



ORIGINAL ARTICLE

WHAT AWAITS US AFTER COVID-19? MUSCULOSKELETAL SYSTEM INVOLVEMENT IN THE ELDERLY POPULATION IN TÜRKİYE AND ITS AFTERMATH

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ABSTRACT

Introduction: Although COVID-19 primarily affects the respiratory system, one of the most frequently effected areas is the musculoskeletal system. COVID-19 associated musculoskeletal problems can cause disability in patients ≥ 65 years. The aim of the study was to define the musculoskeletal problems after the COVID-19 infection and to examine the relationship with the accompanying comorbidities in geriatric population.

Materials and Method: The study was conducted by the members of Geriatric Rehabilitation Study Group of Turkish Physical Medicine and Rehabilitation Society at 11 different hospitals from 7 provinces (Ankara, İstanbul, İzmir, Gaziantep, Adana, Bursa, and Kirikkale) of Türkiye. Individuals aged 65 years and over who had a history of COVID-19 within the last 12 months and experienced persistent/continuous musculoskeletal complaints were included into the study. COVID-19 diagnoses were confirmed from electronic hospital records and the e-Nabız system. Data were collected by face-to-face interviews and after recruiting the first 50 patients from each center, patient recruitment was terminated.

Results: A total of 457 cases in which all questions were answered completely (without any missing data) were included in this observational study. The cases were mainly 65-75 years old, married, and non-smoking women. The most common musculoskeletal involvement was widespread pain (81%), followed by myalgia (63.7%) and arthralgia (44.4%). Other rare involvements (osteonecrosis, myositis, steroid myopathy, arthritis) were significantly more frequent in patients older than 75 years, regardless of gender. Analysis showed that musculoskeletal pain immediately after infection is observed more in cases with comorbid diseases ($p < 0.001$), hypertension ($p < 0.001$), pulmonary involvement ($p = 0.002$) and hospitalization due to COVID-19 ($p < 0.001$). It was determined that the incidence of pain seen immediately after infection increased as the number of comorbidities increased ($p < 0.001$). In conjunction with this, persistent pain after COVID-19 infection were more common in those with osteoarthritis ($p = 0.039$).

Conclusion: Elderly patients may develop musculoskeletal pain in multiple body sites after COVID-19, which is primarily related to presence and number of comorbidities, hospitalization and pulmonary involvement. The long-term consequences of COVID-19 on musculoskeletal health are still being studied, and further research is needed to fully understand the extent and duration of these effects.

Keywords: Aged; COVID-19; Arthralgia; Musculoskeletal Pain.



INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus (SARS CoV-2), primarily targeting the pulmonary system. However, it can also affect the musculoskeletal, cardiovascular, gastrointestinal, and neurological systems. Post-infection period poses challenges for both patients and physicians, with ongoing issues that require management even after one year. These include musculoskeletal (myalgia, arthralgia, etc.), pulmonary (e.g., dyspnea), and cardiovascular (hypertension, arrhythmia, etc.) complications. Therefore, a comprehensive rehabilitation program is crucial for patients to achieve a healthy well-being (1). Concerning the musculoskeletal system, the first step is to be aware of symptomatology during the post-COVID period (2).

Musculoskeletal system involvement in older adults can manifest in muscles (myalgia, muscle weakness, myosis, rhabdomyolysis, necrotizing autoimmune myonecrosis, myopathy, sarcopenia), joints (arthralgia, virus-induced arthritis, inflammatory arthritis), nerves (peripheral neuropathy, Guillain-Barré Syndrome and its variants - Miller Fisher's syndrome, critical illness polyneuropathy), and/or bones (osteoporosis, osteonecrosis) (3). Additionally, pre-existing neuromuscular, muscular, and/or autoimmune conditions can contribute to disability in older adults (4).

The COVID-19 pandemic has been on the world's agenda for nearly four years, causing millions of infections, hospitalizations, weanings, and disabilities. In Türkiye, as of November 2022, 17.042.722 people have been infected, and 101.492 people have died. Unfortunately, no published data is available since then (5). A study by Ek et al., analyzing global data, revealed that deaths due to COVID-19 in individuals over 60 years of age were 35.93% in countries with characteristics similar to Türkiye (6). It can be estimated that the infected elderly population in Türkiye is approximately 6 million people.

Considering a mortality rate of 1%, an estimated 60,000 people have died, and the remaining have experienced various degrees of post-COVID symptoms.

Knowledge regarding COVID-19-associated musculoskeletal system involvement in the geriatric population is limited. The present study aims to define musculoskeletal problems related to COVID-19 in patients aged 65 years and older, as well as to identify confounders of musculoskeletal issues. Data obtained from the study may increase awareness on this matter and pave the way for better management of COVID-19-associated musculoskeletal system problems in older adults.

