European Review for Medical and Pharmacological Sciences 2023; 27: 8291-8300

Post-COVID-19 syndrome in a cohort of hospitalized COVID-19 patients

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Abstract. – OBJECTIVE: The study aimed to investigate the frequency of post-COVID-19 syndrome and associated factors in patients who visited the post-COVID-19 outpatient clinic after hospital discharge in the first, third, and sixth months of the first year of the pandemic.

PATIENTS AND METHODS: The study was a clinical cohort study of patients hospitalized due to COVID-19. The modified British Medical Research Council (mMRC) Dyspnea Scale, the Clinical Frailty Scale (CFS), the Mini Nutritional Assessment short-form (MNA-SF), and the Malnutrition Universal Screening Tool (MUST) were evaluated using a standard form and symptom interview by a specialist physician.

RESULTS: Of the 254 patients in the study group, 50.4% were women, and their ages ranged from 18 to 85 years, with a mean (SD) of 55.3±11.5. Post-COVID-19 syndrome was diagnosed in 57.5% of the patients. It was found that the frequency of some of the symptoms persisted and increased in the first month, decreased significantly in the third month, and did not differ between the third and sixth months. Body mass index (BMI), MNA-SF, MUST, and CFS improved over time. Multiple logistic regression analysis showed that the risk of the post-COVID-19 syndrome was 1.91- and 1.40-fold higher in patients with severe COVID-19 and patients with more symptoms in the first month, respectively.

CONCLUSIONS: COVID-19 is not a short-term infectious disease but an infectious disease with long-term effects. Cohorts of patients who are still symptomatic at the end of the first month after severe COVID-19 should be followed up for a longer period and their clinical outcomes monitored.

Key Words:
Post-COVID conditions, Severity of illness, Follow-up care, Symptom increase.

Introduction

Coronavirus disease-19 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused an ongoing worldwide pandemic. The COVID-19 pandemic has infected and killed many people. In addition, it was mentioned[1-5] that despite being virus-free, residual symptoms lead to functional impairments in physical, cognitive, and psychological aspects. It has been reported1 that symptoms may last longer than six months in some patients. Therefore, the World Health Organization[2] has reported that the period after COVID-19 is important and should be investigated first. With the increased literature on this topic, the subacute or prolonged phase is better defined after COVID-19[1,3,4]. National Institute for Health and Care Excellence (NICE) has recommended the clinical case definitions to identify and diagnose the long-term effects of COVID-19. Signs and symptoms of COVID-19 in the subacute phase between 4 and 12 weeks were defined as ongoing symptomatic COVID-19. The period after 12 weeks is the chronic phase and has been defined post-COVID-19 syndrome. In this phase, signs and symptoms that occur during or after infection with COVID-19 continue for more than 12 weeks, and cannot be explained by an alternative diagnosis[1]. A variety of symptoms, particularly fatigue, muscle and joint pain, sleep disturbances, and depression, have been reported[5] to persist in the period after COVID-19. Although new information about post-COVID-19 syndrome continues to appear in the literature, current data are still controversial due to insufficient and conflicting information[3,6]. There are many studies on symptoms after COVID-19, but more accurate and clear information is needed about these symptoms, their persistence, and their impact on patients. The aim of this study is to assess the persistence of symptoms and their impact in the first, third, and sixth months after COVID-19 in the cohort of hospitalized patients and to determine the frequency of post-COVID-19 syndrome and associated factors.

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Patients and Methods

Study Group

The study is a clinical cohort study consisting of patients hospitalized due to COVID-19, except intensive care patients. It was conducted in a state hospital in a central Anatolian city (Eskisehir), where the incidence of COVID-19 is higher than the Turkish average. Patients hospitalized and discharged from the hospital were assessed in the first, third, and sixth months after discharge for post-COVID-19. Patients hospitalized during the second wave of the COVID-19 pandemic in the province between April 1, 2020, and July 11, 2021, were included in the study. These patients were followed for 6 months. The follow-up of the last patient enrolled in the study ended on January 11, 2022. The study group consisted of 254 patients who completed their application in the first, third, and sixth months after discharge. SARS-CoV-2 infection was diagnosed in all patients by real-time reverse transcription polymerase chain reaction assay using nasopharyngeal swabs or other upper respiratory tract specimens. In addition, computed tomography was able to contribute to the diagnosis in 5 patients. The study was approved by the Ethics Committee of Eskisehir Osmangazi University (No.: 22.03.2022/09). The study was conducted in accordance with the Helsinki Declaration. Informed consent was obtained from participants. Participants were included in the study using an opt-out approach.

