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ABOUT COVER

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WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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The *WJCC* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Current Contents®/Clinical Medicine, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 Edition of Journal Citation Reports® cites the 2021 impact factor (IF) for *WJCC* as 1.534; IF without journal self cites: 1.491; 5-year IF: 1.599; Journal Citation Indicator: 0.28; Ranking: 135 among 172 journals in medicine, general and internal; and Quartile category: Q4. The *WJCC*'s CiteScore for 2021 is 1.2 and Scopus CiteScore rank 2021: General Medicine is 443/826.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Xu Guo*; Production Department Director: *Xiang Li*; Editorial Office Director: *Jin-Lei Wang*.

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Thrice Monthly

EDITORS-IN-CHIEF

Bao-Gan Peng, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati, Ja Hyeon Ku

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

August 6, 2022

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INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

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<https://www.wjgnet.com/bpg/gerinfo/240>

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<https://www.wjgnet.com/bpg/GerInfo/288>

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<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Prospective Study

Predictors of long-term anxiety and depression in discharged COVID-19 patients: A follow-up study

Rabia Kevser Boyraz, Ebru Şahan, Muhammed Emin Boylu, İsmet Kırpınar

Specialty type: Psychiatry**Provenance and peer review:**

Invited article; Externally peer reviewed.

Peer-review model: Single blind**Peer-review report's scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): B

Grade C (Good): C

Grade D (Fair): D

Grade E (Poor): 0

P-Reviewer: Goldstein Ferber S, Israel; Stoyanov D, Bulgaria; Troisi A, Italy**Received:** January 25, 2022**Peer-review started:** January 25, 2022**First decision:** April 18, 2022**Revised:** April 21, 2022**Accepted:** July 6, 2022**Article in press:** July 6, 2022**Published online:** August 6, 2022**Rabia Kevser Boyraz**, Department of Psychiatry, Basaksehir Cam and Sakura Research and Training Hospital, Istanbul 34480, Turkey**Ebru Şahan**, Department of Psychiatry, Marmara University, İstanbul 34854, Turkey**Muhammed Emin Boylu, İsmet Kırpınar**, Department of Psychiatry, Bezmialem Vakıf University, İstanbul 34093, Turkey**Corresponding author:** Rabia Kevser Boyraz, MD, Doctor, Postdoc, Department of Psychiatry, Basaksehir Cam and Sakura Research and Training Hospital, Istanbul 34480, Turkey. rabiasancili@yahoo.com

Abstract

BACKGROUND

Patients who were hospitalized for coronavirus disease 2019 (COVID-19) faced an extremely stressful experience that challenged their mental health and the long-term effects are not definitely known yet.

AIM

To identify both the course of mental symptoms (anxiety and depressive symptoms) and the related risk factors of recovered patients at the 20-22 mo follow-up.

METHODS

One hundred and seventy-two patients were enrolled. The patients were evaluated with a telepsychiatry interview and the Hospital Anxiety and Depression Scale (HADS). Sociodemographic and clinical features were analyzed by regression analysis.

RESULTS

The mean HADS-Anxiety (HADS-A) score was 9.08 ± 4.90 , and the mean HADS-Depression (HADS-D) score was 8.55 ± 4.39 . The mean HADS-A ($P = 0.484$) and HADS-D ($P = 0.011$) scores were increased compared to scores during hospitalization. Being over 50 years old, having lower financial status, and being vaccinated were associated with symptoms of depression (adjusted $R^2 = 0.168$) while being over 50 years old, female sex, being vaccinated, and dyspnea were associated with higher anxiety (adjusted $R^2 = 0.245$).

CONCLUSION

To prevent the deterioration of mental health, psychiatrists should play an active role in identifying emerging mental problems as soon as possible, more vulnerable groups should be characterized, and psychological support should be sustained after discharge.

Key Words: Coronavirus; Anxiety disorders; Depressive disorders; Tele medicine; Psychiatry

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Core Tip: Coronavirus disease 2019 causes various psychiatric outcomes like other coronaviruses. This study aimed to observe the anxiety and depressive symptoms and related factors of recovered patients at the 20-22 mo follow-up. The goal of this study was to identify groups at high risk of anxiety and to raise awareness about providing psychiatric support to these groups.

