30 days after discharge.

### Results

A total of 215 patients were included. The median age was 56 years, and 60.9%(131) were male. There was no statistically significant difference in mood disorders scale scores between male and female. However, there was a weak negative correlation between age and PCL-5 scores ( $\rho$ : -0.157,  $p$ : 0.021). The depression scores ( $p < 0.001$ ), anxiety scores ( $p < 0.001$ ) and PCL-5 ( $p = 0.001$ ) scores were statistically significantly higher in patients with respiratory symptoms at the time of enrollment (after a mean duration of 87.9 days following discharge). Married individuals had statistically significantly lower anxiety, depression, and PCL-5 scores. Beck anxiety scores were statistically significantly higher in patients receiving systemic steroid.

### Conclusion

A substantial portion of patients with COVID-19 suffer from mood disorders after hospital discharge. Those patients with residual symptoms who live alone and receive corticosteroid represent a vulnerable population.

**Key words:** Coronavirus Disease-19, Anxiety, Depression, Post-Traumatic Stress Disorder, Survivors

## Introduction

Coronavirus Disease-19 (COVID-19) first appeared in Wuhan in December 2019 as an unidentified pneumonia. Soon after, it was declared a pandemic by the World Health Organization (WHO). Following the first appearance of the disease, more than a hundred million people were infected, and almost three million people died from it.<sup>1</sup> Countries have taken various measures to fight against the pandemic. The primary measures included isolation, quarantine, and avoidance of mass gatherings. Several studies have shown that all age groups, including children, young adults, and older individuals, have suffered from various mental conditions during periods of social isolation, including anxiety, depression, and post-traumatic stress disorder.<sup>2-4</sup> Loneliness, decrease in income, and the use of face masks have been suggested as possible reasons for these conditions.<sup>2-6</sup>

Mood disorders can develop not only in individuals who have recovered from the infection but also in healthy people who have not been infected with the virus.<sup>7</sup> Several post-pandemic studies revealed that different mood disorders, such as post-traumatic stress disorder and depression, occurred in healthy people during the pandemic.<sup>7-10</sup> In many studies, it has been reported that these conditions are more commonly observed in certain groups of people, such as immigrants, women, and

students.<sup>9-13</sup>

Post-Traumatic Stress Disorder (PTSD) is a mental disorder that arises after a significant traumatic event. It is characterized by hypervigilance, avoidance of stimuli associated with or reminding of the trauma, and re-experiencing the traumatic event through dreams and “flashbacks” and lasts for at least one month. PTSD first appeared in the literature following World War II. It has been reported, however, that it can also occur during outbreaks.<sup>8</sup> PTSD rates have been observed to be higher in individuals who were infected or had a high risk of infection. In the study by Liang et al.<sup>14</sup>, the assessment for the month after the declaration of the pandemic revealed that 12.8% of the participants experienced PTSD.

During the COVID-19 pandemic, several situations that might be stressor have emerged. These may be listed as fears of death, social isolation, getting infected, and financial difficulties. Furthermore, the concern that the healthcare system may be insufficient in fighting against the COVID-19 pandemic can be considered another stressor.<sup>15</sup> During the previous outbreak of severe acute respiratory failure (SARS), both survivors and other healthy individuals experienced high levels of anxiety and depression.<sup>16,17</sup> Since the onset of COVID-19, studies have focused more on the diagnosis and treatment of this virus. However, the effects of COVID-19 on mental health have recently started to be discussed.<sup>18</sup> The

mental health issues experienced by people due to complete lockdowns and restrictions during the COVID-19 pandemic were demonstrated by several studies.<sup>14,16,18</sup> Nevertheless, there is limited research examining the mental health of patients after discharge who were hospitalized due to COVID-19. Therefore, the present study aimed to examine mood disorders in patients discharged from the hospital due to COVID-19.

## Materials and Methods

The study included patients who were admitted to Akdeniz University Medical Faculty Hospital with the diagnosis of COVID-19 and discharged between March 15, 2020, and October 30, 2020. Akdeniz University Faculty of Medicine Hospital is one of the largest tertiary care hospitals in Antalya province and its surrounding areas. With a bed capacity of 983, the hospital admits approximately 3,700 new patients daily and provides services to around 900,000 patients annually from Antalya and neighboring provinces through its 87-bed intensive care units. It is a comprehensive healthcare complex.

