Do Anxiety and Depression Levels Affect the Inflammation Response in Patients Hospitalized for COVID-19

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Objective The whole world is still struggling with the COVID-19 pandemic. Inflammation response, thought to be associated with severe illness and death, is an important research topic in COVID-19. Inflammation is also an essential condition explored in psychiatric illnesses. Our knowledge about the relationship between the inflammation response and psychiatric comorbidities in patients with COVID-19 is very limited. In this study, the relationship between anxiety and depression levels and inflammation response of patients with COVID-19 hospitalized in the hospital was examined.

Methods 175 patients were included in the study. Sociodemographic Data Form, Beck Depression Inventory and Beck Anxiety Inventory were applied to the patients. To evaluate the inflammation responses, blood sedimentation rate, C-reactive protein (CRP), procalcitonin, ferritin, neutrophil/lymphocyte ratio (NLR), and IL-6 levels were examined.

Results In our study, no relationship was found between anxiety and depression levels and inflammatory responses in patients hospitalized with a diagnosis of COVID-19. Anxiety and depression levels of women were higher than men, and NLR, ferritin, IL-6 levels were found to be lower than men. Anxiety levels increase with age. There is a positive correlation between NLR and ferritin levels and duration of hospitalization.

Conclusion Our study examining the relationship of psychiatric comorbidities with the inflammation response and our increasing literature knowledge, together with studies evaluating the mental effects of COVID-19, suggest that determining the relationship between inflammation responses and psychiatric comorbidities in COVID-19, whose pathophysiology has not been clarified yet, maybe an essential step in interventions on the course of the disease.   **Psychiatry Investig 2021;18(6):505-512**

Key Words COVID-19, Anxiety, Depression, Inflammation, Plasma biomarkers.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel RNA virus that emerged in December 2019 in Wuhan, China, and is the cause of coronavirus disease 2019 (COVID-19). The disease has variable symptoms such as fever, cough, sore throat, generalized myalgia and respiratory distress, and some of the patients are hospitalized. It has been reported that approximately 20−30% of hospitalized patients need intensive care due to COVID-19 associated pneumonia.[1,2]

While some of the individuals infected with SARS-CoV-2 survive the disease outpatient, it is not fully understood what causes serious disease development in others. In order to investigate the response of this condition, which cannot be explained by viral load alone, inflammation responses have been investigated in patients.[3] Although advanced age and comorbidities have been shown to be significant risk factors for disease severity in patients with COVID-19, it has been observed that the disease progresses remarkably in young patients without comorbidity. Mortality and disease severity in patients with COVID-19 are thought to be associated with an excessive inflammatory response to SARS-CoV-2.[4] Increased circulating cytokines, lymphopenia and significant mononuclear cell infiltration are thought to be the cause of this condition. Mono-

nuclear cell infiltration detected in the lungs, heart, spleen, lymph nodes and kidney in post-mortem analyzes supports these views.[5-7] It was found that the severity of the disease was associated with inflammatory markers such as C-reactive protein (CRP), D-dimer, and ferritin increased neutrophil-lymphocyte ratio (NLR), and increased serum levels of various cytokines and chemokines.[8-10]

It is thought that the inflammatory response in which IL-6 is involved causes epithelial damage through different pathways. Therefore, attempts are being made to prevent IL-6 signalling in treatment.[11] In a study conducted with 20 patients, 15 (75%) of the patients treated with IL-6 blockage were reported to improve in their clinics,[12] while in another study, only 7 (33%) of 21 patients were reported to benefit.[13]

There is significant literature on the relationship between the immune system and the central nervous system.[14-16] The signal transmissions in which humoral neuronal and cellular pathways play a role, activated by cytokines released as an inflammatory response, reach the brain. These signals are thought to contribute to neuropsychiatric and psychological disorders, depending on where they are activated in the brain and the pathways they trigger.[14,17] Therefore, there is developing literature investigating the relationship between the etiopathogenesis of psychiatric diseases and the inflammation response. It is not known precisely whether inflammation responses change in the etiology of the disease or as a result of the disease. Anxiety disorders and depressive disorders are the most studied psychiatric diseases in inflammation responses. In a study, it was reported that the NLR was significantly higher in patients with the depressive disorder who did not receive antidepressant treatment compared to healthy controls.[18] In another study conducted with adolescents, it was reported that comorbid anxiety disorder increased the inflammation response and NLR and white blood cell counts in adolescents with obsessive-compulsive disorder.[19] Other studies report an increase in proinflammatory cytokines such as interleukin-6 (IL-6) and CRP in Anxiety Disorder.[20-22]

