ORIGINAL ARTICLE

Therapeutic Apheresis and Dialysis

WILEY

Effect of anxiety on COVID-19 infection in hemodialysis patients

Pervin Ozkan Kurtgoz[1] ![ORCID] | Fatih Sackan[2] ![ORCID] |
Muhammet Cemal Kızılarslanoglu[3] ![ORCID] | Ozlem Bilgin[1] ![ORCID] | Ibrahim Guney[1] ![ORCID]

[1]Department of Internal Medicine, Division of Nephrology, University of Health Sciences, Konya City Hospital, Konya, Turkey

[2]Department of Internal Medicine, University of Health Sciences, Konya City Hospital, Konya, Turkey

[3]Department of Internal Medicine, Division of Geriatrics, University of Health Sciences, Konya City Hospital, Konya, Turkey

Correspondence
Pervin Ozkan Kurtgoz, Department of Internal Medicine, Division of Nephrology, University of Health Sciences, Konya City Hospital, Konya, Turkey.
Email: dr.pervinozkan@gmail.com

Abstract

Some evidence suggests that anxiety deteriorate the immune system. We aimed to determine the effect of anxiety on COVID-19 infection in hemodialysis (HD) patients. Our study was conducted with 80 HD patients. State-Trait Anxiety Inventory (STAI), and Beck Anxiety Inventory (BAI) questionnaires were administered between April 15 and May 1, 2020. These patients were followed up for about 8 months and COVID-19 infection, hospitalization, and death rates were recorded. Twenty-one (26%) of the patients were diagnosed with COVID-19 infection. Fourteen out of twenty one (66.6%) of the patients were hospitalized, and 8/21 (38%) of them died due to COVID-19. STAI-S ($p = 0.006$) and BAI ($p = 0.021$) scores were found to be higher and STAI-T ($p = 0.040$) score was found to be lower in HD patients who were infected with COVID-19 compared to without, at the follow-up period. It might be concluded in this study that COVID-19 was more common in anxious HD patients.

KEYWORDS

anxiety, BAI, COVID-19 infection, hemodialysis, STAI

1 | INTRODUCTION

The COVID-19 pandemic, since its first detection, has been affecting all humans over the world. Social distance and isolation are the safest ways to protect against COVID-19 infection. It has been shown that high mortality and complication rates due to COVID-19 are closely related to chronic disease, fragile immune system, and older population. Still, there is a big mystery about when and how this devastating pandemic will end. Therefore, this unknown makes the people more anxious and vulnerable [1].

HD patients are bound to dialysis to live, at least two or three times per week and most of them are in older age with a higher rate of co-morbidities such as hypertension (HT), diabetes mellitus (DM), and cardiovascular

disease (CVD) and higher hospitalization rates compared with younger healthy population. Therefore, HD patients are faced to many medical problems in their life. One of these medical problems is psychiatric disorders like depression and anxiety [2, 3]. Although the prevalence of anxiety in HD patients is not clear, given rates range from 12% to 52% in the literature [4]. It is estimated that these rates may rise even more during the pandemic period [5].

In recent years, the science of psychoneuroimmunology has revealed that anxiety is related to the immunological system and inflammation [6]. In experimental studies, anxiety-like behavior was detected in mice with higher IL-6 and TNF-α levels in their blood [7, 8]. There are many human studies showing that high levels of anxiety impair humoral and cellular immunity and leave

patients vulnerable to infections [9–11]. There are also data showing that increased oxidative stress due to anxiety causes an increase in CRP, IL-6, and TNF-α levels [11].

Based on all these knowledge, it can be easily said that anxiety increases infection rates in people by deteriorating their immune systems. Thus, this interaction may be speculated for COVID-19 infection; however, to the best of our knowledge, this question has not been investigated before. We aimed in the study to investigate the effect of anxiety on development having COVID-19 infection in HD patients.

2 | MATERIALS AND METHODS

2.1 | Study design and patients selection

Eighty patients out of 110 patients aged 18–90 years who underwent dialysis regularly in our HD center were included in the study, after taking written informed consent. The patients participating in the study were selected from patients who had not previously had a COVID-19 infection and had not been in contact with COVID-19 positive patient. Thirty patients were excluded from the study for the following reasons: those who had contact with the COVID-19 infected patient before, those with another focus of infection, those who could not fill out the questionnaires, and those who could not give written consent.