Study Design

The sociodemographic and clinical characteristics of the patients (age, sex, diagnosis date of COVID-19, height, weight, comorbidity, vaccination status, symptoms defined during isolation, date of discharge from the hospital) were taken from the records. Patients presenting to the post-COVID-19 outpatient clinic were assessed using a standard form prepared by a specialist. Patients were asked about their symptoms that persisted after discharge. Body weight was measured. Patients were evaluated for the long-term effects of COVID-19 using the modified British Medical Research Council (mMRC) Dyspnoea Scale, The Clinical Frailty Scale (CFS), Mini Nutritional Assessment short-form (MNA-SF), and Malnutrition Universal Screening Tool (MUST). In addition, chest radiographs and levels of C-reactive protein (CRP), lactate dehydrogenase (LDH), D-dimer, ferritin, and troponin were evaluated at each patient visit.

Definition of Study Parameters

Post-COVID-19 syndrome: Signs and symptoms that develop during or after an infection consistent with COVID-19, continue for more than 12 weeks and are not explained by an alternative diagnosis1. Body mass index (BMI): BMI was calculated by dividing body mass by the square of height. Age-adjusted Charlson Comorbidity Index (ACCI): Patients' comorbidities were rigorously assessed based on a detailed history and defined using International Classification of Diseases (ICD) diagnosis codes. Patients' age was sorted, and ACCI scores were then calculated according to the appropriate formula[7,8]. Fully vaccinated: Patients who received their first reminder dose 3 months after completion of the primary schedule of two doses of mRNA vaccine. Partially vaccinated: Patients who were vaccinated but did not receive all 3 doses were considered partially vaccinated. Severe COVID-19: Severe COVID-19 was defined as the need for a high-flow nasal cannula, noninvasive mechanical ventilation, and invasive mechanical ventilation during hospitalization and the need for oxygen therapy or noninvasive mechanical ventilation at discharge[9]. mMRC scale: Dyspnea in daily life was assessed using the mMRC scale. This is a self-assessment tool that measures the degree of impairment due to dyspnea in activities of daily living on a scale of 0 to 4[10,11]. CFS: The patients' overall fitness or frailty level was assessed by an experienced clinician using CFS on a scale of 1 to 9[12]. MNA-SF: Patients' nutritional status was assessed using MNA-SF on a scale of 0 to 14[13]. MUST: Patients' nutritional status was assessed using MUST, a five-step screening tool to determine adult nutritional status[14]. Chest X-ray evaluation: Two physicians assessed chest X-ray by consensus at early follow-up (at the end of the first month), at midterm follow-up (at the end of the third month), and at late follow-up (at the end of the sixth month) using an 18-point scoring system. The lungs were divided into six zones, upper, middle, and lower, and scored according to the pattern of abnormalities using the scoring system defined by Fogante et al[15].

Statistical Analysis

SPSS (version 15.0, Chicago, IL, USA) was used to analyze the data. MedCalc Statistical Software (version 19.1.16, MedCalc Software Ltd, Ostend, Belgium) was used to calculate the size of the study group and to plot the graphs. Frequency distribution, mean, and standard deviation were used to

plot the data. Measurable data were checked with a normality test and graphs. Mann-Whitney U test and Chi-square test were used for data analysis. The presence of post-COVID-19 syndrome was considered a dependent variable. To determine the independent variables affecting post-COVID-19 syndrome, multivariate logistic regression analysis was performed with variables whose $p<0.10$ in univariate analysis. The statistical significance level was assumed to be $p< 0.05$.

Results

The study group consisted of 254 patients from the cohort of patients who were hospitalized for COVID-19 and then presented to the post-COVID-19 outpatient clinic in the first month. 50.4% of the patients were females, and their ages ranged from 18 to 85 years, with a mean±SD of 55.3±11.5 years. The median number of symptoms at the onset of COVID-19 was 2 (1-7), and the most common symptoms were fatigue and muscle weakness (Table I and Figure 1).

Table I. Characteristics of the study group.

