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Post-COVID syndrome and pain perception in outpatients with COVID-19

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Abstract. – OBJECTIVE: This study aimed to investigate the prevalence of pain symptoms in outpatients with COVID-19 and to analyze the relationship between pain-related, psychological, and cognitive variables in patients with ongoing pain complaints after COVID-19.

PATIENTS AND METHODS: 79 people participated in the research. The focus was on completed demographics (such as age, height, and weight), pain-related (duration and intensity of pain), Modified Medical Research Council (MMRC) Dyspnea Score, and visual analogue scale (VAS) variables.

RESULTS: Significant changes were found in some of the post-COVID symptoms after 3 months. From the 3rd month, the VAS pain scale score, EQ-5D-3L quality of life score, and VAS score obtained from EQ-5D-3L quality of life scale, sitting scores decreased compared to the first measurements. Muscle strength, moderate activity, walking, and total scores increased from the third month.

CONCLUSIONS: We suggest physical pain and inactivity symptoms in patients with COVID regressed in the 3rd month.

Key Words:
COVID-19, Post-COVID syndrome, Pain perception.

Introduction

Musculoskeletal pain (myalgia) is one of the most common symptoms experienced during the acute phase of severe acute respiratory syndrome Coronavirus-19 (SARS-CoV-2) infection[1,2]. In addition, up to 18% of infected individuals with post-COVID symptoms experienced pain during the first year[3]. Characterization of post-COVID pain can help to better understand potential mechanisms and guide personalized treatments. Although post-COVID pain resembles musculoskeletal features[4], neuropathic pain has also been described as a post-COVID sequela[5]. It is possible that post-COVID pain may exhibit features of both musculoskeletal and neuropathic pain6. Preliminary evidence[6-10] suggests the presence of pain in individuals exhibiting post-COVID pain. Vaz et al[7] reported the development of complex regional pain syndrome in a patient who survived COVID-19. Similarly, McWilliam et al[8] reported neuropathic pain as a post-COVID sequela. A recent cohort study[9] of patients with post-COVID pain reported that about 25% showed symptoms of unexplained pain; however, this study collected self-reported symptoms during a telephone interview. Tirelli et al[10] investigated the post-acute sequelae (PASC) in a cohort study. They found that ozone therapy on fatigue reduced PASC symptoms by 67% in all participants. The same authors also declared that there are many therapies for post-COVID syndrome but still many trials are needed to elucidate the pathology of PASC[11].

Pain is one of the important symptoms experienced in viral diseases[12]. As with many infections, pain has been a common symptom of COVID-19 infection. The virus not only affects the respiratory system but also invades different tissues of the body, causing individuals to experience many painful symptoms such as headache, dizziness, abdominal pain, chest pain, and muscle joint pain. Pain may develop due to many reasons in viral diseases, and it is caused by many mechanisms related to this condition. It has been reported that pain develops due to skeletal muscle injury in viral diseases or penetration of the virus into the central nervous system. This clinical feature will stimulate nociceptors.

It is also believed to result from tissue inflammation that will cause the release of inflammatory mediators[13]. Unfortunately, in some cases, pain is only seen during the infection process. It can also cause pain in the individual after infection. As a matter of fact, it has been reported[14] that the pain symptoms of individuals continue after some infectious diseases. Pain experience is influenced by many factors[15].

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According to the theory[16] in the neurophysiology of pain, the individual's psychological state, anxiety, stress, and fears can cause pain perception by activating pain stimuli. In other words, past negative pain experiences can also open the door, and when the door is open, the pain impulses pass, causing intense pain[17]. Individuals experience high levels of fear and stress due to the COVID-19 outbreak[18]. Although there are studies[19,20] showing that individuals with COVID-19 experience pain. There are no studies evaluating the relationship between the fear of pain and quality of life in post-COVID-19 infected patients. Pain, which is a subjective experience, can negatively affect the quality of life of individuals and cause fear of pain[20].

The purpose of this study is to determine the effect of pain experienced during COVID-19 infection on individuals' fear of pain and quality of life.

Patients and Methods

In our retrospective study, 79 patients diagnosed with COVID-19 and receiving outpatient treatment at Gazi Yaşargil Training and Research Hospital were randomly selected and contacted. Pain and clinical conditions during the treatment period, pain status functional status at the end of the 3rd and 4th months, and whether post-COVID syndrome developed or not were evaluated.

