

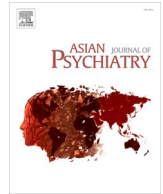


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## Characteristics and outcomes of COVID-19 inpatients who underwent psychiatric consultations

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## ABSTRACT

Patients hospitalized with COVID-19 are at risk of developing many neuropsychiatric disorders, due to the effects of the disease on the brain and the psychosocial pressures of having the disease. The aim of the present study was to evaluate the characteristics and outcomes of patients who were hospitalized with a diagnosis of COVID-19, who underwent psychiatric consultations. The medical records of 892 patients hospitalized due to COVID-19 and the 89 among them who requested psychiatric consultations were analyzed retrospectively. After the psychiatric consultations, patients were most frequently diagnosed with delirium (38.2 %), adjustment disorder (27.0 %), depressive disorder (19.1 %) and anxiety disorder (11.2 %). Patients with delirium had longer hospital stays ( $p < 0.001$ ), were transferred more frequently to intensive care units ( $p < 0.001$ ), and had higher mortality rates during their hospital stays ( $p < 0.001$ ), than all other patients. The need for oxygen ( $p < 0.001$ ) and mechanical ventilation ( $p < 0.001$ ) was also significantly higher in delirium patients, as well as in patients who received other psychiatric diagnoses. Neuropsychiatric disorders develop in patients receiving inpatient treatments in COVID-19 wards, and these disorders negatively affect the prognosis of COVID-19. Our findings suggest that the presence of neuropsychiatric disorders in in-patients with COVID-19 might be associated with the negative outcomes of the disease.

### 1. Introduction

Coronavirus disease 2019 (COVID-19), which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has already affected more than 85 million people and caused over 1.8 million deaths worldwide since the first case was confirmed, in Wuhan, China, in late December of 2019. The clinical presentations of COVID-19 can vary according to the severity of the disease in the individual. However; the most common reported symptoms are fever, cough, dyspnea, and upper respiratory tract symptoms, including myalgias, diarrhea, and smell or taste disorders (Goyal et al., 2020; Guan et al., 2020; Huang et al., 2020; Richardson et al., 2020; Stokes et al., 2020). While SARS-CoV-2 is known to primarily cause disease in the lungs, it is reported that its effects are not limited to the lungs and expands to other organs such as the brain, heart, kidneys, skin, and gastrointestinal organs (Baj et al., 2020; Roberts et al., 2020; Wang et al., 2020; Yuki et al., 2020).

Coronaviruses are known to have neuropathogenic potential (Desforges et al., 2014; Kotfis et al., 2020). It has been demonstrated that severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), which are the other members of the coronaviridae family, have potential neurotrophic effects (Lau et al., 2004; Li et al., 2016; Xu et al., 2005). In a recent meta-analysis study by Rogers et al. (2020), it was demonstrated that coronaviruses have serious psychiatric and neuropsychiatric outcomes, both in the acute stage and in the long term. This systematic review revealed that the most common symptoms among patients admitted to hospitals for SARS or MERS included insomnia (41.9 %), anxiety (35.7 %), impaired memory (34.1 %), depressed mood (32.6 %), and confusion (27.9 %) during the acute stage.

Similarly, growing evidence suggests that SARS-CoV-2 may also cause neurological and psychiatric symptoms by affecting the brain (Troyer et al., 2020; Varatharaj et al., 2020; Vindegaard and Benros,

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2020). In a study by Nalleballe et al. (2020), which evaluated 40,469 COVID-19 infected patients, the neuropsychiatric manifestations rate was found to be 22.5 % ( $n = 9086$ ). While the most common neurologic manifestations in this study were headaches (3.7 %), sleep disorders (3.4 %), and encephalopathy (2.3 %), and the most common psychiatric symptoms were anxiety and other related disorders (4.6 %), as well as mood disorders (3.8 %). These emerging neuropsychiatric manifestations may occur due to the direct effects of the virus on the brain, the indirect immune responses or the medical treatments administered (Rogers et al., 2020). On the other hand, psychiatric disorders developing in the acute period in patients hospitalized for COVID-19 may arise due to concerns about the consequences of the disease (Banerjee, 2020; Xiang et al., 2020), such as social isolation and quarantine (Brooks et al., 2020; Lewnard and Lo, 2020), unemployment, financial difficulties (Chaves et al., 2018), and stigma (Banerjee, 2020).

