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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

COVID-19 HASTALARINDA PSİKİYATRİK BELİRTİLER VE BU BELİRTİLERLE İLİŞKİLİ FAKTÖRLER: PERİFERİK İNFLAMASYON BELİRTEÇLERİ BUNLARDAN BİRİ OLABİLİR Mİ ?

PSYCHIATRIC SYMPTOMS IN COVID-19 PATIENTS AND FACTORS ASSOCIATED WITH THESE SYMPTOMS: COULD PERIPHERAL INFLAMMATION MARKERS BE ONE OF THEM ?

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ÖZET

AMAÇ: Solunum semptomlarına ek olarak, COVID-19 hastalarında psikiyatrik semptomların da arttığına dair veriler bildirilmiştir. Bu çalışmada COVID-19 hastalarında görülen psikiyatrik belirtilerin ortaya konması amaçlanmıştır. Ayrıca bu psikiyatrik semptomlar ile periferik inflamatuar belirteçler arasındaki ilişki araştırılmıştır.

GEREÇ VE YÖNTEM: Hastalar çalışma için araştırıcılar tarafından özel oluşturulmuş "Görüşme Formları" ile değerlendirildi. Hastaların akut ve algılanan stres düzeylerini, depresyon ve anksiyete belirtilerini, durumsal ve genelleştirilmiş kaygı düzeylerini ve bu psikiyatrik belirtilerin farklı sosyal koşullardan nasıl etkilendiğini belirlemek için DSM-V Akut Stres Bozukluğu Ölçeği (ASBÖ); Algılanan Stres Ölçeği-10 (PSS-10); Durumluk-Sürekli Kaygı Envanteri (STAI-T/S); ve son olarak Hastane Anksiyete ve Depresyon Ölçeği (HADÖ) kullanıldı. İnflamatuar belirteçlerden D-dimer, fibrinojen, lenfositler, CRP (C-reaktif protein) ve ferritin seviyeleri dikkate alındı.

BULGULAR: Araştırmamıza 108 yatan, 31 ayaktan izlemi devam eden COVİD 19 hastası dahil edilmiştir. Yatan hastaların ASBÖ, STAİ Süreklilik Ölçeği ve HADS (Hastane Anksiyete Depresyon Skalası) puanları, ayaktan hastalara göre daha yüksek tespit edilmiştir. Kan testlerinde artmış fibrinojen seviyelerinin daha yüksek akut stres bozukluğu skorlarını öngördüğü bulunmuştur. HADS-Depresyon alt ölçeği ve fibrinojen düzeyleri de birbiriyle pozitif korelasyon gösterdiği bulunmuştur.

SONUÇ: Stres, depresyon ve anksiyete belirtileri COVID-19'a eşlik etmektedir. Ayrıca yüksek fibrinojen düzeyleri psikiyatrik belirtilerle ilişkili olabilir. Psikiyatrik belirtiler fiziksel hastalıklardan dolaylı olarak etkilenir. Tüm dünyada korku ve endişeye neden olan bir salgının bireylerde bağışıklık sistemini baskılayabileceğini ve baskılanan bağışıklık sisteminin dolaylı olarak enfeksiyonu daha da karmaşık hale getirebileceğini söyleyebiliriz.

ANAHTAR KELİMELER: COVID-19, Anksiyete, Depresyon İnflamasyon.

ABSTRACT

OBJECTIVE: In addition to respiratory symptoms, there have been reports of increased psychiatric symptoms in COVID-19 patients. In this study, it is aimed to reveal the psychiatric symptoms seen in COVID-19 patients. We also investigated the relationship between these psychiatric symptoms and peripheral inflammatory markers.

MATERIAL AND METHODS: The patients were evaluated with "Interview Forms" specially created by the researchers for the study. DSM-V Acute Stress Disorder Scale (ASDS); Perceived Stress Scale-10 (PSS-10); State-Trait Anxiety Inventory (STAI-T/S); and finally Hospital Anxiety and Depression Scale (HADS) were used to determine patients' acute and perceived stress levels, depression and anxiety symptoms, state and generalized anxiety levels, and how these psychiatric symptoms were affected by different social conditions. D-dimer, fibrinogen, lymphocytes, CRP (C-reactive protein) and ferritin levels were taken into account as inflammatory markers.

