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Research article

Musculoskeletal symptoms in patients with long COVID: A cross-sectional study on Iranian patients

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ABSTRACT

Background and objectives: Latest studies have revealed that an increasing number of Corona Virus Disease of 2019 (COVID-19) patients may continue to feel symptoms after the acute phase. This study aimed to evaluate the prevalence of musculoskeletal symptoms after the acute phase of COVID-19 and its associated factors.
Methods: We designed a cross-sectional study from January 2021 to April 2021. An online questionnaire was designed and sent to patients who had recovered from COVID-19. The questionnaire contained questions on participants' demographic characteristics, COVID-19 course at its acute phase, and musculoskeletal symptoms after recovering from COVID-19. Musculoskeletal symptoms associations with patients' characteristic and COVID-19 course was evaluated.
Result: 239 patients, including 72 (30.1%) males and 167 (69.9%) females with a mean age of 37.96 years (SD = 11.19), were included in the study. 98.74% of our patients had experienced at least one musculoskeletal symptom after recovering from COVID-19, and the most common symptom was fatigue, as 91.2% of participants experienced this symptom, followed by myalgia, headache, and low back pain. High BMI, hospitalization, and ICU admission were associated with a higher risk of musculoskeletal symptoms.
Conclusion: This study indicated a high prevalence of persistent musculoskeletal symptoms among patients who recovered from COVID-19. Modifiable factors, such as BMI, can be targeted to reduce the prevalence of musculoskeletal symptoms in COVID-19 survivors and reduce its burden.

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a new coronavirus responsible for Corona Virus Disease of 2019 (COVID-19). COVID-19 is a syndemic of SARS-CoV-2 and non-communicable diseases affecting population groups [1]. COVID-19, caused by SARS-CoV-2, can range from asymptomatic infection to minimal symptoms to severe pulmonary involvement [2]. Different diagnostic tools have been developed for diagnosing COVID-19 infection like Polymerase Chain Reaction (PCR), Chest Computed Tomography-scan (CT-scan), and anti-viral antibody (Ab), but for a vast majority of patients, the diagnoses are made based on symptoms [2]. The SARS-CoV-2 involves different organs that result in various manifestations. Latest reviews on signs and symptoms found that COVID-19 may have respiratory (cough, dyspnea, chest pain), constitutional (fever, fatigue, chills), musculoskeletal (myalgia, arthralgia), gastrointestinal (diarrhea, abdominal pain), or neurological (confusion, headache) manifestations [3]. In more serious conditions with pulmonary involvement, respiratory symptoms are dominant [2].

Patients may continue feeling the symptoms even after the acute phase, called long-haulers [4], and this condition is referred to as long COVID. About 34% of non-hospitalized and 54% of hospitalized patients may experience symptoms after the acute phase of COVID-19 [5]. The long COVID term is used to describe the symptoms lasting more than four weeks since diagnosis without any other explanation [3, 6], although there is no consensus on its definition yet [7]. The exact mechanism of long COVID is unknown [8]. Incidence of long COVID is higher in patients with comorbidities such as cardiovascular and respiratory diseases

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or severe COVID-19 infection [4, 9]. Also, older ages and a history of psychological issues are associated with a higher risk of developing long COVID [9, 10]. Long COVID signs and symptoms are similar to acute COVID-19 infection [11, 12] and are like post-infection syndrome reported following the SARS coronavirus infection and the Middle East Respiratory Syndrome (MERS) 2012 [13]. The most common symptom of long COVID is fatigue [14, 15]; however, dyspnea, cough, chest pain, myalgia, headache, joint pain, altered taste and smell, diarrhea, and sleep disturbances are commonly reported [6, 16, 17].

Musculoskeletal symptoms are frequently reported in the acute and post-acute phases of COVID-19 [14,18,19]. The reported prevalence of fatigue, arthralgia, and myalgia during the acute phase varies between studies [20, 21]. Myalgia is usually seen in viral infections due to cytokine release, and viral arthralgia has been observed in hepatitis B and parvovirus B19 viremias [21]. However, limited data are available about their incidence after the acute phase of COVID-19. One of the main characteristics of long COVID is chronic fatigue syndrome [22]. Karaaslan et al. found that 72% of hospitalized COVID-19 patients feel one or more rheumatic or musculoskeletal symptoms one month after discharge, and 44% experience fatigue [23].

