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Evaluation of the pain in COVID-19 patients with musculoskeletal pain: A cross-sectional study

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Abstract

Aim: There is no study that have assessed face-to-face using the multidimensional pain scale in COVID-19 patients with musculoskeletal pain. This study aimed to reveal the pain region, character and severity in COVID-19 patients with musculoskeletal pain.

Material and Methods: This cross-sectional study was carried out in 214 patients who had a positive result of the polymerase chain reaction test within the last five days and at least one musculoskeletal pain symptom, such as fatigue, myalgia, and arthralgia/polyarthralgia. The cases were divided into groups as clinically severe and non-severe. Evaluations were made on the first day of admission. Myalgia symptoms were classified as diffuse and local. The McGill Pain Questionnaire was used for pain regions and caharacters while the Visual Analog Scale (VAS) was for pain intensity.

Results: The frequency of involvement was myalgia (96.3%), fatigue (77.6%) and polyarthralgia (62.6%), respectively. The diffuse myalgia was (53.3%) in all patients. The mean myalgia VAS score in the non-severe group was 5.88±1.83 and 6.25±1.24 in the severe group (p=0.192). The most common pain areas were the back, feet, and knees respectively, and throbbing (40.7%), aching (30.8%), and pricking (26.1%) were the most common characteristics. The suffocating character of the pain was significantly higher in the severe group (p<0.05).

Discussion: Defining disease-specific pain regions, character and severity in COVID-19 patients with musculoskeletal pain is important in managing possible chronic pain.

Keywords

COVID-19, Myalgia, Arthralgia, Neuropathic pain, Pain severity

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Introduction

In patients with COVID-19, multisystem symptoms, such as fever, cough, shortness of breath, dizziness, and confusion are detected. These are often accompanied by musculoskeletal symptoms, including fatigue, myalgia, back pain and arthralgia [1,2]. The most common musculoskeletal system symptoms are non-specific musculoskeletal pain; e.g., fatigue, myalgia, back pain, and arthralgia in order of frequency [2].

Although arthralgia is reported as a common symptom, it is often addressed together with myalgia. However, these two need to be considered and defined separately [3]. Additionally, corticosteroids used in the treatment of COVID-19 may increase the severity of myalgia and pain by resulting in damage to the musculoskeletal system.

Zhang et al. [4] suggested that myalgia might be an important predictor of the disease severity in patients with COVID-19 presenting with the tomographic or radiographic involvement of the lung. In this context, it is important to determine the location, sensation character, and severity of musculoskeletal pain, which is present before COVID-19 treatment and in the early symptomatic period of the disease in order to both predict the disease severity and to outline pain management in the long COVID-19 period. In the literature, there are limited studies examining the effects of COVID-19 on the musculoskeletal system [5]. However, to our knowledge, no multi-dimensional prospective study has been conducted with a focus on COVID-19-associated pain and defining the characteristics of this pain. This study aimed to reveal the localization, severity and character of musculoskeletal pain in COVID-19.

Material and Methods

This cross-sectional study was conducted at a University Hospital between July 2021 and December 2021. Approval (2021/09-20) was obtained from the Non-Interventional Research Ethics Committee of the university on 26.05.2021. The study was carried out in accordance with the principles of the Declaration of Helsinki and with permission obtained from the Turkish Ministry of Health.