RESULTS: Our study included 108 inpatients and 31 outpatients with COVID-19. The ASDS, STAI State Scale, and HADS depression scale scores of inpatients patients were found to be higher compared to outpatient patients. Increased fibrinogen levels in blood tests were found to predict higher acute stress disorder scores. HAD-Depression subscale and fibrinogen levels were also found to be positively correlated with each other.

CONCLUSIONS: Stress, depression and anxiety symptoms accompany COVID-19. In addition, high fibrinogen levels may be associated with psychiatric symptoms. Psychiatric symptoms are indirectly affected by physical illnesses. We can say that a pandemic that causes fear and anxiety all over the world may suppress the immune system in individuals and the suppressed immune system may indirectly make the infection more complicated.

KEYWORDS: COVID-19, Anxiety, Depression , Inflammation.

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INTRODUCTION

The virus known as the New Coronavirus affected social life in an unprecedented way and was after named as COVID-19 infection (1-3). Besides the respiratory symptoms of COVID-19, neurological and psychiatric symptoms caused a concern among physicians (1, 2, 4).

Former studies on viral respiratory infectious diseases such as severe acute respiratory syndrome (SARS) have shown that survivors of these ailments had experienced both acute and chronic psychopathological symptoms afterwards (3, 5, 6). In 2003, a study on the psychiatric problems after one month from the recovery of SARS infection showed that most patients had symptoms of anxiety, depression and post-traumatic stress disorder (PTSD) (3, 7). After a different prospective study on SARS survivors, it had been reported that patients had symptoms of PTSD, depression, panic disorder and obsessive-compulsive disorder (OCD) (5, 8, 9).

There is also accumulating evidence that psychiatric symptoms increase in COVID-19 patients (1). A cross-sectional study conducted on 112 patients with COVID-19, indicated that compared to the healthy population, COVID patients showed higher levels of somatization, depression, anxiety, phobias, eating disorders and sleeping disorders (10). A study in which 103 COVID-19 patients were evaluated using online methods, demonstrated that patients showed more symptoms of depression, anxiety, and PTSD compared to non-COVID controls (11). In another study in which COVID-19 patients were evaluated by self-report at a one-month follow-up after treatment; symptoms were found to be 28% for PTSD, 31% for depression, 42% for anxiety, 20% for OCD symptoms, and 40% for insomnia. In general, 56% of the patients scored in the pathological interval in at least one psychiatric clinical diagnosis (12, 13).

In Wuhan, China, a study done with clinically stable patients who stayed in gyms and exhibition centers that had been converted to temporary quarantine hospitals, patients' self-reports showed that the prevalence of COVID-19-related PTSD symptoms were %96,2. The authors reported that this high rate may be due to the collection of data through self-reporting as well as social discrimination against COVID-19 patients, and the rapid transmission of negative news via social media (14).

With COVID-19 spreading actively worldwide, it is getting more evident that psychiatric symptoms are increasing in COVID patients (1). The psychiatric symptoms detected in COVID-19 patients can be caused by fear of the disease, worries about the deterioration of the general health of the individual as a result of infection, as well as economic and domestic concerns and social isolation. Therefore, it is very important to determine the impact of psychological stress on individuals with COVID-19. The psychological stress also has a biological component that may be related to the pathophysiological changes associated with COVID-19 (15). Individuals with mood (16) and anxiety-related disorders (17, 18) have high levels of pro-inflammatory cytokines compared to their healthy controls.