Citation: Boyras RK, Şahan E, Boylu ME, Kırpınar İ. Predictors of long-term anxiety and depression in discharged COVID-19 patients: A follow-up study. *World J Clin Cases* 2022; 10(22): 7832-7843

URL: <https://www.wjgnet.com/2307-8960/full/v10/i22/7832.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v10.i22.7832>

INTRODUCTION

Pandemics may cause major health problems both physically and mentally. Factors such as various biological reasons, difficulties in the treatment process, loss of relatives, quarantine conditions, social isolation, and the uncertainty of the process are among the main factors affecting mental health. Studies on previous infectious epidemics, like severe acute respiratory syndrome, Middle East respiratory syndrome, and Ebola virus disease outbreak, reported that psychological symptoms might persist or arise after the infection with long-term negative outcomes[1].

Neurological and psychiatric outcomes of coronavirus disease 2019 (COVID-19) have been reported in various studies[2,3]. A 6-mo retrospective cohort study of 236379 COVID-19 survivors reported the prevalence and incidence rates of psychiatric and neurologic disorders. A lifetime anxiety disorder rate was 17.39%, a first anxiety disorder rate was 7.11%, while a lifetime and first attack mood disorder rates were 13.6% and 4.22%, respectively. Different from other studies, it was shown that the prevalence of substance use disorders and psychotic episodes increased. The first psychotic episode psychosis diagnosis rate was 0.42% while the first substance use disorder rate was 1.92% and insomnia rate was 2.53%[4].

There have been short-term follow-up studies on how the discharged COVID-19 patients' mental health manifests along with the disease course, but long-term follow-up studies are very few. One of them is from an Italian cohort with 238 patients 4 mo after discharge. In psychiatric assessment, 32.9% and 29.5% of participants showed anxiety and depressive symptoms, respectively. Changes in appetite and sleep patterns emerged in 15.6% and 31.2% of patients[5].

With the pandemic due to the risk of being infected and the prioritization of COVID-19 patients, patient follow-up has become difficult in psychiatry as in many branches. The spread of the use of telepsychiatry after the pandemic made online psychiatric interviews possible. Thus, studies about the pandemic could be continued, as well.

In this context, we aimed to investigate the long-term psychiatric effects of the pandemic on discharged COVID-19 patients through telepsychiatric interviews.

MATERIALS AND METHODS

This study was conducted in accordance with the Declaration of Helsinki Ethical Principles and was approved by the Ethical Committee of the Bezmialem Vakıf University (2021/414).

Setting, design, and participants

This retrospective cohort study focused on the longitudinal follow-up of psychological sequelae in recovered COVID-19 patients 20-22 mo after hospital discharge. Those 281 patients were hospitalized with COVID-19 according to the guidelines of the Turkish Ministry of Health between March 24, 2020 and May 24, 2020 at Bezmialem Vakıf University Hospital (Istanbul/Turkey). In the first part of this study, patients were evaluated psychiatrically during hospitalization and predictors of anxiety and depression were investigated[6]. This study, as a second step, aimed to explore anxiety and depression

levels of the same sample and their correlates after a long period (20-22 mo).

Two hundred and eighty-one patients were planned to be included. Twenty-nine patients refused to participate, 29 died, 25 changed their telephone numbers and new information was not available, 22 could not be reached, and 4 could not speak. Thus, 172 patients, who agreed to undergo a comprehensive telepsychiatric assessment, were enrolled (Figure 1).

Detailed socio-demographic data were recollected. Additionally, patients were asked for their vaccination status, if they lost any relatives and had been reinfected, any persistent physical symptoms, or insomnia after COVID-19 infection. To evaluate their anxiety-depressive symptoms, the Hospital Anxiety and Depression Scale (HADS) was administered through a telephonic interview. Those with significant complaints were advised to take psychiatric support.

Hospital anxiety and depression scale: As a self-report scale, HADS is composed of 14 items, of which seven (HADS-A) evaluate the anxiety and another seven (HADS-D) evaluate the depression severity of patients with physical illness. The cut-off score is 10 for the anxiety subscale and 7 for the depression subscale in the Turkish version[7]. Scales for anxiety and depression showed a high internal consistency, with Cronbach's alpha values ranging between 0.83 and 0.85.

Statistical analysis

All statistical analyses were performed using the IBM Statistical Package for the Social Sciences (SPSS) for Windows version 20.0 (SPSS Inc., Chicago, IL, United States).