As COVID-19 has infected millions of people around the world [8], the number of emerging long-COVID patients is rising, which increases the international burden of the disease [6]. However, few studies have focused on the long COVID, and most studies have evaluated patients in the acute phase of COVID-19 [23,24,25]. Also, limited information is available about musculoskeletal discomforts in patients with long COVID. So in this study, we aimed to evaluate the prevalence of different musculoskeletal symptoms and their associated factors in patients with long COVID. We hypothesized that considering the inflammatory response to COVID-19, the prevalence of musculoskeletal symptoms in patients who had recovered from COVID-19 might be high. Also, we aimed to determine the factors associated with a higher risk of musculoskeletal symptoms in patients with the long-COVID syndrome.

2. Materials & methods

2.1. Design

We designed a cross-sectional study to evaluate the prevalence of post-COVID musculoskeletal symptoms. We conducted the study from January 2021 to April 2021. The ethics committee of the Tehran University of Medical Sciences approved the study protocol (Ethics code: IR.TUMS.IKHC.REC.1399.448).

2.2. Participants

Patients who had recovered from COVID-19 infection were included in the study. Inclusion criteria were: 1) diagnosis of COVID-19 by a physician based on signs and symptoms, imaging, PCR, or Ab, 2) ability to read and write in Persian 3) an at least one-month interval from the disease onset. Patients with musculoskeletal symptoms before contracting COVID-19 were excluded from the study as we wanted to evaluate the new-onset symptoms.

We used convenience sampling to recruit the subjects. We created an online questionnaire using Google form and invited the patients who recovered from COVID-19 to participate in the study. First, we identified the individuals who had been visited in outpatient clinics and those hospitalized due to COVID-19 from January 2021 to April 2021 using Sina hospital records. After that, we sent them a message explaining the study's aims and objectives and invited them to participate in the study. Individuals interested in participating in the study were asked to open the link to the online questionnaire included in the message. There was a question in the online questionnaire on the participants' consent to participate in the study.

Table 1. Basic and demographic characteristics of participants.

Variable		Number (%)
Gender	Female	167 (69.9%)
	Male	72 (30.1%)
Presence of underlying disease		41 (17.2%)
Hospitalization		23 (9.6%)
ICU admission		10 (4.2%)
Intubation		3 (1.3%)
Occupation	Unemployed	71 (29.7%)
	Healthcare worker	46 (19.2%)
	Other	122 (51.0%)
Diagnosis	Definite	149 (62.3%)
	Indefinite	90 (37.7%)

2.3. Questionnaire

The questionnaire contained questions on demographic characteristics, past medical history, the time elapsed since the onset of COVID-19 symptoms, and the COVID-19 diagnosis method. There were also questions on the COVID-19 course at its acute phase, including intubation, hospitalization, ICU admission, and lost days de to COVID-19. Lost days due to COVID-19 were defined as the days the patients needed to rest after the onset of COVID-19 symptoms and could not do their normal activities. Musculoskeletal symptoms, including fatigue, headache, arthralgia, myalgia, neck pain, back pain, hip pain, and leg pain, and their durations were also evaluated [3].

2.4. Statistical analysis

All analyses were performed using IBM SPSS version 24. We calculated mean and standard deviation (SD) for continuous variables and number and percentage for categorical variables. We used the Chi-square test to compare the categorical variables in patients with and without musculoskeletal symptoms. We used the Kolmogorov-Smirnov test to determine whether the continuous variables are distributed normally or not. We used parametric tests, such as independent T-test, to compare the variables with normal distribution in patients with and without musculoskeletal symptoms. To compare variables that did not have a normal distribution, we used non-parametric tests, such as Mann-Whitney and Kruskal-Wallis tests, to compare patients with and without musculoskeletal symptoms. P-value $\leq$ 0.05 was considered statistically significant.

3. Results

Two hundred thirty-nine individuals with a mean age of 37.96 years (SD = 11.19) completed the questionnaire, including 72 men (30.1%). Forty-one patients (17.2%) had underlying diseases, of whom 10 (4.2%) had diabetes, and 7 (2.9%) had hypertension. Among the 23 patients who were hospitalized due to COVID-19, nine (39.1%) were admitted to ICU. Three (1.3%) participants had an intubation history. The mean of days lost due to COVID-19 was 18.19 days (SD = 13.89). Fatigue (91.2%), myalgia (80.3%), and headache (62.3%) were the most common symptoms among the participants. The basic and demographic characteristics of participants are shown in Table 1.

The associations between musculoskeletal symptoms of COVID-19 and other variables are shown in Tables 2 and 3. History of underlying disease was associated with persistence of fatigue for a longer period (P = 0.007). Hospitalization due to COVID-19 was associated with a longer period of arthralgia (P = 0.009), hip pain (P = 0.001), bedridden due to fatigue (P < 0.001), bedridden due to pain (P = 0.024), and exertional dyspnea (P = 0.003). Patients who were admitted to ICU reported low back pain (P = 0.020), bedridden due to fatigue (P = 0.000), and bedridden due to pain (P = 0.003) for longer periods. The female gender

Table 2. Associations between musculoskeletal symptoms and demographic characteristics and COVID-19 course in participants.