Demographic data (age, gender, height/weight, education level, occupation), smoking/alcohol use, chronic disease, and drug use, initial symptoms, and hospital-to-hospital with symptom onset time between hospitalization, visual analogue scale (VAS) pain scale and pain status, post-COVID functional status scale, Modified Medical Research Council (MMRC) dyspnea score, test duration of 5 times sitting up and standing in a chair (for muscle strength assessment), walking speed, the Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) pain scale, EQ-5D-3L quality of life scale, international physical activity questionnaire were applied.

Statistical Analysis

The statistical analysis was performed with IBM® SPSS Statistics version 23 software (IBM Corp., Armonk, NY, USA). To determine differences between groups, Wilcoxon Signed Ranks test and the Friedman test were used. The Kolmogorov-Smirnov test was used to evaluate if variables change over time.

$p<0.05$ was accepted as a significant level.

Results

79 people participated in the research. The mean age of the participants was 40.97, and the standard deviation was 13.02. 52% of the participants are female and 48% are male. When the education level was examined, it was seen that 23% of them were primary school graduates, 7% were secondary school graduates, 31% were high school graduates, 22% were university graduates, and 13% were unanswered.

The average height of women was 162, the standard deviation was 5.6; The mean height of the men was 176, and the standard deviation was 6.2. The mean weight of women was 69.4, the standard deviation was 11.7. The mean for men was 78.2, and the standard deviation was 10.2 (Table I).

While 82% of the participants do not smoke, 17% are smokers. While 98% do not use alcohol, 1% use alcohol (Table II).

Repeated measurements regarding the complaints received from the participants are shared below and summarized in Table III.

In the first measurement, the most common complaints of the participants were joint pain (12%), muscle pain (12%), cough (8%), fatigue (8%), taste (8%), and smell (7%). In the second measurement, the rate of complaint of joint pain decreased to 10% and continued to 10% in the third measurement. The rate of complaint of muscle pain decreased to 8% in the second measurement and continued with 8% in the third measurement. For cough complaints, it decreased to 6% in the second measurement and continued

Table I. Height and weight analysis of participants by gender.

Gender		N	Mean	SD
Height	Female	41	162.71	5.654
	Male	38	176.11	6.294
Weight	Female	41	69.49	11.777
	Male	38	78.24	10.292

SD: Standard deviation.

Table II. Smoking/alcohol use of the participants.

		N	Percentage
Smoking	No	65	82.3
	Yes	14	17.7
	Total	79	100.0
Alcohol	No	78	98.7
	Yes	1	1.3
	Total	79	100.0

Table III. Repeated Measurements of the complaints received from the participants.

	Measurement 1			Measurement 2 (3 months)			Measurement 3 (4 months)		
	N	Percentage	Reply Percentage	N	Percentage	Reply Percentage	N	Percentage	Reply Percentage
Shortness of breath	22	5.8%	28.2%	5	10.6%	25.0%	6	12.8%	28.6%
Cough	31	8.1%	39.7%	3	6.4%	15.0%	3	6.4%	14.3%
Chest pain	9	2.4%	11.5%	0	0.0%	0.0%	1	2.1%	4.8%
Tightness in the chest	4	1.0%	5.1%	0	0.0%	0.0%	0	0.0%	0.0%
Palpitation	5	1.3%	6.4%	0	0.0%	0.0%	0	0.0%	0.0%
Fatigue	32	8.4%	41.0%	0	0.0%	0.0%	0	0.0%	0.0%
Fire	19	5.0%	24.4%	0	0.0%	0.0%	0	0.0%	0.0%
Memory	12	3.1%	15.4%	9	19.1%	45.0%	8	17.0%	38.1%
Headache	22	5.8%	28.2%	1	2.1%	5.0%	1	2.1%	4.8%
Dizziness	3	0.8%	3.8%	2	4.3%	10.0%	1	2.1%	4.8%
Sleep problem	6	1.6%	7.7%	0	0.0%	0.0%	0	0.0%	0.0%
Numbness	3	0.8%	3.8%	0	0.0%	0.0%	0	0.0%	0.0%
Vomiting	3	0.8%	3.8%	0	0.0%	0.0%	0	0.0%	0.0%
Stomachache	1	0.3%	1.3%	0	0.0%	0.0%	0	0.0%	0.0%
Nausea	5	1.3%	6.4%	1	2.1%	5.0%	1	2.1%	4.8%
Diarrhea	7	1.8%	9.0%	1	2.1%	5.0%	0	0.0%	0.0%
Anorexia	7	1.8%	9.0%	0	0.0%	0.0%	0	0.0%	0.0%
Joint pain	47	12.3%	60.3%	5	10.6%	25.0%	5	10.6%	23.8%
Muscle pain	48	12.6%	61.5%	4	8.5%	20.0%	4	8.5%	19.0%
Depression	6	1.6%	7.7%	1	2.1%	5.0%	1	2.1%	4.8%
Anxiety	6	1.6%	7.7%	1	2.1%	5.0%	1	2.1%	4.8%
Seeing	5	1.3%	6.4%	2	4.3%	10.0%	2	4.3%	9.5%
Ear	2	0.5%	2.6%	1	2.1%	5.0%	2	4.3%	9.5%
Throat ache	3	0.8%	3.8%	0	0.0%	0.0%	0	0.0%	0.0%
Taste	29	7.6%	37.2%	3	6.4%	15.0%	4	8.5%	19.0%
Smell	32	8.4%	41.0%	6	12.8%	30.0%	5	10.6%	23.8%
Hair shedding	3	0.8%	3.8%	1	2.1%	5.0%	1	2.1%	4.8%
Sweating	10	2.6%	12.8%	0	0.0%	0.0%	0	0.0%	0.0%
Weakness	0	0.0%	0.0%	1	2.1%	5.0%	1	2.1%	4.8%
Total	382	100.0%	489.7%	47	100.0%	235.0%	47	100.0%	223.8%