Although viral infections are associated with psychiatric symptoms as a direct result of the virus infection in the brain, they are often caused by the activation of a strong immune-inflammatory response (19, 20). Coronaviruses too, can cause psychopathological damage through an indirect immune response (8). The “cytokine storm” involved in the immune response to coronaviruses can cause psychiatric symptoms by accelerating neuroinflammation (21). In a study carried out with quarantined COVID-19 patients (mild cases) in China, it has been detected that CRP (C-reactive protein) levels -which is a peripheral inflammatory indicator- showed positive correlation with Patient Health Questionnaire total scores in patients who exhibits symptoms of depression. Moreover, the change from the onset CRP levels and Patient Health Questionnaire total scores were found negatively correlated. It has been reported that this is an indicator of improvement in depression symptoms (11). In another study executed with COVID-19 patients; Systemic Immune-Inflammation Index-which shows immune response and systemic inflammation based off peripheral lymphocyte, neutrophil, and platelet counts- was found positively related with depression and anxiety scores in follow-ups (12). In both studies, it was emphasized that there is a significant psychological distress in COVID-19 patients and that these symptoms may be related to the markers of inflammation

in patients, underlining the current views on the relationship between psychiatric diseases and inflammation. Considering the available data, psychiatric symptoms-especially stress symptoms (14, 22) have been found to be high in COVID-19 patients in previous studies, and it has been stated that these symptoms may be related to inflammation markers in patients.

The hypothesis of this study is that psychiatric symptoms in COVID-19 patients are associated with some peripheral inflammatory markers that show the severity of the disease. In our study, we aimed to investigate the psychiatric symptoms in COVID-19 patients who were hospitalized and in home-quarantine (mild cases). We identified clinical and social variables that may be associated with psychiatric symptoms. We also tried to detect the relationship between psychiatric symptoms and the levels of peripheral inflammatory markers found in blood tests of COVID-19 patients.

MATERIAL AND METHODS

In this study, patients with positive COVID-19 tests who are hospitalized or home-quarantined from Kutahya Health Sciences University Evliya Celebi State Hospital, Afyonkarahisar State Hospital and Sivas Yıldızeli Family Medicine Center were analyzed. The purpose of this study is to determine the levels of acute and perceived stress, the symptoms of depression and anxiety, the levels of situational and generalized anxiety, as well as to determine how these psychiatric symptoms are affected by different social conditions. In addition, it was aimed to decide whether there is a relationship between psychiatric symptoms, patients' other symptoms and the latest levels of inflammatory markers.

The study was conducted on voluntary patients who filled out the consent form, who were also literate and above 18-year-old. The patients who applied to the mentioned centers in the period of 30.09.20 - 30.12.20 were accepted to the study. The "Interview Form" prepared for this study was applied to the patients by the researchers, which investigated the socio-demographic information and the COVID-19 associated symptoms of the patients. In addition, "Severity of Acute Stress Symptoms-Adult" (Acute Stress Symptoms Scale) -which is a self-assessment scale- were applied to the patient. This scale was published by DSM-5 to assess the severity of acute stress symptoms. The Turkish validity and reliability study of Acute Stress Symptoms Scale was conducted (23).The Perceived Stress Scale-10 (PSS-10), a self-assessment scale developed to measure the degree of stress an individual perceives from certain situations in their life, was also used (24).The Turkish adaptation of PSS-10 was made in 2013 (25). Spielberg's forms of STAI-S (situational anxiety) and STAI-T (general anxiety), which measure the situational and continuing values of anxiety, were also given to patients (26). STAI-S and STAI-T were translated into Turkish by Öner and Le Compte (27) and used in research. The Hospital Anxiety Depression Scale (HADS), which is a self-report scale, was used to detect the symptoms of depression and anxiety of patients. HADS was developed by Zigmond and Snaith (28) to determine the risk of anxiety and depression in the patient, to measure the level of depression and anxiety, and to measure the change of the severity of these symptoms. The validity and reliability study of HADS in Turkey was conducted by Aydemir 1997. HADS is used to diagnose anxiety and depression in a short time and determine the risk group, not for diagnosing patients with physical illness and not on those who apply for primary health care. The D-Dimer, fibrinogen, lymphocyte, CRP and ferritin onset levels of the patients from the centers they were first admitted were also evaluated. These levels were significant in prognostic value for COVID-19 (29 - 31).

Ethical Committee

The study was approved by the Ethics Committee of Kutahya Health Sciences University (IRB:2020/15-11) and conducted in accordance with the Declaration of Helsinki.