Variables	
Age, X±SD, years	55.3±11.5
(min-max)	(19-85)
Sex, n (%)	
Male	126 (49.6)
Female	128 (50.4)
BMI, n (%)	
Normal	50 (19.7)
Overweight	101 (39.8)
Obese	103 (40.6)
Comorbidities, n (%)	
No	81 (31.9)
Hypertension	103 (40.6)
Diabetes	66 (26.0)
Cardiovascular diseases	43 (16.9)
Chronic lung diseases	31 (12.2)
Thyroid disorders	30 (11.8)
Neuropsychiatric disorders	28 (11.0)
Chronic liver disease	4 (1.6)
Chronic renal failure	3 (1.2)
Malignancy	2 (0.8)
Cerebrovascular diseases	1 (0.4)
ACCI, median (min-max)	2 (0-8)
Vaccination status, n (%)	
Unvaccinated	216 (85.0)
Partially vaccinated	9 (3.5)
Fully vaccinated	29 (11.4)
Length of hospital stay, days	
Median (min-max)	20 (3-85)
Mean±SD	19.2±12.1
Severe COVID-19	
No	115 (45.3)
Yes	139 (54.7)

SD: Standard deviation; BMI: Body mass index; ACCI: Age-adjusted Charlson Comorbidity Index.

The most common symptoms of patients in the first month were fatigue and muscle weakness. It was found that the frequency of fatigue or muscle weakness, myalgia or joint pain, dyspnea, amnesia, sleep difficulties, headache, chest pain, cough, taste-smell disorder, and hair loss persisted and increased in the first month, decreased significantly in the third month, and did not differ between the third and sixth months. Rare symptoms such as palpitations, sputum, nausea, and eye symptoms did not change over time (Figure 2).

When the clinical and laboratory results of the patients were compared at the first, third, and sixth months, it was found that BMI (p=0.031), mMRC (p<0.001), MNA-SF (p<0.001), MUST (p<0.001), and CFS (p=0.016) improved over time. Compared with the values in the first month, LDH (p<0.001) and ferritin (p<0.001) levels showed a significant decrease in the third month and D-dimer (p=0.006) and troponin (p=0.005) levels in the sixth month. There was no change in CRP levels (p=0.736) (Table II). One or more symptoms were noted in 86.2% of patients at month 1, in 57.5% at month 3, and 31.0% at month 6. Of the total patient cohort, 149 were diagnosed with post-COVID-19 syndrome. Post-COVID-19 syndrome was more pronounced in obese patients (p=0.045), in patients with an ACCI of 4 or more (p=0.043), in patients with severe COVID-19 (p=0.007), and in patients with a higher number of symptoms (p<0.001) and a higher mMRC Dyspnea Score (p=0.044) at month 1 (Table III). Multiple logistic regression analysis showed that the risk of post-COVID-19 syndrome was 1.91 (1.08-3.37) and 1.40 (1.19-1.63) fold higher in patients with severe COVID-19 and those with more symptoms in the first month, respectively (Figure 3). There was no association between post-COVID syndrome and inflammatory markers.

Discussion

This longitudinal clinical study examined the frequency and impact of post-COVID-19 syndrome in hospitalized patients returning to their social and professional lives after infection. Much research has been done on the characteristics and health outcomes of patients treated in the intensive care unit (ICU) during the pandemic[16,17].

Table II. Comparison of 1st, 3rd, and 6th-month outcomes in patients with COVID-19.

Characteristics	Month 1	Month 3	Month 6	p
BMI, median (min-max)	28.7(16.6-47.6)	29.0 (16.6-44.4)	29.2 (17.3-44.4)	**0.031**
mMRC score, median (min-max)	0* (0-4)	0 (0-4)	0 (0-2)	**<0.001**
CFS score, median (min-max)	2.5 (1-7)	2 (0-7)	1.5 (0-4)	**0.016**
MNA-SF score, median (min-max)	11* (4-13)	13.0 (7-13)	13.0 (7-13)	**<0.001**
MUST score, median (min-max)	0.0** (0-3)	0.0 (0-3)	0.0 (0-2)	**<0.001**
CRP, mg/L median (min-max)	0.95 (0.10-145.30)	0.6 (0.1-114.0)	1 (0.1-51.1)	0.736
LDH, U/L median (min-max)	211* (128-398)	201 (79-393)	95 (0-360)	**<0.001**
D-Dimer, mg/L median (min-max)	0.35** (0.10-5.43)	0.31 (0.19-3.04)	0.34 (0.19-1.17)	**0.006**
Ferritin, µg/L median (min-max)	57* (1-657)	50 (5-565)	45.5 (4-588)	**<0.001**
Troponin, ng/L median (min-max)	1.3** (0.0-378.7)	1.10 (0.5-26.0)	1.1 (1.0-186)	**0.005**
Chest X-ray score, median (min-max)	2* (0-12)	2 (0-8)	0 (0-4)	**<0.001**

*: The value in the first month is different from that in the third and sixth months; **: The value in the first month is different from the sixth month. BMI: Body mass index; mMRC: modified British Medical Research Council, CFS: Clinical Frailty Scale, MN-SF: Mini Nutritional Assessment short-form, MUST: Malnutrition Universal Screening Tool; CRP: C-reactive protein, LDH: Lactate dehydrogenase.