with 6% in the third measurement. The fatigue complaint rate decreased to 0% in the second and third measurements. The rate of taste complaints decreased to 6% in the measurement and increased to 8% in the third measurement. For odor complaints, it decreased to 12% in the second measurement and continued with 10% in the third measurement. The distribution of the pain in the joints of the participants is shared below.

Joint pains were distributed as 36% in the knee, 14% in the foot, 14% in the hand, 5% in the elbow, and 2% in the whole body (Table IV).

The distribution of the participants' pain in their muscles is shared below and summarized in Table V. The distribution of muscle pains is shown as 25% in the thigh, 23% in the back, 10% in the calf, 5% in the waist, and 4% in the arm. Distributions regarding the pain characteristics of the participants are shared below and summarized in Table VI.

When the pain characteristics of the participants were examined, it was seen that 25% of them had pain with movement, 16% were continuous, and 19% were at rest. The distribution of participants' pain time is given in Table VII.

As a result of the Kolmogorov-Smirnov test, which was carried out to determine the test to be carried out to examine whether the scores of the participants from the VAS pain scale changed over time, it was found that the data did not show normal distribution ($p<0.05$). Findings related to the analysis are shared in Table VIII.

A significant difference was found between the groups as a result of the Friedman test, which was carried out to examine whether the scores of the participants on the VAS pain scale changed in the 3rd and 4th months from the first measurement ($\chi^2=76.000$, $p<0.05$). When the averages of the rows were examined, it was seen that the first measurement score was the highest, while the score decreased in the 3rd month and remained the same in the 4th month.

As a result of the Kolmogorov-Smirnov test, which was carried out to examine whether the scores of the participants from the functional status scale after COVID changed over time, it was found that the data did not show normal distribution ($p<0.05$). Findings related to the analysis are shared in Table IX.

There was no significant difference between the groups as a result of the Wilcoxon Signed Ranks test, which was carried out to examine whether the scores they received from the functional status scale after COVID changed in the 3rd and 4th months ($Z=-1.000$, $p>0.05$). Post-COVID functional status scale scores do not change in the 3rd and 4th months.

As a result of the Kolmogorov-Smirnov test, which was carried out to determine the test to be carried out to examine whether the MMRC dyspnea score of the participants changed over time, it was found that the data did not show normal distribution ($p<0.05$). Findings related to the analysis are shared in Table X.

Table IV. Distribution of joint pain locations.

		N	Percentage	Reply percentage
Joint pain area	Knee	42	36.5%	53.2%
	Foot	17	14.8%	21.5%
	Hand	17	14.8%	21.5%
	Elbow	6	5.2%	7.6%
	Whole body	3	2.6%	3.8%
	No	30	26.1%	38.0%
Total		115	100.0%	145.6%

Table V. Distribution of pain locations in the muscles.