Apart from the physical symptoms of COVID-19, it has been reported that anxiety and depressive symptoms can also appear as mental symptoms in those who have the disease.[23] In a study, it was reported that anxiety and depression symptoms were observed at a rate of 20.9% and 18.6%, respectively, in patients treated with the diagnosis of COVID-19.[24] These results bring a question to researchers' minds. Do psychiatric comorbidities affect the inflammatory response in patients with COVID-19? By conducting related studies, the role of psychiatric comorbidities on the inflammation response can be determined, and a positive contribution can be made regarding the course of the disease. At the same time, whether there is a comorbid disease other than COVID-19 may be associated with anxiety and depression levels.[25] Therefore, in our study, the inflammatory responses, anxiety and depression levels of those with and without comorbidity were examined.

We hypothesize that there will be a positive correlation between inflammation response and levels of anxiety-depressive symptoms. According to our knowledge in literature reviews, only one study examines the effect of psychiatric comorbidities on inflammation response in COVID-19.[26] This study showed that the inflammation response was evaluated with more limited parameters (NLR, CRP, oxygen saturation). If psychiatric comorbidities affect the inflammation response, their recognition and treatment seem important in the therapeutic intervention of COVID-19. Our study aimed to determine psychiatric comorbidities in patients hospitalized and treated for COVID-19 and investigate its effect on the inflammation response.

METHODS

Ethical approval was obtained from the Ethics Committee of the University of Health Sciences, Ankara City Hospital with protocol number: E1-20-873. The study was conducted according to the criteria set by the declaration of Helsinki. All participants provided verbal and written informed consent after fully understanding the benefits and risks of participation.

Participants
Patients hospitalized for COVID-19 in Ankara City Hospital, one of the largest pandemic hospitals, between August 20, 2020−September 30, 2020, were included in our study. They all had COVID-19 symptoms and whose computer tomography of the thorax was reported according to the pandemic. Also, their nose and throat swab were positive in PCR. Patients who cannot continue the interview due to a neurocognitive disorder or intellectual disability (n=6), patients with a known psychiatric diagnosis and using psychotropic medication for at least the last month (n=4), foreign nationals who do not speak Turkish (n=8), patients diagnosed with cancer who are followed up for any malignancy and whose treatment is still ongoing (n=5), patients who received immunomodulatory or immunosuppressive therapy due to systemic inflammatory disease (n=3) were excluded from the study. In total, 175 patients over the age of 18 were included in the study.

Data collection tools
Interviews were conducted with the patients by well-trained psychiatrists, and the scales were applied during the first three days of hospital admissions. The sociodemographic characteristics of the patients such as age, gender, marital status, education year, and different medical diseases and psychiatric

histories were recorded during the interview. Then, the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) were administered to the patients.

In order to establish a baseline value, the blood test results requested on the day of hospitalization or the next day were scanned retrospectively from the hospital information system and parameters that may be associated with inflammation: CRP, erythrocyte sedimentation rate (ESR), NLR, procalcitonin, ferritin and IL-6 values were recorded.

Beck Depression Scale

It is a self-assessment scale consisting of 21 questions used to measure the physical, emotional, and cognitive symptoms seen in depression. Each question is scored between 0 and 3, and the total score varies between 0 and 63. The high score indicates the severity of the depression. It was developed by Beck et al.,[27] and its Turkish validity and reliability study has been conducted.[28]

Beck Anxiety Scale

It is a self-assessment scale consisting of 21 questions used to measure the anxiety symptoms experienced by the person. Each question is a Likert type self-rating scale scored between 0 and 3. Higher total scores are related to the severity of anxiety symptoms. It was developed by Beck et al.,[29] and its validity and reliability study in our country was performed by Ulusoy et al.[30]

Statistical analyses

Descriptive statistics of the data were calculated, and the conformity of variables to normal distribution was examined by visual methods (histograms, probability plots), Skewness-Kurtosis values and analytical methods (Kolmogorov-Smirnov test). Sociodemographic data of the patients were compared with chi-square and Student's t-test. Student's t-test was used to compare two independent groups for variables with normal distribution, and the Mann-Whitney U test was used to compare variables that did not show normal distribution. In correlation analysis, Pearson correlation test was used for normally distributed data, and Spearman correlation test was used for data that did not show normal distribution. Significance level was accepted as $p < 0.05$.