The study included voluntary patients aged 18-60 years admitted to the pandemic ward of the hospital, who had a positive result of polymerase chain reaction test within the last five days and described musculoskeletal pain due to COVID-19 with a pain severity of 2 to 8 on the 10-cm Visual Analog Scale (VAS). Patients who had multi-organ involvement due to COVID-19 disease and who required intensive care (critical cases), those that were given corticosteroid therapy due to COVID-19, those with any chronic musculoskeletal disease, inflammatory rheumatic disease (rheumatoid arthritis, ankylosing spondylitis, etc.), or neurological (multiple sclerosis, etc.) or psychiatric disease diagnosed in the pre-COVID-19 period, those who had undergone musculoskeletal surgery in the pre-COVID-19 period, patients with diabetes or any other disease that could cause polyneuropathy, and those with a negative PCR test were excluded from the study. Initially, 218 patients with COVID-19 who had musculoskeletal symptoms (weakness, myalgia, and arthralgia/polyarthralgia) were included in the study. However, two patients were excluded because they did not know their body weight and two patients did not want to complete the evaluation. Therefore, the study was completed with 214 patients who had a positive PCR result. According to the clinical classification of COVID-19, the cases were divided into two groups as severe (n = 116) and non-severe (n = 98). As per the literature, the non-severe group consisted of patients with mild symptoms or fever and respiratory tract infection symptoms, who might have pneumonia findings on imaging (respiratory rate <30/min or oxygen saturation >93%). Patients with at least one of the following conditions formed the severe group: respiratory rate ≥30/minute, oxygen saturation ≤93%, or with lung imaging taken due to COVID-19 before and with the presence of more than half lesion progression in lung imaging during the admission [6].

Written informed consent was obtained from the patients after providing them with information about the study.

Evaluations

A socio-demographic form was used to evaluate the sociodemographic characteristics of the patients. The McGill Pain Questionnaire (MPQ) was used to identify painful regions and evaluate the pain character. The evaluations of the patients were performed on the day of admission to the pandemic ward. MPQ was administered by one investigator only (M.F.O.) in a face-to-face interview with each patient.

Evaluation of myalgia

Myalgia was classified as diffuse and local. The patients were asked where on their bodies they felt myalgia. Pain in the common muscle group was defined as 'diffuse myalgia', while pain localized in one muscle was defined as 'local myalgia'. Two anterior and posterior body images (MPQ-first part) were used to define the painful muscle area. They marked the painful muscle area or areas with a pencil and localized the relevant area with their hands.

Evaluation of painful region and polyarthralgia

The patients were asked to mark with a pencil and localize with their hands the relevant area on two body pictures drawn from the anterior and posterior view (MPQ-first part) for the detection of painful joints and other body parts. Each patient was given a special pen for marking to reduce contact during the evaluations. If the painful region included only a single joint or the spine, it was recorded with the name of the anatomical area involved. Polyarthralgia was defined in the presence of more than one different joint involvement in accordance with the literature [7].

Evaluation of MPQ and pain character

MPQ, a multidimensional pain assessment questionnaire, consists of four parts. In the first part, there are two body pictures drawn from the anterior and posterior views of the body to mark the body region or regions affected by pain. In the second part, there are 20-word groups, each including two to six descriptive words to describe pain in terms of sensation, perception, and evaluation. In the third part of MPQ, the relationship of pain with time and factors that increase or decrease pain is questioned. In the last part, an evaluation is made on a rating scale consisting of words describing the severity of pain. In this study, the last part of MPQ was not used since VAS was preferred to assess the severity of pain and

polyarthralgia.

Evaluation of pain severity

VAS is a scale that converts pain felt by an individual into a numerical form from 0 to 10 points, with 0 representing no pain and 10 representing the most severe pain ever experienced. In this study, the severity of myalgia was assessed using VAS.

Statistical analysis

The study population consisted of patients from a University Hospital in Turkey. The sample size was calculated using G Power (3.1.9, University of Kiel, Germany), taking into account the results obtained by Tuzun et al. [3] The prevalence value was used to calculate the sample size. As a result, the required minimum number of patients was determined as 214 at the 95% confidence interval with a sampling error of 5% and a prevalence of 16.70%.

The arithmetic mean and percentage values were used to present the data related to the demographic characteristics, symptoms and pain characters of the participants. The chi-square test was used to compare two qualitative values, and the Mann-Whitney U test to evaluate parameters that did not show a normal distribution. The significance value was accepted as $p < 0.05$. Statistical analyses were performed with IBM SPSS Statistics (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.).