In descriptive statistics, categorical variables are reported as numbers and percentages. Continuous data are presented as the mean \pm SD. Variables were checked for normal distribution assumption using histogram, skewness, and kurtosis in addition to the Kolmogorov-Smirnov test. HADS scores were analyzed by repeated measures ANOVA for different time points (at baseline and after 20-22 mo). Either Student's *t*-test or one way ANOVA (for independent variables in more than two categorical groups) tests were used to explore HADS-A, HADS-D scores, and related factors.

We did not adjust significance for multiple comparisons because the study is exploratory in nature. Two dependent variables (HADS-A and HADS-D) were included in each group comparison, thus the significance level was adjusted to 0.025. In order to test the association between significant predictors (sex, age, day of hospitalization, medical history, *etc.*) and each of the psychological outcomes above the cut-off scores, univariate logistic regressions were used. Variables that showed statistical significance at a *P*-value of less than 0.05 in the univariate analysis were included in the multivariate regression. Multivariate regression analysis was performed to identify the contribution of each factor associated with anxiety and depression separately. *Post-hoc* Tukey and Games-Howell tests were applied when there was a statistically significant difference in the Kruskal-Wallis test to determine which groups form the difference. A *P* value < 0.05 was considered significant.

RESULTS

The initial data of the follow-up study were evaluated cross-sectionally and published as a preliminary study.

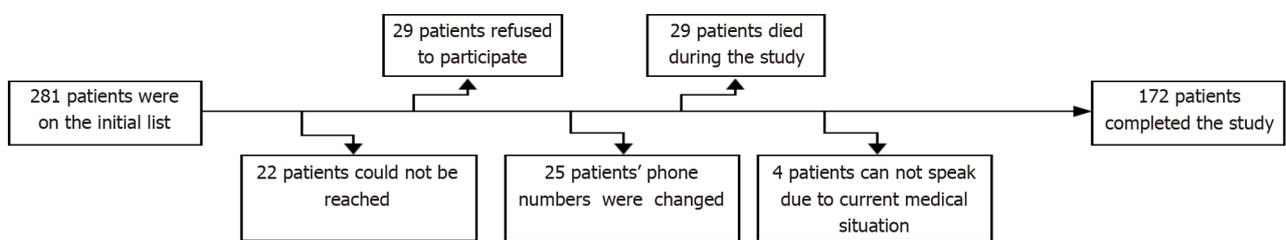
This study focused on the current status of discharged patients 20-22 mo after discharge and compared the results. The sociodemographic and clinical features of participants are shown in Table 1. Of the 172 patients included in the study, 83 (48.3%) were male, and 89 (51.7%) were female. The mean age was 53.23 ± 13.63 (range, 18–86) years. One hundred (58.1%) patients were over 50 years. Most (79.7%) of the participants were married, 13 (7.6%) were single, 7 (4.1%) were divorced, and 15 (8.7%) were widowed. The majority (91.1%) of the patients had child/children. The mean age of children was 24.39 ± 14.25 years. Regarding employment status, 41.3% of the patients were housewives, 30.2% were employed, 2.3% were unemployed, 23.3% were retired, and 2.9% were in the "other" (students and those whose job status was uncertain) category. Most of the participants were from low and middle-income groups (42.4% and 47.7%, respectively), and only 17 (9.9%) participants had a high income. Eighty-five (49.4%) patients had medical comorbidity, and hypertension, diabetes, and pulmonary diseases were the most common ones. Forty-six (26.7%) participants had psychiatric comorbidity, nearly half (11.6%) of them had depressive disorders, and anxiety disorders were the second most common psychiatric disorder (8.7%). Thirty-four (19.7%) patients reported past psychiatric treatment, and more than half of them (11.6%) used selective serotonin reuptake inhibitors. The vaccination rate was 89%; 2 BioNTech was the most commonly preferred vaccination type. Thirty-two (18.6%) patients had been reinfected by COVID-19; 29.7% had lost at least one relative due to COVID-19. Eighty-three (48.3%) patients had residual symptoms like tiredness, palpitation, insomnia, easy fatigue, and dyspnea. Tiredness was the most common one (39%). The mean days of initial hospitalization were 7.28 ± 5.17 . Twenty-nine (16.9%) patients were smokers, and the mean pack-years for the smokers were 21.58 ± 17.31 (range, 1 to 65).