RESULTS

Hundred and seventy-five people participated in the study. The average age of the participants in the study was 52.19 ± 12.6 (min-max: 21−82), 39.4% were female (69/175), 58.3% (102/175) had an additional medical disease, 3.4% (6/175) had a history of psychiatric illness. Sixty-two point three percent

(109/175) of the participants had no current or past smoking history. Sociodemographic data of the participants are given in Table 1.

The age ($p < 0.001$), neutrophil levels ($p = 0.036$) and BAI levels of those with comorbid diseases were significantly higher than those without comorbidities, and their education time ($p = 0.014$) was lower. The comparison of anxiety and depression levels and biochemical values of the patients according to their comorbid illness is shown in Table 2.

The education time ($p < 0.001$), ferritin levels ($p < 0.001$), and NLR ($p = 0.038$) of the women were statistically significantly lower than the men. In addition, anxiety and depression levels of women were significantly higher than men ($p = 0.023$; $p = 0.003$, respectively) (Table 3).

The correlation between blood inflammatory marker levels of the patients and BDI and BAI scores were analyzed. There was no statistically significant correlation between sedimentation rate and BDI levels ($p = 0.504$) and BAI levels ($p = 0.200$). There was no statistically significant correlation between CRP and BDI levels ($p = 0.117$) and BAI levels ($p = 0.088$). There was no statistically significant correlation between IL-6 and BDI levels ($p = 0.450$) and BAI levels ($p = 0.124$). No statistically significant correlation was found between patients' ages and their depression, anxiety levels ($r = -0.1312$, $p = 0.084$; $r = -0.0126$, $p = 0.869$, respectively).

Table 1. Sociodemographic variables of participants

	Mean±SD	Minimium−maximum
Age (years)	52.2±12.6	21−82
Duration of hospitalization (days)	8.9±5.1	2−30
Education (years)	8.3±4.6	0−17
Gender, N (%)		
Female	39.4 (69)	
Male	60.6 (106)	
Smoking, N (%)		
No	87.4 (153)	
Yes	12.6 (22)	
Comorbid medical illness, N (%)		
Yes	58.3 (102)	
No	41.7 (73)	
Comorbidities, N (%)		
Hypertension	23.3 (39)	
Diabetes mellitus	9.1 (16)	
Thyroid dysfunctions	7.4 (13)	
Coronary artery disease	6.9 (12)	
Others	11.4 (20)	
History of psychiatric illness, N (%)		
Psychotic disorders	0.6 (1)	
Anxiety disorders	2.9 (5)	

Table 2. The comparison of anxiety and depression levels and values of inflammatory parameters of the patients according to their comorbid illness

	Patients with comorbid medical illness (N=102) Mean±SD	Patients with no comorbid medical illness (N=73) Mean±SD	t	p
Duration of hospitalization (days)	9.15±5.58	8.51±9.34	0.806	0.422
Age (years)	56.61±10.54	46.06±12.97	5.908	<0.001*
Education (years)	7.58±4.56	9.33±4.52	-2.494	0.014*
Procalcitonin	0.12±0.38 (N=100)	0.10±0.37 (N=72)	0.418	0.676
Sedimentation	35.06±22.55(N=80)	30.08±20.49 (N=56)	1.125	0.263
CRP	0.20±1.40 (N=100)	0.07±1.14 (N=73)	0.781	0.436
IL-6	30.46±35.87 (N=93)	46.55±110.06 (N=68)	-1.318	0.198
BNP	392.65±844.58 (N=23)	120.35±141.80 (N=20)	1.422	0.162
Ferritin	377.89±464.98 (N=102)	392.44±358.39 (N=72)	-0.223	0.824
TSH	2.20±2.87 (N=20)	1.62±1.13 (N=17)	0.778	0.442
T3	2.67±2.87 (N=16)	2.78±0.69 (N=13)	-0.495	0.624
T4	1.24±0.24 (N=18)	1.19±0.15 (N=13)	0.576	0.569
Neutrophil	4.54±2.75	3.84±1.69	2.077	0.036*
Lymphocyte	1.21±0.55	1.61±2.54	-1.308	0.195
NLR§	4.58±4.28	3.96±3.60	1.006	0.316
Beck Depression Scale	13.16±9.13	12.83±8.18	0.247	0.805
Beck Anxiety Scale	14.26±11.24	11.12±8.50	2.010	0.046*
			χ^2	p
Gender (female)	%41.2 (N=42)	%37.0 (N=27)	0.313	0.639
Smoking (none)	%88.2 (N=90)	%86.3 (N=63)	0.145	0.704