Statistical Analysis

Statistical analyses were performed with IBM SPSS Statistics version 23. For continuous variables that did not show a normal distribution, the differences between the groups were evaluated with the Mann Whitney U test. Spearman's correlation analysis was used to determine the relationship between numerical variables. In order to detect the factors which can cause much more symptoms of Acute Stress, a logistic reg-

ression model was created with independent variables that were found to have a significant relationship in univariate analyses. In our study, those who scored higher than the Acute Stress Symptoms Scale average score were defined as having a High Level of Acute Stress Disorder. Also, p<0.05 was taken as the significance level.

RESULTS

108 inpatient and 31 outpatient COVID-19 patients were included in our study. When HADS threshold values were evaluated, 30 (20.5%) of the patients received scores above the threshold in terms of anxiety and 63 (43.2%) in terms of depression **(Table 1)**.

Table 1: Comparison of groups according to scale scores

	Group	n	Mean	Median	SD	p value
Acute Stress Symptoms Scale	Hospital-admitted inpatients	108	7.80	7.00	5.573	0,046
	Home-quarantined patients	31	5.419	6.00	4.319	
PSS Total	Hospital-admitted inpatients	108	15.49	16.00	7.760	0,59
	Home-quarantined patients	31	14.806	15.00	7.901	
STAI-S	Hospital-admitted inpatients	108	43.14	42.00	14.881	0,067
	Home-quarantined patients	31	37.516	36.00	12.355	
STAI-T	Hospital-admitted inpatients	108	46.09	43.00	11.519	<0,001
	Home-quarantined patients	31	36.194	34.00	9.382	
HADS Anxiety	Hospital-admitted inpatients	108	6.88	6.50	4.840	0,083
	Home-quarantined patients	31	5.00	4.00	3.941	
HADS Depression	Hospital-admitted inpatients	108	7.07	7.00	4.400	0,006
	Home-quarantined patients	31	4.742	3.00	4.434	

*p<0.05, PSS-10 : Perceived Stress Scale-10, STAI- S: State-Trait Anxiety Inventory- State , STAI-T: State-Trait Anxiety Inventory-Trait, HADS: Hospital Anxiety Depression Scale

It was found that the scores of Acute Stress Symptoms Scale, STAI-T and HADS-Depression subscale of hospitalized patients were statistically higher than those of home-treated patients (p=0.046, p=0.001, p=0.006, respectively). However, there was no statistically significant difference between the groups in terms of PSS, STAI-S and HADS-Anxiety subscale scores (p=0.59, p=0.067, p=0.083, respectively). Out of the 108 inpatients, 66 (61.11%) were male and 76 (70.37%) were married **(Table 2)**. The mean age of the inpatients was 43.3±14.7.

Table 2: Comparison of Acute Stress Symptoms Scale according to sex and marital status of the groups

		Acute Stress Symptoms Scale				
		n	Mean	Median	SD	p value
Sex	Male	66	6.95	6.000	05.59	0.027
	Female	42	9.12	8.00	5.343	
Marital Status	Married	76	7.80	7.00	05.29	0.627
	Single	32	7.78	6.000	6.293	

*p<0.05

It was found that the Acute Stress Symptoms Scale levels of women showed statistically higher significance than men (p=0.027) whereas there was no statistically significant difference between the groups according to the marital status variable (p=0.6279). In **Table 3**, Acute Stress Symptoms Scale scores are observed according to the current symptoms of patients hospitalized with a COVID-19 diagnosis.

Table 3: Evaluation of Acute Stress Symptoms Scale Scores According to The Symptoms of Patients Hospitalized with the Diagnosis of COVID-19