Table 1. Demographic characteristics of patients with COVID-19 according to disease severity

	Non-severe (n_1 = 98)		Severe (n_2 = 116)		Total (n = 214)		z/x^2	p
	X ± SD		X ± SD		X ± SD			
Age (years)	43.23 ± 10.13		50.6 ± 7.27		47.25 ± 9.44		-5.672	<0.001
Height (cm)	166.03 ± 8.42		166.80 ± 9.02		166.44 ± 8.74		-0.543	0.587
Weight (kg)	70.71 ± 9.31		72.80 ± 8.51		71.84 ± 8.93		-1.201	0.23
Body mass index	25.73 ± 2.60		26.20 ± 2.62		25.98 ± 2.61		-1.503	0.133
	n	%	n	%	n	%		
Gender								
Male	38	38.8	49	42.2	87	40.7	0.264	0.607
Female	60	61.2	67	57.8	127	59.3		
Area of residence								
Rural	13	13.3	17	14.7	30	14	0.104	0.949
District	10	10.2	11	9.5	21	9.8		
City center	75	76.5	88	75.9	163	76.2		
Education level								
Illiterate	6	6.1	7	6	13	6.1	10.633	0.014
Primary school	39	39.8	61	52.6	100	46.7		
Secondary school	25	25.5	35	30.2	60	28		
Higher education	28	28.6	13	11.2	41	19.2		
Occupation								
Worker	4	4.1	13	11.2	17	7.9	18.974	0.002
Civil servant	21	21.4	8	6.9	29	13.6		
Housewife	38	38.8	56	48.3	94	43.9		
Self-employed	28	28.6	38	32.8	66	30.8		
Student	4	4.1	1	0.9	5	2.3		
Unemployed	3	3.1	0	0	3	1.4		
Presence of comorbidity								
Yes	28	28.6	73	62.9	101	47.2	25.165	<0.001
No	70	71.4	43	37.1	113	52.8		
Comorbid disease								
None	70	71.4	42	36.2	112	52.3	31.414	<0.001
Hypertension	17	17.3	32	27.6	49	22.9		
Coronary artery disease	8	8.2	39	33.6	47	22		
Atrial fibrillation	2	2	1	0.9	3	1.4		
Benign prostatic hyperplasia	1	1	2	1.7	3	1.4		

n: number, %: percentage, kg: kilogram, cm: centimeter, z: Mann-Whitney U statistic, x^2: chi-square test statistic, $p < 0.05$

Results

A total of 214 patients diagnosed with COVID-19 (98 non-severe, 116 severe) were included in the study. Table 1 presents the demographic characteristics of the participants according to disease severity. As per the data in Table 1, there was a statistically significant difference between the patients' age, education level and the presence of comorbid disease according to the severity of the disease.

In the evaluation of myalgia with VAS, the mean score in the non-severe group was 5.88±1.83, while it was 6.25±1.24 in the severe group (p=0.192). Musculoskeletal Pain Distribution in terms of Disease Severity is shown in Table 2.

When the patients' musculoskeletal symptoms were examined according to the severity of the disease, common myalgia was observed at a rate of 53.3% in the severe group and 55.1% in the non-severe group (Table 3).

Evaluation of Pain Characters is shown in Table 3. The three most common pain characteristics were throbbing (40.7%), aching (30.8%), and pricking (26.1%). The presence of suffocating, another pain character, was significantly higher in the non-severe group than in the severe cases (p = 0.037). When pain character was examined in terms of pattern over time in all COVID-19 patients, it was described as 'constant' (n=129; 60.3%), 'rhythmic' (n= 72; 33.6%) and 'intermittent' (n=13; 6.1%).

Discussion

Patients infected with SARS-CoV-2 may show a wide range of symptoms involving different systems. In the literature, it has been reported that musculoskeletal symptoms may occur

Table 2. Musculoskeletal pain distribution of COVID-19 patients in terms of disease severity