The first case of COVID-19 in our country was detected on March 11, 2020. A prepared questionnaire consisting of 40 questions including evaluation of COVID-19 awareness of the participants, State-Trait Anxiety Inventory (STAI), and Beck Anxiety Inventory (BAI) were applied to the our patients between April 15 and May 1, 2020 which was the time nearly the first COVID-19 pandemic wave seen in our country. Then, these patients were followed up for about 8 months and COVID-19 infection, hospitalization, and death rates were recorded. COVID-19 positivity defined as follows: the presence of COVID-19 pneumonia in chest computed tomography (CT) and/or the real-time reverse transcription polymerase chain reaction (RT-PCR) positivity [12].

2.2 | Measurement of the BAI levels of the patients

Development of this scale was carried out by Beck et al. and a study showing its reliability and validity in Turkish was done by Ulusoy et al. It consists 21 items which measures physical and psychological aspects of anxiety. Total score range is between 0 and 63. The score of higher than

7 points was considered as having anxiety. Higher scores reflect severe anxiety [13, 14].

2.3 | Measurement of the STAI levels of the patients

This questionnaire, developed by Spielberger et al. and adapted to Turkish by Oner et al., consists 40 items and have two different scales, STAI-S (state anxiety) and STAI-T (trait anxiety). Each scale has 20 items and each item is given scores ranged from 1 to 4 points; therefore, total scores change between 20 and 80 points for each scale. The score of higher than 39 points reflects anxiety symptoms. Each scale evaluates the patients' anxiety levels; however, STAI-S is mostly affected by temporary emotional state, while STAI-T particularly shows patients anxiety status regardless of situation and circumstances [15, 16].

2.4 | Statistical analyses

All the statistical analyses were made by using Statistical Package for the Social Sciences (SPSS) version 22.0. Categorical variables, given in the tables, were presented as numbers and percentages. All the comparisons were analyzed by using Fisher Exact or Chi-square tests which is appropriate for categorical variables. Continuous variables were assessed by Kolmogorov–Smirnov test, histogram, and variation coefficients to find out whether or not they have normal or skew distribution. As the all numerical parameters, assessed in our study, had skew distribution, they were presented as median (interquartile range [IQR]). Comparisons between two numerical parameters that show skew distribution were analyzed by Mann–Whitney U test. The p-value lower than 0.05 was accepted as statistical significance.

3 | RESULTS

The first COVID-19 infected patient from the participants was detected on June 5, 2020. During the study follow-up period, 21 (26%) of the patients were infected with COVID-19. The median age of the patients with COVID-19 was 60 years (18–83), 12/21 (57%) were male, 14/21 (66.6%) were hospitalized, and 8/21 (38%) could not survive. HD durations and co-morbidity rates were similar between the groups categorized as patients with and without COVID-19 infection. When the patients' BAI, STAI-T, and STAI-S scores compared between patients with and without COVID-19 infection, it was observed that the

patients with COVID-19 infection had higher BAI ($p = 0.021$) and higher STAI-S scores ($p = 0.006$) and lower STAI-T ($p = 0.040$) scores (Tables 1 and 2; Figure 1).

The patients categorized into two groups according to BAI and STAI-S scores. The score higher than 7 points was considered as anxiety according to BAI while the score higher than 39 points was considered as anxiety according to STAI-S. Anxious HD patients were found to be more likely to get COVID-19 infection during the study follow-up period compared with non-anxious ones