*statistically significant. CRP: C-reactive protein, IL: interleukin-6, BNP: Brain Natriuretic Peptide, NLR: Neutrophil Lymphocyte Ratio, TSH: thyroid stimulating hormone, T4: thyroxine T3: triiodothyronine

A negative, moderate and statistically significant correlation was found between the blood TSH levels of the patients and BAI levels (r=-0.4873, p=0.002) but no statistically significant correlation between BDI levels (r=-0.2285, p=0.174). There was also no relationship between NLR and BDI levels (p=0.427) and BAI levels (p=0.674). A statistically significant positive correlation was found between patients' BDI levels and BAI levels (r=0.7555, p<0.001)

There was no statistically significant correlation between the duration of hospitalization and BDI levels (p=0.192), BAI levels (p=0.387). A statistically significant positive correlation was found between the duration of hospitalization and NLR (r=0.209, p=0.006) and ferritin (r=0.219, p=0.004) levels. The correlation analysis, which evaluates the relationship of inflammatory parameters with each other and the duration of hospitalization is shown in Table 4.

DISCUSSION

The main findings of this cross-sectional study are:
a) No relationship was found between ferritin, ERS, CRP, IL-6, NLR levels and anxiety-depression levels.

b) Anxiety and depression levels of the female are higher than male.

c) Ferritin, NLR and IL6 levels of the female are lower than male.

d) A positive correlation was found between the NLR and ferritin levels and the duration of hospitalization.

e) The age of those with the comorbid disease is older, and their anxiety levels are higher.

The role of inflammation in the etiology of the disease in anxiety disorders and depression is an important topic in developing literature. It has been investigated by measuring inflammatory markers such as white blood cell counts and NLR, CRP, and cytokines such as IL-6.[18,20,31] In a meta-analysis evaluating 61 studies, IL-6 levels were reported to positively correlate with depression.[32] In a study conducted by O'Donovan et al.,[33] it was reported that there was a relationship between IL-6 and anxiety levels, but no relationship was found between IL-6 and depression levels. This situation has been explained as that the psychosomatic pathway that determines the stress-related production of IL-6 may differ in a depressive mood.

Table 3. Comparison of anxiety, depression levels and values of inflammatory parameters by gender

	Female (n:69) Mean±SD	Male (n:106) Mean±SD	t	p
Duration of hospitalization (days)	8.17±4.39	9.36±5.46	-1.523	0.130
Age (years)	51.44±12.66	52.67±12.70	-0.627	0.532
Education (years)	6.79±4.67	9.26±4.31	-3.577	<0.001*
Procalcitonin	0.05±0.09 (N=168)	0.14±0.47 (N=104)	-1.907	0.059
Sedimentation	35.67±22.68 (N=52)	31.84±21.16 (N=84)	0.997	0.320
CRP	0.04±0.04 (N=68)	0.20±1.36 (N=105)	-0.969	0.334
IL-6	20.98±27.77 (N=62)	47.45±94.02 (N=99)	-2.624	0.010*
BNP	323.44±951.49 (N=18)	224.64±239.38 (N=25)	0.500	0.620
Ferritin	181.60±311.91 (N=69)	516.85±434.90 (N=105)	-5.534	<0.001*
TSH	2.48±3.05 (N=17)	1.48±1.06 (N=20)	1.372	0.179
T3	2.61±0.61 (N=12)	2.80±0.59 (N=17)	-0.847	0.405
T4	1.18±0.26 (N=13)	1.25±0.15 (N=18)	-1.000	0.326
Neutrophil	3.91±2.29	4.48±2.43	-1.548	0.123
Lymphocyte	1.31±0.52	1.42±2.14	-0.401	0.689
NLR	3.54±3.02	4.82±4.49	-2.088	0.038*
Beck Depression Scale	14.91±9.10	11.80±8.29	2.334	0.021*
Beck Anxiety Scale	15.78±10.96	11.11±9.42	3.002	0.003*
			χ^2	p
Comorbid medical illness (yes)	%60.9 (N=42)	%56.6 (N=60)	0.313	0.639
Smoking (no)	%91.3 (N=63)	%84.9 (N=90)	1.557	0.212

*statistically significant. CRP: C-reactive protein, IL: interleukin-6, BNP: Brain Natriuretic Peptide, NLR: Neutrophil Lymphocyte Ratio, TSH: thyroid stimulating hormone, T4: thyroxine T3: triiodothyronine