The initial mean HADS-A score was 8.73 ± 5.422 , while the HADS-D score was 7.12 ± 5.508 during hospitalization for COVID-19. At the 20-22 mo follow-up, the mean HADS-A score was 9.08 ± 4.90 , and

Table 1 Sociodemographic and clinical features of participants

Sociodemographic features		n (%)
Sex	Female	89 (51.7)
	Male	83 (48.3)
Age (yr)	18-50	72 (41.9)
	50-86	100 (58.1)
Marital status	Married	137 (79.7)
	Single	13 (7.6)
	Divorced	7 (4.1)
	Widowed	15 (8.7)
Household	Family	137 (79.7)
	Roommate	3 (1.7)
	Partner	23 (13.4)
	Alone	9 (5.2)
Children	No	17 (9.9)
	Yes	155 (90.1)
Employment	Employed	52 (30.2)
	Unemployed	4 (2.3)
	Retired	40 (23.3)
	Housewife	71 (41.3)
	Other	5 (2.9)
Financial status	Low income	73 (42.4)
	Middle income	82 (47.7)
	High income	17 (9.9)
Smoking history	Yes	29 (16.9)
	No	143 (83.1)
Alcohol	Yes	6 (3.5)
	No	166 (96.5)
Clinical features		
Chronic disease	No comorbidity	85 (49.4)
	Hypertension	10 (5.8)
	Diabetes	8 (4.7)
	Cardiovascular	6 (3.5)
	Cancer	3 (1.7)
	Pulmonary	13 (7.6)
	Neurologic	3 (1.7)
	Gastrointestinal	1 (0.6)
	Thyroid	1 (0.6)
	Allergic	2 (1.2)
	Rheumatologic	1 (0.6)
	Endocrinology	1 (0.6)
	Metabolic	1 (0.6)
Other infections	1 (0.6)	

	Fibromyalgia	1 (0.6)	
	2 medical diseases, one from first 5	16 (9.3)	
	2 medical diseases, two from the first 5	2 (1.2)	
	2 or more of first 5	17 (9.9)	
Psychiatric comorbidity	Yes	46 (26.7)	
	No	126 (73.3)	
Reinfection	Yes	32 (18.6)	
	No	140 (81.4)	
Vaccination	Yes	153 (89)	
	No	19 (11)	
Which vaccine	None	17 (9.9)	
	2 Sinovac	22 (12.9)	
	3 Sinovac	33 (19.3)	
	2 BioNTech	55 (32.2)	
	2 Sinovac+1 BioNTech	36 (21.1)	
	2 Sinovac+2 BioNTech	3 (1.8)	
	1 BioNTech	4 (2.3)	
	1 Sinovac	1 (0.6)	
	Death of relatives caused by COVID-19	Yes	51 (29.7)
		No	121 (70.3)
Persistent symptoms	Yes	83 (48.3)	
	No	89 (51.7)	
	Tiredness	67 (39)	
	Palpitation	30 (17.4)	
	Dyspnea	30 (17.4)	
	Sleep disorders	5 (2.9)	
	Easy fatigue	5 (2.9)	
	Other symptoms	9 (5.2)	



DOI: 10.12998/wjcc.v10.i22.7832 Copyright ©The Author(s) 2022.

Figure 1 Flowchart of excluded cases.

the mean HADS-D score was 8.55 ± 4.39 . The mean HADS-A ($P = 0.484$) and HADS-D ($P = 0.011$) scores were increased when compared to those during hospitalization. Repeated measures ANOVA revealed that changes in HADS-D scores at follow-up were significant (Wilks' Lambda Sig.: 0.011; Partial Eta Squared: 0.038), while HADS-A score changes were not significant (Wilks' Lambda Sig.: 0.484; Partial Eta Squared: 0.003).

As shown in Table 2, we evaluated the associations between HADS-A and HADS-D scores at the 20-22 mo follow-up and sociodemographic and clinical features. Female patients had more anxiety symptoms than males. Participants over 50 years had more anxiety and depression symptoms than