The results have been quite tragic[17]. ICU mortality during the first wave of the COVID -19 pandemic ranged from 40% to 85% among patients admitted to the ICU[16]. This study examined the health outcomes of hospitalized patients who were not treated in the ICU. In our study, 57.5% of our patients were diagnosed with post-COVID-19 syndrome. The most common symptoms were fatigue or muscle weakness, amnesia, myalgia or joint pain, and dyspnea. Although many clinical and laboratory parameters improved over time, they persisted at month 6. It was found that the risk of post-COVID-19 syndrome was higher in patients with severe COVID-19 and more symptoms at month 1.

Since the outbreak of the pandemic, millions of people worldwide have become infected with COVID-19. The impact of COVID-19 on human

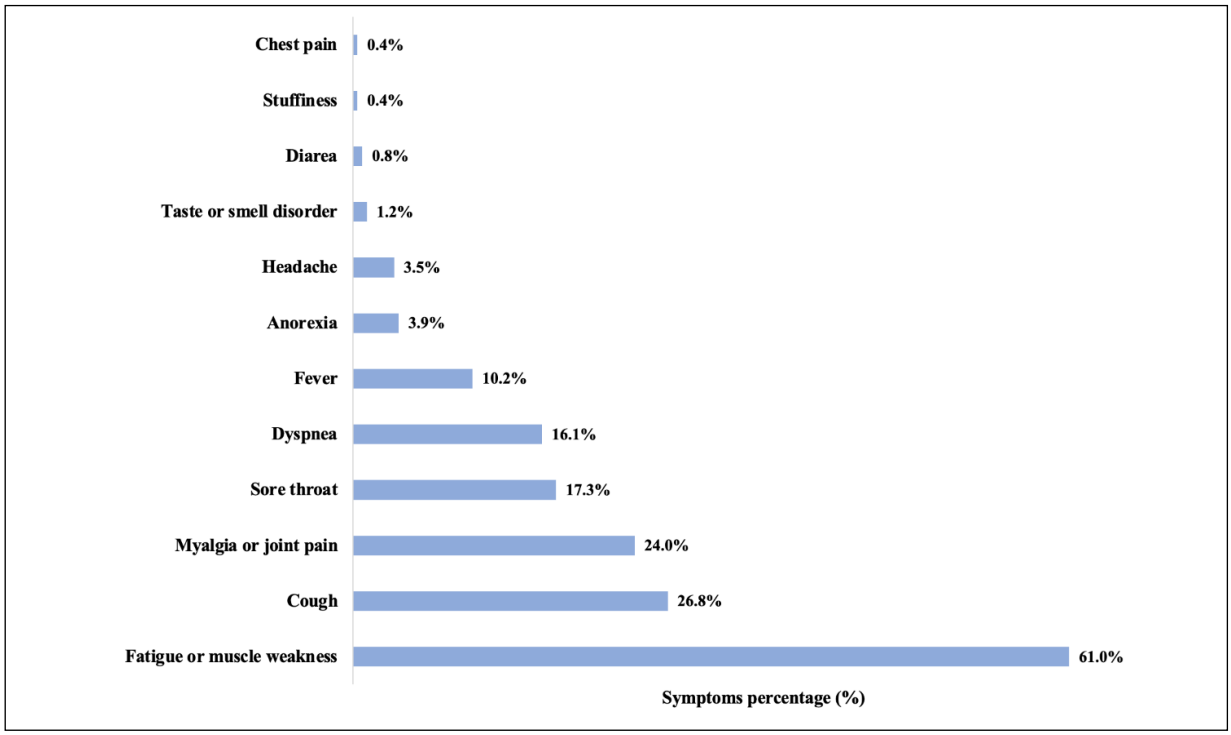

Figure 1. Percentage of symptoms at disease onset in the COVID-19 patient cohort.

Table III. Comparison of patient characteristics according to the post-COVID-19 syndrome.