MATERIALS AND METHOD

Study design and settings

This multi-center cross sectional study was conducted by the Geriatric Rehabilitation Study Group of the Turkish Physical Medicine and Rehabilitation (PMR) Society. An invitation letter was sent to all members of the Study Group and PMR departments of eleven hospitals from seven provinces of Türkiye (Ankara, Istanbul, Izmir, Gaziantep, Adana, Bursa, and Kırkkale) have informed that they want to participate in the study. Afterwards the study protocol was approved by the Clinical Research Ethics Committee of the Hacettepe University Medical Faculty (Date: 19.04.2022, No: 16969557750).

A comprehensive patient registration form has been created and a consortium was formed to produce the final version of the questionnaire by all centers. Patients who applied to the PMR clinics (after having COVID-19) were evaluated in the scope of the study and recruited by the sequential method. Only older adults who had the history of COVID-19 and meeting the following criteria were included in the study: a-Aged 65 years or older, b-Diagnosed with COVID-19 within

the last 12 months, c-Individuals with persistent/continuous musculoskeletal complaints, and d-Those who agreed to participate in the study. COVID-19 diagnoses were confirmed by electronic hospital records and the e-Nabız system and all the interviews were conducted in the hospital. A written informed consent was obtained from each patient. All data were collected face-to-face and deposited using a web-based method. Patient recruitment was terminated at each center after reaching 50 patients meeting the acceptance criteria.

Musculoskeletal complaints were differentiated and listed, including widespread pain, arthralgia, arthritis, myalgia, myositis, myopathy, neuropathy, osteonecrosis, and falls.

Pain was divided into different categories such as pre existing pain, immediate pain after infection (lasting around seven days), pain lasting from 1-3 weeks, 4-8 weeks, 8 weeks to 3 months, 3-6 months, 6-9 months, 9-12 months, and persistent pain (lasting more than three months) after infection. The analysis of pain was based on its presence, duration, and location.

Assessment procedure

Survey questions were asked face-to-face by the specialists at the PMR clinics. Completed questionnaires were transferred to electronic media. A total of 550 patients from 11 centers were collected within the scope of the study, and 457 patients in which all questions were answered completely (without any missing data) were included and analyzed.

Statistical analysis

The data were entered into and analyzed by the SPSS software version 28.0.1.1 (IBM Corp., Armonk, NY, USA). All categorical variables were given as number and percentage values. Chi-squared test was used to compare categorical variables. Significance level was set at $p < 0.05$.

RESULTS

A total of 457 patients from 11 centers were included in this observational study. Majority of the cases were female, aged 65-75 years, vaccinated, married, primary school graduates, and had at least one chronic disease. They were non-smokers and living with their families/spouses. The demographic characteristics of the cases are given in Table 1.

Among the cases included in the study, 91 (19.9%) of them were hospitalized during the COVID-19 course. Of the hospitalized patients, 77% were admitted for pulmonary problems, 60% (52) had a hospitalization duration of less than 2 weeks, and 12 (10.2%) patients were hospitalized for more than 4 weeks. It is noteworthy that 174 (38.1%) patients did not take medication at the time of infection, and fifty-four patients (11.8%) took medication without a prescription. The COVID-19 related data of signs and symptoms and medication status are presented in Table 2.

Overall 94.1% of the patients had comorbidities and the most common comorbidity was hypertension (73.1%), followed by osteoarthritis (32.6%), diabetes mellitus (27.8%), and coronary artery disease (24.5%) (Table 3). Four hundred and thirty-eight (96.7%) patients were taking medication for these diseases. Of 162 (35.44%) patients taking medications, 47 (10.2%) taking more than 5 medications per day had polypharmacy (Table 2).

Pain was present in 370 (81%) of the cases included in the study. In 95 (25.67%) of these cases, pain lasted longer than six months. The most common sites of pain were the spine (48.9%) including the lumbar and thoracic regions and the lower extremities including the hip and knee. In 261 (80.6%) of the patients with pain, pain was present prior to COVID-19 and increased in terms of value. Arthralgia was present in 203 (44.4%) cases and was most common in the knee (60.6%) and hip (40.9%). Post COVID pain and its characteristics are shown in Table 4. Post-infection 123 cases (26.9%)



Table 1. The demographic data of the patients (n=457)

