




Prevalence of Post-COVID-19 Syndrome and Related Factors among University Employees: A Prospective Cohort Study

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ABSTRACT

Objective: The term post-COVID (coronavirus disease) is used to refer to the presence of prolonged symptoms 12 weeks or more after the disease treatment. This study aimed to evaluate the presence of symptoms and anxiety in patients with COVID-19 who did not require inpatient care at the third and sixth months following symptom onset.

Materials and Methods: The study is a prospective cohort study involving 471 university employees who contracted COVID-19 between October 2020 and October 2021. Data were obtained through the disease contact follow-up program implemented at the university and phone interviews conducted at the third and sixth months from symptom onset.

Results: The study group comprised 361 individuals at three months and 109 at six months from symptom onset. The study found that symptoms persisted in 116 (32.1%) people in the third month and in 47 (13.0%) people in the sixth month. The most common symptoms at three months were shortness of breath, fatigue, and fatigue, while fatigue, fatigue, and shortness of breath were the most common symptoms at six months.

Conclusion: Understanding the long-term effects of coronavirus will enhance the management of the disease. As a result, the follow-up of symptomatic COVID-19 and post-COVID-19 patients will become more systematic and effective.

Keywords: COVID-19, SARS-CoV-2, Post-COVID Syndrome, common symptoms, prospective cohort study

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INTRODUCTION

In 2011, post-SARS syndrome was defined as the prolongation of symptoms such as fatigue, sleep disorders, muscle pain, and depression in patients infected by a coronavirus (SARS-CoV) (1). Similarly, patients with Coronavirus Disease-2019 (COVID-19) have reported persistent symptoms after infection. The post-COVID-19 syndrome was first reported in the literature by Peter Novak in September 2020 in a case who had chronic fatigue, orthostatic dizziness, brain fog associated with orthostatic hypoperfusion, and painful neuropathy (2). Following this case report, Lamprecht reported in a review that the disease causes physical, cognitive, and psychological functional limitations with residual symptoms despite microbiological normalization, and the symptoms can last up to six months in some cases (1). Studies are still ongoing to ensure standardization in definitions, but for now, the term post-COVID is used for the presence of prolonged symptoms 12 weeks and beyond after the disease treatment (3, 4).

Many studies have investigated the post-recovery health status of patients infected with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) (5, 6). It has been determined that the majority of patients diagnosed with the post-COVID syndrome cannot return to their pre-disease physical and psychological states until the sixth month, and symptoms persists due to the involvement of many systems. The presence and severity of symptoms may vary over time, and a worsening or alleviation of symptoms may be observed throughout this process (7, 8). Most studies have been performed on patients who required inpatient care services or intensive care units during their treatment period. However, it is known that 80% of patients are outpatients, and, therefore, there is still a lack of data on this group of patients. This study aims to evaluate the presence of symptoms and anxiety in the third and sixth months in patients who have had COVID-19 but have not required inpatient care.

MATERIALS and METHODS

Study Sample

The present study is a prospective cohort study carried out on university employees who had COVID-19 between October 2020 and October 2021, without hospitalization. Among the 5,751 university employees,

471 (8.0%) tested positive for the virus through a nasopharyngeal swab polymerase chain reaction (PCR) test between October 1, 2020, and April 30, 2021. Patients who were followed up from the onset of their illness as part of the disease contact tracing program implemented at the university were included in the study. Of the 471 people who tested positive, 17 were excluded from the study due to inpatient treatment, 79 could not be reached, and 14 refused to participate in the study. Informed consent was obtained from all participants, and standardized questions were asked during the interviews.

At the third month, 361 people were phoned and asked questions, and 116 reported ongoing symptoms. When these 116 people were called back in sixth month, seven could not be reached or refused to participate in the study, and only 47 reported prolonged symptoms. As a result, 116 (32.1%) of 361 patients in the third month, and 47 (13.0%) of 109 patients in the sixth month reported prolonged symptoms (Fig. 1).