Symptom		Gender			Presence of underlying disease			Hospitalization			ICU admission			Occupation			
		Male	Female	P-value	Yes	No	P-value	Yes	No	P-value	Yes	No	P-value	Unemployed	HCW	Other	P-value
Fatigue	No	3 (4.2%)	18 (10.8%)	0.132	3 (7.3%)	18 (9.1%)	**0.007**	2 (8.7%)	19 (8.8%)	0.169	1 (10.0%)	20 (8.7%)	0.984	7 (9.9%)	1 (2.2%)	13 (10.7%)	0.055
	0–4 weeks	41 (56.9%)	74 (44.3%)		17 (41.5%)	98 (49.5%)		8 (34.8%)	107 (49.5%)		5 (50.0%)	110 (48.0%)		27 (38.0%)	21 (45.7%)	67 (54.9%)	
	4–12 weeks	14 (19.4%)	46 (27.5%)		6 (14.6%)	54 (27.3%)		5 (21.7%)	55 (25.5%)		2 (20.0%)	58 (25.3%)		20 (28.2%)	17 (37.0%)	23 (18.9%)	
	>12 weeks	14 (19.4%)	29 (17.4%)		15 (36.6%)	28 (14.1%)		8 (31.8%)	35 (16.2%)		2 (20.0%)	41 (17.9%)		17 (23.9%)	7 (15.2%)	19 (15.6%)	
Headache	No	30 (41.7%)	60 (35.9%)	0.461	8 (19.5%)	82 (41.4%)	0.059	9 (39.1%)	81 (37.5%)	0.459	3 (30.0%)	87 (38.0%)	0.339	16 (22.5%)	22 (47.8%)	52 (42.6%)	0.059
	0–4 weeks	29 (40.3%)	79 (47.3%)		23 (56.1%)	85 (42.9%)		8 (34.8%)	100 (46.3%)		4 (40.0%)	104 (45.4%)		42 (59.2%)	16 (34.8%)	50 (41.0%)	
	4–12 weeks	10 (13.9%)	16 (9.6%)		7 (17.1%)	19 (9.6%)		3 (13.0%)	23 (10.6%)		1 (10.0%)	25 (10.9%)		8 (11.3%)	4 (8.7%)	14 (11.5%)	
	>12 weeks	3 (4.2%)	12 (7.2%)		3 (7.3%)	12 (6.1%)		3 (13.0%)	12 (13.0%)		2 (20.0%)	13 (5.7%)		5 (7.0%)	4 (8.7%)	6 (4.9%)	
Arthralgia	No	26 (36.1%)	66 (39.5%)	0.163	16 (39.0%)	76 (38.4%)	0.186	9 (39.1%)	83 (38.4%)	**0.009**	5 (50.0%)	87 (38.0%)	0.491	25 (35.2%)	18 (39.1%)	49 (40.2%)	0.106
	0–4 weeks	37 (51.4%)	64 (38.3%)		13 (31.7%)	88 (44.4%)		5 (21.7%)	96 (44.4%)		2 (20.0%)	99 (43.2%)		26 (36.6%)	20 (43.5%)	55 (45.1%)	
	4–12 weeks	5 (6.9%)	15 (9.0%)		4 (9.8%)	16 (8.1%)		2 (8.7%)	18 (8.3%)		1 (10.0%)	19 (8.3%)		6 (8.5%)	6 (13.0%)	8 (6.6%)	
	>12 weeks	4 (5.6%)	22 (13.2%)		8 (19.5%)	18 (9.1%)		2 (30.4%)	19 (8.8%)		2 (20.0%)	24 (10.5%)		14 (19.7%)	2 (4.3%)	10 (8.2%)	