	Group	n	Mean	Median	SD	p value
Fever	No	93	7.67	7.00	5.551	0.487
	Yes	15	08.60	8.00	5.841	
General body pain	No	82	7.04	6.000	5.201	0.017
	Yes	26	10.19	08.50	6.12	
Cough	No	58	6.638	6.000	4.941	0.025
	Yes	50	09.14	07.50	6.00	
Dyspnea	No	84	07.36	6.000	05.56	0.055
	Yes	24	09.33	9.00	5.467	
Headache	No	85	07.25	6.000	5.226	0.059
	Yes	23	09.83	9.00	06.43	
Fatigue	No	80	07.31	6.000	5.483	0.093
	Yes	28	09.18	8.00	05.70	
Sore throat	No	89	07.31	6.000	5.147	0.133
	Yes	19	10.05	8.00	6.972	
Diarrhea	No	102	07.73	7.00	5.647	0.386
	Yes	6	9.00	08.50	4.336	
Chest pain	No	93	07.33	6.000	5.440	0.025
	Yes	15	10.67	10.00	5.715	
Other symptoms	No	106	07.75	7.00	5.610	0.288
	Yes	2	10.50	10.50	2.121	
The presence of at least one symptom	No symptom/ complaint	39	6.359	6.000	5.183	0.022
	At least one symptom present	69	08.61	8.00	05.66	

*p<0.05

It was found that the Acute Stress Disorder Scale levels of the patients who complained of body pain, cough and chest pain showed statistically higher significance compared to the

patients who did not describe these symptoms (respectively p=0.017 for p=0.025; p=0.025). In our study, it was found that Acute Stress Symptoms Scale scores were higher in patients with at least one symptom than in those without any (p=0.022). There was no significant statistical difference of Acute Stress Symptoms Scale scores between those with or without the symptoms of fever, shortness of breath, headache, fatigue, sore throat and diarrhea (p=0.487, p=0.055, p=0.059, p=0.093, p=0.133, p=0.386, respectively). Inpatient patients were divided into two groups as High Acute Stress Disorder Scale or Low Acute Stress Symptoms Scale according to whether they scored higher or lower than the average Acute Stress Symptoms Scale score determined in our study. The findings of the Logistic Regression Analysis which was applied in order to identify the predictors of obtaining a high Acute Stress Symptoms Scale are shown in the **Table 4**.

Table 4: Analysis of the predictors of obtaining the High Acute Stress Symptoms Scale by Logistic Regression

					95% Confidence Interval	
Variant	**Regression Coefficient**	**Standard Error**	**p**	**Odds Ratio**	**Lower Limit**	**Upper Limit**
Constant	231.636	145.858	0.112	10.139	0.5813	176.821
D-Dimer	1.06e-4	3.50e-4	0.763	1.000	0.9994	1.001
Fibrinogen	-0.00737	0.00367	**0.044**	0.993	0.9855	1.000
Ferritin	-0.00653	0.00443	0.140	0.993	0.9849	1.002
Lymphocyte	0.05199	0.27231	0.849	1.053	0.6177	1.796
Fever	-0.04954	141.349	0.972	0.952	0.0596	15.193
Cough	0.12292	0.74200	0.868	1.131	0.2641	4.841
Dyspnea	107.379	122.309	0.380	2.926	0.2662	32.169
Chest Pain	211.808	139.582	0.129	8.315	0.5392	128.231

Nagelkerke r2 = 0.192, *p<0.05

As a result of the logistic regression analysis; from the d-dimer, fibrinogen, ferritin, lymphocyte level, fever, cough, shortness of breath, chest pain variables, only the fibrinogen variable was found to be related with being included in the High Acute Stress Symptoms Scale group. Corresponding model was found to explain %19.2 of the variants.

In **Table 5**, the correlation analysis findings of the scale scores of the inpatient patients, acute phase reactants and age variables are shown. It has been found that there is a positive significant relationship between D-dimer scores and STAI-S and STAI-T scores (Rho=0.247, Rho=0.377). It was also found that there is a positive correlation between the HADS-Depression subscale and levels of Fibrinogen (Rho=0.386). There is a relationship between Acute Stress Symptoms Scale and the following PSS, STAI-S, STAI-T, HADS anxiety and HADS depression scores (Rho=0.334, Rho=0.388, Rho=0.327, Rho=0.718, Rho=0.487, respectively).