In Turkey, the first confirmed case of COVID-19 was reported on March 11th, 2020. In the time period since, the data leading up to January 6th 2020 shows that there have been 2,283,921 people diagnosed with the disease, including 22,070 people that have died as a result of the disease in Turkey (Republic of Turkey Ministry of Health Corona Table, 2021). Since the confirmation of the first case, many public and private hospitals were declared "pandemic hospitals" by the government, to combat COVID-19. In this context, new inpatient wards where only COVID-19 patients were treated were established.

The aim of this study was to quantify the characteristics and outcomes of patients who were hospitalized in the pandemic wards of Istanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty Hospital at the height of the outbreak with a diagnosis of COVID-19 and who received psychiatric consultations. A further objective of this study was to identify factors associated with the neuropsychiatric symptoms these patients experienced.

## 2. Methods

### 2.1. Study population and COVID-19 diagnosis

All patients over the age of 18 who were hospitalized during the COVID-19 pandemic in the wards of Istanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty Hospital and received consultations from the department of psychiatry between the 10th of March 2020, and 26th of June 2020, were included in the study. The patients were divided into two groups; "confirmed cases" and "probable cases", according to the case definitions of the World Health Organization (WHO, 2020). Regardless of clinical signs and symptoms, individuals with laboratory confirmations of COVID-19 were categorized as "confirmed cases." The "probable cases" included: (1) patients who met clinical criteria (acute onset of fever and cough; or acute onset of any three or more of the following signs or symptoms: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnoea, anorexia/nausea/vomiting, diarrhoea, altered mental status) and were in contact with an individual with a probable or confirmed case, or epidemiologically linked to a cluster of individuals, at least one of whom had a confirmed case; (2) suspected cases due to chest imaging findings suggestive of COVID-19 disease; and (3) people with a recent onset of anosmia or ageusia in the absence of any other identified cause. Criteria for inclusion were as follows: (1) being over 18 years of age; (2) having a diagnosis of COVID-19 according to the case definition of the WHO (confirmed or probable cases); (3) having received in-patient treatment in a COVID-19 ward. Patients whose file information was not available and whose first hospitalization took place in the intensive care units (ICU) were not included in the study.

Nasal and pharyngeal swab specimens were collected on admission to the hospital. The diagnosis of COVID-19 was confirmed by reverse transcriptase-polymerase chain reaction (RT-PCR) assays for SARS-Cov-2 RNA.

### 2.2. Data collection

The consultations were retrospectively reviewed using information obtained from medical file records and electronic medical records. Two consultant psychiatrists and an infectious disease specialist prepared a structured data collection form in order to determine the sociodemographic and clinical features of the patients. This form included questions on the patients' age and gender, the clinical features of their COVID-19 diagnosis, their PCR test results, chest imaging findings, hospitalization period dates, ICU transfer information, intubation status and final status. The form also included information on their reason for requesting a psychiatric consultation, their psychiatric history, the psychiatric diagnosis given to them, the treatment recommendations made and whether there was need for reconsultation. The structured data collection form was filled out by three psychiatry residents from the department of consultation-liaison psychiatry.

### 2.3. Consultation procedure

Patients were evaluated by a psychiatrist at their consultations in the COVID-19 wards where they were hospitalized. The consultants entered the rooms of patients with COVID-19 cases with personal protective equipment provided for them in order to reduce their risk of exposure. Personal protective equipment included a gown, gloves, respirators (N95), medical masks, goggles, and disposable face shields. The anamnesis, examination findings, pre-diagnosis and treatment recommendations of the patients were recorded in the consultation forms in their medical files and in the electronic medical record system. Psychiatric diagnoses were made according to the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10), which is the classification list of WHO (1992).