Data		Number (n)	Percentage (%)
Gender	Women	296	64.8
	Men	161	35.2
Age group	65-75	294	64.3
	76-85	126	27.6
	>86	37	8.1
Marital status	Single/Divorced/Widowed	155	31.7
	Married	312	68.3
Education level	Illiterate	78	17.1
	Primary school	226	49.4
	High school	74	16.2
	University	79	17.3
Working status	Retired	213	46.7
	Housewife	207	45.3
	Still working	37	12.5
Life style	With family/spouse	365	79.9
	Caregiver/Nursing home/Other relatives	35	7.6
Cigarette status	Alone	57	12.5
	Non-smoking	336	74
	Smoking	119	26

Table 2. The data of COVID-19 related signs and symptoms (n=457)

		Number (n)	Percentage (%)
Time after COVID-19 infection	<1 month	25	5.5
	1-3 months	38	8.3
	3-6 months	66	14.4
	6-9 months	75	16.4
	9-12 months	89	19.5
	>12 months	164	35.9
Vaccination status	No vaccination / Didn't want to specify	137	19.3
	Inadequate / Insufficient vaccination	58	17.4
	Full vaccination	262	63.3
Hospitalization for COVID-19	Yes	91	19.9
	No	366	80.1
Medication at the time of infection	With prescription	229	50.1
	Without prescription	54	11.8
	No medication	174	38.1
Medication during COVID-19	Anticoagulation	259	56.7
	Antiviral	246	53.8
	Corticosteroid	68	14.8
	Biological agent	22	4.8

Inadequate/insufficient vaccination: 1 dosage of sinovac/1 dosage of biontech/ 2 dosage of sinovac/1 dosage of sinovac+1 dosage of biontech vaccination

Full vaccination: 3 dosage of sinovac/3 dosage of biontech/ 2 dosage of sinovac+2 dosage of biontech/3 dosage of sinovac+2 dosage of biontech vaccination

Table 3. The comorbidities of the patients (n=457)

Comorbidities	Number of Patients (n)	Percentage (%)
Overall	430	94.1
Hypertension	334	73.1
Osteoarthritis	149	32.6
Diabetes mellitus	127	27.8
Coronary artery disease	112	24.5
Osteoporosis	78	17.1
Gastro-intestinal diseases	59	12.9
Depression	33	7.2
Obesity	31	6.8
Chronic kidney disease	26	5.7
Stroke	25	5.5
Movement disorders	22	4.8
Thyroid diseases	22	4.8
Chronic obstructive pulmonary diseases	16	3.5
Asthma bronchiale	12	2.6
Liver diseases	9	2

Table 4. Post-COVID pain and its characteristics (n=457)

		Yes number (n)	Yes percentage (%)	No number (n)	No percentage (%)
Presence of pain after infection		370	81	87	19
Duration of pain after infection	<1 week	39	8.5		
	1-3 weeks	80	17.5		
	4-8 weeks	68	14.8		
	8 week- 3 months	38	8.3		
	3-6 months	50	10.9		
	6-9 months	95	20.7		
	9-12 months	27	5.9		
Localization of pain after infection	Backbone/lomber spine	181	48.9		
	Dorsal	162	43.8		
	Hip	119	32.2		
	Knee	118	31.9		
	Shoulder	99	26.8		
Characteristic of prior pain	Prior pain and increase in	261	80.6	63	19.4
	Prior treatment for pain	229	70.7	95	29.3
Disability impact	Difficulty of walking	123	26.9	334	73.1
	Device usage	76	16.6	381	83.4
	Cane	46	60.5		
	Walker	22	28.9		
	Wheelchair	15	19.7		



Table 5. Post-COVID musculoskeletal system problems (n=457)

	Number of Patients (n)	Percentage (%)
Widespread pain	370	81
Myalgia	291	63.7
Arthralgia	203	44.4
Arthritis	15	3.3
Muscle weakness	74	16.2
Myositis	2	0.4
Steroid myopathy	6	1.3
Falls	53	11.6
Osteoporosis (detected in post-COVID period)	93	20.4
Osteonecrosis	1	0.2
Neuropathy	38	8.3
Peripheral	9	1.9
Polyneuropathy	29	6.3

had difficulty of walking and 76 (16.6%) patients felt the need to use an assistive device and the most commonly used device was a cane in 46 (60.5%) cases.

The most prevalent complaint, observed in 457 cases, was widespread pain (81%), followed by myalgia (63.7%) and arthralgia (44.4%). Post-COVID musculoskeletal system problems are presented in Table 5. The most rare involvements were osteonecrosis (1 patient, 0.2%) and myositis (2 patients, 0.4%).