Methodology

The study collected sociodemographic information (age, gender, job description, duty place), smoking status, presence of chronic disease, presence of COVID-19-related symptoms before the COVID-19 PCR test (asymptomatic/symptomatic), presence of prolonged symptoms (at the third and sixth month), course of the disease (those who required inpatient care and intensive care unit), fear of contracting COVID-19 disease again, willingness to be vaccinated against COVID-19, recommendation of vaccination to relatives, and data about the presence of COVID-19 in the family using prepared forms. The Coronavirus Anxiety Scale was used to measure the level of anxiety associated with

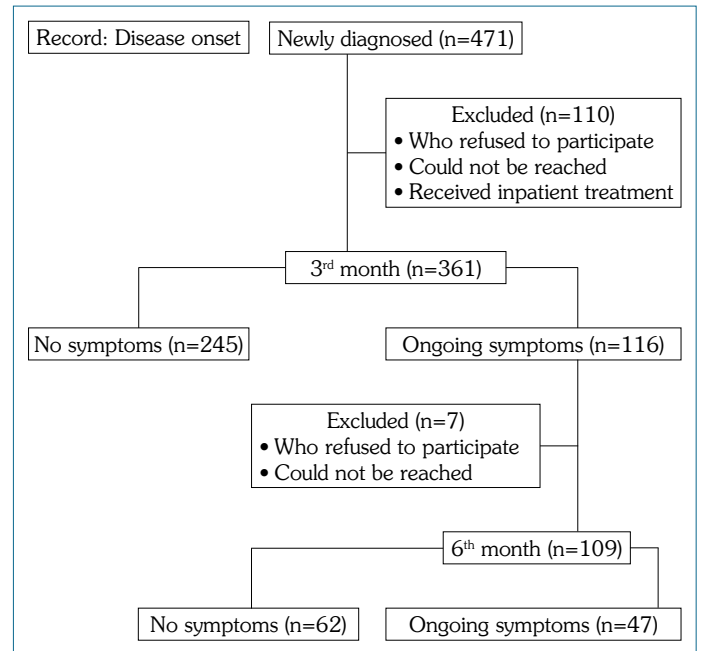


Figure 1. Flow chart

COVID-19. This scale was developed by Lee in 2020 to identify possible dysfunctional anxiety cases associated with the COVID-19 pandemic (9), and its validity and reliability were evaluated in a Turkish study conducted by Evren et al. (10). The scale consists of five questions in a 5-point Likert scale format. The scoring of the scale is as follows: 0 indicates “never”, 1 indicated “rarely or less than a day or two”, 2 indicates “a few

Table 1. Some sociodemographic characteristics and statements on COVID-19 of the study group at the 3rd month

	n	%		n	%
Age groups (years)			Having ongoing symptoms		
18–29	173	47.9	No	245	67.9
30–44	143	39.6	Yes	116	32.1
45 and more	45	12.5	Fear of getting re-infected		
Gender			No	168	46.5
Male	193	53.5	Yes	173	47.9
Female	168	46.5	Indecisive	20	5.5
Smoking status			Willingness to get vaccinated against COVID-19		
Never smoker	210	58.2	No	62	17.2
Former smoker	29	8.0	Yes	270	74.8
Someday smoker	35	9.7	Indecisive	29	8.0
Everyday smoker	87	24.1	Suggesting vaccinations to relatives		
Having chronic disease			No	12	3.3
No	272	75.3	Yes	288	79.8
Yes	89	24.7	Indecisive	61	16.9
Having symptoms before testing			Another family member with COVID-19		
No	17	4.7	No	93	25.8
Yes	344	95.3	Yes	268	74.2
Total	361	100.0	Total	361	100.0

Table 2. Distribution of ongoing symptoms in the third month and some related variables