Table 5: Correlation analysis of scale scores, acute phase reactants and age variables of inpatients

		1	2	3	4	5	6	7	8	9	10	11
1	Age	—										
2	CRP	0.223*	—									
3	D-Dimer	0.337**	0.316**	—								
4	Fibrinogen	0.448**	0.632**	0.380**	—							
5	Ferritin	0.392**	0.424**	0.188	0.324**	—						
6	Lymphocyte	-0.100	-0.491**	-0.241*	-0.385**	-0.199*	—					
7	Acute Stress Symptoms Scale	0.087	0.012	0.009	-0.240	-0.064	-0.086	—				
8	PSS	-0.036	0.038	-0.044	-0.116	0.108	-0.021	0.334**	—			
9	STAI-S	0.324**	-0.138	0.247*	-0.182	-0.040	-0.010	0.388**	-0.047	—		
10	STAI-T	0.297**	-0.017	0.377**	0.098	0.103	-0.023	0.327**	0.155	0.694**	—	
11	HADS Anxiety	0.018	0.024	0.033	-0.221	-0.028	-0.107	0.718**	0.455**	0.425**	0.467**	—
12	HADS Depression	0.002	-0.010	-0.017	-0.386**	0.026	-0.069	0.586**	0.487**	0.389**	0.476**	0.770**

* p < 0.05, ** p < 0.01, CRP: C Reactive Protein, PSS-10 : Perceived Stress Scale-10, STAI- S: State-Trait Anxiety Inventory- State , STAI-T: State-Trait Anxiety Inventory-Trait, HADS: Hospital Anxiety Depression Scale

DISCUSSION

In this study, it was intended to determine whether there is a relationship between psychiatric symptoms and levels of inflammatory markers. Inpatient patients were divided into two groups as High Acute Stress Symptoms Scale or Low Acute Stress Symptoms Scale according to whether they scored higher or lower than the average Acute Stress Symptoms Scale score discovered in our study. In order to determine the predictors of obtaining a high Acute Stress Symptoms Scale score, a logistic regression analysis was performed. It was also determined that the fibrinogen variable predicted inclusion in the High Acute Stress Symptoms Scale group. It was found that there was a positive significant relationship between D-dimer scores and STAI-S scale scores and STAI-T scale scores (Rho=0.247, Rho=0.377). It was also found that there was a positive correlation between the HADS-Depression subscale sco-

re and Fibrinogen levels (Rho=0.386). Patients with COVID-19 have hyper-coagulability caused by an immune response to coronavirus-2 infection and they also often experience severe acute respiratory syndrome. Fibrinogen elevation and concomitant D-dimer elevation occur in many patients. D-dimer has become a part of routine laboratory tests for COVID-19 patients with critical illness and has been accepted as an indicator of disease severity (30). D-dimer elevation has been reported as a predictor of death in Chinese patients with COVID-19 (32). In addition, there are studies that have previously reported an association between D-dimer and hyper-coagulability factors and symptoms of depression, anxiety and stress (33). The relationship of fibrinogen and D-dimer with psychiatric symptoms may be related to the severity of the disease and inflammation.

Both the relationship of fibrinogen and D-dimer with psychiatric symptoms and the presence of physical symptoms require consideration of the psychoneuroimmunological framework of COVID-19. In addition, the presence of depression and anxiety symptoms can be highly correlated with the severity of the physiological condition, as reflected in the levels of peripheral inflammation markers in the blood of the patients having these psychological symptoms during a COVID-19 infection (34). In the study of Guo et al., symptom severity levels and CRP levels were found to be related with depression symptoms (11). A study conducted by Mazza and colleagues conducted that the fundamental systemic inflammation index (SII) -which is a reflection of systemic inflammation and immune response based on peripheral lymphocyte, neutrophil, and platelet counts- was found to be positively associated with depression and anxiety scores in patient follow-ups (12). The immune response to coronaviruses induces local and systemic production of cytokines, chemokines and other inflammatory mediators (35). It is known that coronaviruses can indirectly cause psychopathological symptoms through immune response (8). It has been proven that COVID-19 infection triggers the excessive production of pro-inflammatory cytokines that may be associated with neuropsychiatric symptoms, including IL-6(interleukin-6), IL-8 (interleukin-8), IL-10 (interleukin-10), IL-2R (interleukin-2 receptor), and tumor necrosis factor TNF-alpha (4). It is known that the irregularity of cytokines may cause depression symptoms (36 - 38) and anxiety symptoms (39). It makes sense to consider viral infections and subsequent immune activation as a form of stress. The irregularity of stress can interact with the pathogenesis of psychiatric symptoms. This situation can also be affected by other variables such as anti-inflammatory treatments (34).