### 2.4. Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences, version 22.0 (SPSS Inc, Chicago, IL). Characteristics of patients were described using mean and standard deviations, median or counts and proportions, as appropriate. Differences between the groups (patients who received no consultations, patients with delirium, and patients with other psychiatric diagnoses) were tested using the chi-square test for categorical variables and a one-way analysis of variance (ANOVA) for continuous variables.

## 3. Results

We investigated the patient records of 927 individuals above 18 years of age, who were hospitalized with a diagnosis of COVID-19. The records of all patients were accessed. Thirty-five patients hospitalized at first in the ICU with the above diagnoses were excluded. Out of a total of 892 patients (Male = 412, 46.2 %), 89 patients (10.0 %; Male = 36, 40.5 %) requested psychiatric consultations. The average age was 55.6 years (Table 1). Patients were consulted mostly on the first day of their

**Table 1**  
Reasons for the psychiatric consultations.

| Reasons                                    | $n = 89$ | %    |
|--|----------|------|
| Psychomotor agitation/restlessness         | 23       | 25.8 |
| Impairment of sleep                        | 21       | 23.6 |
| Evaluation of prior psychiatric treatments | 15       | 16.7 |
| Anxiety/fear                               | 13       | 14.6 |
| Suicidal ideation                          | 8        | 9.0  |
| Refusal of medical treatment               | 4        | 4.5  |
| Crying spells                              | 3        | 3.4  |
| Confusion                                  | 3        | 3.4  |
| Suicidal attempt                           | 1        | 1.1  |
| Loss of appetite                           | 1        | 1.1  |

hospitalization (19.3 %), with a median consultation date of their third day (range = 1–89). RT-PCR positivity was detected in 46 patients (51.7 %) in the first or consecutive test.

The most common reasons for requesting psychiatric consultation were psychomotor agitation/restlessness (25.8 %), impairment of sleep (23.6 %), evaluation of prior psychiatric treatment (16.7 %), anxiety/fear (14.6 %), and suicidal ideation (9.0 %) (Table 1). After the psychiatric evaluations were performed during their consultations, the patients were diagnosed with either delirium (38.2 %), adjustment disorder (27.0 %), depressive disorder (19.1 %), or anxiety disorder (11.2 %) (Table 2).

Gender distribution was similar across the compared groups. Patients with delirium were significantly older than the other two groups ( $p < .001$ ). The hospital stays were significantly longer for patients with delirium in comparison to the other two groups. The hospital stays of patients diagnosed with other psychiatric disorders were also longer than patients who did not seek psychiatric consultations at all.

A chi-square test (where group X had prior neuropsychiatric diseases) showed that the frequency of prior neuropsychiatric disorders differed by group ( $X^2(2, n = 892) = 135.91, p < .001$ ), and patients with delirium, as well as patients with other diagnoses, were significantly more likely to have had prior neuropsychiatric disorders ( $p < .05$ , post hoc analyses with Bonferroni correction). A chi-square test (where group X had prior medical diseases) showed that the frequency of prior medical diseases differed by group ( $X^2(2, n = 892) = 45, p < .001$ ), and that patients with delirium, as well as patients with other diagnoses were significantly more likely to have had prior medical diseases ( $p < .05$ , post hoc analyses with Bonferroni correction). A chi-square test (where group X were transferred to the ICU) showed that the frequency of consequent ICU transfer differed by group ( $X^2(2, n = 892) = 64.29, p < .001$ ), and that patients with delirium were significantly more likely to have had to be transferred to the ICU ( $p < .05$ , post hoc analyses with Bonferroni correction). A chi-square test (where group X were under consequent intubation) showed that the frequency of consequent intubation differed by group ( $X^2(2, n = 892) = 98.27, p < .001$ ), and that patients with delirium and other diagnoses were significantly more likely to be consequently intubated ( $p < .05$ , post hoc analyses with Bonferroni correction). A chi-square test (where group X had an oxygen requirement) showed that the frequency of oxygen requirement differed by group ( $X^2(2, n = 892) = 84.99, p < .001$ ), and that patients with delirium and other diagnoses were significantly more likely to require oxygen ( $p < .05$ , post hoc analyses with Bonferroni correction). A chi-square test (where group X had clinical outcomes) showed that clinical outcomes differed by group ( $X^2(4, n = 892) = 24.76, p < .001$ ), and that patients with delirium were significantly more likely to die during hospitalization ( $p < .05$ , post hoc analyses with Bonferroni correction). The comparison of the sociodemographic and clinical characteristics of all patients is shown in Table 3.