	Ongoing symptom at 3 months						p	Ongoing symptom at 6 months						p
	No		Yes		Total			No		Yes		Total		
	n	%*	n	%*	n	%**		n	%*	n	%*	n	%**	
Age groups (years)														
18–29	120	69.4	53	30.6	173	47.9	0.780*	31	66.0	16	34.0	47	43.1	0.238*
30–44	94	65.7	49	34.3	143	39.6		24	49.0	25	51.0	49	45.0	
≥45	31	68.9	14	31.1	45	12.5		7	53.8	6	46.2	13	11.9	
Gender														
Female	119	61.7	74	38.3	193	53.5	0.007*	41	58.6	29	41.4	70	64.2	0.783*
Male	126	75.0	42	25.0	168	46.5		21	53.8	18	46.2	39	35.8	
Smoking status														
Never smoker	140	66.7	70	33.3	210	58.2	0.661*	37	56.9	28	43.1	65	59.6	0.605*
Former smoker	22	75.9	7	24.1	29	8.0		4	66.7	2	33.3	6	5.5	
Someday smoker	22	62.9	13	37.1	35	9.7		9	69.2	4	30.8	13	11.9	
Everyday smoker	61	70.1	26	29.9	87	24.1		12	48.0	13	52.0	25	22.9	
Having symptoms before testing														
No	193	71.0	79	29.0	272	75.3	0.036*	47	63.5	27	36.5	74	67.9	0.042*
Yes	52	58.4	37	41.6	89	24.7		15	42.9	20	57.1	35	32.1	
Drug use status														
No	14	82.4	3	17.6	17	4.7	0.287*	2	66.7	1	33.3	3	2.8	1.000*
Yes	231	67.2	113	32.8	344	95.3		60	56.6	46	43.4	106	97.2	
CAS score (Median, IQR; %25–75)	0	0–0	0	0–2	0	0–0	<0.001[§]	0	0–0	0	0–0	0	0–0	0.033[§]
CAS score (Mean Rank)	165.7		213.3					52.1		58.9				
Total	245	67.9	116	32.1	361	100.0		62	56.9	47	43.1	109	100.0	

*: Row percentage; **: Column percentage; *: Chi-square test; §: Mann-Whitney U test. CAS: Coronavirus Anxiety Scale; IQR: Interquartile range

days”, 3 indicated “more than 7 days”, and 4 indicates “almost daily in the last two weeks” (with a minimum score of 0 and a maximum score of 20 points). A higher score on the scale indicates higher levels of anxiety (10).

Statistical Analyses

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) software for Windows version 15.0 (Statistical Package for the Social Sciences, SPSS, Inc., Chicago, IL, USA). Frequency distribution, mean and standard deviation values were used to present the data. Mann Whitney-U, Chi-square test, Wilcoxon, and McNemar test were used for data analysis. The significance level was set at 0.05 in all statistical analyses.

Ethics Approval

This study was approved by Institute Ethics Committee and it adhered to the tenets of the Declaration of Helsinki (E-25403353-050.99-134583 Decision number: 48, 12.30.2020).

RESULTS

The study group consisted of 361 people at three months and 109 people at six months from the onset of symptoms. In the study group, at three months, 193 (53.5%) of the patients were

female, and 168 (46.5%) were male. Their ages ranged from 18 to 60, with a mean of 32.50 ± 9.64 years. As a result of the three-month interview with COVID-19 patients in the study group, it was found that 116 (32.1%) people still had ongoing symptoms. It was determined that 47.9% of the study group were afraid of having COVID-19 again. While 74.8% of the patients wanted to be vaccinated, 79.8% stated that they would recommend their relatives be vaccinated. In the study group, 268 (74.2%) people stated that they also had someone in their family who had COVID-19. Some sociodemographic characteristics and statements about COVID-19 of the study group in the third month are given in Table 1.

In the study, 38.3% of females and 25.0% of males had symptoms in the third month. It was determined that the symptoms continued in 43.3% of the patients with chronic disease, and the most common chronic diseases among the patients were hypertension and thyroid diseases. While 43.3% of those with any chronic disease had ongoing symptoms in the third month, 29.2% of those without any chronic disease had symptoms in the third month ($p=0.011$). The rate of those using drugs for COVID-19 was determined as 95.3%. It was found that 47 out of 361 (13.0%) people still had ongoing symptoms in the sixth month. Table 2 shows the distribution of symptoms persisting for three months in the study group, according to some variables that may be related.