Due to different factors such as social isolation, perceived fear of the illness being dangerous, uncertainty, physical discomfort, drug side effects, fear of infecting others, and negative news on social media; COVID-19 patients may experience symptoms of anxiety, depression, and post-traumatic stress. In our study, mean Acute Stress Symptoms Scale score was found to be 7.2 (7.8 in inpatients/5.419 in outpatients). In the validity and reliability study of Acute Stress Symptoms Scale conducted in Turkey, the average healthy group score was found to score 3.13 (23). Our findings indicate that patients who have tested positive for COVID-19, have symptoms of acute stress that are much more in quantity compared to healthy population (23). Stress symptoms were found to be high both in previous studies conducted with COVID patients and in studies conducted during the SARS epidemic (11, 12, 14). When HADS was evaluated according to the threshold values, 30 (20.5%) of the patients received scores above the threshold in terms of anxiety and 63 (43.2%) of the patients were above the threshold in terms of depression. In previous coronavirus outbreaks depression levels were %24.7–40.9, while anxiety levels were % 27.6–44.2 among patients (40). In a study conducted by Mazza et al., in which COVID-19 patients were evaluated by self-assessment at one month's follow-up after treatment, depression symptoms were found to be 31% and anxiety symptoms were 42% (12). In a study in which 103 COVID-19 patients were evaluated by online methods, depression symptoms were reported by 60.2% and anxiety symptoms were reported by 55.3% (11). Although the numbers may vary depending on the scale and method chosen, the symptoms of depression and anxiety were generally found to be high in this group of patients.

In our study, it was found that the scores of Acute Stress Symptoms Scale, STAI-T and HADS-Depression subscale of hospitalized patients were statistically higher than those of home-treated patients (p=0.046, p=0.001, p=0.006, respectively). In addition, it was found that there was a statistically significant positive relationship between age and STAI-S scale scores and STAI-T scale scores (Rho=0.324, Rho=0.297, respectively). One of the main consequences of the pandemic is the increase of social isolation, which is a significant risk factor strongly associated with depression, self-harm and suicide (41 - 43). The increase in social isolation in hospital conditions and the inability to find adequate social support in those conditions may have led to these results. Older adults are known to be quite vulnerable to the mental health consequences of social isolation, especially those in residential care (44). It was found that the Acute Stress Disorder Scale levels of women showed statistically higher significance than men. It has also been stated in various previous studies that women are psychopathologically more affected from the Covid-19 pandemic (11, 12, 45 - 47).

In this study, it was found that the Acute Stress Symptoms Scale levels of patients suffering from body pain, cough and chest pain were statistically significantly higher than those who did not describe any of these symptoms (p=0.017, p=0.025, p=0.025, respectively). Also in our study, it was found that Acute Stress Symptoms Scale scores were higher in patients with at least one symptom than in those without any (p=0.022). In a study made in China with 1738 participants, physical symptoms such as cough, body aches, chills and fever were found significantly associated with followed scale scores of High Impact of events Scale (IES-R), stress, anxiety or depression sub-scales of Depression Anxiety Stress Scale (DASS) (48).

In this study, we revealed the presence of comorbid stress, depression and anxiety symptoms in COVID-19 patients, and it was concordant to the literature. Given the alarming impact of COVID-19 on mental health, we think that these patients should also be evaluated from a psychiatric point of view starting from the time they are first diagnosed. We have also shown that fibrinogen elevation and D-dimer elevation may be associated with psychiatric symptoms in Covid-19 patients.

Our study has some limitations. First of all, psychiatric symptoms were collected with self-report scales. No clinical interviews were conducted with the patients to make an additional psychiatric diagnosis. In addition, our study is cross-sectional in nature. There is a need for follow-up studies that can give a cause-effect relationship on the subject. In future studies, the relationship between Covid-19, inflammation and psychiatric symptoms needs to be investigated further. This will also contribute to decipher the relationship between inflammation and psychiatric symptoms and improve our knowledge of the etiopathogenesis of these psychiatric disorders.

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