Myalgia	No	13 (18.1%)	34 (20.4%)	0.326	6 (14.6%)	41 (20.7%)	**0.007**	6 (26.1%)	41 (19.0%)	0.066	3 (30.0%)	44 (19.2%)	0.052	11 (15.5%)	6 (13.0%)	30 (24.6%)	0.052
	0–4 weeks	48 (66.7%)	92 (55.1%)		21 (51.2%)	119 (60.1%)		9 (39.1%)	131 (60.6%)		2 (20.0%)	138 (60.3%)		38 (53.5%)	29 (63.0%)	73 (59.8%)	
	4–12 weeks	6 (8.3%)	19 (11.4%)		3 (7.3%)	22 (11.1%)		2 (8.7%)	23 (10.6%)		3 (30.0%)	22 (9.6%)		9 (12.7%)	8 (17.4%)	8 (6.6%)	
	>12 weeks	5 (6.9%)	22 (13.2%)		11 (26.8%)	16 (8.1%)		6 (26.1%)	21 (9.7%)		2 (20.0%)	25 (10.9%)		9 (12.7%)	3 (6.5%)	11 (9.0%)	
Neck pain	No	52 (72.2%)	113 (67.7%)	0.591	22 (53.7%)	143 (72.2%)	**0.009**	18 (78.3%)	147 (68.1%)	0.270	8 (80.0%)	157 (68.6%)	0.755	46 (64.8%)	30 (35.2%)	89 (73.0%)	0.214
	0–4 weeks	14 (19.4%)	30 (18.0%)		8 (19.5%)	36 (18.2%)		2 (8.7%)	42 (19.4%)		1 (10.0%)	43 (18.8%)		14 (19.7%)	8 (17.4%)	22 (18.0%)	
	4–12 weeks	3 (4.2%)	9 (5.4%)		3 (7.3%)	9 (4.5%)		0 (0.0%)	12 (5.6%)		0 (0.0%)	12 (5.2%)		2 (2.8%)	5 (10.9%)	5 (4.1%)	
	>12 weeks	3 (4.2%)	15 (9.0%)		8 (19.5%)	10 (5.1%)		3 (13.0%)	15 (6.9%)		1 (10.0%)	17 (7.4%)		9 (12.7%)	3 (6.5%)	6 (4.9%)	
Back pain	No	43 (59.7%)	91 (54.5%)	0.704	19 (46.3%)	115 (58.1%)	0.319	14 (60.9%)	120 (55.6%)	0.769	9 (90.0%)	125 (54.6%)	0.126	38 (53.5%)	26 (56.5%)	70 (57.4%)	0.119
	0–4 weeks	19 (26.4%)	43 (25.7%)		11 (26.8%)	51 (25.8%)		4 (17.4%)	58 (26.9%)		0 (0.0%)	62 (27.1%)		20 (28.2%)	8 (17.4%)	34 (27.9%)	
	4–12 weeks	6 (8.3%)	17 (10.2%)		5 (12.2%)	18 (9.1%)		3 (13.0%)	20 (9.3%)		1 (10.0%)	22 (9.6%)		4 (5.6%)	9 (19.6%)	10 (8.2%)	
	>12 weeks	4 (5.6%)	16 (9.6%)		6 (14.6%)	14 (7.1%)		2 (8.7%)	18 (8.3%)		0 (0.0%)	20 (8.7%)		9 (12.7%)	3 (6.5%)	8 (6.6%)	
Low Back pain	No	37 (51.4%)	82 (49.1%)	0.257	16 (39.0%)	103 (52.0%)	0.094	10 (43.5%)	109 (50.5%)	0.262	4 (40.0%)	115 (50.2%)	**0.020**	28 (39.4%)	26 (56.5%)	65 (53.3%)	0.235