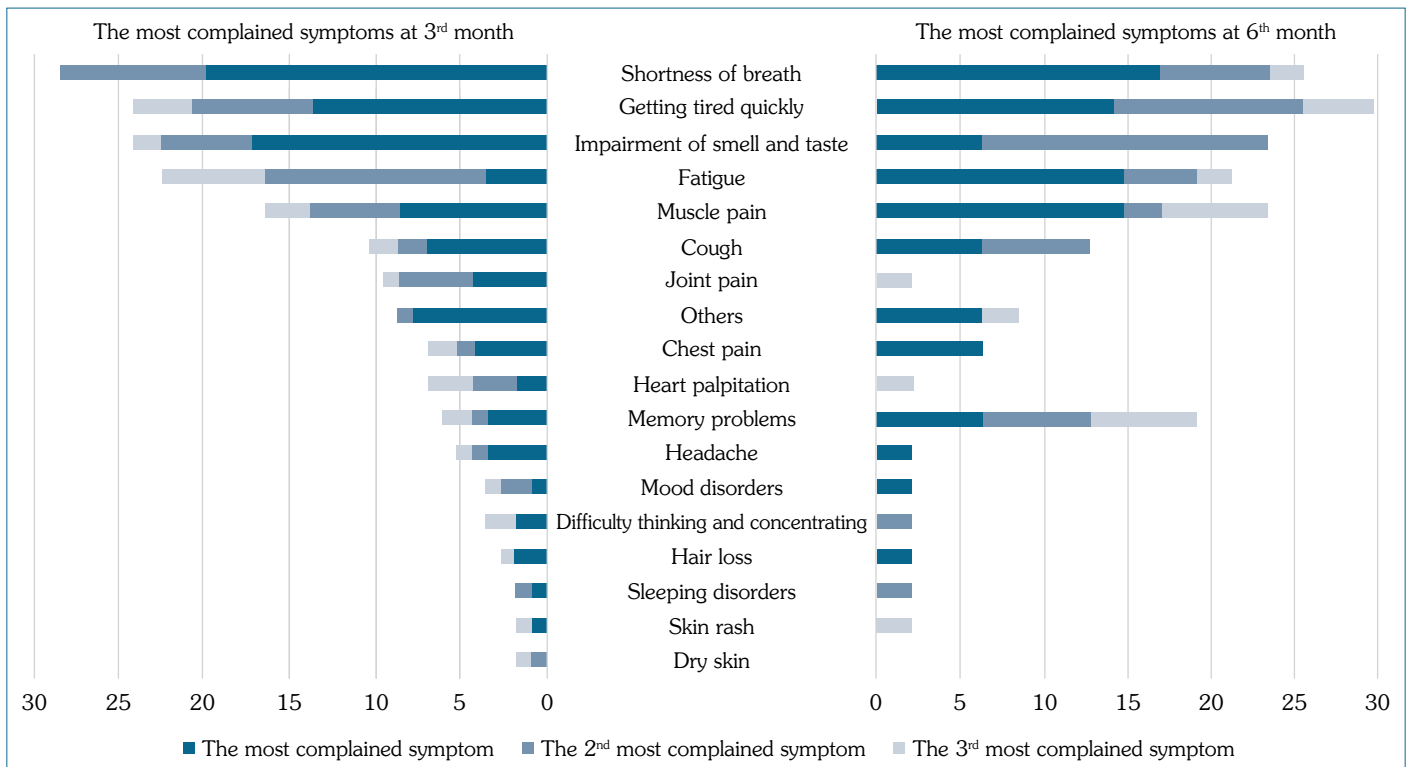


Figure 2. The most common symptoms of the patients at the third and sixth months

In the third month, patients reported the most common symptoms were dyspnea (19.8%), loss of smell-taste (17.2%), and getting tired quickly (13.8%). The next most common symptoms were fatigue (12.9%), shortness of breath (8.6%), and getting tired quickly (6.9%). In the sixth month in the study group, the most common symptoms were dyspnea (17.0%), joint pain (14.9%), and fatigue (14.9%). The most common symptoms of the patients at the third and sixth months are shown in Figure 2.

Among the 361 people in the study group, the three most common symptoms in the third month were shortness of breath, getting tired quickly, and fatigue, while the most common symptoms in the sixth month were getting tired quickly, fatigue, and shortness of breath. In addition, an analysis was conducted to compare person’s symptoms before and after the third and sixth month assessments. Fatigue, heart palpitation, getting tired quickly, impairment of smell and taste, cough, shortness of breath, and muscle pain symptoms decreased significantly from the third to sixth month (McNemar test, $p < 0.001$). The percentage changes of these symptoms, which decreased gradually over time, ranged from 50.1% to 95.2%, with heart palpitation showing the most significant decrease. The distribution of ongoing symptoms in the third and sixth months of the patients is shown in Figure 3.

