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The effect of having COVID-19 on insomnia, fatigue, and quality of life: A comparative study with vaccinated and unvaccinated COVID-19–negative patients

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ABSTRACT

Aim: To compare insomnia, fatigue, and activities of daily living of patients who were infected during the coronavirus disease-2019 (COVID-19) pandemic with those who did not have the infection, according to their vaccination status.

Methods: A total of 176 volunteers (104 women and 72 men) participated in the study. The study group was divided into three groups: patients who had COVID-19, individuals who did not have COVID-19 and were vaccinated, and those who did not have COVID-19 and were not vaccinated. The data collection tools were a personal information form; insomnia, fatigue and activities of daily living short questionnaire; and anxiety and depression inventories, which evaluated psychological status.

Results: There was no difference in terms of depression, insomnia, fatigue, and quality of life scale scores between the groups. Work and education status did not affect scores. The fatigue rate was higher in those who had COVID-19 (10.7%, *p*=0.007). Women's fatigue scores were higher (*p*<0.001), and their physical and psychological health scores in the quality of life scale were lower than men's (*p*=0.025 and *p*=0.007, respectively). The anxiety score of married participants was higher (*p*=0.021). The rate of insomnia was high in the entire study group (41.7%). Depression and anxiety were positively correlated with insomnia and fatigue. Depression was negatively correlated with all sub-parameters of quality of life, and anxiety was negatively correlated with physical, psychological health, and environment. There was no difference between insomnia, fatigue, depression, and quality of life scale scores between the groups, irrespective of COVID-19 infection.

Conclusion: The high rates of insomnia and depression suggested that the progression of the pandemic also brought about chronic health problems. Therefore, it is important to conduct extensive preventive health programs for the population.

Key words: COVID-19 pandemic, insomnia, fatigue, quality of life scale, anxiety, depression.

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Introduction

It has been 1.5 years since the emergence of coronavirus disease-2019 (COVID-19). Headache, fatigue, and widespread pain lasting weeks to months in the post-COVID-19 period are among the causes of admission to neurology outpatient clinics. During this period, limitations in lifestyle, fear of illness, and unknowns have changed the psychological and social lives of many people and brought additional problems. Prolonged curfews, reduction of close and friendly meetings, changes in work patterns, the transition to distance education in schooling, and the increase in the time spent at home and alone are

issues that the pandemic has brought to our lives. While the COVID-19 pandemic continues, restrictions continue to a certain extent. Every day brings different information about both COVID-19 and vaccines. The change in our lifestyle and habits has also changed our sleep-wake cycle. Increased prevalence of anxiety, depression, and sleep disorders have been observed [1]. Many studies among the normal population and students found high percentages of sleep disorders [2]. A comparison of individuals by age found that the younger population was more affected by this condition [3].

Fatigue and quality of life are other aspects that need to be evaluated. Post-COVID-19 fatigue is a condition that begins after COVID-19 and continues uninterrupted for 3-6 months. Although there are deficiencies in the definition and there are issues that need to be investigated, this is a serious condition that interrupts and disrupts daily life activities. Both medical and psychological causes can manifest themselves as fatigue. Psychological state fatigue and fatigue also affect our quality of life.

In our study, we planned to investigate the effect of being vaccinated against COVID-19 and having the infection. Has getting vaccinated and having an infection reduced fears and fixed our daily routine? Is the severity of insomnia and fatigue different from the normal population in patients with COVID-19? How does vaccination affect this situation? Our study aimed to investigate the effect of the COVID-19 pandemic on sleep, fatigue, and quality of life.

Materials and methods

Study design and participants

This was a cross-sectional study performed on volunteers aged over 18 years living in Istanbul, Tekirdağ, and Izmit (all of these provinces are

metropolitan cities) between June 1st and September 1st, 2021. The patients were divided into three groups as patients who had COVID-19 (group 1), vaccinated and uninfected patients (group 2), and unvaccinated and uninfected patients (group 3). The sociodemographic characteristics of the patients, accompanying systemic diseases, drugs used, whether they had previous sleep disorders, whether they had COVID-19 (whether they received inpatient or outpatient treatment for this), and whether they were vaccinated were recorded. The forms were completed by the patients themselves during face-to-face interviews. The fatigue of the patients was measured using the Fatigue Severity Scale, insomnia was measured using the Insomnia Severity Index, and quality of life was measured using the short form of the World Health Organization Quality of Life Scale. In addition, the Beck Depression Inventory (BDI) and COVID-19 Brief Anxiety Inventory were used to determine the accompanying neuropsychiatric status.