Nineteen of 34 patients with delirium (56 %) and four of the 55 patients with a psychiatric diagnosis (7.4 %) had previous neuropsychiatric conditions.

#### 4. Discussion

In the present study, psychiatric consultations requested by patients

**Table 2**  
Psychiatric diagnoses after consultations.

| Final psychiatric diagnosis | n = 89 | %    |
|-----------------------------|--------|------|
| Delirium                    | 34     | 38.2 |
| Adjustment disorder         | 24     | 27.0 |
| Depressive disorder         | 17     | 19.1 |
| Anxiety disorder            | 10     | 11.2 |
| Sleep disorder              | 3      | 3.4  |
| Other                       | 1      | 1.1  |

hospitalized with a probable or confirmed diagnosis of COVID-19 in pandemic wards in a tertiary hospital were retrospectively examined.

In this study, we found that a psychiatric consultations were requested by 10.0 % of patients hospitalized in COVID-19 wards. In studies conducted in Europe (Huysse et al., 2001; Rothenhäusler et al., 2001), and Turkey (Özmen and Aydemir, 1993; Aslan ve ark., 2003; Canan et al., 2008; Ekmekçi Ertek and Öztürk, 2019), the rate of requesting psychiatric consultations for inpatients in general hospital wards varies between 1.2 % and 2.8 %. It can be said that this rate is high. However, there are studies reporting that the prevalence of psychiatric disorders in inpatients varies between 26.1 % and 38.7 % (Silverstone, 1996; Arolt et al., 1997; Martucci et al., 1999; Hansen et al., 2001).

According to the results of our study, it has been observed that the most common reasons for requesting psychiatric consultations were psychomotor agitation/restlessness, impairment of sleep, evaluation of prior psychiatric treatments, anxiety/fear and suicidal ideation, respectively. In general, it can be said that the reasons for requesting consultations in the present study (although the frequency and order varied) did not differ from the results of previous studies of patients in general hospital wards (Göktaş et al., 2006; Wilson et al., 2012; Eser et al., 2018). However, a small number of studies conducted with patients with COVID-19 found that these complaints were more common in patients after psychiatric evaluations (Helms et al., 2020; Iqbal et al., 2020). In a recent study investigating psychiatric morbidity in patients with COVID-19 (Iqbal et al., 2020) who were referred to the consultation-liaison psychiatry service, it was reported that the most common symptoms of patients were insomnia (70 %), anxiety (64 %), agitation (50 %) and depressive mood (42 %). Similarly, the study conducted by Xie et al. (2020) looked at patients who were experiencing the first episode of their mental disorders and were hospitalized with or without a diagnosis of COVID-19. The study went onto compare the two groups to show that the most common symptoms in those diagnosed with COVID-19 were insomnia (72 %), aggressive behaviors (64.0 %), delusion (40.0 %), and severe anxiety (36.0 %).