Coronavirus Anxiety Scale (CAS) scores of 361 patients in the study group ranged from 0 to 14 in the third month, and the mean score was 0.70 ± 2.01 (median: 0). When the patients were questioned again in the sixth month, the scores of 109 patients on the Coronavirus Anxiety Scale ranged from 0 to 9, with a mean score of 0.25 ± 1.10 (median: 0). In the study group, the CAS scores of 47 patients with ongoing symptoms in the sixth month ranged from 0 to 9, and the mean score was 0.51 ± 1.22 (median: 0).

When the third and sixth-month scores of 109 patients were compared, it was observed that 35 patients had a decrease, one patient had an increase, and 73 patients had no change in score (Wilcoxon test, $z = -5.202$, $p < 0.001$). The changes in the third and sixth-month scores of the patients from CAS are shown in Figure 4.

DISCUSSION

It has been reported that more than 10 million people have been diagnosed with COVID-19 in Türkiye during the pandemic (11). Viral mutations affect the contagiousness and severity of the disease, thus affecting the number of outpatients, hospitalization, and mortality rates (12). Even after serological recovery, functional limitations are observed in many symptomatic COVID-19 and post-COVID syndrome cases due to the effects of COVID-19 (13). Our cohort study observed that the number of symptomatic COVID and post-COVID syndrome cases was not low even after six months. Approximately one-third of the patients remained symptomatic in the third month, and in approximately half of these patients, the symptoms continued in the sixth month.

In a multicenter study conducted in Spain, only 20% of the patients were shown to have completely recovered, while 34.4% of the patients reported various symptoms at the third-month follow-up (14). Our study observed that various symptoms were still present in 32.1% (116/361) of the university employees who were serologically positive in the third month after the diagnosis. The most common symptoms in the third month were shortness of breath (27.6%), getting tired quickly (27.6%), and fatigue (24.1%). Arnold et al. (15) reported similar post-COVID symptoms at 12 weeks in a British cohort study. In the second interview in the sixth month, it was observed that at least one symptom persisted in 13.0%