		N	Percentage	Reply percentage
Muscle pain area	Thigh	26	25.7%	36.1%
	Calf	11	10.9%	15.3%
	Waist	5	5.0%	6.9%
	Back	24	23.8%	33.3%
	Arm	4	4.0%	5.6%
	no	31	30.7%	43.1%
Total		101	100.0%	140.3%

As a result of Wilcoxon Signed Ranks test, which was conducted to examine whether the MMRC dip dyspnea le score of the participants changed in the 3rd and 4th months, no significant difference was found between the groups (Z=-1.000, p>0.05). The MMRC dip dyspnea line score does not change at 3 and 4 months.

As a result of the Kolmogorov-Smirnov test, which was carried out to determine the test to be carried out to examine whether the evaluation of the participants' muscle strength and walking speed changed over time, it was found that the data did not show normal distribution (p<0.05). Findings related to the analysis are shared in Table XI.

As a result of the Wilcoxon Signed Rows test, which was carried out to examine whether the evaluation of the participants' muscle strength and walking speed changed in the 3rd and 4th months, it was found that there was a significant difference between the groups in muscle strength (Z=-2.563b, p<0.05), while there was no significant difference

Table VI. Distribution of participants' pain characteristics.

	N	Percentage
0	31	39.2
In motion	20	25.3
Continuous	13	16.5
At rest	15	19.0
Total	79	100.0

Table VII. Distribution of participants' pain time.

	N	Percentage
1	39	49.4
2	2	2.5
3	15	19.0
4	9	11.4
5	2	2.5
7	9	11.4
10	3	3.8
Total	79	100.0

Table VIII. Friedman test conducted to examine whether VAS pain scale scores change over time.

	Order mean	N	Chi-square	df	p
VAS Measurement 1	2.49	78	76.000	2	0.000
VAS 3 Months	1.76				
VAS 4 Months	1.76				

VAS: visual analogue scale.

Table IX. Wilcoxon signed ranks test conducted to examine whether their scores from the post-COVID functional status scale change over time.

		N	Order mean	Order sum	Z	p
Post-COVID functional status scale 4th month - post-COVID functional status scale 3rd month	Negative order	0[a]	0.00	0.00	-1.000[b]	0.317
	Positive order	1[b]	1.00	1.00		
	Equations	78[c]				
	Total	79				

[a]Post-COVID functional status scale 4th month<Post-COVID functional status scale 3rd month. [b]Post-COVID functional status scale 4th month>Post-COVID functional status scale 3rd month. [c]Post-COVID functional status scale 4th month=Post-COVID functional status scale 3rd month.

Table X. Wilcoxon Signed Ranks test conducted to examine whether the MMRC dyspnea score changes over time.

		N	Order mean	Order sum	Z	p
MMRC dyspnea score 4 months - MMRC dyspnea score 3 months	Negative order	1[a]	1.00	1.00	-1.000[b]	0.317
	Positive order	0[b]	0.00	0.00		
	Equations	78[c]				
	Total	79				

[a] Score to MMRC dyspnea at 4 months < Score at MMRC dip at 3 months. [b] Score to MMRC dyspnea at 4 months > Score at MMRC dip at 3 months. [c] MMRC dyspnea score 4 months = MMRC dyspnea score 3 months.

Table XI. Wilcoxon Signed Ranks test conducted to examine whether muscle strength and walking speed change over time.

		N	Order mean	Order sum	Z	p
Muscle strength 4th month - Muscle strength 3rd month	Negative order	13[a]	18.50	240.50	-2.563[b]	0.010
	Positive order	28[b]	22.16	620.50		
	Equations	38[c]				
	Total	79				
Walking speed 4 months - Walking speed 3 months	Negative order	14[d]	8.89	124.50	-1.746[c]	0.081
	Positive order	4[e]	11.63	46.50		
	Equations	61[f]				
	Total	79				

[a]Muscle strength 4th month<Muscle strength 3rd month. [b]Muscle strength 4th month>Muscle strength 3rd month. [c]Muscle strength 4th month=Muscle strength 3rd month. [d]Walking speed 4th month<Walking speed 3rd month. eWalking speed 4th month>Walking speed 3rd month. [f]Walking speed 4th month=Walking speed 3rd month.