Musculoskeletal symptom	Non-severe (n_1 = 98)		Severe (n_2 = 116)		Total (n = 214)		z/x^2	p
	n	%	n	%	n	%		
Diffuse myalgia Present	54	55.1	60	51.7	114	53.3	0.243	0.622
Local myalgia Present	36	36.7	56	48.3	92	42.9	3.326	0.06
Affected region								
Foot	13	13.3	9	7.8	22	10.3	6.906	0.647
Knee	4	4.1	9	7.8	13	6.1		
Neck	5	5.1	5	4.3	10	4.7		
Waist	1	1.0	0	0.0	1	0.4		
Hand-wrist	1	1.0	1	0.9	2	0.9		
Hip	1	1.0	1	0.9	2	0.9		
Elbow	5	5.1	7	6.0	12	5.7		
Shoulder	3	3.1	4	3.4	7	3.3		
Upper back	28	28.6	29	25.0	57	26.6		
Polyarthralgia Present	37	37.7	51	43.9	88	41.1	-0.918	0.359

n: number, %: percentage, z: Mann-Whitney U statistic, x^2: chi-square statistic, $p < 0.05$

before the development of respiratory system symptoms and findings in COVID-19 [8, 9], and myalgia may be an important predictor of the severity of the disease [4], which increases the importance of evaluating musculoskeletal symptoms in patients with COVID-19. Among the most common musculoskeletal symptoms are fatigue, myalgia, arthralgia, and muscle weakness [10]. In this context, it is essential to not only identify the presence of musculoskeletal pain in COVID-19 but also define the localization and character of pain and determine its relationship with time. However, we found no study in the literature evaluating early musculoskeletal pain associated with COVID-19 using a multidimensional pain scale. The aim of our study was to describe the localization, character and severity of musculoskeletal pain experienced by COVID-19 patients.

Table 3. Evaluation of pain character in patients with COVID-19 according to disease severity

Pain Character	Non-severe (n_1 = 98)		Severe (n_2 = 116)		Total (n = 214)		x^2	p
	n	%	n	%	n	%		
Throbbing								
Present	34	35	53	46	87	40.7	2.662	0.103
Absent	64	65	63	54	127	59.3		
Aching								
Present	30	30.6	36	31.0	66	30.8	0.004	0.947
Absent	68	69.4	80	69.0	148	69.2		
Pricking								
Present	30	30.6	26	22.4	56	26.1	1.848	0.174
Absent	68	69.4	90	77.6	158	73.8		
Sharp								
Present	8	8.2	6	5.2	14	6.5	0.777	0.378
Absent	90	91.8	110	94.8	200	93.5		
Stabbing								
Present	8	8.2	11	9.5	19	8.9	0.114	0.735
Absent	90	91.8	105	90.5	195	91.1		
Piercing								
Present	6	6.1	6	5.2	12	5.6	0.091	0.763
Absent	92	93.9	110	94.8	202	94.4		
Pressing								
Present	6	6.1	14	12.1	20	9.3	2.217	0.136
Absent	92	93.9	102	87.9	194	90.7		
Tearing								
Present	4	4.1	6	5.2	10	4.7	0.142	0.706
Absent	94	95.9	110	94.8	204	95.3		
Hurting								
Present	4	4	7	6	11	5.1	0.415	0.519
Absent	94	96	109	94	203	94.9		
Terrifying								
Present	3	3.1	4	3.4	7	3.3	0.025	0.874
Absent	95	96.9	112	96.6	207	96.7		
Flashing								
Present	3	3.1	2	1.7	5	2.3	0.416	0.519
Absent	95	96.9	114	98.2	209	97.6		
Suffocating								
Present	2	2.0	10	8.6	12	5.6	4.345	0.037
Absent	96	98	106	91	202	94.4		
Tingling								
Present	1	1.0	3	2.6	4	1.9	0.710	0.399
Absent	97	99.0	113	97.4	210	98.1		

n: number, %: percentage, x^2: chi-square statistic, $p < 0.05$

Chronic diseases that are more commonly seen in advanced ages also increase the severity of COVID-19 in this patient group [11]. In a study by Wang et al. [12], examining the findings of 138 COVID-19 cases, it was shown that 46.4% of the patients had comorbidities, and those admitted to the intensive care unit had a higher age than those who did not require intensive care. We found the frequency of comorbidities and mean age to be higher in the severe disease group than in the non-severe group, which is consistent with the literature.