Table 2 Comparison of anxiety and depression scores by different variables

	HADS-A score (mean ± SD)	P value	HADS-D score (mean ± SD)	P value
Sex				
Female	10.65 ± 5.16	0.0	8.65 ± 4.14	0.76
Male	7.40 ± 4.01		8.44 ± 4.67	
Age (yr)				
≤ 50	7.50 ± 4.73	0.000	7.12 ± 4.66	0.0
> 50	10.23 ± 4.73		9.58 ± 3.90	
Marital status				
Married	8.73 ± 4.93	0.003 (between married and widowed)	8.59 ± 4.34	> 0.05
Single	8.38 ± 4.48		6.61 ± 4.42	
Divorced	10.57 ± 6.57		9.42 ± 6.60	
Widowed	12.2 ± 2.98		9.40 ± 3.54	
Having children				
No	8.64 ± 4.22	0.69	6.94 ± 4.13	0.11
Yes	9.13 ± 4.98		8.72 ± 4.40	
Employment				
Employed	7.11 ± 4.57	0.000 (between employed and housewife)	7.76 ± 4.80	> 0.05
Unemployed	5.50 ± 3.51		8.50 ± 8.34	
Retired	9.00 ± 3.96		9.15 ± 3.81	
Housewife	10.80 ± 5.19		9.05 ± 4.13	
Other	8.80 ± 3.49		4.80 ± 2.28	
Financial status				
Low income	9.86 ± 4.25	> 0.05	9.16 ± 3.60	0.009 between low income and high income; 0.03 between middle income and high income
Middle income	8.79 ± 5.26		8.59 ± 4.78	
High income	7.17 ± 5.36		5.70 ± 4.66	
Household				
Family	8.68 ± 4.87	> 0.05	8.31 ± 4.52	> 0.05
Roommate	10.00 ± 5.29		8.66 ± 1.52	
Partner	11.08 ± 4.07		9.73 ± 3.10	
Alone	9.77 ± 6.55		9.11 ± 5.77	
Smoking				
No	9.33 ± 5.08	0.14	8.58 ± 4.38	0.81
Yes	7.86 ± 3.73		8.37 ± 4.53	
Chronic medical disease				
No	9.01 ± 4.48	0.84	8.59 ± 4.25	0.90
Yes	9.16 ± 5.32		8.51 ± 4.55	
Lifetime psychiatric disorder				
No	8.28 ± 4.90	0.00	8.29 ± 4.51	0.20
Yes	11.28 ± 4.24		9.26 ± 4.02	
Family member death caused by COVID-19				

No	8.71 ± 4.80	0.13	8.38 ± 4.27	0.43
Yes	9.96 ± 5.07		8.96 ± 4.69	
Vaccination				
No	6.00 ± 5.2	0.003	4.36 ± 4.07	0.00
Yes	9.47 ± 4.73		9.07 ± 4.16	
Reinfection				
No	8.82 ± 4.83	0.14	8.44 ± 4.31	0.49
Yes	10.21 ± 5.12		9.03 ± 4.80	
Symptoms				
No	8.00 ± 5.26	0.002	7.98 ± 4.85	0.082
Yes	10.25 ± 4.21		9.15 ± 3.78	
> tiredness				
No	8.30 ± 5.27	0.10	8.06 ± 4.77	0.01
Yes	10.26 ± 4.06		9.19 ± 3.59	
> palpitation				
No	8.71 ± 5.01	0.03	8.29 ± 4.44	0.09
Yes	10.83 ± 4.00		9.76 ± 3.99	
> dyspnea				
No	8.68 ± 4.99	0.18	8.49 ± 4.50	0.70
Yes	11.00 ± 3.99		8.83 ± 3.92	
> sleep disorders				
No	9.02 ± 4.90	0.33	8.53 ± 4.41	0.81
Yes	11.20 ± 4.96		9.00 ± 4.18	
> easy fatigue				
No	9.07 ± 4.90	0.81	8.64 ± 4.40	0.10
Yes	9.60 ± 5.54		5.40 ± 2.70	

Adjusted $P < 0.025$. HADS-A: Hospital anxiety and depression scale-anxiety score; HADS-D: Hospital anxiety and depression scale-depression score.

patients younger than 50 years. Marital status had a significant association with anxiety symptoms but had no significant association with depressive symptoms. In the *post hoc* analysis, widowed patients had a higher mean HADS-A score than married patients (Games-Howell test; $P = 0.003$). Employment status was significantly associated with anxiety symptoms as well. In the *post hoc* analysis, housewives had a significantly higher mean HADS-A score than employed patients (Tukey test; $P = 0.000$). Additionally, financial status had a significant association with depressive symptoms, but no significant association with anxiety symptoms. In the *post hoc* analysis, patients with a low and middle income showed more depressive symptoms than patients with a high income (Tukey test; $P = 0.009$ and $P = 0.03$, respectively). Vaccinated patients had significantly higher mean HADS-A and HADS-D scores compared to unvaccinated ones. There was no significant difference between the vaccination preferences of the individuals. When all the residual symptoms were considered, the mean HADS-A score of those with residual symptoms after COVID-19 was significantly higher. Tiredness caused a significantly higher mean HADS-D score ($P = 0.01$). On the other hand, being reinfected was not associated with higher anxiety and depression scores.