Patients' demographic data, such as age and sex, as well as symptoms at initial admission, thoracic computerized tomography (CT) findings, COVID-19 reverse transcription polymerase chain reaction (rRT-PCR) results, and length of hospital stay in the hospital, were retrieved from the hospital automation system and recorded in the data collection form. In addition, the unit where the patient was treated during the patient's stay (intensive care unit, ward), the length of stay, comorbidities, residual symptoms, and medications administered due to COVID-19 were recorded. Residual symptoms are defined as symptoms that persist after the initial diagnosis and continue after discharge.

**Table 1; General patient characteristics**

		n (%)
Sex	Female	84 (29.1)
	Male	131 (60.9)
Marital status (n=213)	Married	181 (85.0)
	Single	22 (10.2)
	Widowed/Divorced	10 (4.7)
Smoking (n=212)	Smoker	10 (4.7%)
	Never	76 (35.3%)
	Never	126 (58.6%)
Need for Intensive Care		42 (19.6%)
CT findings (n=145)	Ground-glass	116 (80)
	Consolidation	10 (6.8)
	Other	7 (4.8)
	Normal	12 (8.4)
Comorbidities	Hypertension	65 (30.2)
	Diabetes Mellitus	56 (26.0)
	Chronic lung disease (Asthma and/or COPD)	23 (10.7)
	Chronic kidney disease	15 (7.0)
	Malignancies	8 (3.7)

**CT: Computed Tomography; COPD: Chronic obstructive pulmonary disease**

Post-Traumatic Stress Disorder (PTSD) Checklist - Civilian Version (PCL-5), and Beck Anxiety and Depression Inventories were administered to the patients at least 30 days after discharge. The questionnaires were filled out by calling the patients via phone. They also administered face-to-face to the patients who did not want to respond via phone but came to the outpatient clinic after discharge. Interviews conducted by the researchers. Patients with a positive COVID-19 PCR result in an oral or nasal swab were included in the study. Patients with any psychiatric disorders during their hospital stay, possible COVID-19 cases, those who were COVID-19 compatible on CT but PCR negative, those who could not be accessed via phone, those who died from COVID-19, those with cognitive disorders such as dementia and Alzheimer's, those who did not want to answer questions, and those aged  $\leq 18$  years were excluded from the study.

**PTSD Civilian Version (PCL-5):** It is a checklist that questions and assesses PTSD based on the DSM-V criteria. It is a self-reported measure. The instrument consists of 20 items in total. Patients rate how much they have been bothered by the symptoms given in the list over the past month. Each item is rated on a 5-point Likert-scale and is scored from 0 to 4. The total score of the scale is the arithmetic sum of the responses to the items. A scale score of 0–19 is interpreted as asymptomatic, 20–39 as mildly, 40–59 as moderately, 60–79 severely, and  $> 80$  as extremely symptomatic.<sup>19</sup> The Turkish reliability study of the instrument was conducted by Boysan et al.<sup>20</sup>

**The Beck Depression Inventory (BDI):** It is a 21-item self-assessment scale that measures the somatic, affective, cognitive, and impulsive symptoms of depression. Each item is scored from 0 to 3. The total score range of the inventory is 0–63; higher scores indicate greater depressive severity. The purpose of the inventory is not to diagnose depression but to objectively quantify the severity of symptoms. There are two forms of the BDI. The first one is the original form developed by Beck in 1961.<sup>21</sup> The second form was also developed by Beck in 1978.<sup>22</sup> The BDI-1978 was adapted into Turkish by Hisli.<sup>22</sup> The Turkish version of the BDI-1978 was used in this study.

**The Beck Anxiety Inventory (BAI):** It is a 21-item self-report scale that aims to determine the frequency of anxiety symptoms experienced by individuals. Each item is scored from 0 to 3. The total score range of the inventory is 0–63. Higher scores indicate more severe anxiety experienced by the individual. The original inventory was developed by Beck et al.<sup>23</sup>. The inventory was adapted into Turkish by Ulusoy et al.<sup>24</sup>.

The Akdeniz University Faculty of Medicine Clinical Research Ethics Committee approved the study on November 11, 2020, with Decision No: KAEK-861.

## Statistical Analysis

Descriptive data were presented as percentage distribution, mean, standard deviation, median, and minimum–maximum values. The Chi-square test was used to compare the categorical variables.