Measurement tools

Sociodemographic data records: The patients' age, education, marital status, whether they were working, whether there was a change in work patterns during the COVID-19 pandemic, whether they worked shifts, their medical history, medications used, and whether they had previous sleep disorders were recorded. It was recorded whether the patients had had COVID-19, whether they were at home or in the hospital, the treatments they received, their vaccination records (vaccine name and the number of doses administered), and whether there was a death of relatives due to COVID-19.

Insomnia severity index (ISI): Insomnia severity is determined by 7 items. Each item is

scored as 4 points with 0 and the total score is between 0 and 28. A score of 0-7 indicates no insomnia, a score of 8-14 indicates a low threshold for insomnia, a score of 15-21 indicates moderate, and a score of 22 and above indicates severe insomnia [4].

The short form of the World Health Organization Quality of Life Scale (WHOQOL-BREF): The WHOQOL-BREF defines quality of life as "how an individual perceives their life concerning their goals, expectations, standards, and concerns within the culture and value system in which they live." There is one more question about the environment in Turkey's adaptation and it covers a total of 27 questions [5]. This questionnaire evaluates five sub-parameters: general health (two questions), physical health (seven questions), psychological health (six questions), social relations (three questions), and environmental parameters (eight questions). The total score and subgroup scores are evaluated separately. A high score indicates a high quality of life.

Fatigue severity scale (Fatigue) (FSS): The validity and reliability study of the FSS, which was developed by Krupp et al. [6] in 1989, was conducted by Armutlu et al. in Turkey in 2007 [7]. A 9-item FSS was created by choosing fatigue characteristics. Each item is scored from 1 (I do not agree) to 7 (I agree). Less than 2.8 indicates no fatigue, and over 6.1 indicates chronic fatigue.

Beck depression inventory (BDI): The inventory contains 21 self-assessment statements scored on a 4-point scale. A high total score indicates a high level of intensity of depression. A score of 0-10 points indicates no depression, 11-17 mild depression, 18-23 moderate depression, and 24 or above severe depression [8-9].

The short form of the Coronavirus Anxiety Scale: The Turkish validity and reliability of the Coronavirus Anxiety Scale (CAS), which was developed by Lee et al. [10] to identify patients with possible dysfunctional anxiety associated with the COVID-19 crisis, was established [11]. The scale consists of five questions and scores from 0 to 4. The higher the score, the greater the severity of anxiety.

Data collection
The study was conducted face-to-face with volunteer participants aged over 18 years. All participants were informed about the study and their consent was obtained. The volunteers completed the measurement tools. Approval for the study was obtained from the ethics committee of Prof. Dr. Cemil Taşçıoğlu City Hospital (Date: 24.05.2021, No.: E-48670771-514.10).

Statistical analysis
Statistical Package for the Social Sciences-PC Version 25.0 (SPSS 25.0) package program was used for statistical analysis of the data. Mean ± standard deviation and percentage values were calculated for all variables. The conformity of the quantitative data to normal distribution was measured using the Kolmogorov-Smirnov test and its graphical evaluations. Pearson's Chi-square test and Fisher's exact test were used for comparing categorical variables. Non-parametric differences between two groups in terms of numerical variables were determined using the Mann-Whitney U test. Spearman correlation analysis was used to evaluate the relationships between quantitative variables. The Kruskal-Wallis test was used for comparisons of groups of three or more that did not show normal distribution, and Tomhone's T2 test was used for pairwise comparisons. The results of the research were evaluated by accepting the

$p<0.05$ value as significant in the 0.95 confidence interval.