Multiple linear regression analysis showed that being vaccinated, having a low income, and being over 50 years old were associated with increased depressive symptoms (adjusted $R^2 = 0.170$) (Table 3).

Being vaccinated, being over 50 years old, female sex, and dyspnea were significantly associated with increased anxiety symptoms (adjusted $R^2 = 0.245$) (Table 4).

Changes in HADS scores (HADS scores at the 20-22 mo follow-up minus those at the hospitalization/baseline) were analyzed by multivariate regression for associated factors as well. The "tiredness" and HADS-D score changes were associated with increased anxiety symptoms (adjusted $R^2 = 0.487$) (Table 5). Being vaccinated and baseline HADS-D were significantly associated with increased depressive symptoms (adjusted $R^2 = 0.671$) (Table 6).

Table 3 Multivariate regression analysis of factors associated with depressive symptoms

Coefficients							
Model	Unstandardized coefficients		Standardized coefficients	T	Sig.	95.0% confidence interval for B	
	B	Std. error	Beta			Lower bound	Upper bound
(Constant)	5.381	1.8439		2.92679	0.004	1.750	9.012
Vaccination	4.172	1.002	0.298	4.162	0.000	2.193	6.151
> 50 yr	1.644	0.643	0.185	2.558	0.011	0.375	2.912
Financial status	-1.174	0.478	-0.173	-2.455	0.015	-2.118	-0.230

Table 4 Multivariate regression analysis of factors associated with anxiety symptoms

Coefficients							
Model	Unstandardized coefficients		Standardized coefficients	T	Sig.	95.0% confidence interval for B	
	B	Std. error	Beta			Lower bound	Upper bound
(Constant)	8.678	2.232		3.887	0.000	4.270	13.086
Vaccination	3.355	1.108	0.215	3.028	0.003	1.167	5.543
> 50 yr	1.656	0.695	0.167	2.384	0.018	0.284	3.028
Dyspnea	1.747	0.874	0.135	2.000	0.047	0.022	3.472
Sex	-2.747	0.702	-0.280	-3.914	0.000	-4.133	-1.361
Marital status	0.641	0.364	0.121	1.761	0.080		1.360
Psychiatric comorbidity	-1.348	0.789	-0.122	-1.709	0.089		0.209

Table 5 Tiredness” and hospital anxiety and depression scale-depression score changes are associated with increased anxiety symptoms

Coefficients							
Model	Unstandardized coefficients		Standardized coefficients	T	Sig.	95.0% confidence interval for B	
	B	Std. error	Beta			Lower bound	Upper bound
(Constant)	-1.226	1.151		-1.065	0.288	-3.499	1.047
Delta HADS-D	0.634	0.054	0.675	3.028	0.000	0.528	0.740
Tiredness	1.793	0.761	0.131	2.384	0.020	0.290	3.296
Vaccination	0.002	1.209	0.000	2.000	0.999	-2.386	2.389

Delta-HADS-D: Delta-hospital anxiety and depression scale-depression score.

DISCUSSION

It is known that major pandemics negatively affect mental health for many reasons. Going through a severe COVID-19 infection, being hospitalized, and being taken to the intensive care unit can cause great stress in patients and leave them with psychiatric problems. Long-term follow-up studies about the COVID-19 outbreak are newly established, but the difficulty of accessing patients due to the risk of contamination also limits the studies in this area. Although the use of telepsychiatry serves to reduce this limitation, it also raises questions when compared to the detailed and efficient evaluation of face-to-face interviews. There are also studies showing that online interviews and treatments using the telepsychiatry method which has become widespread, especially after the epidemic in Turkey, have similar effectiveness to face-to-face interviews[8].

In our study, we conducted a follow-up interview among patients who underwent psychiatric evaluation while receiving inpatient care for COVID-19 between March-May 2020 20-22 mo later (in January 2022). We updated the initial data for 172 patients to maintain comparisons only with those

Table 6 Being vaccinated and baseline HADS-D score are significantly associated with increased depressive symptoms

Coefficients							
Model	Unstandardized coefficients		Standardized coefficients	T	Sig.	95.0% confidence interval for B	
	B	Std. error	Beta			Lower bound	Upper bound
(Constant)	4.592	1.113		4.125	0.000	2.394	6.789
Reinfection	0.600	1.113	0.032	0.723	0.471	-1.038	2.238
Vaccination	4.680	1.012	0.204	4.626	0.000	2.683	6.677
HADS-A	-0.014	0.093	-0.010	-0.149	0.881	-0.197	0.170
HADS-D	-1.015	0.093	-0.773	0.10951	0.000	-1.198	-0.832