Two important roles of IL-6 in depression have been emphasized. First, regulation of the local inflammatory response by interacting with macrophage and glia melatonin production is linked to local epigenetic modulation via methyl CpG-binding protein 2 (MeCP2). Second, the inductive role of IL-6 in the systemic regulation of tryptophan. Especially in these two ways, IL-6 has a broad psychiatric effect, including the processes that trigger depression. Lamers et al.[34] reported that in both cross-sectional and two and six-year follow-up, CRP levels were not associated with depressive symptoms and severity, but IL-6 levels were a predictor for chronicity. Intracellular multiplication of SARS-CoV-2 results in increased levels of the proinflammatory IL-6. Classically, in cis-mediated signalling, Janus kinases (JAKs) activation and signal transducer and activator of transcription 3 (STAT3) activation occur.[35] This increased inflammation response in patients with COVID-19 may cause psychiatric comorbidities, and psychiatric comorbidities may also strengthen this response. There may be several reasons why no relationship was found between CRP and IL-6 levels and anxiety and depression levels in our study. One of the reasons for the high inflammatory response in depression and anxiety is that the corticolimbic cycle is affected by the released mediators and emotional-behavioural changes may

occur.[36] In this case, as the inflammation response increases, depressive complaints and anxiety may increase. Since there was no longitudinal follow-up in our study, the mood changes of patients with high inflammation response for a long time cannot be known. On the other hand, in previous studies showing the relationship between CRP and IL-6 levels with depression and anxiety, it was noted that it was not known that high CRP and IL-6 represented an association, a mediating risk factor, or a causal factor for depression.[16]

The NLR is the research subject as a predictor of disease or a severity marker in many psychiatric illnesses.[37] In a study, it was reported that there is a positive relationship between the severity of depression and NLR in patients with depression.[38] In a large study involving 13,888 patients in the UK, it was reported that the NLR was higher in dementia, alcohol dependence, schizophrenia, bipolar affective disorder, depression, non-phobic anxiety disorders compared to the control group.[39] In a meta-analysis study examining the relationship between NLR and psychiatric disorders, it was reported that there is evidence that NLR can predict prognosis in non-psychiatric disorders. However, a similar prognostic measure has not been developed in psychiatry yet. It was suggested to investigate whether NLR is similarly predictive in psychiatric disorders

Table 4. Correlation analysis between the inflammatory parameters of patients

	Procalcitonin		Sedimentation		IL-6		Ferritin		Lymphocyte		NLR		T3	
	r	p	r	p	r	p	r	p	r	p	r	p	r	p
Duration of hospitalization†	0.066	0.390	0.093	0.279	0.150	0.058	0.219	0.004*	-0.120	0.113	0.209	0.006*	-0.505	0.005*
Procalcitonin			0.065	0.461	0.258	0.001*	0.134	0.081	-0.037	0.628	0.331	<0.001*	-0.383	0.049*
Sedimentation					0.057	0.530	0.210	0.014*	-0.096	0.264	0.117	0.176	-0.333	0.112
IL-6							0.237	0.003*	0.012	0.877	0.196	0.013*	-0.270	0.164
Ferritin									-0.003	0.973	0.191	0.012*	-0.212	0.269
Lymphocyte											-0.143	0.059	0.524	0.004*
NLR													-0.443	0.016

Positive correlations: Duration of hospitalization and ferritin, Duration of hospitalization and NLR. Procalcitonin and IL-6, NLR and IL-6, Procalcitonin and NLR, Ferritin and NLR.Ferritin and Sedimentation, Lymphocyte and T3. Negative correlations: Procalcitonin and T3, Duration of hospitalization and T3. *statistically significant, †Spearman analysis. NLR: Neutrophil Lymphocyte Ratio, T3: triiodothyronine, IL-6: interleukin-6

with prospective studies and to determine whether it is used in clinical practice.[40] A study in the literature evaluated the relationship between NLR and depression-anxiety levels in patients with COVID-19, and this study reported no relationship between depression-anxiety scores and NLR-CRP levels.[25] In the same study, similar to our study, it was found that NLR was lower in women. It is known that the inflammatory response is a complex process affected by many factors. In our study, although the patient group was homogenized as patients who did not need intensive care and who were evaluated by taking baseline blood values on the day of hospitalization, there may be no association with psychiatric comorbidity in inflammation responses due to the mixed pathophysiology of inflammation.