Results

The data were collected through face-to-face interviews during the third wave of the pandemic between June 1st and September 1st, 2021. The study was conducted with a total of 176 participants, 104 (59%) women, and 72 (4%) men. The mean age was 35.76±11.84 (range, 18-69) years. Sociodemographic characteristics according to the groups are shown in Table 1. In the pairwise comparison, the mean age of the COVID-19 group was not different from groups 2 and 3. There were differences in age only between groups 2 and 3

($p<0.001$), which was related to the vaccination policy (the elderly were prioritized). There was no difference between the three groups in terms of concomitant diseases. The most common comorbidities were hypertension, diabetes mellitus, and thyroid dysfunction. When evaluated in terms of habits (smoking and/or alcohol use), group 2 had a rate of 50.8%, which was higher than in the other groups. The rate was 28.6% in group 1 and 27.8% in group 3 ($p=0.006$). There was no statistically significant difference in terms of anxiety, depression, insomnia, and fatigue and WHOQOL-BREF scores and WHOQOL-BREF subgroups scores between the groups (Table 2).

Table 1. Sociodemographic characteristics of the study group.

Parameters	Group 1	Group 2	Group 3	*P*-value
Age				
Mean ± SD	35.82±1.47	40.62±1.55	31.01±1.37	***<0.001***
Median (min-max)	34.5 (18-63)	40 (20-69)	28 (18-55)	
Sex	N (%)	N (%)	N (%)	
Female	26 (46.4)	32 (54.2)	42 (68.9)	*0.158*
Male	30 (53.6)	27 (45.8)	19 (31.1)	
Marital status				
Single	24 (42.8)	20 (33.9)	35 (57.4)	***0.033***
Married	32 (57.1)	39 (66.1)	26 (42.6)	
Education level				
Primary	9 (14.3	5 (8.5)	9 (13.1)	*0.368*
Secondary	11 (19.6)	12 (20.3)	22 (36.0)	
University	36 (64.3)	42 (71.2)	30 (49.2)	
Job status				
Yes	41 (73.2)	48 (81.4)	34 (55.7)	***0.008***
No	15 (26.8)	11 (18.6)	17 (44.3)	
Change in work pattern				
Yes	13 (23.2)	18 (30.5)	11 (18.0)	*0.274*
No	43 (76.8)	41 (69.5)	27 (44.3)	
Working shifts				
Yes	4 (7.1)	2 (3.4)	0 (0)	*0.066*
No	52 (92.9)	57 (96.6)	61 (100)	

Group 1=COVID-19(+); Group 2=vaccine (+), COVID-19 (-); Group 3=vaccine (-), COVID-19(-); Pearson Chi-square test.

Table 2. Comparison of depression, anxiety, fatigue, insomnia, and quality of life scores of the groups.

Parameters	Group 1	Group 2	Group 3	P-value
Anxiety	0 (0-16)	0 (0-11)	0 (0-12)	0.282
Depression	9 (0-37)	9 (0-39)	11 (0-41)	0.056
Insomnia	6 (0-34)	6 (0-17)	7 (0-25)	0.333
Fatigue	36 (1-63)	36 (0-56)	39 (14-61)	0.298
General health status	6.5 (3-9)	7 (4-10)	7 (3-10)	0.204
Physical health	27 (16-35)	28 (13-35)	27 (13-35)	0.276
Psychological health	22 (12-29)	23 (10-30)	22 (13-30)	0.150
Social relationship	11 (6-15)	11 (3-15)	11 (6-15)	0.455
Environment	28 (14-40)	28 (12-40)	27 (13-40)	0.800

The values are given as median (min-max).

Table 3. Comparison of the groups according to the degree of depression, insomnia, and the presence of fatigue.

Parameters	Group 1 (n, %)	Group 2 (n, %)	Group 3 (n, %)	*P*-value
Depression severity				
None	31 (55.4)	31 (52.5)	24 (39.3)	
Mild	14 (25.0)	19 (32.2)	18 (29.5)	*0.343*
Moderate	9 (16.1)	7 (11.9)	13 (21.3)	
Severe	2 (3.6)	2 (3.4)	6 (9.8)	
Insomnia Severity				
None	33 (58.9	37 (62.7)	35 (57.4)	
Mild	16 (28.6)	21 (35.6)	22 (36.1)	*0.426*
Moderate	4 (7.1)	1 (1.7)	2 (3.3)	
Severe	3 (5.4)	0 (0)	2 (3.3)	
Death of a relative				
No	47 (83.9)	51 (86.4)	45 (73.8)	*0.170*
Yes	9 (16.1)	8 (13.6)	16 (26.2)	
Fatigue				
No	50 (89.3)	59 (100)	60 (98.4)	***0.007***
Yes	6 (10.7)	0 (0)	1 (1.6)	