Variables	Post-COVID-19 syndrome		
	Yes	No	*p*
Age X±SD, years (min-max)	56.1±10.9 (25-83)	54.1±12.2 (19-85)	0.170
Sex, n (%)			
Male	71 (47.7)	55 (52.4)	0.458
Female	78 (52.3)	50 (47.6)	
Vaccination status			
Unvaccinated	126 (84.6)	90 (85.7)	0.470
partially vaccinated	7 (4.7)	2 (1.9)	
Fully vaccinated	16 (10.7)	13 (12.4)	
BMI, n (%)			
Normal	22 (14.8)	28 (26.7)	**0.045**
Overweight	60 (40.3)	41 (39.0)	
Obese	67 (45.0)	36 (34.3)	
ACCI, n (%)			
<4	114 (76.5)	91 (86.7)	**0.043**
≥4	35 (23.5)	14 (13.3)	
Symptom number at onset, median (min-max)	2 (1-5)	2 (1-7)	1.0
Severe COVID-19			
No	57 (38.3)	58 (55.2)	**0.007**
Yes	92 (61.7)	47 (44.8)	
At 1st months after COVID-19			
Symptom number, median (min-max)	3 (0-9)	2 (0-9)	**<0.001**
mMRC score			
0	82 (53.6)	71 (46.4)	**0.044**
1-4	67 (66.3)	34 (33.7)	
CFS score, median (min-max)	3 (1-7)	2 (1-4)	0.203
MNA-SF score	11 (5-13)	12 (4-13)	0.320
MUST score, median (min-max)	0 (0-3)	0 (0-3)	0.258
CRP, mg/L, median (min-max)	1 (0.1-145.3)	0.9 (0.1-28.1)	0.600
LDH, U/L, median (min-max)	213.0 (128-398)	210.5 (137-388)	0.766
D-Dimer, mg/L, median (min-max)	0.3 (0.1-5.4)	0.4 (0.1-2.6)	0.853
Ferritin, µg/L, median (min-max)	59 (3-657)	49 (1-640)	0.776
Troponin, ng/L, median (min-max)	1.3 (0.1-36.7)	1.3 (0.1-37.7)	0.605
Chest X-ray score, median (min-max)	4 (0-8)	1 (0-12)	0.249

SD: Standard deviation; BMI: Body mass index; ACCI: Age-adjusted Charlson Comorbidity Index; COVID-19: coronavirus disease – 19; mMRC: modified British Medical Research Council; CFS: Clinical Frailty Scale, MNA-SF: Mini Nutritional Assessment short-form, MUST: Malnutrition Universal Screening Tool; CRP: C-reactive protein, LDH: Lactate dehydrogenase.

health was assessed at the beginning of the pandemic using morbidity and mortality data. However, as disease symptoms progressed, the magnitude of the disease burden changed. Knowing how long and how severe the symptoms of infected individuals persisted can help determine the significance and magnitude of the disease burden. Several studies[9,18-24] have shown that a significant proportion of patients are symptomatic after COVID-19, symptoms persist for a long time, and affect workability and quality of life. For this reason, it is important to perform regular follow-up examinations to detect post-COVID-19 syndrome after COVID-19 and to engage patients in appropriate treatment and rehabilitation programs.

COVID-19 has not proceeded like a short-term infectious disease, information about the duration of the disease has changed since its onset. Several mechanisms, including viral damage, oxidative stress, immunologic abnormalities, and inflammatory damage, are responsible for the clinical picture in post-COVID-19 syndrome[18]. Long-term complications have been reported[4] because of the effects on multiple organs and systems, particularly the pulmonary, neuropsychiatric, cardiovascular, musculoskeletal, and gastrointestinal systems.

A study[9] from China, the country of origin of the pandemic, reported that 76% of patients were symptomatic 6 months after COVID-19. A study[19] with a median follow-up of 60 days from Italy, one of the European countries where the effects

