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Depression, Anxiety, Sleep Quality, and Biological Rhythms between Patients with COVID-19

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ABSTRACT

Objectives: This study aimed to explore depression, anxiety, sleep quality, biological rhythms, and risk factors related to taste and smell loss in COVID-19 patients.

Methods: This case-control study was conducted as a single-center study between January 1 and May 15, 2021. The study included COVID-19 patients and healthy adults as the control group. Depression Anxiety Stress Scale Short form (DASS-21), Biological Rhythms Assessment Interview in Neuropsychiatry, and Pittsburgh Sleep Quality Index (PSQI) were administered to the patients and control group.

Results: A total of 247 individuals (123 [49.7%] patients with COVID-19 and 124 [50.3%] control group) were included in the study. A total of patients with COVID-19 include 60 (48.7%) hospitalized-treated groups (HTG) and 63 (51.3%) home-treated groups (HOG). DASS-21 score, BRAIN score, and PSQI score in the patient group were higher than the control group (20.0 ± 11.5 vs. 8.8 ± 4.8 , $p < 0.001$ for DASS-21 score, 40.1 ± 8.6 vs. 33.4 ± 6.3 , $p < 0.001$ for BRAIN score, 5.2 ± 3.0 vs. 2.9 ± 1.5 , $p < 0.001$ for PSQI score). Anxiety score and PSQI score in the HTG were significantly higher than the HOG (7.4 ± 3.7 vs. 5.1 ± 4.2 , $p < 0.001$ for anxiety score, 5.8 ± 2.9 vs. 4.6 ± 3.0 , $p = 0.013$ for PSQI score). Age (Odds Ratio [OR]=1.038, 95% confidence interval [CI]=1.010–10.67, $p = 0.007$) and gender (OR=6.012, 95% CI=2.533–14.271, $p < 0.001$) were determined as risk factors for developing taste/smell loss in COVID-19.

Conclusion: It can be stated that patients with COVID-19 have a higher risk of developing mood disorders, irregularity in biological rhythms, and sleep disorders compared to the control group. In addition, age and gender variables are directly related to taste and smell disorders in COVID-19.

Keywords: Anosmia, biological rhythms, COVID-19, depression, loss of taste



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INTRODUCTION

Coronavirus infections have played a role in neuropsychiatric disorders during and after Severe Acute Respiratory Syndrome (SARS) and Middle-East Respiratory Syndrome (MERS) pandemics.^[1] In a study carried out after SARS in the 1st month, about 35% of the patients had medium or severe levels of anxiety or depressive symptoms. As for longer-term studies, the prevalence of psychiatric disorders was determined as 33.3% in a survey carried out on the 30th month with 90 patients with SARS disease.^[2]

There are over 79% structural and genetic similarities between SARS-CoV-2 and SARS-CoV and over 50% between SARS-CoV-2 and MERS-CoV.^[3] During the coronavirus disease 2019

(COVID-19) pandemic, the third biggest coronavirus epidemic in the last two decades, relatively high anxiety, depression, post-traumatic stress disorder (PTSD), psychological distress, and stress frequency have been reported in the general public in eight countries.^[4] In a survey of patients with COVID-19, the frequency of patients who have received psychopathological scores as follows: 28% of the patients in terms of PTSD, 31% in terms of depression, 42% in terms of anxiety, 20% in terms of obsessive-compulsive disorder, and 40% in terms of insomnia on the 1st month. In general, 56% of the patients received scores in the pathological range in at least one clinical dimension.^[5] In COVID-19, psychiatric effects emerge due to potential reasons such as the virus' direct impact on the central nervous system, the neuropsychiatric effects of systemic and central nervous system inflammation, contact isolation, and being stigmatized due to the contagious disease and function disorder related to having a severe illness.^[6]