Considering the depression rate (mild, moderate, and severe), a rate of 44.7% was found in those who had COVID-19 (group 1), 47.5% in group 2, and 60.6% in group 3. Although not statistically significant, the depression rate of group 3 was higher. When the FSS total score was divided into two groups as chronic fatigue above 6.1 and below 6.1, the presence of fatigue was 10.7% in patients who had COVID-19, whereas it was 0% in group 2

and 1.6% in group 3. There was a significant difference between the groups (p=0.007). When the patients who had COVID-19 with fatigue were evaluated according to whether they were working, no significant difference was found (*p*=0.515). When our entire study group was evaluated, the rate of insomnia was found as mild in 33.5%, moderate in 5.4%, and severe in 2.8%. When those who had COVID-19 were evaluated separately, this rate was 28.6% for mild, 7.1% for moderate, and 5.4% for severe insomnia. There was no difference in the frequency and degree of insomnia between groups 1 and 2 and those who had COVID-19 (*p*=0.426) (Table 3).

The Mann-Whitney U test was used to evaluate anxiety, depression, fatigue, insomnia, and WHOQOL-BREF scores by sex. Fatigue scores were significantly higher in women than in men (*p*<0.001). There was also a significant difference in terms of physical health and psychological health scores, which were sub-parameters of WHOQOL-BREFs, between the sexes. Men scored higher from these subgroups (*p*=0.025 and *p*=0.007, respectively).

The Mann-Whitney U test was used to compare the working and non-working groups and there was no difference in terms of depression, fatigue, anxiety, and insomnia. However, WHOQOL-BREF general health status (*p*=0.004), physical (*p*=0.020), and psychological (*p*=0.001) subgroups scores were significantly higher in the working population. Changes in work patterns, whether work was in shifts, and previous sleep disorders were not associated with insomnia.

There was no statistically significant difference between insomnia, fatigue, anxiety, depression, and WHOQOL-BREF scores when the age groups under 25 years, 25-65 years, and over 65 years were compared (*p*>0.005).

According to educational status, (primary school, high school, and university) there was no statistically significant difference in terms of anxiety, depression, fatigue, and activities of daily living (ADL) (*p*>0.005).

When we evaluated the participants according to marital status using the Mann-Whitney U test, it was found that anxiety scores were higher in married participants (p=0.021).

Table 4. Correlations between anxiety, depression, fatigue, insomnia, and quality of life scores of the study group

Study group (N=176)	1	2	3	4	5	6	7	8
	r	r	r	r	r	r	r	r
1.Anxiety	1							
2. Depression	0.319**	1						
3. Fatigue	0.188*	0.277**	1					
4. Insomnia	0.354**	0.414**	0.204**	1				
5. General health status	-0.141	-0.342**	-0.291**	-0.341**	1			
6. Physical health	-0.172	-0.333**	-0.416**	-0.339**	0.523**	1		
7. Psychological health	-0.152*	-0.482**	-0.389**	-0.316**	0.584**	0.585**	1	
8. Social health	0.031	-0.156*	-0.092	-0.053	0.331**	0.387**	0.413**	1
9. Environment	-0.160*	-0.277**	-0.115	-0.271**	0.430**	0.513**	0.493**	0.446**

*p<0.05, **p<0.01 Spearman correlation analysis in the study group.

Table 5. Correlations between anxiety, depression, fatigue, insomnia and quality of life scores of the COVID-19 group.