In the present study, the most common diagnosis made after the psychiatric consultations was delirium. Delirium is a syndrome of acute brain failure that is common in medical wards (Inouye et al., 2014; Thom et al., 2019), and is a well-known complication of respiratory diseases such as pneumonia (O'Hanlon and Inouye, 2020). Knowledge about the neuroinvasive character of SARS-CoV-2 (Iadecola et al., 2020; Kotfis et al., 2020; Li et al., 2020; Orsini et al., 2020) and the neuropsychiatric consequences of the disease it causes (Mao et al., 2020; Orsini et al., 2020; Rogers et al., 2020) increases with every day. In this context, it can be said that it is no surprise that COVID-19 causes delirium. To our knowledge, in the only study evaluating psychiatric consultations in COVID-19 wards, Iqbal et al. (2020) reported that delirium was 26 % in a sample of 98 % males with a mean age of 43.9. In our study, the rate of delirium diagnosis was higher in patients who requested a consultation (38.2 %). This may be due to the higher mean age of our sample (55.6). Studies that examined the geriatric population hospitalized with COVID-19, reported that the delirium rate was between 26.7 % (Annweiler et al., 2020), 27.5 % (Marengoni et al., 2020) and 42 % (McLoughlin et al., 2020). In another recent study in which 707 patients over the age of 50 were evaluated, the delirium rate was found to be 33 % (Garcez et al., 2020). The results of our study show that more than half of the delirium patients (56 %) had a neuropsychiatric diagnosis and almost all of them (97 %) had a chronic medical disease. It is known that these two conditions predispose the development of delirium. In hindsight, it can be said that delirium develops at high rates during COVID-19, and that clinicians should focus more on this situation (Garcez et al., 2020; O'Hanlon and Inouye, 2020).

We found that psychiatric consultations were requested by patients hospitalized in COVID-19 wards, mostly within the first three days of their admission. Bianchetti et al. (2020) found that the most frequent symptom of onset was delirium (67 %) among dementia patients

**Table 3**

Comparison of the sociodemographic and clinical characteristics of patients with delirium, patients with other psychiatric diagnoses, and all other patients.

| Characteristics<br>n (%)                          | Patients with<br>delirium<br>n=34 | Patients with other psychiatric diagnoses<br>n=55 | Patients with no<br>consultation<br>n = 803 | Chi square/<br>F | df | p                   |
|---|-----------------------------------|---|---|------------------|----|---------------------|
| Age   | 73.8 (SD = 15)                    | 55.5 (SD = 13.7)                                  | 54.9 (SD = 16.2)                            | 22.64            | 2  | < .001 <sup>c</sup> |
| Males   | 14 (41.2)                         | 22 (40.0)   | 376 (46.9)                                  | 1.34             | 2  | .51                 |
| Presence of chronic medical diseases <sup>a</sup> | 32 (97 %)                         | 38 (70.4)   | 362 (45.1)                                  | 45.00            | 2  | < .001              |
| Prior neuropsychiatric diagnosis <sup>b</sup>     | 19 (56)                           | 4 (7.5)   | 28 (3.5)                                    | 135.91           | 2  | < .001              |
| Hospital stay length (days)                       | 17.8 (SD = 11)                    | 12.9 (SD = 10)                                    | 7.9 (SD = 5.9)                              | 47.60            | 2  | < .001 <sup>d</sup> |
| Oxygen treatment                                  | 38 (70.4)                         | 30 (88.2)   | 216 (28.9)                                  | 84.99            | 2  | < .001              |
| Consequent ICU transfer                           | 18 (52.9)                         | 12 (21.8)   | 76 (9.5)                                    | 64.29            | 2  | < .001              |
| Consequent mechanic ventilation<br>usage          | 14 (41.2)                         | 11 (20.0)   | 30 (3.7)                                    | 98.27            | 2  | < .001              |
| Death during hospitalization                      | 9 (26.5)                          | 3(5.5)  | 50 (6.2)                                    | 20.8             | 2  | < .001              |
| Clinical outcomes                                 |                                   |   |   | 24.26            | 4  | < .001              |
| Recovered   | 20 (58.8)                         | 48 (87.2)   | 698 (87.1)                                  |                  |    |                     |
| Deceased  | 9 (26.5)                          | 3 (5.5)   | 50 (6.2)                                    |                  |    |                     |
| Transferred to another unit                       | 2 (5.9)                           | 2 (3.6)   | 53 (6.6)                                    |                  |    |                     |

ICU = Intensive care unit.