**Table 2; The detailed table of the patients' mental status scale scores**

Scale	Severity	n (%)
Beck Depression Score (n=215)	Minimal (0–9)	175 (81.4)
	Mild (10–16)	26 (12.1)
	Moderate (17–29)	10 (4.7)
	Severe (30–63)	4 (1.9)
Beck Anxiety Score (n=215)	Minimal (0–9)	148 (68.8)
	Mild (10–16)	39 (18.1)
	Moderate (17–29)	18 (8.4)
	Severe (30–63)	10 (4.7)
PCL-5 (n=215)	Asymptomatic (0–19)	182 (84.7)
	Mildly (20–39)	18 (8.4)
	Moderately (40–59)	11 (5.1)
	Severely (60–79)	4 (1.9)
	Extremely (> 80)	0 (0)

**PCL-5: posttraumatic stress disorder checklist for DSM-V**

**Table 3. Association between variables and scales**

		Beck Depression	Beck Anxiety	PCL-5
Sex	Female	6.9	7.4	11.6
	Male	5.2	6.9	8.0
	p	0.834	0.739	0102
Age	<40	5.3	6.0	10.7
	40–64	5.9	7.8	10.8
	>64	5.1	6.3	6.1
	p	0.485	0.567	0.188
Residual symptom	No	4.5	5.1	6.8
	Yes	7.3	10.3	13.8
	p	<0.001	<0.001	0.001
Marital status	Single	7.5	11.0	16.5
	Married	5.2	6.3	8.0
	Widowed/Divorced	8.4	12.7	22.0
	p	0.030	0.001	0.001
Need for intensive care	Yes	5.2	7.5	7.4
	No	5.7	7.0	10.0
	p	0.174	0.540	0.792
CT findings	No	11.0	8.4	19.8
	Unilateral	8.7	10.0	9.4
	Bilateral	6.3	8.4	11.0
	p	0.658	0.675	0.976
Favipiravir therapy	Yes	5.6	7.0	9.0
	No	4.6	6.9	10.4
	p	0.338	0.847	0.743
Steroid therapy	Yes	6.0	8.2	8.7
	No	5.2	6.4	9.5
	p	0.066	0.026	0.343

**CT: Computed Tomography; PCL-5: posttraumatic stress disorder checklist for DSM-V**

The Kolmogorov-Smirnov test was used to analyze the normality of distribution. The Kruskal-Wallis analysis of variance was used to compare more than two groups and the Mann-Whitney U test to compare two groups. The logistic regression method was used for multivariate analyses. A cut-off value of 16, 16 and 39 was determined for Depression, Anxiety and PTSD scores, respectively, as the dependent variables Presence of Residual Symptoms, Marital Status, Steroid Therapy, which were the variables with a significant difference identified by univariate analysis, age and sex were included in the Logistic Regression model to explain Anxiety by Logistic Regression Analysis. Analyses were performed using SPSS 18.0. A p value of < 0.05 level was considered significant.

**Results**

There were 385 individuals treated as inpatients in the Akdeniz University Hospital COVID-19 Referral Clinic between March 15, 2020, and October 30, 2020. We were able to contact 215 (55.8%) of these patients. A total of 170 (44.2%) patients were excluded because 29 patients died in the hospital, 14 patients refused to participate in the study, and 127 patients could not be reached by phone. The median age was 56 years among the patients reached, and 60.9% (131) were male. The group that could not be contacted was statistically older (56 vs 64; p <0.001). Among the patients included in the study, 64% (144) were older than 50 years old. Among the patients who agreed to participate in the study, 121 (56.2%) answered the survey questions over the phone, while the remaining 94 (43.8%) were included in the study during their outpatient follow-up visits.

The patients were included in the study after a mean duration of 87.9±43.4 days following discharge. The most common complaints of the patients at COVID-19 diagnosis were fever (26.5%), dyspnea (18.6%), and cough (13.5%), while 38.1% (82) of the patients had residual symptoms at the time of enrollment. The most common residual symptoms were dyspnea (12.6%), fatigue (8.4%), and cough (4.7%). The length of hospital stay was 8 (1–90) days, and the mean length of stay in the intensive care unit for those requiring intensive care was 9.7 days. Thoracic CT was performed in 145 (67.4%) patients, while chest radiography was performed in all patients. The most common chest radiographic finding was consolidation (46%) and the most common CT finding was ground-glass infiltration (80%). There was at least one comorbidity in 164 (76.3%) patients, and the most common comorbidities were hypertension (30.2%) and diabetes mellitus (26.0%). The general characteristics of patients are presented in Table 1.