HADS-A: Hospital anxiety and depression scale-anxiety score; HADS-D: Hospital anxiety and depression scale-depression score.

who completed the follow-up study. We observed that the mean HADS-A and HADS-D scores were increased in the follow-up compared to the baseline status. Sixty-five (38.5%) patients had over-the-threshold anxiety and 68 (39.5%) had over-the-threshold depression during hospitalization while these figures were 111 (64.5%) for anxiety and 63 (36.6%) for depression at the follow-up.

Despite that we expected a decrease in anxiety after recovery from COVID-19, it increased according to both the mean scores and the cut-off values of HADS-A. Further analysis revealed that being over 50 years old, female gender, marital status (widowed), psychiatric comorbidity, and dyspnea as a residual symptom were factors associated with this increase. Old age is a period of increased physical/mental fragility. Thus, the incapacity to face major life crises may be related to anxiety (also to depression). The fact that the curfew lasted for a long time for people over 65 years in Turkey, isolation from their relatives due to the risk of contamination, and being subjected to travel ban may be among the factors that have increased their anxiety. Besides, being widowed is the loss of closest social support and relationship, and it is more common in the elderly. Residual dyspnea can also increase anxiety by causing health concerns. Female gender and comorbid psychiatric diseases are notable risk factors for anxiety disorders as in the general population[9]. Additionally, the ongoing pandemic process, the persistence of uncertainty, the loss of relatives and friends, the need for repeated vaccinations, and the economic problems experienced after the pandemic can be related to the rise in anxiety symptoms.

When depression is considered, the mean depression score was increased, but there was no significant increase in the percentage of patients who had over-the-threshold depression. Even though the acute phase of the pandemic with no vaccine has passed, we observed an increase in the depression scores while we had expected a decrease. Having a low income, being older than 50 years, and being vaccinated were found to be associated with increased depressive symptoms. Low financial status and being elderly were both expected and understandable risk factors for depression, apart from COVID-19. Moreover, it may be necessary to distinguish between the loss of loved ones, grieving processes, and other negative effects of the pandemic.

In contrast to our results, the current literature shows that vaccinated people reported decreased mental distress levels. As expected, vaccinated people become less worried about getting infected, they may become more active socially, or they may venture into different work opportunities[10]. The correlation between vaccination and HADS-A and HADS-D scores in our study may be related to the tendency of people with anxiety and depression to be vaccinated.

After the first study, the decrease in the rate of medical comorbidity in our sample was due to the death of 29 people with comorbidities. We thought that losing a relative, being reinfected, having a comorbid medical disease, and having residual complaints would be associated with an increase in anxiety and depression, but we could not find a significant difference. This may be due to the small size of our sample and should be replicated in further studies. Lack of a significant increase in anxiety in reinfected patients may be explained by the "habituation with repeated exposure".

In Wuhan, following COVID-19 treatment in the hospital during the general quarantine period, 782 discharged patients were re-evaluated 1 mo later in home isolation. The prevalence rates of insomnia, anxiety, and depressive symptoms among discharged COVID-19 patients during the centralized quarantine period were 44.37%, 31.59%, and 27.62%, respectively. Afterward, the prevalence rates during the home isolation were 27.11%, 17.26%, and 16.11%, respectively[11]. Inconsistent with our results, anxiety and depressive symptoms were decreased. Unlike our study, they observed that mental symptoms decreased significantly when home isolation started but the period after discharge was only 1 mo in this sample. Similar to our study, being women, being elderly, and having previous medical history were associated with anxiety and depressive symptoms. In our study, the mean HADS-A score was higher in patients with medical comorbidity compared to those without, but there was no significant statistical difference. The small size of our sample compared to this study may be the reason why we could not find a difference. Surprisingly, the mean depression score was lower in those with

chronic illness, although it was not statistically significant. In a study in Wuhan, fewer mental health problems were detected in alcohol and cigarette users. In our study, we also found the mean scores of both anxiety and depression in smokers to be lower, although not significantly. As stated in this study, this is possible because most of the smokers and drinkers were men who had fewer mental health problems than women. On the other hand, the decrease in psychiatric complaints was surprising since smokers may have difficulties in managing stress.

