Evaluation of Early Cognitive Functions in Patients With COVID-19 Infection

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Abstract: In December 2019, some pneumonia cases emerged in Wuhan, China. It was named as coronavirus 2019 (COVID-19) by the World Health Organization. Patients developed anxiety and sleep problems after treatment. Patients with confirmed COVID-19 (n = 57) admitted to our study and whose treatment was completed 3 months ago were included in the study. This is a case-control study, and 22 patients included the control group. We found statistical significance between the average score of Beck anxiety and Pittsburgh Sleep Quality Index (p = 0.03, p = 0.01). In our study, we investigated the psychological conditions that may occur in the postacute COVID-19 period. We recommend that patients should be directed to appropriate clinics for rehabilitation. Clinicians must be aware that prompt and correct diagnosis with careful management is essential for recovery.

Key Words: COVID-19, cognitive functions, depression

In December 2019, some unknown pneumonia cases emerged in Wuhan, Hubei, China. Patients’ clinical presentations were resembling viral pneumonia. It was named as coronavirus 2019 (COVID-19) by the World Health Organization (WHO) (Lai et al., 2020). The worldwide spread of COVID-19 led the WHO to declare the COVID-19 pandemic on March 11, 2020.

Patients diagnosed with this disease must be treated in isolation. Furthermore, anxiety, depression, and sleep problems may occur after isolation treatment. Developing anxiety caused decreasing immunity and other physiological events (Rajeswari and SanjeevaReddy, 2019). Studies suggest that patients with COVID-19 experience depression, anxiety, and insomnia (Rogers et al., 2020). Except for isolation treatment, the uncertainty of the future, stigma, and traumatic memories of severe illness experienced by patients during COVID-19 are significant psychological stressors of psychopathological outcome (Brooks et al., 2020; Carvalho et al., 2020).

On the other hand, coronaviruses can affect the central nervous system (CNS) directly or indirectly via an immune response (Wu et al., 2020). Postmortem studies showed that coronaviruses are neurotropic and can cause neurological diseases (Desforges et al., 2019). We consider that postacute COVID-19 patients are likely to have highly psychiatric conditions. In our study, we evaluated factors such as anxiety, depression, and sleep quality disorder in COVID-19 patients, as well as their relationship with indirect cognition, and directly examine the relationship of COVID-19 with cognition.

METHODS

Design and Participants
This study is approved by the local ethics committee.

Patients with confirmed COVID-19 (n = 57) were admitted to Medicana Hospital, and whose treatment was completed 3 months ago were included in the study between November 2020 and March 2021. This study is a case-control study, and 22 patients were included the control group. Patients were informed about the study, and written informed consent was obtained from all patients.

Data Collection and Statistical Analysis
The study population included patients aged 18 or older with a positive diagnosis of COVID-19. Thirty-one patients were men, and 26 patients were women. For COVID-19–positive diagnosis, we used PCR-positive. Sociodemographic and clinical data were collected using a data extraction form, including age, sex, psychiatric history, and baseline inflammatory markers. Baseline inflammatory markers during acute COVID-19 were extracted from electronic documents charts: C-reactive protein (CRP), neutrophil and lymphocyte counts, D-dimer levels, and ferritin levels.

Current sleep quality and psychological assessments were measured using the following questionnaires: Beck Anxiety Inventory (a total score of 0–7 is interpreted as a “minimal” level of anxiety, 8–15 as “mild,” 16–25 as “moderate,” and 26–63 as “severe”), Beck Depression Inventory (scores from 0 through 9 indicate no or minimal depression; scores from 10 through 18 indicate mild to moderate depression; scores from 19 through 29 indicate moderate to severe depression; and scores from 30 through 63 indicate severe depression), Pittsburgh Sleep Quality Index (score of five or more indicates poor sleep quality; the higher the score, the worse the quality), and Montreal Cognitive Assessment (cutoff point is 26).

Statistical analyses were performed using SPSS software (Version 22 for Windows; SPSS Inc, Chicago, IL). Descriptive analysis was conducted on the basic characteristics of residents by frequency and composition ratio, and compared their differences by basic situation and mental health statuses among various demographics by Mann-Whitney U-test and correlation analysis. The data were tested for normal distribution. A value of p < 0.05 (two-tailed) was considered statistically significant.

RESULTS
All patients completed the study without data leakage. The demographic and clinical characteristics of the 57 patients (53.94 years; 31 males and 26 females) and 22 healthy controls (54.27 years; 9 males and 13 females) are outlined in Table 1. When the demographic data of the patients were evaluated, we found no significant difference between the control group and the patient groups in terms of age, sex, smoking, and education.

In the patient group, B-anxiety and B-depression mean scores were 12.78 ± 10.12 and 10.87 ± 10.67, respectively. The average score of Beck depression in the two groups was not statistically significant (p = 0.18). We found a statistical significance between the average score of Beck anxiety and Pittsburgh Sleep Quality Index (p = 0.03, p = 0.01). No significant difference was observed between the groups in terms of cognition (p = 0.908). Our test results are outlined in Table 2. No significant difference was observed when the correlation analysis of Montreal Cognitive Assessment (MoCA)
value with inflammatory markers was performed in patients ($p > 0.05$ for all inflammatory markers).

**DISCUSSION**

In our study, we evaluated anxiety, depression, sleep disorders, and cognitive dysfunctions in patients with postacute COVID-19 patients. As a result, we found a statistically significant increase in anxiety and sleep disorders compared with the normal population. In our study, we found no significant change in cognitive dysfunction between the control and the patient groups. Considering that COVID-19 has systemic effects rather than a disease that only involves the lungs, we think that patients may have anxiety and sleep disorders, and it will be beneficial to arrange their treatment in this direction in the early period.