**Table 4. Anxiety Assessment by Logistic Regression Analysis**

Variable	B	SE	OR	95% CI	p
Age*	-0.008	0.013	0.992	0.968–1.018	0.548
Male <sup>a</sup>	0.057	0.379	1.059	0.503–2.227	0.881
Residual Symptom <sup>b</sup>	1.895	0.361	6.655	3.278–13.511	<0.001**
Single <sup>c</sup>	1.490	0.558	4.437	1.488–13.232	0.008**
Widowed/Divorced <sup>c</sup>	2.883	0.902	17.865	3.048–104.703	0.001**
Steroid <sup>d</sup>	0.532	0.379	1.702	0.810–3.576	0.160

**B: regression coefficient, SE: standard error, OR: Odds Ratio**

**\*Continuous variables \*\*p < 0.05**

**Reference category: a) Female, b) Absence of residual symptoms, c) Being married, d) Non-receipt of steroid therapy.**

**Nagelkerke R<sup>2</sup>: 0.317**

The most common treatment combination was favipiravir, systemic steroid, and non-specific antibiotic treatment. Out of the patients, 4.7% (10) received invasive mechanical ventilation, 3.3% (7) received non-invasive mechanical ventilation, and 0.9% (2) received high-flow oxygen therapy. In addition, all patients received oxygen support. With a cutoff point of 16 for Beck depression and anxiety scores, the incidence rates of depression and anxiety were 6.6% and 13.1%, respectively. With a cutoff point of 39 for PCL-5, the rate of PTSD was 7%. The Beck depression, Beck anxiety, and PCL-5 scores of the patients are presented in detail in Table 2.

There was no statistically significant difference in mood disorder scale scores between male and female. However, there was a weak negative correlation between age and PCL-5 scores ( $\rho$ : -0.157,  $p$ : 0.021). The depression scores ( $p$  < 0.001), anxiety scores ( $p$  < 0.001) and PCL-5 ( $p$  = 0.001) scores were statistically significantly higher in patients with complaints at the time of enrollment (after a mean duration of 87.9 days following discharge). Married individuals had statistically significantly lower anxiety, depression and PCL-5 scores. While there was no statistically significant difference in the mental status scale scores of patients receiving favipiravir treatment, the Beck anxiety scores of patients receiving systemic steroid treatment were statistically significantly higher (Table 3). There are no statistical differences in the rates of anxiety, PTSD, and depression between those with greater initial illness severity (ICU patients) and those with lesser initial illness (non-ICU patients).

The results of the logistic regression analysis on anxiety revealed that residual symptoms and being single, or widowed/divorced caused a significant difference. Accordingly, it is possible to say that those with residual symptoms had 6.7 times the odds of anxiety compared to those without residual symptoms. Furthermore, individuals who were single had 4.4 times the odds of anxiety, while those who were widowed or divorced had 17.9 times the odds of anxiety compared to those who were married (Table 4).

## Discussion

Shortly after the onset of the COVID-19 pandemic, it was predicted that people might experience changes in mental status. There are increasing studies on this subject. It has been emphasized in the literature that post-COVID anxiety and depression scores are high, and that post-traumatic stress disorder is experienced intensely during the

pandemic.<sup>8,16–18,25–28</sup> Unlike the literature, the present study assessed mood disorders only in hospitalized patients and found that the presence of residual symptoms and being single caused anxiety, depression and post-traumatic stress disorder.

Several recent studies highlighted the neurological and psychiatric outcomes of COVID-19. The study by Taquet et al.<sup>25</sup> which included one of the largest case series in the literature, analyzed the electronic records of more than 200,000 patients and identified significantly high anxiety and depression scores. However, the study by Taquet et al. was conducted using only electronic records and the authors indicated that it would not be appropriate to generalize the results to all COVID-19 patients since it did not include patients who did not present to hospital after COVID-19 treatment. The study also did not evaluate socioeconomic and living standards in detail. A systematic review found that post-COVID-19 syndrome is linked to a high frequency of clinically significant depression and depressive symptoms, with certain factors like female sex, previous psychiatric history, and psychopathology at one-month follow-up acting as moderators.<sup>10</sup> The study also revealed that COVID-19 patients experience higher levels of neuropsychiatric symptoms, such as impulsivity and insomnia, compared to psychiatric patients and healthy individuals, and they often have various emotional experiences and concerns during their treatment<sup>10,29</sup>. Our study, included only hospitalized patients, administered a face-to-face questionnaire to most of these patients after discharge and via phone to the remaining patients. Besides, we believe that our study is valuable because the patients' sociodemographic findings and COVID-19-related clinical findings were examined in more detail.