The psychiatric results of infectious diseases vary.^[7] Some contagious diseases are related to sleep disorders. Infectious agents such as viruses and bacteria infect the central nervous system with the immune response developed against the infection or the direct effects of the pathogen and cause sleep disorders. Biological rhythms, also known as the circadian rhythm, express the cyclical variations in physiological and behavioral functions and consist of the daily sleep-wake cycle, hormonal metabolism, diet patterns, social anxiety, and ultradian and seasonal rhythms.^[8] Biological rhythm disorders mediated by lifestyle cause individuals to be more susceptible to various psychiatric disorders, including mood disorders such as unipolar and bipolar disorders. Anxiety and mood disorders are among the most common mental health problems in the general population of countries throughout the world.^[1] The number of studies on many complex connections between common anxiety and mood disorders and contagious viral diseases has increased in recent years.

In this study, it was aimed to explore depression, anxiety, sleep quality, biological rhythms, and risk factors related to taste and smell loss in COVID-19 patients.

METHOD

This case-control study was conducted as a single-centered multi-unit study in the Kafkas University Health, Application, and Research Hospital Clinics between January 1 and May 15, 2021. The study included patients who agreed to participate in the study and met the criteria of being over 18 years of age and who applied to COVID-19 clinics with symptoms such as fever, cough, weakness,

fatigue, joint pain, loss of taste or smell; and who were diagnosed with COVID-19 by PCR test, anamnesis, physical examination or radiological tests. Patients, some of whom received 5-day medication at home and some of whom were hospitalized, were interviewed within a maximum of 2 weeks after their treatment was completed. Afterward, healthy individuals with similar characteristics in terms of age and gender were included in the control group. Participants with a history of psychiatric illness or active psychiatric illness in clinical interviews and electronic medical records were excluded from the study.

Socio-demographic Data Form

The patient's demographic information was obtained: Age, gender, education level, marital status, regular income, income level, and smoking habit. In addition, the patients were asked whether they were hospitalized for treatment of COVID-19 and if they were hospitalized, its duration, whether other family members had COVID-19, whether they were aware of whom they contracted COVID-19, and whether any family members lost their lives due to COVID-19. Finally, the patients' general knowledge level about COVID-19 was measured through a survey consisting of five questions, and their habit of learning about COVID-19 was evaluated. Before the study, detailed anamnesis of the patients was conducted, and they were asked whether they were exposed to taste or smell loss symptoms.

Depression Anxiety Stress Scale (DASS-21)

DASS-21 is a 4-point Likert scale that evaluates the depression, anxiety, and stress dimensions of the individuals in the past week, which consists of seven items, each in clinical and non-clinical samples.^[9] The points that can be received from each sub-dimension range between 0 and 21, and as the points obtained from the sub-dimensions increase, the levels of depression, anxiety, or stress also increase. A validity and reliability study of the Turkish version of the DASS-21 Short Form was conducted.

Biological Rhythms Interview of Assessment in Neuropsychiatry (BRIAN)

BRIAN was developed to measure individuals' daily cyclic rhythm and functionality.^[10] The scale consists of 4 points Likert type 21 items. It has five subscales: sleep, activity, social, diet habits, and dominant rhythm patterns. The dominant rhythm pattern scores are not included in the total score when the total score is calculated. High scores express irregularities in the biological rhythm. The Turkish version of the scale was utilized in this study.

Pittsburgh Sleep Quality Index (PSQI)

PSQI consists of seven sub-components that evaluate subjective sleep quality, sleep latency, sleep duration, sleep disturbances, use of sleeping medication, and daytime dysfunction.^[11] The total score of the seven components is the total PSQI score. The self-report scale gives detailed information about the type and intensity of sleep quality and sleep disorders within the past month. The total score from the scale ranges between 0 and 21, and high values indicate that sleep quality is bad and sleep disorder level is high. A score of ≥ 5 shows that clinical sleep quality is significantly impaired. The Turkish version of the scale was utilized in this study.

