75367_Auto_Edited.docx

WORD COUNT	3152	TIME SUBMITTED	18-MAY-2022 10:46PM
		PAPER ID	86092935

Name of Journal: *World Journal of Clinical Cases*
Manuscript NO: 75367
Manuscript Type: ORIGINAL ARTICLE

Retrospective Cohort 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

Abstract

BACKGROUND

Patients who are hospitalized for coronavirus disease 2019 (covid-19) face an extremely stressful experience that might challenge 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

The patients were evaluated with a telepsychiatric interview and the Hospital Anxiety and Depression Scale (HADS). Sociodemographic and clinical features were analyzed with regression. 172 patients were enrolled.

RESULTS

The mean HADS-Anxiety -A (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=.484) and HADS-D (p=.011) scores were increased compared to scores during hospitalization. Being over 50

years old, lower financial status, and being vaccinated were associated with symptoms of depression (adjusted R square= .168) while being over 50 years old, female sex, being vaccinated and dyspnea were associated with higher anxiety (adjusted R square= .245).

CONCLUSION

To prevent the deterioration of mental health psychiatrists should play an active role in identifying the 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; Retrospective cohort; Tele medicine; Psychiatry

Boyraz 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; In press

Core Tip: Covid-19 causes various psychiatric outcomes like other coronaviruses. This study aims to observe anxiety and depressive symptoms and related factor at 20-22 mo follow-up. The goal of this study is to identify groups at high risk of anxiety and to raise awareness about providing psychiatric support to these groups.

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 SARS, the Middle East respiratory syndrome (MERS), and the Ebola Virus Disease (EVD) outbreak reported that psychological symptoms might persist or arise after the infection with long-term negative outcomes [1].

Neurological and psychiatric outcomes of covid 19 have been reported in various studies [2, 3]. A 6-month retrospective cohort study of 236.379 covid-19 survivors reported prevalence and incidence rate 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 prevalence of substance use disorders and psychotic attack were increased. The first attack psychosis diagnosis rate was 0.42% while the first substance use disorder rate was 1.92% and insomnia was 2.53% respectively [4].

We see 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 yet. One of them is from an Italian cohort with 238 patients, after 4 mo of discharge. In psychiatric assessment, 32.9% and 29.5% of participants showed anxiety and depressive symptoms, respectively. Changes in appetite and sleep patterns emerged for 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

MATHERIALS 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 after 20-22 mo of hospital discharge. Those 281 patients were hospitalized with covid-19 according to the guideline of the Turkish Ministry of Health between March 24th, 2020, and May, 24th, 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).

281 patients were planned to include. 29 patients refused to participate, 29 patients died, 25 patients changed their telephone numbers and new information was not available, 22 patients could not be reached, and 4 people could not speak. Thus, 172 patients, who agreed to undergo a comprehensive telepsychiatric assessment, were enrolled, and 271 data were available for the statistical analyses (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 (HADS): As a self-report scale HADS is composed of 14 items, 7 items (HADS-A) evaluate the anxiety and 7 items (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 alphas 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, Illinois, USA).

In descriptive statistics, categorical variables were reported as numbers and percentages. Continuous data were presented as mean ± standard deviation (Mean ± SD). Variables were checked for normal distribution assumption using histogram, skewness, and kurtosis in addition to the Kolmogorov-Smirnov test. Either Student's t-test or One Way ANOVA 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 planned to be 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. Correlates 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. Tukey and Games-Howell tests were applied for post-hoc

analysis when there was a statistically significant difference in the Kruskal-Wallis test to determine which groups form the difference. A p-value <.05 was considered significant.

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 (ranged 18–86) years. 100 patients (58.1%) were over 50 years. Most of the participants (79.7%) were married, 13 participants (7.6%) were single, 7 participants (4.1%) were divorced and 15 participants (8.7%) were widowed. 91.1% of the patients had child/children. The mean childrens' age was 24.39± 14.25. Regarding employment status, 41.3% of 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 is uncertain) category. Most of the participants were from low and middle-income groups (42.4% and 47.7%, respectively), only 17 (9.9%) participants had a high income. 85 patients (49.4%) had medical comorbidity, hypertension, diabetes, and pulmonary diseases were the most common ones. 46 participants (26.7%) had psychiatric comorbidity, nearly half of them had (11.6%) depressive disorders, anxiety disorders had been seen as the second most common psychiatric disorder (8.7%). 34 (19.7%) patients reported past psychiatric treatment, 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. 32 patients (18.6%) had been reinfected by covid-19; 29.7% of patients had lost at least one relative due to covid-19. 83 patients (48.3%) had residual symptoms like tiredness, palpitation, insomnia, easy fatigue, and dyspnea. Tiredness was the most common one (39%). The mean day of hospitalization at initial was 7.28 ± 5.17. 29 (16.9%) patients were smokers, and the mean pack-years for the smokers was 21.58 ± 17.31 (ranged 1–65).