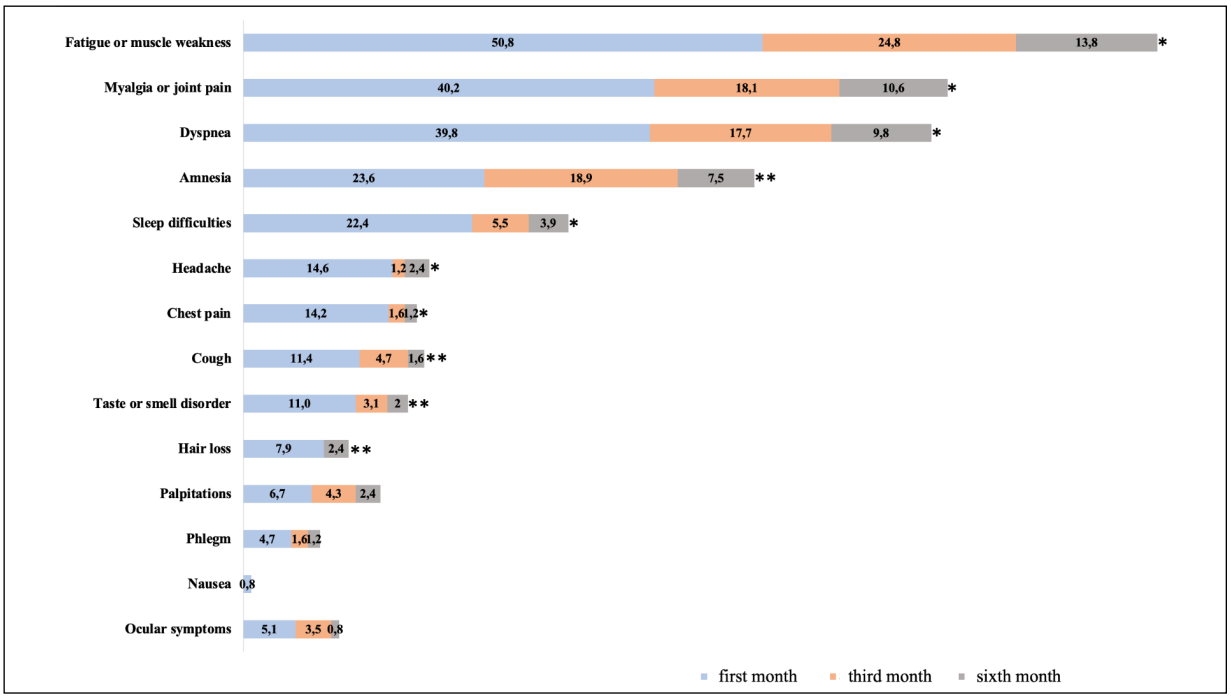

Figure 2. Percentage of symptoms at 1st, 3rd, and 6th month after COVID-19. *: $p<0.001$; **: $p<0.01$.

of the pandemic were felt the most, reported that 87% of patients were symptomatic. Another study[20] from France reported that 68% of patients had at least one symptom at three months and 60% at six months. A study[21] examining more than 250,000 patients in England reported that