The statistical analysis of the data obtained from the participants in this study was done with the Statistical Package for the Social Sciences software's version 22.0. In the descriptive analysis, frequency, percentage, mean, standard deviation, median, minimum and maximum were used. Kolmogorov–Smirnov test was to evaluate the normal distribution state of the data. In assessing the difference between the groups, a significance test for the difference between the two means (Student's t-test) was used for the continuous variables that achieved the parametric test assumption. The Mann–Whitney-U test was used for those not reaching the parametric test assumption. In the analysis of qualitative variables, the Chi-square test was used. In the correlation between the continuous variables, Pearson correlation analysis was used when two scales were parametric, and Spearman correlation analysis was used when one of the variables was non-parametric. The correlation coefficient (*r*) evaluation was ranked as "low" between 0 and 0.24; "medium" between 0.25 and 0.49; "good" between 0.50 and 0.74 and "very good" between 0.75 and 1.0. Binary logistic regression analysis was applied to the variables that showed significant differences in Chi-square analyses to determine the effect of independent variables on the dependent variables of taste or smell loss. A $p < 0.05$ was accepted as significant.

RESULTS

A total of 247 individuals and 123 (49.7%) patients with COVID-19 and 124 (50.3%) control group were included. The socio-demographic and COVID-19-related characteristics according to groups are summarized in Table 1.

According to the correlation analysis between the scales applied to all participants, a statistically significant positive correlation was observed between total DASS-21 and BRIAN scores ($r=0.526$, $p < 0.001$), total PSQI and BRIAN scores ($r=0.465$, $p < 0.001$), total PSQI and DASS-21 scores

($r=0.482$, $p < 0.001$). DASS-21, BRIAN, and PSQI scores according to groups are summarized in Table 2.

A total of 123 patients with COVID-19 include 60 (48.7%) hospitalized-treated groups (HTG) and 63 (51.3%) home-treated groups (HOG). When comparing HTG and HOG according to socio-demographic and COVID-19-related characteristics, there was no significant difference between the groups in terms of gender, marital status, and history of psychiatric disorders in the family ($p=0.951$, $p=0.103$, $p=0.235$, respectively). The mean age in the HTG was higher compared to the HOG (55.1 ± 14.4 vs. 33.9 ± 9.9 , $p < 0.001$). There was a significant difference between the groups regarding education level; the frequency of college or university graduates was 49 (77.8%) in the HOG and 10 (16.7%) in the HTG ($p=0.001$). There was also a significant difference between the HTG and HOG groups in terms of income level and who had a job with a regular income (6 [10.0%] vs. 37 [58.7%], $p=0.001$ and 34 [56.7%] vs. 56 [88.9%], $p=0.001$, respectively). The frequency of smoking was 3 (5.0%) in the HTG and 19 (30.2%) in the HOG ($p=0.001$). Moreover, there were 33 (55.0%) in the HTG and 10 (15.9%) in the HOG with comorbid chronic diseases ($p=0.001$). In terms of characteristics related to COVID-19, in terms of time spent on COVID-19, 40 (66.6%) in HTG and 25 (39.6%) in HOG spent 1 h or more ($p=0.004$). In addition, in terms of COVID-19 knowledge levels, 40 (66.7%) in HTG and 57 (90.5%) in HOG were found to have good to very good knowledge levels ($p=0.861$). There was no significant difference between the groups in terms of having family members with COVID-19 and losing family members due to COVID-19 (36 [60.0%] in the HTG vs. 35 [55.6%] in the HOG, $p=0.618$ and 7 [11.7%] in the HTG and 8 [12.7%] in the HOG, $p=0.861$, respectively).

Among the DASS-21 subscales, stress subscale scores were 7.6 ± 3.7 in the HTG and 7.8 ± 4.7 in the HOG, anxiety subscale scores were 7.4 ± 3.7 in the HTG and 5.1 ± 4.2 in the HOG, depression subscale scores were 6.3 ± 3.9 in the HTG and 6.1 ± 4.7 in the HOG ($p=0.782$, $p < 0.001$, $p=0.548$, respectively). DASS-21, BRIAN, and PSQI scores in the home-treated group and HTG of COVID-19 patients are summarized in Table 3.