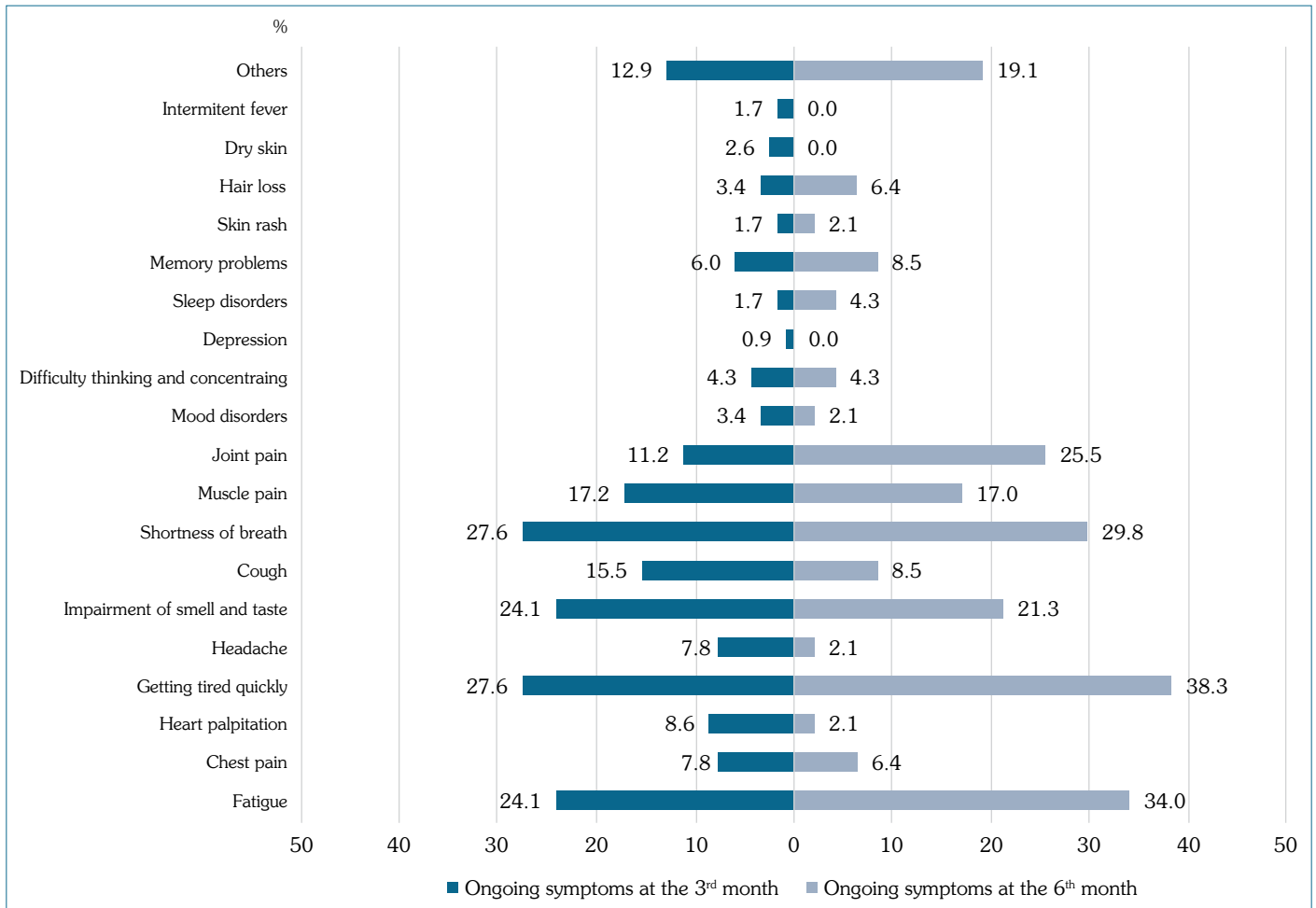


Figure 3. The distribution of ongoing symptoms at the third and sixth months of the patients

(47/361) of the patients. The most common symptoms at this time were getting tired quickly (38.3%), fatigue (34.0%), and shortness of breath (29.8%). In a cohort study conducted by Augustin et al. (16), it was reported that the most common symptom observed in patients was anosmia at both the fourth, and seventh months of follow-up. Additionally, it was noted that fatigue, which is considered among the symptoms of post-COVID persistent COVID, could meet the criteria for chronic fatigue syndrome (CFS) (8, 17, 18), and the distinction between the two might be difficult. Considering that the most important causes of CFS are immune system defects, stress, and various infections (19), it should be kept in mind that COVID-19 disease may also be involved in the infective reasons of CFS in the future.

In the Long-COVID cohort study conducted by Davis et al. (7) with data collected from 56 different countries, it was reported that the rate of bone pain, and auditory symptoms such as tinnitus increased over time while fatigue, shortness of breath, and cognitive impairment symptoms decreased. Similarly, the rate of symptoms of fatigue, chest pain, palpitations, weakness, headache, impaired smell and taste, cough, dyspnea, and muscle pain significantly decreased in the sixth month compared to the third month. It can be thought that since the study population consists of active working university employees, their active work may have caused insufficient rest time and, therefore, delay in recovery times.

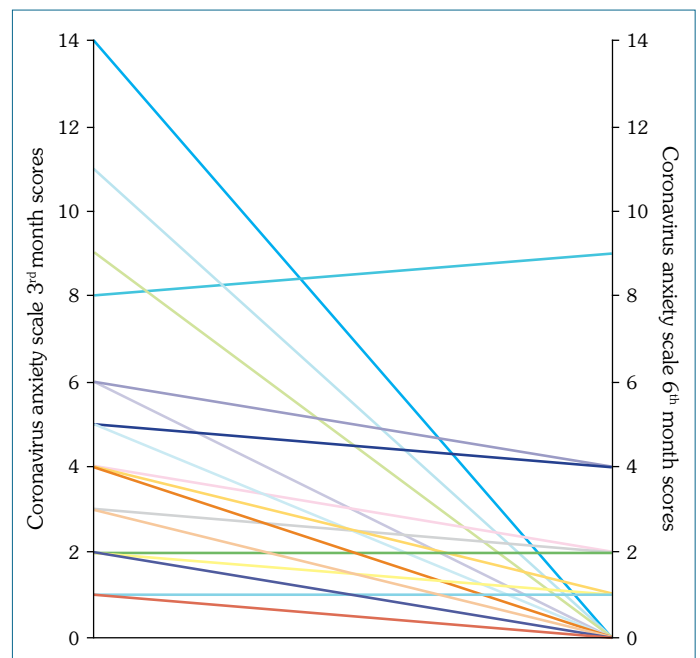


Figure 4. The changes in the third and sixth month scores of the patients from CAS