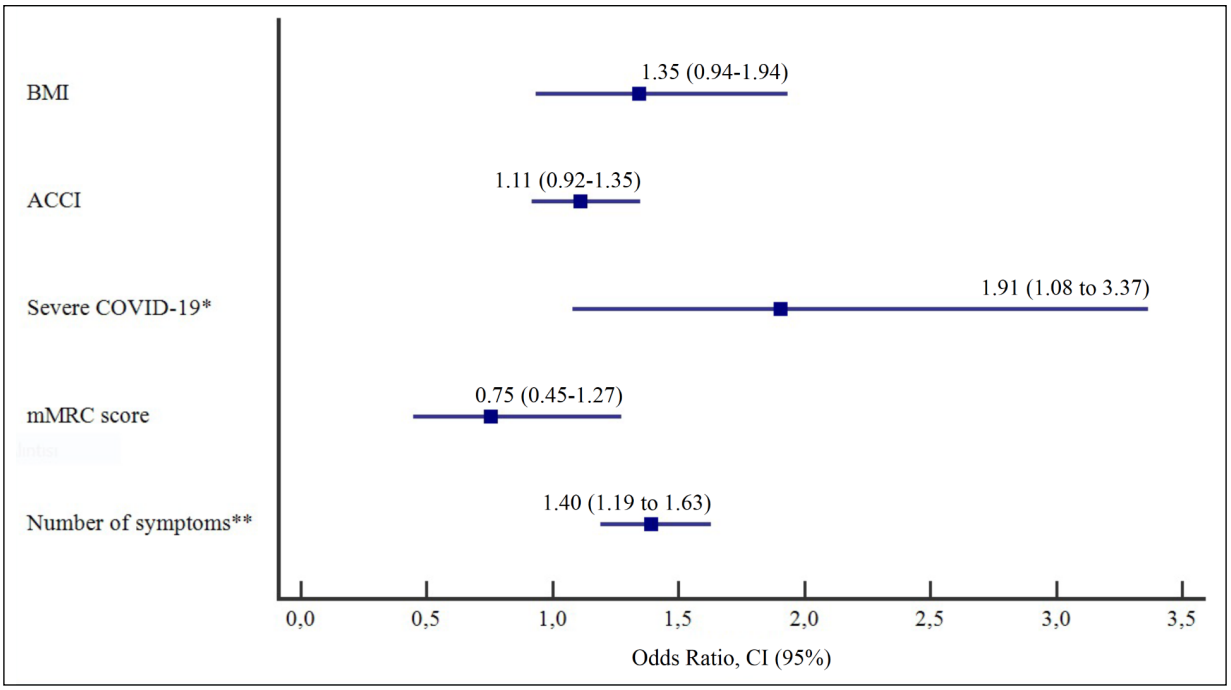

Figure 3. Forest plot showing odds ratio and 95% CI of factors associated with post-COVID-19 syndrome. *: $p=0.027$; **: $p<0.001$. BMI: Body mass index; ACCI: Age-adjusted Charlson Comorbidity Index; COVID-19: coronavirus disease-19; mMRC: modified British Medical Research Council.

37% of patients were symptomatic between 3 and 6 months. In the United States[22], it was reported that at least one-third of patients were symptomatic in the period after COVID-19. Our study found that 86.2% of patients had one or more symptoms in the first month, 57.5% in the third month, and 31.0% in the sixth month, which is consistent with the literature. The difference in the frequency of symptoms after COVID-19 in the different studies might be due to the heterogeneity of the patient group and data sources.

Fatigue, shortness of breath, chest pain, cognitive impairment, arthralgia, and decreased quality of life were the most common symptoms observed during the period after COVID-19[19-24]. In the study by Carfi et al[19], more than half of the patients had three or more symptoms. Fatigue (53.1%), dyspnea (43.4%), joint pain (27.3%), and chest pain (21.7%) were the most commonly reported symptoms. In the study by Ghosn et al[20], it was reported that 24% of patients had three or more symptoms in the sixth month. In the study by Huang et al[9], fatigue or muscle weakness (63%) ranked first, sleep disorders (26%) second, and anxiety or depression (23%) third. Ceban et al[25], in their systematic review and meta-analysis that included 81 studies, found a proportion of 32% of fatigue and a proportion of 22% of cognitive impairment after COVID-19. In another study[26] of more than ten thousand patients, the most common symptoms after COVID-19 were fatigue (37%), brain fog (32%), memory issues (28%), attention disorder (22%), and neuropsychiatric disorders such as sleep disturbances (31%), anxiety (23%), and depression (17%). New-onset dementia was reported[27] in 3%, particularly in patients who had developed pneumonia.

Taniguchi et al[28] showed that 31% of ICU-treated patients were frail after 90 days, and 70% of them were not previously frail. Mueller et al[29] found that the median frailty score 3 months after COVID-19 was 3, and more than 21% of patients had a CFS of 4 or higher. The authors noted that CFS correlated with the St. George's Respiratory Questionnaire, pulmonary function tests, the 6-minute walk test, and the mMRC dyspnea score. A higher mMRC Dyspnea Score was an important risk factor for frailty after COVID-19[29]. In some studies[9,19,23,24], quality of life has worsened in a significant proportion of patients who were symptomatic for a long time after COVID-19. This situation prevented about one-third of active workers from returning to work after 6 months[20]. In the study by Arnold et al[23], despite the high symptom burden (74%), clinically significant abnormalities on chest radiographs, exercise testing, blood tests, and spirometry were less common (35%), and in patients with mild disease, this rate was even lower (7%).

The symptoms observed in our study were consistent with the literature. The symptom burden and symptoms observed in our study group, 85% of whom were unvaccinated and more than half of whom were severely ill, are consistent with the course of the pandemic and the literature. Also, consistent with the literature, we found that CFS and mMRC scores decreased in parallel with improvement over time. BMI, MNA-SF, and MUST scores improved during the recovery period.

Some studies[30,31] have shown that inflammation persisted in parallel with symptoms. The cross-sectional study by Maamar et al[31] examined the association between inflammatory markers and post-COVID-19 syndrome. The authors demonstrated that women with the highest tertile of neutrophil count, fibrinogen level, or neutrophil-to-lymphocyte ratio (NLR) had a 4-5-fold increased risk of post-COVID-19 syndrome. D-dimer levels were found[32] to be increased in patients with tomographic findings in the third month. In our study, inflammatory markers were also examined to objectively evaluate the effects of post-COVID-19 syndrome on the human body and to discuss possible mechanisms. LDH, D-dimer, ferritin, and troponin levels have decreased over time in parallel with symptom improvement. However, we showed that there was no association between post-COVID syndrome and inflammatory markers.