Chi-squared test was used to compare categorical variables (significance level was set at $p < 0.05$) (Table 6). According to the results of the analysis carried out, it was found that musculoskeletal pain immediately after infection is observed more frequently in cases with comorbid diseases ($p < 0.001$), hypertension ($p < 0.001$), and hospitalization due to COVID-19 ($p < 0.001$). It was determined that the incidence of pain seen immediately after infection increased as the number of comorbidities increased ($p < 0.001$). In conjunction with this, persistent pain after

COVID-19 infection were more common in those with osteoarthritis ($p = 0.039$).

DISCUSSION

This study reveals that musculoskeletal involvement during the post-COVID period in older adults referred to PMR clinics is an important issue. In the scope of our study patients who applied to the PMR clinics were evaluated by the sequential method. The predominant involvements include widespread pain (81%), myalgia (63.7%) and arthralgia (44.4%). Majority of the cases were female (64.8%). The reason for this situation may be due to the fact that our sample in which the survey was conducted consisted of more women and also women may had more persistent pain. But it can't be claimed that the percentage of women infected with COVID-19 was higher. However, rarer involvements, such as osteonecrosis, myositis, steroid myopathy, and arthritis, were more common in patients older than 75 years, irrespective of gender.

In terms of pain and its determinants, the study

Table 6. The relationship between comorbidities and musculoskeletal pain and persistent pain

		Musculoskeletal pain immediately after infection (lasting about 7 days)		Persistent pain (that lasts for more than three months) after infection	
		Number (%)	p	Number (%)	p
Presence of comorbidities	No	41 (56.9%)	<0.001	47 (65.3%)	0.602
	Yes	361 (83%)		270 (62.1%)	
Hypertension	No	88 (71%)	0.001	68 (54.8%)	0.086
	Yes	286 (84.6%)		215 (63.6%)	
Chronic liver disease	No	369 (81.5%)	0.072	279 (61.6%)	0.318
	Yes	5 (55.6%)		4 (44.4%)	
Osteoarthritis	No	247 (79.2%)	0.199	181 (58%)	0.039
	Yes	127 (84.7%)		102 (68%)	
Number of comorbidities	No	13 (48.1%)	<0.001	13 (48.1%)	0.311
	Only 1 disease	94 (76.4%)		74 (60.2%)	
	2 or 2 < diseases	267 (85.6%)		196 (62.8%)	
COVID vaccination	No	8 (61.5%)	0.163	11 (84.6%)	1.000
	Yes	255 (79.2%)		264 (82%)	
Pulmonary involvement	No	270 (77.6%)	0.002	219 (62.9%)	0.196
	Yes	104 (91.2%)		64 (56.1%)	
Hospitalization due to COVID	Yes	88 (94.6%)	<0.001	50 (53.8%)	0.097
	No	286 (77.5%)		233 (63.1%)	

finds that musculoskeletal pain immediately after infection is observed more in cases with comorbid diseases, hypertension, pulmonary involvement and hospitalization due to COVID-19. It was determined that the incidence of pain seen immediately after infection increased as the number of comorbidities increased. And persistent pain after COVID-19 infection were more common in those with osteoarthritis.

Over the approximately four-year duration of the COVID-19 pandemic, which infected millions worldwide, the infection posed challenges to the musculoskeletal system. The primary aim of this descriptive study was to examine post-COVID musculoskeletal involvement in older adults. The characteristics of the study population align with those of previous studies from Türkiye, with the

majority being women, married, housewives, and having at least one medical comorbidity (7).

Myalgia, rhabdomyolysis, myositis, rarely necrotizing autoimmune myositis, and critical illness myopathy may be observed as post-COVID muscle involvement. In the current study, myalgia (63.7%) and muscle weakness (16.2%) were the most reported complications, with myopathy (1.2%) and myositis (0.4%) were being very rare. Patel et al. stated that among persistent symptoms, myalgia (23.14%) had a higher prevalence (8). In this review where long-term COVID effects were analyzed, the authors specified the long COVID period as around the first 70 days after infection.

Jacobs et al. reported that symptoms associated with the infection, particularly joint pain, myalgia and generalized pain, tended to disappear around



the 4th week (9). However, our observations suggest a fluctuating course, with a tendency to decrease towards the end of the first month, followed by an increase afterwards. Karaaslan et al conducted a single-center cohort study, comprising 300 participants, with phone interviews and found 21% arthralgia and 22% myalgia after the first month of infection (10). In the study carried out as a continuation of the first research, the rates of myalgia and arthralgia were 18.6 % and 15.1 %, respectively in the sixth month (11). It is also higher than Wang's medical chart review of post-acute sequela of COVID-19 (19%) and similar to the rate (64%) in Lippi et al.'s article on long-term sequelae of COVID-19 published in 2023 (12, 13). In a study designed as a cross-sectional, single-center case series, the rate of myalgia and arthralgia were 68.0% and 43.3% respectively in hospitalized adults (14). The disparity in results compared to Karaaslan, Patel, and Wang may arise from the methodology implemented in our study, involving face-to-face interviews by a medical doctor during the long COVID period (9-12 months).