TABLE 1 Comparison of clinical and demographic data of patients

		Total, $n = 80$	COVID-19 (+), $n = 21$	COVID-19 (−), $n = 59$	p
Age		52 (18–83)	60 (18–83)	50 (19–83)	0.431
Gender	Female	37 (46.3%)	9 (42.8%)	28 (47.4%)	0.717
	Male	43 (53.8%)	12 (57.1%)	31 (60.7%)	
Marital status	Single	25 (31.3%)	9 (42.8%)	16 (27.1%)	0.181
	Married	55 (68.8%)	12 (57.1%)	43 (72.8%)	
Educational status	Literate	59 (73.8%)	16 (76.1%)	43 (72.8%)	0.767
Co-morbidity	Yes	54 (67.5%)	14 (66.6%)	40 (67.7%)	0.924
DM	Yes	25 (31.3%)	7 (33.3%)	18 (30.5%)	0.810
HT	Yes	52 (65%)	14 (66.6%)	38 (64.4%)	0.852
CAD	Yes	20 (25%)	8 (38.0%)	12 (20.3%)	0.107
Lung Disease	Yes	12 (15%)	5 (23.8%)	7 (11.8%)	0.188
Psychotropic medication use	Yes	4 (5%)	2 (9.5%)	2 (3.3%)	0.281
HD duration (months)		66 (6–288)	36 (12–168)	72 (6–288)	0.069
Contact with COVID-19 patient	Yes	13 (16.3%)	8 (38.1%)	5 (8.5%)	0.002
Hospitalization	Yes	14 (17.5%)	14 (66.7%)	0 (0%)	<0.001
Mortality	Yes	10 (12.5%)	8 (38.1%)	2 (3.4%)	<0.001

Abbreviations: CAD: coronary artery disease; DM, diabetes mellitus; HD, hemodialysis; HT, hypertension.

TABLE 2 The BAI, STAI-S, and STAI-T levels of patients

	Total, $n = 80$	COVID-19 (+), $n = 21$	COVID-19 (−), $n = 59$	p
The BAI score	6 (0–35)	9 (1–35)	5 (0–34)	0.021
The STAI-S score	44 (21–79)	50 (24–79)	40 (21–62)	0.006
The STAI-T score	18 (0–27)	17 (10–26)	19 (0–27)	0.040

Abbreviations: BAI, Beck Anxiety Inventory; STAI-S, State-Trait Anxiety Inventory-State; STAI-T, State-Trait Anxiety Inventory-Trait.
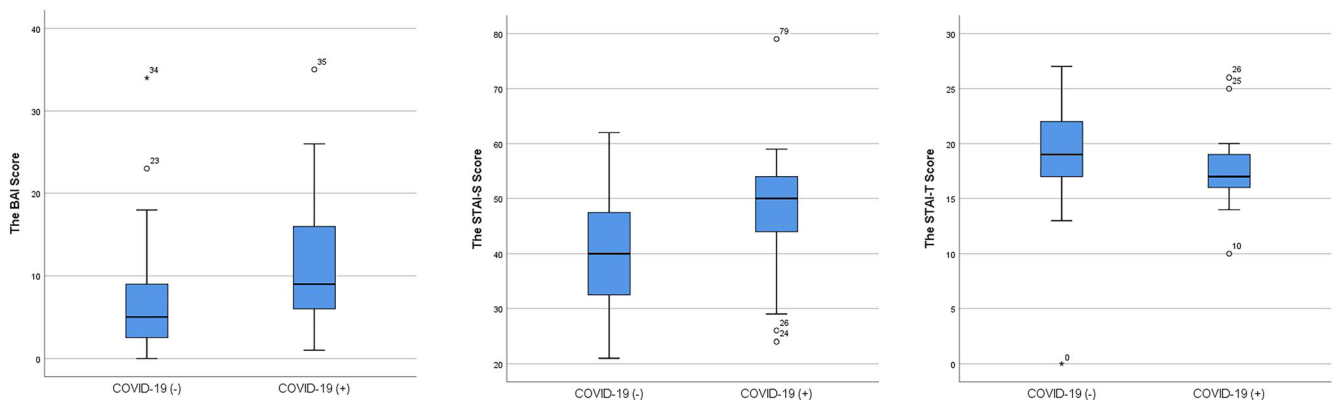

FIGURE 1 This figure demonstrates the levels of patients' BAI, STAI-S, and STAI-T

TABLE 3 Comparison of COVID-19 infection rates according to BAI and STAI-S levels

		Total, $n = 80$	COVID-19(+), $n = 21$	COVID-19 (−), $n = 59$	OR (95% CI)	p
Beck anxiety status[a]	Absent	42 (52.5%)	7 (33.3%)	35 (59.3%)	5.800 (1.542–21.811)	0.041
	Present	38 (47.5%)	14 (66.6%)	24 (40.7%)		
State anxiety status[b]	Absent	32 (40.0%)	3 (14.3%)	29 (49.1%)	2.197 (1.025–8.297)	0.005
	Present	48 (60.0%)	18 (85.7%)	30 (50.9%)		