<sup>a</sup> Hypertension, diabetes mellitus, asthma bronchiale, chronic obstructive pulmonary disease, cancer and other diseases; <sup>b</sup>dementia, depression, cerebrovascular event and other diseases; <sup>c</sup>patients with delirium > patients with other psychiatric diagnoses, and patients with no consultation; <sup>d</sup>patients with delirium > patients with other psychiatric diagnoses > patients with no consultation.

diagnosed with COVID-19. Similarly, Poloni et al. (2020) emphasized that delirium may be representative of an early-phase clinical feature of COVID-19, especially in elderly patients. In this context, it becomes clear that clinicians should be alert of the fact that delirium may develop, especially in the first days of hospitalization.

Delirium is known to be a negative prognostic predictor (Inouye et al., 2014). Early studies indicated that delirium in elderly patients with COVID-19 was strongly associated with in-hospital mortality (Garcez et al., 2020; Marengoni et al., 2020). We found that delirium patients stayed longer in hospitals, were transferred to the ICU more frequently than other patients, and needed more oxygen treatment and mechanical ventilation. Their mortality rates were also higher during hospitalization. Given these results, frequent delirium screenings are of great importance for the assessment and management of COVID-19 (O'Hanlon and Inouye, 2020).

In our study, the most common diagnosis made after the psychiatric consultations, following delirium, were adjustment disorder, depressive disorder and anxiety disorder, respectively. The COVID-19 pandemic can trigger a range of stressors related to an individuals' health status. Some of these may include being in quarantine, unemployment, financial difficulties and stigma, that can lead to adaptation difficulties in many suffering from the disease. Unsurprisingly, this complex array of stressors can lead to psychiatric problems such as adjustment disorder, depression, and anxiety (Kazlauskas and Quero, 2020; Lotzin et al., 2020; Mazza et al., 2020; Xie et al., 2020).

One of the important results of our study was that comorbid medical diseases, the need for oxygen treatment and mechanical ventilation were significantly higher in patients with psychiatric disorders than patients without. Considering that patients with adjustment disorder (24/55, 43.6 %) and anxiety disorder (10/55, 18.2 %) are 61.8 % of all psychiatric patients, their oxygen requirement may be expected to be higher due to the distress triggered by COVID-19 in this group. However, the fact that patients with a psychiatric diagnosis stay in the hospital for a longer period of time compared to other patients, alongside the high intubation rates of these patients, indicates that the presence of psychiatric diseases has a negative effect on the course of COVID-19. Based on this, it can be said that patients with psychiatric disorders have a worse course of COVID-19 and that clinicians should be wary of psychiatric disorders in the fight against COVID-19.

This study had several limitations. Firstly, data collection was limited to information obtained from medical file records and electronic medical records, due to the retrospective nature of the study. When saving the documents, it is noteworthy that there may have been incomplete and/or erroneous records. Secondly, the fact that physicians

have an intense and stressful work environment, especially during the height of COVID-19, may have caused patients' psychiatric complaints to be overlooked and some patients with less severe psychiatric disorders to have been ignored. It should be kept in mind that this may have caused instances of measurement bias in the outcome assessments. Finally, the data were collected from a single tertiary hospital in Istanbul and, the majority of the patients were those living in urban areas. It is important to note that all of these circumstances limit the generalizability of these findings.

## 5. Conclusion

It can be said that various psychiatric disorders develop in patients who are hospitalized for COVID-19, as a result of both the effects of the disease on the central nervous system and the psychosocial problems caused by the disease. After the psychiatric consultations, we found that the most common diagnosis was delirium, and that the development of it negatively affected the prognosis of COVID-19. On the other hand, we observed that other psychiatric disorders such as adjustment disorder, depression and anxiety were common in patients hospitalized in COVID-19 wards and were associated with a more severe course of COVID-19. Our findings indicate that the presence of neuropsychiatric disorders in patients hospitalized with COVID-19 may be associated with the negative outcomes of the disease. In this context, our study is important as it draws attention to the fact that in-patients with COVID-19 should be evaluated frequently for neuropsychiatric disorders resulting from the disease. It is clear that consultation-liaison psychiatry services will make important contributions to combating the global COVID-19 pandemic.

## Financial disclosure

None.

## Ethical statement

This study was approved by the Istanbul University - Cerrahpaşa, Cerrahpaşa Medical Faculty's Ethical Committee.

## Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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None.

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