There was 67 (54.4%) of the patient group in the study that had loss of taste or smell. The group's mean age with taste or smell loss was lower than those without taste or smell loss (40.6 ± 15.9 vs. 48.6 ± 15.7 , $p=0.006$). The frequency of females in the group with taste or smell loss was considerably higher than those without taste or smell loss (42 [62.7%] vs. 13 [23.2%], $p < 0.001$). The number of smokers was 54 (80.6%) in the group with taste or smell loss and 47

Table 1. Socio-demographic and COVID-19-related characteristics according to groups

	Patient Group (n=123)	Control Group (n=124)	p
Age (years)	44.3±16.2	42.2±13.0	0.267*
Gender			
Female	55 (44.7)	60 (48.4)	0.652 [†]
Male	68 (55.3)	64 (51.6)	
Education Level			
Other (not educated or have other courses)	13 (10.6)	12 (9.7)	<0.001 [†]
Primary	30 (24.4)	2 (1.6)	
High-school	21 (17.1)	7 (5.6)	
College or university	59 (48.0)	103 (83.1)	
Marital Status			
Single	35 (28.5)	67 (54.0)	<0.001 [†]
Married	88 (71.5)	57 (46.0)	
Income Level			
<2800 TL	17 (13.8)	8 (6.5)	0.025 [†]
2800-8000 TL	63 (51.2)	54 (43.5)	
>8000 TL	43 (35.0)	62 (50.0)	
A regular job with an income			
Yes	90 (88.9)	34 (27.4)	<0.001 [†]
No	33 (26.8)	90 (72.6)	
Smoking			
Yes	22 (17.9)	54 (43.5)	<0.001 [†]
No	101 (82.1)	70 (56.5)	
Presence of any psychiatric illness in first- and second-degree relatives			
Yes	35 (28.5)	23 (18.5)	0.092 [†]
No	88 (71.5)	101 (81.5)	
Additional Diseases			
Yes	43 (35.0)	28 (22.6)	0.045 [†]
No	80 (65.0)	96 (77.4)	
Time spent per day for COVID-19 disease			
Less than 1 h	58 (47.2)	90 (72.6)	<0.001 [†]
1–2 h	53 (43.1)	25 (20.2)	
3 h or more	12 (9.8)	9 (7.3)	
COVID-19 knowledge level			
Very bad or bad	10 (8.1)	6 (4.8)	0.347 [†]
Medium	16 (13.0)	16 (12.9)	
Good	52 (42.3)	44 (35.5)	
Very Good	45 (36.6)	58 (46.8)	
Family members with COVID-19			
Yes	71 (57.7)	45 (36.3)	0.001 [†]
No	52 (42.3)	79 (63.7)	
Death of any family member due to COVID-19			
Yes	15 (12.2)	24 (19.4)	0.171 [†]
No	108 (87.8)	100 (80.6)	

TL: Turkish liras.

Data is presented as mean±standard deviation and n (%).

*T-test in independent groups, [†]Chi-square test.