[a]The score higher than 7 points was considered as anxiety according to BAI.
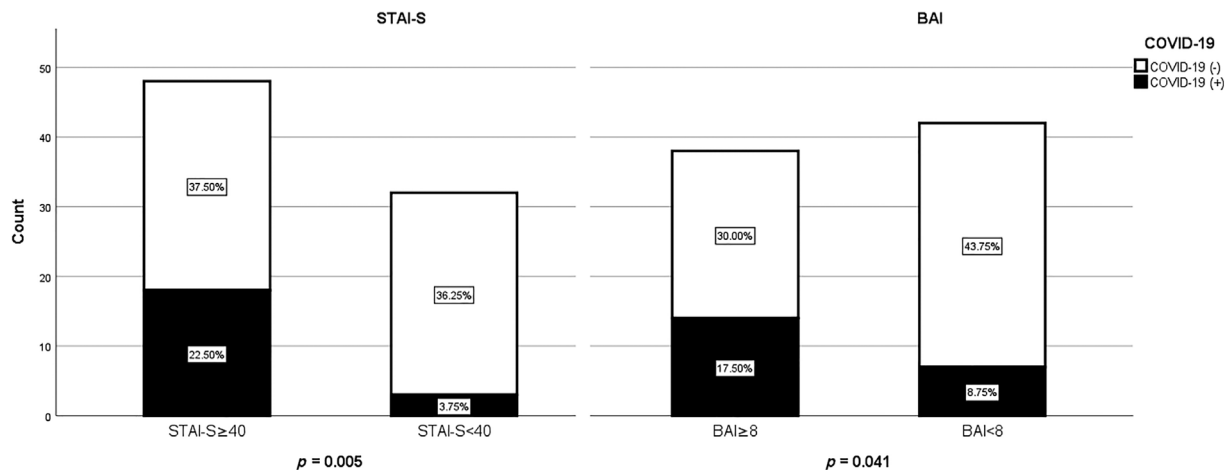[b]The score higher than 39 points was considered as anxiety according to STAI-S.

FIGURE 2 This figure demonstrates the rates of development of COVID-19 infection in HD patients according to anxiety levels

when evaluated with both anxiety screening tools, BAI and STAI-S (OR: 5.8; 95% CI: 1.5–21.8 and OR: 2.2; 95% CI: 1.0–8.3, respectively; Table 3; Figure 2).

4 | DISCUSSION

It has been demonstrated that anxious HD patients are more likely to be infected COVID-19 compared with non-anxious ones in this study follow-up period. We think that high level of anxiety may pose a risk for COVID-19 infection in HD patients. This finding can be explained by two possibilities. First, high anxiety levels are not protective and can increase the risk of making mistakes. Second, anxiety levels can affect the immune system.

HD patients must spend a certain time in dialysis centers to live, where the patients are faced to risk of near contact other people or patients [17, 18]. Thus, social isolation and the direction "stay at home" are two difficult suggestions to avoid COVID-19 such patients who should regularly go health centers for their life. Therefore, in the pandemic era, the HD patients are worried about their health status and what they will do if the pandemic makes them away from HD centers [3]. They are also afraid of transmitting this virus to their families or

relatives if they become infected with COVID-19 [19]. Taking all these ways into account, it is possible to say that HD patients are at increased risk of anxiety due to the COVID-19 pandemic.

Twenty-one of our HD patients were infected in 8 months period, but at different times at the same dialysis center. We have taken some precautions in our hospital and dialysis center during the COVID-19 period to protect our patients. A single and separate dialysis room was organized for the COVID-19 positive patient, and a different and single nurse took care of this patient. After the dialysis was completed, the HD machine was properly disinfected. The COVID-19 positive patient, reached the dialysis center by own vehicle. If they have not own vehicle, our dialysis shuttle transported them alone. COVID-19 positive patients were constantly informed about the isolation. A great effort has been made to ensure for other patients and healthcare personnel do not contact with COVID-19 positive patients. Unfortunately, despite all these precautions, in our follow-ups, we found that COVID-19 positive group had more contact with infected COVID-19 patients than those without. In fact, COVID-19 positive patients were more anxious and they would have been expected to take further measures to avoid infection. In previous outbreaks, a positive

correlation was found between high anxiety levels and increased personal protective measures. At the same time, the rates of benefiting from health services increased with increasing anxiety levels, and they went to the hospital more frequently. Although anxious patients have taken more measures to prevent the disease, frequent hospital visits have increased their risk of becoming infected [20]. Also, Leung et al. determined in their study, moderate anxious patients were more successful in taking precautions against the pandemic. It has been observed that people with high or low levels of anxiety have increased rate of making mistakes, so unable to control the epidemic [21]. In our study, more COVID-19 infections were detected in patients with high anxiety levels and this finding support the literature.