In many studies investigating the psychological effects of COVID-19 on individuals, it has been reported that the anxiety and depression levels of women are higher than men.[26,41,42] In a study conducted by Pierce et al.[43] with 53,351 participants, evaluating the mental effects before and during the pandemic, it was reported that women were more affected by the pandemic than men. In our study, it was found that anxiety and depression levels of women were higher than men, in accordance with the literature.

Sex-disaggregated data for COVID-19 show that the rates of men and women getting sick are close. However, depending on possible variables such as immunological, hormonal or smoking status based on gender, increased disease severity and mortality differences against SARS-CoV-2 infection have been reported.[1,44,45] A study conducted with 317 patients diagnosed with COVID-19 in Wuhan, China, IL-6, ferritin, procalcitonin, LDH and hsCRP were found to be lower in women compared to men.[46] Biological sex is known to influence adaptive immune responses.[47] However, our knowledge about immune response changes based on gender in COVID-19 is still very limited. In previous studies in patients with a diagnosis of CO-VID-19, it has been reported that hsCRP, Ferritin, LDH, IL-6 levels differ according to gender.[46,48] In our study, although women had higher anxiety and depression scores, ferritin, NLR and IL-6 levels were found to be lower than men. This situation can be interpreted as the difference associated with sex hormones has a more significant effect on the inflammation response than psychiatric comorbidities.[49] However, it seems that further studies are needed regarding the gender difference in inflammation response for COVID-19.

Factors that determine the severity of the disease and affect hospitalization duration in patients hospitalized for COVID-19 are an important research topic. A study conducted by Tezcan et al.,[50] high ferritin levels, hypoalbuminemia and increased lactate dehydrogenase levels were found to be associated with prolonged hospitalization. In another study, higher serum ferritin was found to predict an increased risk of disease severity in patients with COVID-19.[51] Gottlieb et al.,[52] in a study conducted in which 8,673 patients with COVID-19 were examined, male gender, presence of congestive heart disease, and increased NLR was reported as factors associated with critical illness. Many factors affect the hospitalization of patients. In our study, a significant relationship was found between NLR and ferritin levels and duration of hospitalization. This result may contribute to the knowledge of the literature on developing cheap and easy-to-use biomarkers to predict the duration of hospitalization.

Deaths in the COVID-19 pandemic occurred mostly in elderly individuals and those with chronic disease.[25] This situation is frequently stated in public information, television channels and social media, and curfews are still implemented for older people in our country. As a result of all these, it is expected that people with other medical diseases have higher anxiety in accordance with this.

Limitations

The present findings must be interpreted in light of several limitations. The most important limitation of our study is that the change in inflammation responses of the patients during the hospitalization period was not evaluated. Analyzing the same inflammation parameters again at the discharge of the patients and examining their relationship with the levels of anxiety and depression may make it easier to match other variables related to the disease. The second limitation is that the inflammatory responses of the patients were evaluated together with ESR, CRP, NLR, ferritin, and IL-6 levels. Apart from these parameters, more specific markers of inflammation response and which may be cell-mediated immune activation markers in depression and anxiety can be investigated in future studies. Disease severity of patients is an important variable in the inflammatory response. In our study, we tried to keep this situation constant by taking a patient group that is clinically stable and does not need intensive care. However, evaluating the clinical findings such as oxygen saturation, heart rate, and respiratory rate and the change of inflammation responses and psychiatric comorbidities may help evaluate the relationship between the inflammation response due to the disease and the inflammation response due to psychiatric comorbidity.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: Aybeniz Civan Kahve, Sureyya Barun, Hasan Kaya. Data curation: Erol Goka, Merve Okuyucu, Aybeniz Civan Kahve. Formal analysis: Aybeniz Civan Kahve, Yunus Hacimusalar, Hasan Kaya. Funding acquisition: Aybeniz Civan Kahve. Investigation: Sureyya Barun, Erol Goka, Hasan Kaya. Methodology: Sureyya Barun, Merve Okuyucu, Aybeniz Civan Kahve. Project administration: Aybeniz Civan Kahve, Hasan Kaya. Resources: Merve Okuyucu, Erol Goka, Hasan Kaya. Software: Aybeniz Civan Kahve, Yunus Hacimusalar. Supervision: Yunus Hacimusalar, Erol Goka. Validation: Hasan Kaya, Sureyya Barun. Visualization: Aybeniz Civan Kahve, Merve Okuyucu, Hasan Kaya. Writing—original draft: Aybeniz Civan Kahve, Yunus Hacimusalar. Writing—review & editing: Sureyya Barun, Erol Goka.

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