The term 'myalgia' is often used to describe musculoskeletal symptoms associated with COVID-19. However, some studies have reported that this term is not sufficient and may be confused with joint pain [3.13]. Therefore, the classification of myalgia as diffuse and local and the detailed localization of painful regions can be considered as the strong characteristics of our study. The etiopathogenesis of myalgia and arthralgia due to COVID 19 involves direct damage by the virus to muscle tissue, synovium and cortical bone [14]. Consistent with the literature, the presence of diffuse myalgia was higher than local myalgia in all COVID-19 patients in our study [3]. Furthermore, we detected myalgia as a musculoskeletal symptom in all patients with severe clinical COVID-19. Similarly, in a meta-analysis including 55 studies investigating the effect of clinical symptoms on disease severity in COVID-19 cases, it was emphasized that the frequency of myalgia was higher in the presence of severe disease [15]. Similar to the findings in the literature, a more aggressive inflammatory response in the severe disease group may have triggered myalgia symptoms [16].

In our study, we determined that the severity of myalgia in COVID-19 patients was above moderate level, and there was no significant difference between the groups in terms of pain intensity. In a previous study, in which biopsychosocial factors predicting pain in individuals with COVID-19 were retrospectively evaluated, pain intensity was evaluated using VAS, and the mean VAS score of the patients was found to be 4.04 (SD = 2.23) [17]. The higher pain intensity of our patients may be due to our study being conducted in the acute and painful period of COVID-19. Furthermore, we consider that patients' increased fear related to the COVID-19 disease in the acute phase and possible sleep problems they experienced may have affected the intensity and perception of pain [18].

It has been stated that the etiopathogenesis of joint and muscle involvement may be common in COVID-19 patients [13]. Therefore, there is a possible relationship between arthralgia and myalgia. In this context, it is also important to define the localization of single joint, spine and multiple joint pain due to COVID-19 in the early period. In our study, the regions of single joint and spine pain caused by COVID-19 were found to be the back, feet, and knees, in order of frequency. In a study investigating pain symptoms in COVID-19, the back and lower limbs were shown to be the most frequently involved musculoskeletal regions [19]. Similar to our study, Tuzun et al. [3], who evaluated musculoskeletal pain associated with COVID-19, noted back and foot pain as one of the most common symptoms.

In our study, the patients described the characteristic of their

pain felt as throbbing, aching, and pricking in that order. Furthermore, although suffocating pain was detected in a few patients, it was determined at a significantly higher rate in those with severe clinical symptoms. In the study in which pain syndromes were evaluated in the acute phase of mild to moderate COVID-19, the pain character was defined as numbing, burning, and pressing in order of frequency [7]. Identification of different pain characters compared to our study may be due to the authors' inclusion of patients who used medication for COVID-19, the elderly, and those with comorbidities that could cause neuropathic pain, as well as the absence of an evaluation performed with a multidimensional pain scale in the previous study. Identifying the pain character in COVID-19 patients with musculoskeletal pain may provide an understanding of different pain mechanisms, which will, in turn, affect the choice of medical treatment. Furthermore, reviewing the current literature, we did not find a study that questioned the character of neuropathic pain in detail and evaluated its localization in COVID-19-patients with musculoskeletal pain.

Majority of our patients described the pattern of their current pain in terms of its relationship with time as 'constant'. IgM antibodies can be detected from the seventh to the 21st day of the infection in SARS-CoV-2 [20]. Therefore, the continuation of possible viral replication at the time of the evaluation of the patients in our study might have been a factor in the constant nature of pain. We consider that this finding would guide scientific studies investigating the relationship between COVID-19-associated musculoskeletal pain and time.

Differences in some socio-demographic data between groups may have led to a limitation in interpreting the results of the multi-dimensional assessment of pain. This can be stated as a limitation of our study.

Conclusion

It is known that COVID-19 may result in the development of neuropathic pain within weeks or months. Therefore, pain should be detected early, defined, and localized. This study will make an important contribution to the literature by providing early detection of regions of pain, its severity and especially its character in COVID 19 patients with musculoskeletal pain.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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