While state anxiety determines how an individual feels at a certain moment and under certain conditions, trait anxiety generally determines how an individual feels, regardless of the situation and circumstances. State anxiety levels are more closely related to stressful events. Such ongoing and uncertain events, such as a pandemic, can increase state anxiety levels [22]. Therefore, it can be expected that the pandemic will affect the state anxiety levels more than the trait anxiety levels. Also, the state anxiety levels of our patients were higher than in other studies conducted before the pandemic; however, trait anxiety levels were lower [23]. Our patients had higher BAI and STAI-S scores than STAI-T scores at the beginning of the pandemic. This confirms that our patients were affected by the pandemic. In addition, according to our study, high BAI and STAI-S scores may have an effect on having COVID-19 infection.

In an experimental study, mice were divided into two groups as anxious and non-anxious by light/dark choice test and total lymphocyte counts, IgA, and IgE levels were lower in anxious ones compared with others [24]. Therefore, this finding may explain the reason how the anxiety cause immunodeficiency which makes more vulnerable of the patients to take COVID-19. Some clinical studies showed that IFN-γ, TNF-α, IL-6, and IL-1ß levels increased in self-reporting anxiety. Thus, this evidence may show there is a stress induced inflammatory activity [25, 26]. On the other hand, immune response may be precipitated more aggressively in the situations with newly emerging stressors [27–29]. The main cause of death in COVID-19 infection is cytokine storm and the exhaustion of the immune system. The excessive inflammation is thought to be caused by over-production of IL-6 and TNF-α levels [30, 31]. Since we were unable to measure cytokine levels in our study, we do not know the inflammatory changes that may develop due to anxiety in our patients. However, the increased incidence of COVID-19 infection in patients with high anxiety supports that anxiety affects the immune response.

Strengths of this study were: co-morbidity rates and psychotropic drug use rates were similar between the groups with and without COVID-19 infection. Thus, the interaction between anxiety and COVID-19 infection was more clearly documented regardless of the effect of co-morbidities.

This study had some limitations. First, study population was limited; however, the patients included in the study were nearly the all of HD patients followed-up in our center. Our study could have been planned as a multicenter, but at the time we started the study, the centers working as pandemic hospitals were limited in our province. Even so, we think that our study can set an example for more comprehensive studies. Second, immunodeficiency could not be evaluated in HD patients and inflammatory markers such as IL-1, IL-6, and TNF-α could not be studied. Further studies may investigate these interactions with prospectively designed researches. Beside these limitations, we believe that our study will raise awareness about the effect of anxiety on the course of COVID-19 in HD patients.

In conclusion, anxiety might affect the immune system; therefore, it is easy to say that the HD patients with anxiety should be considered as a patient with impaired immune-system those may make the patients more prone to get COVID-19 infection and have more severe disease course. Thus, we recommend that HD patients should be routinely investigated for anxiety in HD centers and appropriate treatment modalities should be considered as soon as possible with the support of psychiatrists.

CONFLICT OF INTEREST

The authors declare they have no conflict of interest.

ETHICS STATEMENT

The Medical Specialty Training Board of Konya Training and Research Hospital and Hamidiye Scientific Research Ethical Committee approved our study protocol (with IRB numbers: 48929119/774 and 46 418 926-050.03.04, respectively).

ORCID

Pervin Ozkan Kurtgoz https://orcid.org/0000-0002-4206-0525
Fatih Sackan https://orcid.org/0000-0003-0257-8917
Muhammet Cemal Kızılarslanoglu https://orcid.org/0000-0002-7632-6811
Ozlem Bilgin https://orcid.org/0000-0003-3245-1511
Ibrahim Guney https://orcid.org/0000-0002-1646-2811

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