Table 2. DASS-21, BRIAN, and PSQI scores according to groups

	Patient Group (n=123)	Control Group (n=124)	p
Total stress sub-scale score	7.7±4.2	3.6±2.3	<0.001*
Total anxiety sub-scale score	6.2±4.2	2.9±2.2	<0.001*
Total depression sub-scale score	6.2±4.3	2.3±1.7	<0.001*
Total DASS-21 score	20.0±11.5	8.8±4.8	<0.001*
Total sleep sub-scale score	13.0 (1.0–20.0)	9.0 (1.0–16.0)	<0.001†
Total social sub-scale score	7.0 (4.0–16.0)	9.0 (4.0–16.0)	0.477†
Total activity sub-scale score	11.0 (5.0–20.0)	7.0 (5.0–19.0)	<0.001†
Total diet sub-scale score	8.0 (4.0–16.0)	8.0 (4.0–16.0)	0.280†
Total BRAIN score	40.1±8.6	33.4±6.3	<0.001*
Total dominant rhythm sub-scale score	6.0 (3.0–12.0)	6.0 (3.0–12.0)	0.194†
Subjective sleep quality	1.0 (0.0–3.0)	1.0 (0.0–3.0)	<0.001†
Sleep latency	0.0 (0.0–3.0)	0.0 (0.0–3.0)	<0.001†
Sleep duration	0.0 (0.0–3.0)	0.0 (0.0–3.0)	0.076†
Habitual sleep efficiency	0.0 (0.0–3.0)	0.0 (0.0–3.0)	0.017†
Sleep disturbances	0.0 (0.0–3.0)	0.0 (0.0–3.0)	<0.001†
Use of sleeping medication	0.0 (0.0–3.0)	0.0 (0.0–3.0)	0.338†
Daytime dysfunction	1.0 (0.0–3.0)	1.0 (0.0–3.0)	<0.001†
Total PSQI score	5.2±3.0	2.9±1.5	<0.001*

BRAIN: Biological rhythms assessment interview in neuropsychiatry; DASS-21: Depression anxiety stress scale short form; PSQI: Pittsburgh sleep quality index. Data is presented as mean±standard deviation and median (min-max).

*Independent group t-test, †Mann Whitney U test.

Table 3. DASS-21, BRIAN, and PSQI scores in the home-treated group and hospitalized-treated group of COVID-19 patients

	Home-treated group (n=63)	Hospitalized-treated group (n=60)	p
Total DASS-21 score	18.9±12.7	21.3±10.1	0.242*
Total sleep sub-scale score	12.0 (5.0–20.0)	9.0 (5.0–20.0)	0.003†
Total social sub-scale score	6.0 (4.0–16.0)	9.0 (4.0–14.0)	0.006†
Total activity sub-scale score	11.0 (5.0–20.0)	9.0 (5.0–19.0)	0.703†
Total diet sub-scale score	7.0 (4.0–16.0)	9.0 (4.0–13.0)	0.028†
Total BRAIN score	42.1±9.1	37.9±7.5	0.007*
Total dominant rhythm sub-scale score	8.0 (3.0–12.0)	5.0 (3.0–12.0)	0.001†
Subjective sleep quality	1.0 (0.0–3.0)	1.0 (0.0–3.0)	0.145†
Sleep latency	0.0 (0.0–3.0)	0.0 (0.0–3.0)	0.344†
Sleep duration	0.0 (0.0–3.0)	0.0 (0.0–3.0)	0.001†
Habitual sleep efficiency	0.0 (0.0–3.0)	0.0 (0.0–3.0)	0.199†
Sleep disturbances	0.0 (0.0–3.0)	0.0 (0.0–3.0)	0.001†
Use of sleeping medication	0.0 (0.0–3.0)	0.0 (0.0–3.0)	0.435†
Daytime dysfunction	1.0 (0.0–3.0)	1.0 (0.0–3.0)	0.187†
Total PSQI score	4.6±3.0	5.8±2.9	0.013*

BRAIN: Biological rhythms assessment interview in neuropsychiatry; DASS-21: Depression anxiety stress scale short form; PSQI: Pittsburgh sleep quality index. Data is presented as mean±standard deviation and median (min-max).

*Independent group t-test, †Mann Whitney U test.

(83.9%) in those without taste or smell loss ($p=0.807$). The number of people having another chronic disease was 47 (70.1%) in the group with taste or smell loss and 33 (58.9%) in those without taste or smell loss ($p=0.267$). Among the scale scores, only DASS-21's depression subscale score in the group with taste or smell loss was significantly higher than those in the group without taste or smell loss (7.1 ± 4.6 vs. 5.1 ± 3.9 , $p=0.014$).