Covid-19 (+) group (N=56)	1	2	3	4	5	6	7	8
	r	r	r	r	r	r	r	r
1.Anxiety	1							
2. Depression	0.428**	1						
3. Fatigue	0.368**	0.383**	1					
4. Insomnia	0.502**	0.567**	0.300*	1				
5. General health status	-0.195	-0.450**	-0.422**	-0.400**	1			
6. Physical health	-0.261	-0.352**	-0.576**	-0.382**	0.613**	1		
7. Psychological health	-0.183	-0.622**	-0.467**	-0.294*	0.545**	0.435**	1	
8. Social health	0.160	-0.124	-0.054	0.056	0.262	0.350**	0.532**	1
9. Environment	-0.175	-0.498**	-0.228	-0.400**	0.516**	0.513**	0.603**	0.465**

*p<0.05, **p<0.01 Spearman correlation analysis in the COVID-19 positive group.

Anxiety scores were not associated with the death of close relatives (p=0.060). According to marital status, the WHOQOL-BREF physical health subgroup score was significantly higher in single participants (p=0.014).

Spearman correlation analysis was performed for the variables among the numerical data. A moderate and significant relationship was found between depression and insomnia and fatigue (p<0.001). It was observed that depression showed a significant correlation in all parameters of the WHOQOL-BREF. Insomnia was significantly correlated with WHOQOL-BREF general health status, physical, and psychological health status subgroups scores.

Anxiety was also found to be moderately and highly correlated with depression and insomnia, and weakly but significantly correlated with fatigue (Table 4). Similar results were found when the correlation table of patients who had COVID-19 was evaluated separately (Table 5).

Discussion

There was no difference in terms of anxiety, depression, fatigue, and WHOQOL-BREF scores between the group that had COVID-19 during the pandemic and the groups that did not, the latter were vaccinated and unvaccinated. The rate of chronic fatigue was higher in those who had COVID-19. Fatigue scores were higher in women than in men. No statistically significant relationship was found between marital status, work status, and fatigue. The rate of insomnia was found to be high in the entire study group. Depression was weakly or moderately correlated with all evaluated parameters. We found a moderate and significant correlation between depression, insomnia, and fatigue. Anxiety was moderately correlated with insomnia and weakly correlated with fatigue. Depression, insomnia, fatigue, and activities of daily living were correlated to varying degrees.

The relationship between depression and insomnia was also demonstrated in pre-

pandemic studies [12]. In a study conducted in China, an increase in insomnia was observed during the pandemic period. This was thought to be associated with psychological state and poor sleep hygiene [13]. Insomnia was shown to be a very common symptom [14]. This rate was found to be high especially in women and those living in the city. In the study of Hasan et al., approximately 13% of the participants (98 out of a total of 756) had insomnia symptoms. There was a significant difference in terms of insomnia between the sexes; women were more prone to insomnia. In addition, middle class (as income status), urban residence, smoking status, lack of physical exercise, poor health status, and multiple comorbidities were also strongly associated with insomnia. Fear of COVID-19, risk of COVID-19, and mental health problems (i.e. depression, anxiety, and suicide) were associated with insomnia [15]. In our study, anxiety, depression, and fatigue were positively correlated with insomnia, and general health status, physical and psychological health, and environmental scores were negatively correlated with insomnia.

It was revealed that the young population was more affected by sleep disorders [3]. In our study, there was no difference in terms of insomnia, fatigue, anxiety, and depression scores between those aged under and over 25 years. We did not make comparisons between urban and rural areas, concentrating on urban populations. Educational status was mostly high in our patient group.

The insomnia rate was 37% in a Greek study and 86% in a Chinese study. Both rates are higher than the pre-pandemic rate of 3.9-22% [16]. In a study conducted in Malaysia during the third wave, the rate of insomnia was found as 29.7% [17]. Similar rates in different parts of the world, such as Europe and the Far East, have been interpreted as widespread

consequences of the pandemic. Despite the late period of the pandemic, this rate is serious. In our study, when all groups were evaluated, the rate of insomnia was found as 41.7%, and when only the COVID-19 group was evaluated, it was found as 39.8%, both of which were high rates. This shows that even though the pandemic is becoming chronic, sleep problems continue. This is also important because patients with chronic insomnia will emerge in the long term. Insomnia was found less frequently in Indians, those with higher education levels, and married people [17]. We found no relationship between education level and marital status, and insomnia.