As far as we could see in the literature, the longest follow-up study was a cohort study evaluating patients between 24-60 wk after COVID-19. Similar to our study, symptom scale scores for depression, insomnia, and posttraumatic stress disorder were increased at the long-term follow-up[12]. As far as we can see, our study is both the longest follow-up study in the literature and the first follow-up study in Turkey investigating anxiety and depression symptoms.

The fact that anxiety and depression scores increased especially in women, the elderly, patients with lower financial status, and patients with psychiatric comorbidity compared to the baseline indicates that special support by psychological counseling should be given to these groups. Women may have been affected more than men due to their gender roles (caring for children and sick family members, more responsibility for housework). People over the age of 50 may be at greater risk of anxiety and depression due to their general health concerns and their potential to experience a decrease in general functionality. Psychiatric comorbidity has always been a predictor of new psychiatric problems. Additionally, in the telepsychiatry interview, patients frequently complained about the economic difficulties experienced during the pandemic process which may cause as many adverse psychological effects as the pandemic. For this reason, the economic support strategy seen in many countries is an appropriate and necessary step to be taken.

Limitations: Post-pandemic various issues such as boredom of living with pandemic conditions, the obligation to wear a mask, the obligation to be vaccinated, vaccine hesitancy, and economic difficulties may have an impact on the increase in anxiety and depression in Turkey. National identity and each country's unique socio-political interventions towards the pandemic process also change the course of the pandemic as a confusing factor[13]. It is a limitation of our study, not to review the impact of such various events separately with a control group. In this way, we have associated everything that affects anxiety and depression in the long follow-up period of about two years with COVID-19. The lack of face-to-face interviews and the limitations of self-report scales are our other shortcomings.

CONCLUSION

The course of long-term psychiatric symptoms related to COVID-19 is still uncertain. Contrary to what we expected in our study, we observed that anxiety and depression scores increased even more in long-term follow-up. As this is the longest follow-up study in the literature, we would like to emphasize the importance of our results in clinical practice. To prevent the deterioration of mental health, psychiatrists should play an active role in identifying emerging mental problems as soon as possible, and psychological support should be offered for discharged patients, especially for more vulnerable groups. For this purpose, we need stronger data with larger samples to properly identify the consequences of the COVID-19 pandemic on mental health and detect patients who might be more in need of further support and care.

ARTICLE HIGHLIGHTS

Research background

The authors designed a prospective study to compare the scores at baseline (hospitalization) of patients diagnosed with coronavirus disease 2019 (COVID-19) on a rating scale measuring anxiety and depression with their scores at the end (after 20-22 mo). This is the longest follow-up study in the literature.

Research motivation

The course of long-term psychiatric symptoms related to COVID-19 is still unknown.

Research objectives

To evaluate how anxiety and depression progress and identify the factors that play a role in this course by long-term follow-up.

Research methods

A large number of patients were reached in a short time using the telepsychiatry method.

Research results

In our study, we observed that anxiety and depression scores increased during the follow-up. The continuation of long-term follow-up studies will contribute to the clarification of the subject.

Research conclusions

The authors found that the mean scores of anxiety and depression increased in the follow-up after recovery in patients who had COVID-19. This confirmed the knowledge that there may be various permanent or temporary mental symptoms related to COVID-19. The authors observed that the symptoms of anxiety and depression secondary to COVID-19 increased while we expected them to decrease in the long follow-up. For this reason, patients with COVID-19 should be examined as soon as possible and necessary treatments should be given.

Research perspectives

More comprehensive follow-up studies for psychiatric symptoms secondary to COVID-19 should be continued and the importance of early intervention should be emphasized.

FOOTNOTES

Author contributions: Boyraz RK contributed to literature search, figure preparation, study design, data analysis and interpretation, and draft writing; Boylu ME contributed to data collection and interpretation, and statistical analysis; Şahan E contributed to literature search, figure preparation, study design, data analysis and interpretation, and revision and supervision of the manuscript; and Kirpınar İ contributed to supervision of the manuscript.

Institutional review board statement: This study was conducted in accordance with the Declaration of Helsinki Ethical Principles and was approved by the Ethical Committee of the BezmialemVakıf University (2021/414).

Informed consent statement: All study participants provided informed consent prior to study enrollment.

Conflict-of-interest statement: All authors report no relevant conflicts of interest for this article.

Data sharing statement: Additional SPSS data could be shared when requested.

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S-Editor: Ma YJ

L-Editor: Wang TQ

P-Editor: Ma YJ

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