Similarly, radiologic findings[9,15,23,24,32] have been shown to persist in the post-COVID-19 period. Moreno-Pérez et al[24] found that in their study group, radiologic changes persisted in 19% of patients at 77 days of follow-up, and most findings were mild. In contrast, Balbi et al[32] found that more than 80% of patients had parenchymal changes at CT three months after symptom onset. These findings were associated with worsening pulmonary function tests, whereas the vessels were less affected[32].

The identification of patients at risk for post-COVID-19 syndrome and a better understanding of the mechanisms are very important for prevention and treatment as well as for follow-up and rehabilitation[33]. Numerous clinical trials are currently underway investigating antioxidant supplements, exercise, and other pharmacological approaches to reduce the effects of post-COVID-19 syndrome[34]. Some authors[20,24,35-37] investigated the risk factors for the development of post-COVID-19

syndrome. Moreno-Pérez et al[24] found that no demographic, baseline clinical characteristics, comorbidities, or severity of acute illness were associated with post-COVID-19 syndrome. On the other hand, only involvement greater than 50% on chest radiographs and tachycardia on admission were associated with post-COVID-19 syndrome[24]. Ghosn et al[20] found that the risk of having three or more symptoms in the sixth month was higher in women, in patients with three or more symptoms in the acute phase, and in patients who required follow-up in the intensive care unit.

In another study[37] using logistic regression analysis to detect post-COVID-19 syndrome, it was found that women, patients with respiratory distress, lethargy, and prolonged and severe illness were at increased risk. In the study by Yoo et al[35], the risk of post-COVID-19 syndrome was high in patients hospitalized for COVID-19, diabetes, and a high BMI, whereas the risk was low in patients who had an organ transplant. In the study by Sudre et al[36], prolonged COVID-19 was characterized by symptoms such as fatigue, headache, shortness of breath, and anosmia and was more common in older age, high body mass index, and female sex. More than five symptoms in the first week of illness were also associated with long-term COVID-19[36]. Another study[37] reported that the risk of post-COVID-19 syndrome was higher in women, in patients with a high number of initial symptoms, and in patients who required ICU follow-up, and that IgG antibodies were higher in post-COVID-19 syndrome. In our study, multivariate analysis revealed that the risk for post-COVID-19 syndrome was increased in patients with severe COVID-19 and more symptoms in the first month. Our results suggest that those with severe COVID-19 should be followed up for at least 6 months and enrolled in a rehabilitation program if necessary.

Limitations

The main limitation of the study is that it referred to patients hospitalized for COVID-19 and did not include outpatients. Long-term effects beyond six months were not assessed because patients were followed up only up to six months. Another limitation was the lack of assessment of neurologic and psychiatric effects in patients.

Conclusions

COVID-19 is not only an acute infection, but a disease that tends to be a chronic process. The symptoms of patients persist for a long time, even if the contribution of the disease to functional deterioration is less in the post-disease period. We found that symptom burden and inflammatory markers decreased over time, and radiological findings improved. Cohorts of patients with severe COVID-19 and patients who are still symptomatic at the end of the first month should be followed up for a longer period and their clinical outcomes monitored.

Ethics Approval

The study was approved by the Turkish Ministry of Health and the Ethics Committee of the Faculty of Medicine at Eskişehir Osmangazi University (Date: 22.03.2022, No.: 09).

Informed Consent

Participants were included in the study using an opt-out approach.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflict of Interest

The authors declare that they have no competing interests.

Funding

No funding was received for this study-

Authors' Contributions

Selma Metintas and Guntulu Ak conceived the study, designed the project, and wrote the final draft of the manuscript. Selma Metintas and Muzaffer Metintas performed the statistical analysis, critically revised data, and made substantial contribution in the interpretation of results. Yasar Bildirici, Anıl Ucan, and Sebnem Eker Guvenc revised the manuscript and made substantial scientific contributions. Anıl Ucan and Sebnem Eker Guvenc collected the data and wrote the first draft of the paper. All authors revised the manuscript and approved the final version

Acknowledgements

We would like to thank all authors for sharing valuable data obtained as a result of the literature review and the COVID-19 Intensive Care team for their diligent follow-up of patients.

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