CAS: Coronavirus Anxiety Scale

Although older age has been shown as a risk factor for post-COVID in the literature (20, 21), no relationship was found between age groups and the presence of symptoms persisting in the third and sixth months in the study. The reason may be that the members of the study group were consisting of active workers and young individuals. While the rate of presence of symptoms in the third month was 38.3% in female cases, it was 25.0% in males. Similarly, it was found that the male gender was associated with a lower risk for post-COVID syndrome in various studies (16, 21) but no gender association was found in another study (22). Differences in ethnicity and possibly socio-economic status might explain such contrasting results.

In our study, hypertension and thyroid diseases were the most common chronic diseases among the patients. While 43.3% of those with any chronic disease had ongoing symptoms in the third month, only 29.2% of those without any chronic disease had symptoms in the third month ($p=0.011$). Additionally, 60% of patients with chronic diseases also reported symptoms in the sixth month ($p=0.033$). This is consistent with previous studies that have shown post-COVID syndromes to be prolonged and persistent in the presence of chronic diseases (21, 23).

COVID-19 disease is known to be associated with psychological and neurological health problems in both acute and chronic periods (17, 24, 25). These can include cognitive disorders, anxiety, depression, and sleep disorders (25, 26). In the literature, coronavirus anxiety, “coronaphobia” with its new definition, was measured using CAS (27), and it has been reported to be common among young adults, pregnant women, and patients with cancer (28–30). However, the scores obtained from the CAS were low in the 109 patients in our study group. In addition to ethnic and socio-cultural differences, the stress stemming from the interruption of face-to-face education, closure of workplaces, and economic concerns may have predominated over coronaphobia.

There were several limitations in our study. The university employees in our study group may not be representative of the general population. Patient data were collected via telephone interviews instead of face-to-face. Another limitation of the study is that patients' statements were taken as a basis in this process and the presence or severity of the symptoms could not be confirmed by clinical tests. Additionally, the same patients had to be called repeatedly over a 6–7 month period. Finally, the dynamic nature of the pandemic and repeated mutations in the virus may have affected the results of the study by worsening or improving some symptoms.

CONCLUSION

COVID-19 is not only a disease with acute symptoms but can also cause morbidity in the following periods. Knowing the long-term effects of the coronavirus will enhance the management of the disease. Since the number of post-COVID patients in the community is higher than expected as was shown in this study, this disease's social and economic burden will be more severe in the future. Thus, the follow-up of symptomatic COVID-19 and post-COVID-19 patients will become more systematic and effective. In order to provide more specialized care for these patients, it is recommended to open Post-COVID outpatient clinics in health institutions and provide a multidisciplinary approach to the patients.

Ethics Committee Approval: The Eskişehir Osmangazi University Non-interventional Clinical Research Ethics Committee granted approval for this study (date: 30.12.2020, number: 48).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – FNÖM, SM, MFÖ, AÜ, DA, AK, SS, SDGK; Design – FNÖM, SM, MFÖ, AÜ, DA, AK, SDGK; Supervision – FNÖM, SM, MFÖ, AÜ, DA, AK; Resource – FNÖM, SM, MFÖ, AÜ, DA, AK, SDGK; Materials – FNÖM, SM, MFÖ, AÜ, DA, AK, SDGK; Data Collection and/or Processing – FNÖM, SM, MFÖ, AK, SS; Analysis and/or Interpretation – FNÖM, SM, MFÖ, AK, SS; Literature Search – FNÖM, SM, MFÖ, AK, SS, SDGK; Writing – FNÖM, SM, MFÖ, AK, SS; Critical Reviews – FNÖM, SM, MFÖ, AK, SS.

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