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Table 2 (*continued*)

Symptom		Gender			Presence of underlying disease			Hospitalization			ICU admission			Occupation			
		Male	Female	P-value	Yes	No	P-value	Yes	No	P-value	Yes	No	P-value	Unemployed	HCW	Other	P-value
	0–4 weeks	27 (37.5%)	53 (31.7%)		14 (34.0%)	66 (33.3%)		6 (26.1%)	74 (34.3%)		1 (10.0%)	79 (34.5%)		28 (39.4%)	12 (26.1%)	40 (32.8%)	
	4–12 weeks	6 (8.3%)	15 (9.0%)		4 (9.8%)	17 (8.6%)		3 (13.0%)	18 (8.3%)		2 (20.0%)	19 (8.3%)		6 (8.5%)	6 (13.0%)	9 (7.4%)	
	>12 weeks	2 (2.8%)	17 (10.2%)		7 (17.1%)	12 (6.1%)		4 (17.4%)	15 (6.9%)		3 (30.0%)	16 (7.0%)		9 (12.7%)	2 (4.3%)	8 (6.6%)	
Hip pain	No	55 (76.4%)	130 (77.8%)	0.599	29 (70.7%)	156 (78.8%)	0.434	15 (65.2%)	170 (78.7%)	**0.001**	9 (90.0%)	176 (76.9%)	0.464	47 (66.2%)	38 (82.6%)	100 (82.2%)	0.088
	0–4 weeks	13 (18.1%)	22 (13.2%)		7 (17.1%)	28 (14.1%)		3 (13.0%)	32 (14.8%)		0 (0.0%)	35 (15.3%)		13 (18.3%)	6 (13.0%)	16 (13.1%)	
	4–12 weeks	2 (2.8%)	5 (3.0%)		1 (2.4%)	6 (3.0%)		0 (0.0%)	7 (3.2%)		0 (0.0%)	7 (3.1%)		3 (4.2%)	1 (2.2%)	3 (2.5%)	
	>12 weeks	2 (2.8%)	10 (6.0%)		4 (9.8%)	8 (4.0%)		5 (21.7%)	7 (3.2%)		1 (10.0%)	11 (4.8%)		8 (11.3%)	1 (2.2%)	3 (2.5%)	
Leg pain	No	35 (48.6%)	63 (37.7%)	0.248	10 (24.4%)	88 (44.4%)	0.085	9 (39.1%)	89 (41.2%)	0.141	5 (50.0%)	93 (40.6%)	0.296	24 (33.8%)	17 (37.0%)	57 (46.7%)	0.173
	0–4 weeks	25 (34.7%)	62 (37.1%)		17 (41.5%)	70 (35.4%)		5 (21.7%)	82 (38.0%)		1 (10.0%)	86 (37.6%)		26 (36.6%)	19 (41.3%)	4 2 (34.4%)	
	4–12 weeks	7 (9.7%)	17 (10.2%)		6 (14.6%)	18 (9.1%)		3 (13.0%)	21 (9.7%)		2 (20.0%)	22 (9.6%)		6 (8.5%)	6 (13.0%)	12 (9.8%)	
	>12 weeks	5 (6.9%)	25 (15.0%)		8 (19.5%)	22 (11.1%)		6 (26.1%)	24 (11.1%)		2 (20.0%)	28 (12.2%)		15 (21.1%)	4 (8.7%)	11 (9.0%)	
Chest pain	No	38 (52.8%)	105 (62.9%)	0.134	19 (46.3%)	124 (62.6%)	0.176	11 (47.8%)	132 (61.1%)	0.058	6 (60.0%)	137 (59.8%)	0.279	36 (50.7%)	30 (65.2%)	77 (63.1%)	0.343
	0–4 weeks	21 (29.2%)	45 (26.9%)		17 (41.5%)	49 (24.7%)		5 (21.7%)	61 (28.2%)		1 (10.0%)	65 (28.4%)		24 (33.8%)	11 (23.9%)	31 (25.4%)	
	4–12 weeks	6 (8.3%)	12 (7.2%)		3 (7.3%)	15 (7.6%)		4 (17.4%)	14 (6.5%)		2 (20.0%)	16 (7.0%)		8 (11.3%)	8 (8.7%)	6 (4.9%)	
	>12 weeks	7 (9.7%)	5 (3.0%)		2 (4.9%)	10 (5.1%)		3 (13.0%)	9 (4.2%)		1 (10.0%)	11 (4.8%)		3 (4.2%)	1 (2.2%)	8 (6.6%)	
Bedridden due to fatigue	No	41 (56.9%)	97 (58.1%)	0.070	20 (48.8%)	118 (59.6%)	0.102	3 (13.0%)	135 (62.5%)	**0.001>**	0 (0.0%)	138 (60.3%)	**0.001>**	36 (50.7%)	26 (56.5%)	76 (62.3%)	0.465
	0–4 weeks	28 (38.9%)	46 (27.5%)		13 (31.7%)	61 (30.8%)		13 (56.5%)	61 (28.2%)		6 (60.0%)	68 (29.7%)		23 (32.4%)	16 (34.8%)	35 (28.7%)	
	4–12 weeks	2 (2.8%)	10 (6.0%)		2 (4.9%)	10 (5.1%)		3 (13.0%)	9 (4.2%)		1 (10.0%)	11 (4.8%)		4 (5.6%)	2 (4.3%)	6 (4.9%)	
	>12 weeks	1 (1.4%)	14 (8.4%)		6 (14.6%)	9 (4.5%)		4 (17.4%)	11 (5.1%)		3 (30.0%)	12 (5.2%)		8 (11.3%)	2 (4.3%)	5 (4.1%)	
Bedridden due to pain	No	61 (84.7%)	114 (68.3%)	**0.037**	29 (70.7%)	146 (73.7%)	0.097	13 (56.5%)	162 (75.0%)	**0.024**	5 (50.0%)	170 (74.2%)	**0.003**	41 (57.7%)	36 (78.3%)	98 (80.3%)	**0.018**
	0–4 weeks	10 (13.9%)	37 (22.2%)		7 (17.1%)	40 (20.2%)		5 (21.7%)	42 (19.4%)		2 (20.0%)	45 (19.7%)		20 (28.2%)	8 (17.4%)	19 (15.6%)	
	4–12 weeks	0 (0.0%)	5 (3.0%)		0 (0.0%)	5 (2.5%)		1 (4.3%)	4 (1.9%)		0 (0.0%)	5 (2.2%)		2 (2.8%)	1 (2.2%)	2 (1.6%)	
	>12 weeks	1 (1.4%)	11 (6.6%)		5 (12.2%)	7 (3.5%)		4 (17.4%)	8 (3.7%)		3 (30.0%)	9 (3.9%)		8 (11.3%)	1 (2.2%)	3 (2.5%)	