In our study, the rates of anxiety, depression and PTSD were 13.1%, 6.6%, and 7%, respectively. These rates are lower than those reported by similar studies in the literature.<sup>18</sup> Most of the studies in the literature were conducted with COVID-19 patients who were treated as outpatients or in a more general population such as students, healthcare professionals and pregnant women.<sup>25,26,28,30–32</sup> We could identify, only a single study investigating mental health among hospitalized patients.<sup>18</sup> In their study conducting an online survey in Wuhan in the early days of the pandemic, Chen et al. reported the rates of anxiety, depression and PTSD as 16.4%, 21%, and 13.2%, respectively. There are some methodological inadequacies in Chen et al.'s study. The

authors did not specify how many days after discharge the patients were included in the study. In our study, patients were included about 3 months after discharge. The overall low scores in our study may be due to the younger patient group and the longer time since discharge compared to other studies.

It was reported that hospitalized patients might experience serious mental problems during the pandemic. Such problems may be due to neurological involvement by COVID-19, as well as medications such as corticosteroids and hydroxychloroquine administered in the hospital, and pandemic-related stress.<sup>18,33-35</sup> In our study, anxiety scores were statistically significantly higher for the group receiving corticosteroids, but there was no association with other scores. We believe that this may be due to the more severe respiratory distress in the steroid group and the higher risk of death compared to the other groups.

Recently, a post-COVID-19 syndrome has been defined.<sup>36</sup> According to this definition, patients may experience symptoms such as fatigue months after recovering from COVID-19. An Italian study, which was similar in number of patients and length of hospital to our study, but assessed patients approximately 2 months after discharge, found the rate of post-COVID-19 residual symptoms to be 87.4%.<sup>37</sup> In our study, this rate was 38.1%. However, our study was performed approximately 3 months after discharge. This suggests that the effects of COVID-19 may decrease over the course of time. Although the physical effects of the disease have passed, these patients may continue to experience persistent mental problems.<sup>38</sup> Our study found patients with residual respiratory symptoms to have high scores on all anxiety, depression and PTSD.

A significant relationship was shown between mental health and marital status.<sup>39</sup> Studies reported that married individuals had better mental health.<sup>40</sup> The survey studies conducted during the COVID-19 pandemic observed that married individuals exhibited more anxiety and depression symptoms compared to those living alone during lockdowns.<sup>41,42</sup> In our study, all anxiety, depression and PCL-5 scores of married individuals were statistically significantly better than single individuals. This finding shows the importance of social support for mental health during outbreaks. It may be important to provide social support to patients discharged from the hospital during the lockdowns.

Burnout syndrome is another important public health issue within mood disorders. Some studies have emphasized the need for the development and adaptation of a burnout syndrome scale.<sup>8,43</sup> However, in our study, burnout syndrome was not investigated.

The management of mood disorders is a complex treatment involving multiple variables. Behavioral communication can be effectively administered through online platforms, particularly during challenging times. It's important to note that everyone's experience with mood disorders is unique, and what works for one person may not work for another. Consulting with a qualified mental health professional and developing an individualized treatment plan is crucial for effectively managing mood disorders.

Our study has certain limitations. First of all, the enrolled patient group was younger than the patients who were unable to contact group. Therefore, results of our study are not applicable to all age groups. However, most of the patients included in the study were over the age of 50. The single-

center setting and lack of a control group are other limiting factors. Moreover the study did not explore about burnout.

In conclusion, a substantial portion of patients with COVID-19 suffer from mood disorders after hospital discharge. Those patients with residual symptoms, who lives alone, and who receives corticosteroid therapy represent vulnerable population. Therefore, this group of patients should follow up closely after discharge. On the other hand, the results of this study should be supported by other studies.

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