Logistic regression analysis was performed to investigate possible predictors of the patient group's taste or smell loss risk. The model consisted of age, gender, and mean score on the depression subscale of the DASS-21. The model, including all predictors, was statistically significant ($\chi^2=31.21$, $p<0.001$). The factors related to taste or smell loss are summarized in Table 4 (Cox and Snell $R^2=22.4\%$ and Nagelkerke $R^2=36.3\%$).

DISCUSSION

This study aimed to explore depression, anxiety, sleep quality, biological rhythms, and risk factors related to taste and smell loss in COVID-19 patients. According to the results of this study, it can be stated that individuals with COVID-19 have a higher risk of developing mood disorders and impairments in their biological rhythms and sleep quality than the control group. In addition, it can be stated that patients in the HTG, in other words, patients with severe symptoms, are at greater risk in terms of anxiety disorder and impairment in sleep quality than patients without severe symptoms. This study found that impairment in the sense of taste or smell in COVID-19 is seen more frequently in younger people and females. In addition, depression scores were significantly higher in individuals with taste or smell loss.

In a meta-analysis, depression, anxiety, and sleep disturbance prevalence in COVID-19 patients was reported as 45%, 47%, and 34%, and in the general population as 33.7%, 31.9%, and 20.1%, respectively.^[12] In this study, the

scores related to depression, anxiety, and sleep quality impairment in the patient group were higher than the control group, similar to the literature. In addition, biological rhythm irregularity was higher in the patient group than in the control group in this study. Therefore, it can be suggested that biological rhythm irregularity contributes to the psychiatric symptoms in the patient group as well. COVID-19 patients are expected to be exposed to a significant mental disorder wave.^[13] In an extensive study carried out with 62,354 COVID-19 patients, 18.1% were diagnosed with a psychiatric disorder on the 14th and 90th days after the disease. Furthermore, this risk was found to be much higher in comparison to influenza and other respiratory tract viruses. COVID-19 has become a condition that triggers adverse psychological effects that can increase individuals' anxiety, depression, and stress levels depending on the damage caused by the disease.^[14] In this study, the depression, anxiety, and stress total and sub-scale score means were significantly higher than the control group, similar to the literature.

Accompanying severe illnesses can be shown as a contributing factor to increasing the prevalence of depression in COVID-19.^[12] In this study, the frequency of chronic diseases was significantly higher in the patient group than in the control group. In the literature, it has been found in some studies that an increase in the frequency of family members having COVID-19 is a situation that increases the risk of developing depressive symptoms in COVID-19 patients.^[15] Similar to this finding, the frequency of depressive symptoms in the patient group and the frequency of family members contracting COVID-19 were higher in the patient group than in the control group in this study. Another factor related to developing depression in COVID-19 patients might be the intensity of the disease. A significant difference in depression scores was not found in this study between the HTG with severe symptoms and the individuals without severe symptoms who received outpatient treatment. In another study, no relationship was found be-

Table 4. The factors related to taste or smell loss

	β	SE	Wald	p	Odds ratio	95%CI
Age	0.037	0.014	7.361	0.007	1.038	1.010-10.67
Gender						
Female/Male (ref)	1.794	0.441	16.541	<0.001	6.012	2.533-14.271
Total depression sub-scale score	-0.072	0.051	1.996	0.158	0.931	0.843-1.028
Constant	-2.457	0.841	8.533	0.003	0.086	

CI: Confidence interval; SE: Standard error.