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Table 2 (*continued*)

Symptom		Gender			Presence of underlying disease			Hospitalization			ICU admission			Occupation			
		Male	Female	P-value	Yes	No	P-value	Yes	No	P-value	Yes	No	P-value	Unemployed	HCW	Other	P-value
Shortness of breath in rest	No	43 (59.7%)	120 (71.9%)	0.126	15 (36.6%)	135 (68.2%)	0.260	10 (43.5%)	153 (70.8%)	**0.003**	2 (20.0%)	158 (69.0%)	0.352	33 (46.5%)	31 (67.4%)	61 (50.0%)	0.106
	0–4 weeks	24 (33.3%)	32 (19.2%)		12 (29.3%)	46 (23.2%)		10 (43.5%)	46 (21.3%)		4 (40.0%)	52 (22.7%)		18 (25.4%)	14 (30.4%)	32 (26.2%)	
	4–12 weeks	3 (4.2%)	10 (6.0%)		6 (14.6%)	10 (5.1%)		1 (4.3%)	12 (5.6%)		2 (20.0%)	13 (5.7%)		10 (14.1%)	1 (2.2%)	15 (12.3%)	
	>12 weeks	2 (2.8%)	5 (3.0%)		8 (19.5%)	7 (3.5%)		2 (8.7%)	5 (2.3%)		2 (20.0%)	6 (2.6%)		10 (14.1%)	0 (0.0%)	14 (11.5%)	
Shortness of breath in activity	No	31 (43.1%)	83 (49.7%)	0.754	28 (68.3%)	99 (50.0%)	0.617	4 (17.4%)	110 (50.9%)	**0.022**	5 (50.0%)	112 (48.9%)	0.253	41 (57.7%)	20 (43.5%)	91 (74.6%)	0.883
	0–4 weeks	21 (29.2%)	42 (25.1%)		10 (24.4%)	51 (25.8%)		7 (30.4%)	56 (25.9%)		4 (40.0%)	59 (25.8%)		21 (29.6%)	13 (28.3%)	21 (17.2%)	
	4–12 weeks	10 (13.9%)	24 (14.4%)		3 (7.3%)	28 (14.1%)		5 (21.7%)	29 (13.4%)		0 (0.0%)	32 (14.0%)		5 (7.0%)	9 (19.6%)	7 (5.7%)	
	>12 weeks	10 (13.9%)	18 (10.8%)		0 (0.0%)	20 (10.1%)		2 (8.7%)	21 (9.7%)		1 (10.0%)	26 (11.4%)		4 (5.6%)	4 (8.7%)	3 (2.5%)	

Values are reported as number (%). Statistically significant values are bolded.

was associated with a higher risk of being bedridden due to pain ($P = 0.037$).

Patients who were bedridden due to fatigue were significantly older, had higher BMIs, and had lost more days due to COVID-19 than those who were not ($P < 0.05$). BMI and lost days due to COVID-19 were significantly higher in patients who had experienced shortness of breath at rest, chest pain, arthralgia, and myalgia for longer periods ($P < 0.05$).

4. Discussion

Studies have estimated that 10% of COVID-19 patients may continue feeling the symptoms even after the acute phase, referred to as long-COVID [4]. Many studies on patients with COVID-19 have evaluated its manifestations, including musculoskeletal symptoms, but to the best of our knowledge, no study has explicitly worked on musculoskeletal discomforts in Iran, focusing on the post-acute phase. The current study evaluated the prevalence of post-COVID musculoskeletal symptoms and associated factors. We found that BMI, gender, hospitalization due to COVID-19, and intubation are associated with a higher risk of lasting musculoskeletal symptoms in patients with COVID-19.

In our study, fatigue (91.2%), myalgia (80.3%), and headache (62.3%) were the most common symptoms. The high prevalence of fatigue in our study is consistent with the high rate of fatigue reported in previous studies, estimated to be 30–72% [12, 23]. Almost all studies on COVID-19 symptoms and limited studies on long-COVID symptoms have shown that fatigue is the most common symptom in these patients [23, 26, 27]. However, the exact etiology of fatigue is unknown. Neurotransmitter level alterations, inflammation and cytokine release, stress-induced hormones such as Cortisol, substrate metabolism, and even psychological distress are the potential contributing factors [28]. Due to various factors involved in causing fatigue, it is one common and persistent symptom in acute and chronic phases of COVID-19, which should be considered for long-term management of symptoms. It gets more critical considering that fatigue is associated with more days lost among our participants, which can increase the burden of the disease.