The mean HADS-A score was 9.08 ± 4.90, and the mean HADS-D score was 8.55 ±4.39. The mean HADS-A (p=.484) and HADS-D (p=.011) scores were increased compared to hospitalization.

In Table 2, we evaluated the associations between HADS-A and HADS-D scores and sociodemographic and clinical features. Female patients had more anxiety symptoms than males. Participants over 50 years had more anxiety and depression symptoms than 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 higher mean HADS-A than married patients (Games-Howell test; P = 0.003). Employment status was significantly associated with anxiety symptoms as well. In 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 post hoc analysis, patients from low and middle income showed more depressive symptoms than patients from high income (Tukey test; P = 0.009 and P = 0.03 respectively). Vaccinated patients had significantly higher HADS-A and HADS-D mean 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 low income and being over 50 years old were associated with increased depressive symptoms (adjusted R square= .170) (Table 3).

Multiple linear regression analysis showed that being vaccinated, being over 50 years old, female sex and dyspnea were significantly associated with increased anxiety symptoms (adjusted R square= .245) (Table 4).

DISCUSSION

It is known that major pandemics negatively affect mental health for many reasons. Going through a severe covid-19 infection, being hospitalized, 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 about a detailed and efficient evaluation as in face-to-face interviews. There are also studies showing that online interviews and treatments with the telepsychiatry method, which has become widespread especially after the epidemic in our country, have similar effectiveness with face-to-face interviews [8].

In our study, we conducted a follow-up interview 20-22 mo later (in January 2022) with patients who underwent psychiatric evaluation while receiving inpatient care for covid-19 between March-May 2020. We updated the initial data for 172 patients to maintain comparisons only with those who completed the follow-up study. We observed that the mean HADS-A and HADS-D levels were increased in the follow-up compared to the baseline status. 65 patients (38.5%) had over the threshold anxiety and 68 patients (39.5%) had over the threshold depression during hospitalization while this rate was 111 (64.5%) for anxiety and 63 (36.6%) for depression at the follow-up.

Despite 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, 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 our country, 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. 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. Being from low income, 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.

The correlation between vaccination and HADS-A and HADS-D scores 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 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 significant increase in anxiety in reinfected patients may be explained by the "habilitation with repeated exposure".

In Wuhan following covid-19 treatment in hospital during the general quarantine period, 782 discharged patients were re-evaluated one month 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 [9]. 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 one month in this sample. Similar to our study, being women, elderly, and having previous medical history was 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 difference. The small size of our sample compared to this study may be the reason why there was no significant 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 PTSD were increased at long-term follow-up [10]. As far as we can see, our study is both the longest follow-up study in the literature and the first follow-up study from our country investigating anxiety and depression symptoms in our country.

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 for new psychiatric problems. Additionally, in the telepsychiatric 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, not all vaccines are accepted in international travel and economic difficulties may have an impact on the increase in anxiety and depression in our country. 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 2 years with covid-19. The lack of face-to-face interviews and the limitations of self-report scales are our other shortcomings.

CONCLUSION

To prevent the deterioration of mental health psychiatrists should play an active role in identifying the 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.

75367_Auto_Edited.docx

ORIGINALITY REPORT

10%
SIMILARITY INDEX

PRIMARY SOURCES

1	www.frontiersin.org Internet	171 words — 5%
2	dusunenadamdergisi.org Internet	48 words — 1%
3	researchinpsychotherapy.org Internet	45 words — 1%
4	covid19-data.nist.gov Internet	36 words — 1%
5	www.nature.com Internet	22 words — 1%
6	storage.googleapis.com Internet	21 words — 1%

EXCLUDE QUOTES	ON	EXCLUDE SOURCES	< 1%
EXCLUDE BIBLIOGRAPHY	ON	EXCLUDE MATCHES	< 10 WORDS