Logistic regression analysis.

tween the severity of the disease and depression, similar to this finding.^[16] However, another study found that exposing the condition severely is related to depression among COVID-19 patients.^[15] In another study carried out about 1 month after having COVID-19, it was indicated that half of the participants reported at least a slight level of depression and common anxiety. However, medium and severe anxiety was reported at 10.4%, and severe depression at 19%. This study said that individuals with severe symptoms developed more intense psychiatric symptoms.^[17] Although depression scores were generally higher in the patient group than the control group in this study, there was no significant difference between the HTG and HOG in terms of depression scores. In this research, the reason for this result might be based on the differences in criteria for disease severity, the sample size, and the use of DASS-21 for depression.

In this study, the anxiety and stress sub-scale scores mean were found to be significantly higher in the patient group compared to the control group besides the depression sub-scale of the DASS-21 scale. The relationship between stressful life events and psychiatric illness is more vital than connecting with medical or physical conditions. The psychiatric outcomes of SARS-CoV-2 infection might emerge due to both the virus' immune reaction to itself and psychological stress factors such as social isolation, the psychological effect of a new, severe, and potentially deadly disease, and concerns about transmitting the infection to others and being stigmatized.^[5] Thirty-four percent of the hospitalized COVID-19 patients displayed anxiety symptoms, and it was found that the possibility of developing anxiety symptoms is higher in patients exposed to the disease severity.^[18] In addition, studies in the literature indicate that social isolation and loneliness also cause negative results in mental health.^[19] In this study, the patients' anxiety scores of the hospitalized group (patients with severe symptoms) were significantly higher than those of the home-treated group. Thus, these results were in line with the conclusions of the literature.

A family history of mood disorders increases the risk of mood disorders in individuals two to four times.^[20] Since there was no significant difference between the patient and control groups in terms of family history of psychiatric illness and none of the participants in this study had a history of psychiatric illness, it can be said that the significantly higher levels of depression, anxiety, and stress in the patient group compared to the control group are significantly related to COVID-19 and related factors.

It has been reported that viral infections affect circadian

rhythms. It is well-known that viruses reprogram the host cell metabolism, and this carries the potential to regulate circadian hour components.^[21] It has been reported that circadian impairment causes a hyperinflammatory condition along with more severe results after viral infections and that hypoxia, which is seen in cases such as COVID-19, can change body temperature, metabolic rate, the release of physiological variables such as cortisol and melatonin release, in other words, the biological rhythms.^[22] Therefore, it is considered that in COVID-19, both the change that takes place in individuals' sleeping, eating, and drinking habits and interpersonal relationships based on a new lifestyle caused by the pandemic and SARS-CoV-2 affecting the host cells infected during the infection in multiple ways and making itself a part of the physiological processes of the cells in the body, their immune response, and basic cellular mechanisms are conditions which can affect biological rhythms. In this study, the irregularity in the biological rhythms of COVID-19 patients was higher than in the control group. It was found that BRIAN subscales of sleep and activity dimensions' score medians were significantly higher in the patient group compared to the control group. Therefore, according to this study, there is more irregularity in the sleep and activity habits of individuals with COVID-19 compared to the control group. However, exposing the disease severity was not parallel to this study's impairment of biological rhythm. The total score means of the biological rhythm of the HOG without severe symptoms were significantly higher than those of the HTG. In the HTG, the sleep and diet sub-scale scores were lower or more regular than the HOG. It can be suggested that this was due to HTG patients' eating, drinking, activity, and sleep conditions continuing more routinely based on the rules of the hospitals. In addition, inadequate sleep quality has been defined as an essential and permanent symptom in individuals with COVID-19.^[23] In this study, the score medians indicating impairment in the sleep quality of COVID-19 patients were significantly higher than the control group. Similarly, there are findings in the literature about sleep disorders in COVID-19 patients and survivors of the disease. Mazza et al.'s study on 402 patients with COVID-19 was carried out in about the 1st month; symptoms related to sleep disorders were seen in about 40% of the participants.^[5] Similar to this study, in a study including COVID-19 patients without a previous psychiatric disorder, the frequency of sleep disorder diagnosis reached a high frequency of 9% at 90-day follow-up.^[13] In a study involving 85 hospitalized COVID-19 patients, sleep disturbances were reported in 54% of the participants.^[24] In a study involving 202 hospitalized COVID-19 patients, the risk of sleep disturbances was higher in patients with accompanying chronic illnesses.^[25] Similarly, the frequency