Depression, insomnia, and fatigue scores were higher in women. In addition, the scores were worse in those who lived alone [18]. In another study, fatigue was found to be higher in elderly and female populations [19]. Participants who reported fatigue, cognitive problems, recurrent falls, and stress, sadness, and sleep problems were significantly related to chronic fatigue syndrome (CFS) possibility or probability [19]. In our study, there was no relationship between age and fatigue, but the rate of chronic fatigue was higher in women and the COVID-19 group. A fatigue-enhancing effect of depression was reported [18]. However, there was no difference between men and women in our group in terms of depression and insomnia scores. In addition, the rates of depression were similar between the groups. Therefore, it can be thought that this high rate was related to COVID-19. Perceived stress was found to be higher in those living alone at home [20]. On the contrary, we found higher anxiety scores in married people.

The study of Mareilla et al. [21] found high rates of anxiety and depression in those with COVİD-19-like symptoms. More studies are needed to reveal whether it is due to the direct or indirect effect of COVİD-19. However, we

found high rates of depression in the groups that did not have COVID-19, even in the group that was not vaccinated. It is necessary to investigate the effect of pandemic life habits on depression in detail.

Among our patients who had had COVID-19, 53 (94.6%) were treated at home and three (5.4%) were treated in hospitals. However, the fatigue rate was found to be high. Patients evaluated 1 year after hospitalization for COVID-19 had muscle fatigue, insomnia, anxiety, or depression [22]. It is recommended that fatigue assessments should be performed on patients hospitalized for a long time. Post-COVID-19 fatigue is common, but like other post-infectious fatigue conditions, it usually resolves within months. Post-COVID-19 fatigue is caused by end-organ injury, mental health conditions, or post-COVID-19 idiopathic fatigue [23]. While knowledge, attitudes and behaviors regarding COVID-19 preventive measures are important for preventing disease transmission, they are also associated with participant's fatigue [24].

Restrictions in physical activities during the pandemic affected all segments of society and increased depression and negatively affected quality of life [25]. The general health, physical health, and psychological subgroups scores of the quality of life scale were significantly higher in those who were working. Being active during the pandemic made people less affected by restrictions and they felt better.

Another study evaluating anxiety and quality of life found that older women had high anxiety and poor quality of life [26]. When children aged 7-17 years were evaluated in terms of quality of life, it was found that the scores were much lower than before COVID-19 (from 40.2% to 15.3%), and two-thirds of them felt very intense pressure. Patients with low socioeconomic status, migrant families, and those with limited living space were more affected [27]. As expected, the whole world and all age groups were affected by the pandemic in various ways. We found women to have lower physical and psychological health scores and were more affected in these areas than men. Although these results suggest that there are different levels of impairment in different domains between the sexes, additional studies are needed to evaluate the contribution of different roles in society and families.

It is important to be vaccinated in terms of preventive and public health. However, similar depression and anxiety rates in the vaccinated group showed that there was no rapid community normalization. Having COVID-19 or being vaccinated did not affect anxiety-depression rates. Although new information about vaccines and the disease is produced every day, it is clear that there are many unresolved and unknown issues.

The strengths of our study were that we reached a large number of participants, we evaluated different segments of society, and the questionnaires were completed through face-to-face interviews. In addition to insomnia, fatigue, quality of life, and psychological conditions were evaluated and compared in detail. The limitation of our study was that the predominant group among those who had COVID-19 was those who were treated at home. Our rate of hospitalized patients was low. In addition, when we administered the questionnaires, we did not wait for a fixed period after the COVID-19 infection. We evaluated all patients in the same group regardless of whether they had the infection 3 months or 1 year ago.

Conclusion
Our study is valuable because it compares different groups. Fatigue related to COVID-19 should be evaluated and emphasized. Although

the acute period of the pandemic has passed, the rates of sleep disorders and depression remain high. Insomnia, fatigue, and psychological states interact with quality of life to varying degrees. The pandemic affects the entire population whether previously infected or vaccinated, thus it is important to expand preventive treatment and rehabilitation programs for physical and psychological health.

Conflict of Interest: *The authors declare that they have no conflict of interest.*

*Ethical statement***:** *Approval for the study was obtained from the ethics committee of Prof. Dr. Cemil Taşçıoğlu City Hospital (Date: 24.05.2021, No.: E-48670771-514.10).*

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