The most important factor associated with a longer period of musculoskeletal symptoms in our study was higher BMI, associated with arthralgia, myalgia, chest pain, bedridden due to fatigue, and exertional dyspnea. This finding is consistent with Karaarslan et al. study as they found that higher BMI is associated with a higher risk of lasting musculoskeletal symptoms in patients with COVID-19 [23]. They evaluated fatigue, myalgia, arthralgia, back pain, low back pain, and neck pain among 300 COVID-19 patients one month after discharge from the hospital and found that persistence of fatigue, myalgia, and arthralgia was related to higher BMIs [23]. BMI is a modifiable factor associated with a higher risk of long-COVID musculoskeletal symptoms, and it can be targeted in interventions to decrease the incidence of long COVID musculoskeletal symptoms. It gets more important as physical activity levels have reduced during the COVID-19 pandemic, leading to overweight and obesity among populations [29]. Designing interventions specified for the pandemic situation to improve the physical activity levels and enhance the healthy lifestyles among populations during the pandemic may be beneficial in helping people keep their BMI levels at normal levels and reducing the burden of long COVID [30]. Improvement of physical activity levels may also have additional benefits considering its role in alleviating musculoskeletal symptoms [31, 32].

In our study, hospitalization due to COVID-19 was associated with bedridden, arthralgia, and exertional dyspnea. ICU admission was also associated with bedridden and back pain. In another similar study, with a mean 110.9 days follow-up after the hospital admission of COVID-19 patients, 55.0% reported fatigue as the most common symptom. Also, most patients who were hospitalized had persistent symptoms [27]. Carvalho-Schneider et al. followed non-critical COVID-19 patients for two months and found that persistent symptoms until day 30 were associated with hospital admission and clinical dyspnea and older ages but were not associated with underlying disease [33]. Hospitalization

Table 3. Associations between musculoskeletal symptoms and age, BMI, and lost days due to COVID-19.