Studies have shown that coronavirus diseases not only affect physical health but also human psychology. For example, during the SARS pandemic, anxiety and depression increased and sleep was affected in the general population. Some previous studies showed that respiratory infections and tuberculosis assumed disability in daily life, respectively (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018; Murray et al., 2018).

In patients with COVID-19, older age and severe disease were major factors of disability and mortality (Zhou et al., 2020a). However, anxiety and sleep disturbances that develop in patients cause prolonged hospital stay and negatively affect mortality. In a meta-analysis, it was found that many COVID-19 patients experience depression, anxiety, and/or sleep disturbances. The cause of these psychiatric disorders is multifactorial. One major factor is a lack of contact with families (Dubey et al., 2020). Others are isolation and stigma of disease. These problems continue in the posttreatment period (Guan et al., 2020; Zhou et al., 2020a). Therefore, we investigated the psychological conditions that may continue in post-COVID period COVID-19 patients. We found a significant increase in sleep disturbance and anxiety in the follow-up after COVID-19.

Clinical symptoms are associated with inflammatory factor storms and elevated CRP, ferritin, D-dimer, fibrinogen, and lactate dehydrogenase levels in patients with COVID-19 (Zeng et al., 2020). In our study, we found that the aforementioned markers increased in the acute phase in most of our patients. COVID-19 changes peripheral immune cells and elicits a cascade of immune responses, finally resulting in a damaging cytokine storm (Yang et al., 2020). Several studies have shown that a critical role of inflammation was involved in the pathological process of mild cognitive impairment (Shen et al., 2020). However, we evaluated cognitive functions with the MOCA test in the post-COVID period, and we did not find any significant cognitive dysfunction in the patients. Also, we did not find a relationship between inflammatory markers and MOCA test.

Anxiety and depression may have a negative impact on patient immune system (Leonard, 2001). Patients with depression may also have negative attitudes toward antiviral therapy, which may reduce their treatment adherence and recovery. The prevalence of depression among patients with SARS was 18%, 1 month after their discharge (Wu et al., 2005), and 15.6% at 30-month assessment after SARS outbreak (Mak et al., 2009). A new study in an isolation unit of a general hospital that examined the mental health status of 106 patients with COVID-19 early stage of the outbreak found a prevalence of depression of 49.06% (Zhao et al., 2020). In our study, we did not find a significant increase in depression in the postacute period in patients with COVID-19.

Cognitive dysfunction in patients with viral infection has been commonly reported in prior studies. Moreover, viral infection that involves the CNS and cardiopulmonary failure may be associated with neurologic sequelae, delayed neurodevelopment, and reduced cognitive functioning (Chang et al., 2007). In a recent study, it was found that there is a significant correlation between continuous attention function changes at presentation and CRP levels in COVID-19 patients (Zhou et al., 2020b).

Previous studies on mental health in the COVID-19 pandemic have been conducted in the general population and health professionals but not in the patient population. Our study is different from the others in terms of evaluating anxiety, depression, and sleep disorders in postacute stage COVID-19 patients. In our study, we found that the prevalence of anxiety in outpatients with COVID-19 was 48%, which is a substantial increase compared with prepandemic anxiety levels. On the other hand, we used MoCA test to evaluate the cognitive functions of the patients. Although no significant loss of cognition was observed in the post-COVID period, the mean MoCA level was found to be low because elderly patients were included in our control and patient groups.

**CONCLUSIONS**

Following the acute phase, health care services are planning rehabilitation strategies. Postacute COVID-19 refers to persistent symptoms 3 weeks after COVID-19 infection, whereas “chronic COVID” describes symptoms lasting more than 12 weeks (Halpin et al., 2021). COVID-19 will cause longer-term mental and physical health problems, work disability, and reduced quality of life in survivors. Because of that, the number of patients needing follow-up care and rehabilitation due to COVID-19 will be unprecedented. In our study, we investigated the psychological conditions that may occur in the postacute COVID-19 period. According to the results of our study, we recommend that patients should be directed to appropriate clinics for rehabilitation. Clinicians must be aware that prompt and correct diagnosis with careful management is essential for recovery.

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**DISCLOSURE**

The study is approved by the Ethics Committee of KTO Karatay University, Medical Faculty:

The author declares no conflict of interest.

This publication has not been presented or published anywhere else.

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**TABLE 1.** Demographic Features of Patients

| Control Group, $n = 22$ | COVID-19 Patients, $n = 57$ | $p$ |
|------------------------|-----------------------------|-----|
| Age 54.273 ± 13.932     | 53.946 ± 16.662             | 0.662 |
| Sex 5/22                | 9 female, 13 male           | 0.409 |
| Smoking 9/5             | 14/57                       | 0.733 |
| Education 9/4           | 9.947 ± 4.505               | 0.618 |

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**TABLE 2.** COVID-19 Infection's Effect on Sleep, Mood, and Cognition

|                      | Control Group | COVID-19 Patients | $p$   |
|----------------------|---------------|-------------------|-------|
| Beck Anxiety Inventory| 7.409 ± 4.2612| 12.789 ± 10.1291  | 0.031 |
| Beck Depression Inventory| 6.864 ± 4.6115| 10.877 ± 10.6772  | 0.183 |
| Pittsburgh Sleep Quality| 3.909 ± 2.1137| 6.561 ± 4.3178    | 0.010 |
| Index                | 19.091 ± 5.0982| 18.930 ± 6.2873   | 0.908 |

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