Joint involvement is another condition that is as common as myalgia. In the systematic review by Claffi et al., only one study focussing on arthralgia was found and the rate was mentioned to be 2.5% (15). Joints were the third most frequent site of involvement and was observed in 44.4% of cases in our study. This rate is higher than the study by Wang et al, which assessed post-acute sequela of COVID-19 (21%), and the study by Moreno-Pérez et al, which evaluated up to 14 weeks (19.2%) (12,16). However, it is also lower than the rate in the study of Lippi et al. (13).

This study's findings on joint involvement differ from previous studies, suggesting diverse post-COVID presentations, possibly influenced by variant differences, emphasizing the importance of specialized evaluations, as symptoms of COVID-19, especially musculoskeletal symptoms, exhibit a diverse and fluctuating course. Arthritis

has been reported in various studies (16-18) and on careful diagnosis, viral arthritis and arthritis in particular can be distinguished by the quick response to nonsteroidal anti-inflammatory drugs (3). In our study, the rate of arthritis was 3.3%, which was not very rare. None of our patients with arthritis had a background of chronic inflammatory arthritis. The presenting pictures might be post-viral arthritis. Yet, we do not have information on their follow-up.

Nerve involvement includes peripheral neuropathy, critical illness polyneuropathy, and Guillan-Barré syndrome and its variants (3). In this study, neuropathy was observed in 8.3% of the patients, and most of them were diagnosed with polyneuropathy. Two patients (0.4%) had Guillan Barré Syndrome, one patient had transverse myelitis (0.2%), and 13 patients (2.8%) were diagnosed with sensorimotor polyneuropathy during COVID-19 infection. It is noteworthy that there were 16 (3.5%) patients who developed sensorimotor polyneuropathy after that period. Although the frequency of neurological involvement is quite high in the early period, nerve involvement can also occur in the post-COVID period (19).

It seems that the post-COVID era will never be the same. The infection, which has been on the global agenda for the past four years or so, is difficult to characterize because of the variety of systems involved, the differences in age, sex, and presentation, and the wide range of co-morbidities in patients. The involvement of the musculoskeletal system can lead to disability and mobility during the post-COVID period (20). An analysis of these characteristics; female gender, age between 65-75 years, and presence of at least one comorbidity are predisposing factors for post-COVID syndrome. Older individuals have to deal with more severe pain, especially in the presence of concomitant osteoarthritis. However, this study finds encouraging evidence of pain reduction after the 12th month of treatment.

Aspects that need to be improved: In this observational study we evaluated the first 12 months after infection. This period, referred to as post-COVID in the literature, could have been extended to examine long symptoms. Additionally, it would have been beneficial to analyze these three periods separately, providing detailed insights into the musculoskeletal involvement of patients during the primary infection. Given the known differences between variants, these symptoms could have been investigated in cases with genetic analysis. However, the study was conducted during a time when the concept of post-COVID was just established, and the details of musculoskeletal involvement were still being determined, making it challenging to address all these questions. Nonetheless, it is essential to conduct future studies incorporating these characteristics for both the older population and all other age groups.

Positive aspects: To the best of our knowledge, our study represents the first descriptive analysis of musculoskeletal disorders in older people in our country, even though it was conducted when information about musculoskeletal disorders was limited. This study marks the face-to-face investigation in Türkiye with patients over 65 years of age at PMR clinics. The results encompass data from eleven PMR clinics across seven provinces in the country, spanning the Aegean, Marmara, Central Anatolia, Mediterranean, and Southeastern Anatolia regions. In this regard, it stands out as the study with the broadest range of known characteristics.

CONCLUSION

There are potential musculoskeletal effects of COVID-19 in older adults. Arthralgia and myalgia are common symptoms associated with COVID-19. Elderly patients with pre-existing musculoskeletal conditions, such as osteoarthritis, may experience exacerbated symptoms during or after a COVID-19 infection. Also, factors such as the presence and

number of other comorbidities, hospitalization and pulmonary involvement play considerable roles. The long-term consequences of COVID-19 on musculoskeletal health are still under investigation, and further research is necessary to fully comprehend the extent and duration of these effects.

Ethics Committee Approval: The study protocol was approved by the University of Hacettepe Clinical Research Ethics Committee (Date: 19.04.2022, No: 16969557750). The study was conducted under the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available.

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