of impairment in sleep quality and accompanying chronic diseases in the HTG was also higher in this study. Another study found that impairments in sleep quality are related to depression, and there is no significant difference in terms of anxiety.^[26] In Wang et al.'s study involving 484 hospitalized COVID-19 patients, sleep disturbance prevalence was 42.8%, and high anxiety increases the risk of sleep disturbances.^[27] Similarly, the sleep disturbance and anxiety scores were significantly higher in both the patient and control groups and the HTG than the HOG in this study.

COVID-19 has become a condition that triggers adverse psychological effects that can increase individuals' anxiety, depression, and stress levels depending on the damage caused by the disease. Although depression scores were generally higher in the patient group than the control group in this study, there was no significant difference between the HTG and HOG in terms of depression scores. Our smaller sample size and use of DASS-21 for depression and anxiety may have given us different results.

This study also investigated the loss of taste or smell in COVID-19 patients and its association with different variables. The literature expresses that the senses of taste and smell impairments are caused by the direct damage given by the virus to the smell and taste receptors. Changes in the sense of smell are associated with the damage delivered by the virus to the olfactory bulbous or olfactory nerve. In contrast, the importance of taste impairments is related to the damage given to the ACE2 receptor located in the oral cavity.^[28] In this study, 54.4% of our patient group had a loss of taste or smell. In other studies, taste or smell loss was found in half of the COVID-19 patients or more.^[29] In this study, the group's mean age with taste or smell loss was younger than the group without taste or smell loss, and the frequency of females was higher in this group. The literature shows that taste or smell loss is seen more in younger ages and the female gender.^[30] In this study, when the other factors related to age and gender variables were fixed, this increased the risk of taste or smell loss in COVID-19 patients. Therefore, the result is in line with the literature.

There was no significant difference between groups with and without taste or smell loss regarding smoking and having another chronic illness in this study. Another study similarly determined no relationship between taste or smell loss in COVID-19 patients and smoking.^[31] In this study, the DASS-21 score means of the group with taste-smell loss was higher enough to be significant than those without taste-smell loss. There was no significant difference between the two groups regarding the mean of the anxiety sub-scale score. Still, the depression sub-scale score means

were significantly higher in the taste and smell loss group.

In a study involving COVID-19 patients, taste and smell loss were related to anxiety and depressive state.^[32] In this study, taste or smell loss was found to be only associated with the development of depressive symptoms. Our results might be attributed to the differences in the used surveys. Speth et al.'s study was a prospective study and applied their surveys to their patients during the period they had COVID-19 and the application of our surveys within 2 weeks after the disease.^[32]

The limitation of the study is that although this study has strength in having a well-matched control group with the patient group, our sample size may not be sufficient to evaluate the results of a pandemic such as COVID-19 adequately. Therefore, the results of this study cannot be generalized to all COVID-19 patients. In addition, this study evaluated the patients' conditions in the first 2 weeks after discharge. It lacked the long-term follow-up to present the progress of mental results.

CONCLUSION

As a result, there was higher depression, anxiety, stress levels, impairment in sleep quality, and irregularity in biological rhythms in individuals with COVID-19 compared to the control group in this study. In addition, individuals with severe symptoms of anxiety and sleep quality impairment levels were higher than those without severe symptoms. In addition, complaints of taste or smell loss in COVID-19 were related to the depression level. In COVID-19 patients, the age factor increased taste or smell loss 1.0 times, and the gender factor increased the taste or smell loss 6.0 times. COVID-19 inevitably has psychiatric consequences besides medical consequences. Therefore, it seems necessary to identify mental effects by approaching COVID-19 patients from a psychiatric point of view.

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