		Age (year)			BMI (kg/m^2)			Lost days due to COVID-19		
		Mean	SD	P-value	Mean	SD	P-value	Mean	SD	P-value
Fatigue	No	34.00	11.84	0.071	25.463	4.87	0.112	17.94	18.31	**0.016**
	0–4 weeks	37.04	10.76		31.964	28.11		15.44	10.18	
	4–12 weeks	37.65	10.79		26.443	4.30		21.31	12.89	
	>12 weeks	41.70	10.52		31.075	21.29		21.32	19.24	
Headache	No	37.67	11.38	0.271	29.031	18.68	0.681	18.24	12.11	0.076
	0–4 weeks	37.72	10.32		30.450	23.85		16.06	12.33	
	4–12 weeks	42.64	12.47		26.939	3.20		21.76	10.79	
	>12 weeks	37.40	8.78		35.908	36.12		26.92	29.96	
Arthralgia	No	37.40	11.55	0.224	29.019	21.67	**0.032**	16.30	10.89	**0.048**
	0–4 weeks	37.51	9.96		31.234	26.01		17.03	10.88	
	4–12 weeks	41.16	14.21		28.152	4.29		19.71	13.59	
	>12 weeks	41.50	9.01		28.515	4.14		28.67	26.28	
Myalgia	No	37.83	12.3	0.276	25.111	4.13	**0.004**	19.43	14.58	**0.028**
	0–4 weeks	37.71	10.1		32.014	27.79		16.26	10.19	
	4–12 weeks	36.88	11.14		27.806	4.08		15.50	6.52	
	>12 weeks	42.69	12.1		28.457	4.14		29.38	26.19	
Neck pain	No	37.99	10.77	0.112	31.161	25.79	0.379	17.31	11.85	0.505
	0–4 weeks	36.81	11.434		26.581	4.64		17.07	11.24	
	4–12 weeks	38.08	10.77		26.098	5.41		21.55	14.74	
	>12 weeks	43.67	10.54		27.937	3.08		27.36	29.19	
Back pain	No	38.07	11.64	0.959	31.459	27.73	0.697	17.36	13.04	0.054
	0–4 weeks	38.37	10.03		28.164	12.02		18.98	11.31	
	4–12 weeks	37.43	9.72		26.612	2.73		13.45	5.41	
	>12 weeks	39.40	10.74		27.926	3.73		26.12	26.49	
Low back pain	No	38.03	11.50	0.367	31.777	29.14	0.341	19.39	16.73	0.819
	0–4 weeks	38.20	9.50		27.899	10.86		16.84	10.76	
	4–12 weeks	36.70	13.21		27.403	3.35		17.19	9.42	
	>12 weeks	40.94	10.73		28.224	3.25		18.13	11.22	
Hip pain	No	37.73	11.02	0.560	29.954	23.73	0.262	18.15	14.37	0.885
	0–4 weeks	38.71	10.28		29.648	15.35		17.61	11.05	
	4–12 weeks	40.86	10.69		28.326	5.24		21.60	21.56	
	>12 weeks	42.25	11.73		28.857	3.59		19.38	11.53	
Chest pain	No	37.59	10.93	0.422	28.605	20.97	**0.016**	17.18	14.56	**0.036**
	0–4 weeks	38.02	10.97		31.102	21.39		18.34	13.57	
	4–12 weeks	43.76	11.67		28.261	4.03		23.70	9.27	
	>12 weeks	38.50	8.37		39.524	39.72		22.00	11.35	
Leg pain	No	37.65	10.85	0.652	27.332	10.08	**0.015**	16.84	10.19	0.436
	0–4 weeks	37.55	10.33		30.413	26.36		17.01	12.00	
	4–12 weeks	40.41	13.99		32.987	29.78		19.22	8.86	
	>12 weeks	40.23	10.49		33.974	27.02		25.83	26.54	
Bedridden due to fatigue	No	35.95	9.93	**0.035**	27.640	15.32	**0.003**	16.67	11.28	**0.063**
	0–4 weeks	40.18	10.85		34.545	32.24		18.13	9.62	
	4–12 weeks	45.64	15.38		26.541	2.42		31.11	21.09	
	>12 weeks	44.07	11.28		29.061	4.95		24.73	34.70	
Bedridden due to pain	No	37.85	10.76	0.097	28.732	17.20	0.143	17.62	11.90	0.830
	0–4 weeks	37.26	11.60		34.247	35.87		17.60	11.02	
	4–12 weeks	42.80	8.87		27.080	3.45		21.33	8.08	
	>12 weeks	45.55	11.28		30.054	4.95		32.57	42.43	
Shortness of breath in rest	No	36.54	10.44	0.092	27.95	16.82	**0.006**	14.80	9.99	**0.002**
	0–4 weeks	38.68	12.17		35.033	35.23		18.58	12.01	
	4–12 weeks	41.15	10.67		27.168	3.92		27.48	22.64	
	>12 weeks	40.25	9.54		29.120	4.56		19.54	12.65	
Exertional dyspnea	No	37.44	11.58	0.055	29.917	23.76	0.156	15.60	9.90	**0.004**
	0–4 weeks	39.55	9.05		30.153	18.87		22.00	15.74	
	4–12 weeks	43.15	10.37		28.616	3.97		30.64	30.94	
	>12 weeks	35.17	6.97		27.059	2.97		28.00	11.64	

Statistically significant values are bolded.

history indicates a more severe disease and causes a higher period of immobility, leading to longer-lasting symptoms. A higher prevalence of musculoskeletal symptoms in hospitalized patients suggests a need for rehabilitation programs for these patients to facilitate restoring their physical capacity in these patients [34].

4.1. Limitations

There are several limitations of this study worth mentioning. First, few patients in our study had been admitted to ICU or had been intubated. Due to the small sample size, our study may not have the appropriate power to evaluate their associations with musculoskeletal symptoms. Second, our study had a cross-sectional design, and we could not evaluate causal relationships. Third, the interval between the onset of COVID-19 symptoms and our study varied from one month to more than three months among participants, which is another limitation of this study as the length of follow-ups was not equal for all patients. Fourth, recall bias is another limitation of this study. Finally, about 70% of our participants were females, which should be considered in the interpretation of our findings considering the biological differences between males and females in pain perception, especially the lower threshold of females in pain perception [35].

5. Conclusion

This study indicated a high prevalence of persistent musculoskeletal symptoms among patients who recovered from COVID-19. These musculoskeletal symptoms may reduce people's function and productivity, increasing the burden of COVID-19. Modifiable factors, such as BMI, can be targeted to reduce the prevalence of musculoskeletal symptoms in COVID-19 survivors and reduce its burden. Also, cohort studies may be beneficial for further evaluating the association between COVID-19 and persistent musculoskeletal symptoms.

Declarations

Author contribution statement

Mohaddeseh Azadvari: Conceived and designed the experiments; Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Afarin Haghparast; Amin Nakhostin-Ansari: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Seyede Zahra Emami Razavi; Maryam Hosseini: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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