Table XII. Wilcoxon Signed Ranks test was conducted to examine whether S-LANSS pain scale score changes over time.

		N	Order mean	Order sum	Z	p
S-LANSS pain scale 4th month - S-LANSS pain scale 3rd month	Negative order	0[a]	0.00	0.00	.000[b]	1.000
	Positive order	0[b]	0.00	0.00		
	Equations	79[c]				
	Total	79				

[a]S-LANSS pain scale 4th month<S-LANSS pain scale 3rd month. [b]S-LANSS pain scale 4th month>S-LANSS pain scale 3rd month. [c]S-LANSS pain scale 4th month=S-LANSS pain scale 3rd month.

Table XIII. Wilcoxon Signed Rank test conducted to examine whether L VAS score changes over time.

		N	Order mean	Order sum	Z	p
L Vas 4th month - L VAS 3rd month	Negative order	0[a]	0.00	0.00	-1.000[b]	0.317
	Positive order	1[b]	1.00	1.00		
	Equations	78[c]				
	Total	79				

[a]L Vas 4th month<L VAS 3rd month. [b]L Vas 4th month>L VAS 3rd month. [c]L Vas 4th month=L VAS 3rd month.

Table XIV. Friedman test conducted to examine whether EQ-5D-3L quality of life scale scores change over time.

	Order mean	N	Chi-square	df	p
EQ-5D-3L quality of life scale 1st measurement	2.13	79	19.419	2	0.000
EQ-5D-3L quality of life scale 3rd month	1.93				
EQ-5D-3L quality of life scale 4th month	1.94				

[a]L Vas 4th month<L VAS 3rd month. [b]L Vas 4th month>L VAS 3rd month. [c]L Vas 4th month=L VAS 3rd month.

Table XV. Friedman Test Conducted to Examine Whether EQ-5D-3L Quality of Life Scale VAS Scores Change Over Time.

	Order mean	N	Chi-square	df	p
EQ-5D-3L quality of life scale VAS 1st measurement	2.15	79	18.167	2	0.000
EQ-5D-3L quality of life scale VAS 3rd month	1.94				
EQ-5D-3L quality of life scale VAS 4th month	1.91				

Table XVI. Friedman test conducted to examine whether scores from the international physical activity questionnaire have changed over time.

	Order mean	N	Chi-square	df	p
UFAA vigorous activity 1st measurement UFAA vigorous activity 3rd month UFAA vigorous activity 4th month	2.01 1.99 1.99	79	2.000	2	0.368
UFAA moderate activity 1st measurement UFAA moderate activity 3rd month UFAA moderate activity 4th month	2.08 1.97 1.95	79	12.286	2	0.002
UFAA walking 1st measurement UFAA walking 3rd month UFAA walking 4th month	2.07 1.96 1.97	78	10.333	2	0.006
UFAA seating 1st metric UFAA residency 3rd month UFAA sitting 4th month	1.92 2.02 2.06	79	11.143	2	0.004
UFAA total score 1st measurement UFAA total score 3rd month UFAA total score 4th month	2.09 1.95 1.96	79	12.071	2	0.002

between the groups in walking speed (Z=-1.746, $p>0.05$). When the averages of the rows were examined, it was seen that the muscle strength score increased in the 4th month compared to the 3rd month. Walking speed does not change in the 3rd and 4th months.

As a result of the Kolmogorov-Smirnov test, which was carried out to determine the test to be carried out to examine whether the S-LANSS pain scale score of the participants changed over time, it was found that the data did not show normal distribution ($p<0.05$). Findings related to the analysis are shared in Table XII.

As a result of the Wilcoxon Signed Rank test conducted to examine whether the participants' S-LANSS pain scale scores changed in the 3rd and 4th months, it was found that there was no significant difference between the groups (Z=-1.000, $p>0.05$). The S-LANSS pain scale score does not change in the 3rd and 4th months.

As a result of the Kolmogorov-Smirnov test, which was carried out to determine whether the L VAS score of the participants changed over time, it was found that the data did not show normal distribution ($p<0.05$). Findings related to the analysis are shared in Table XIII.

As a result of the Wilcoxon Signed Ranks test, which was carried out to examine whether the L VAS score of the participants changed in the 3rd and 4th months, it was found that there was no significant difference between the groups (Z=-1.000, $p>0.05$). L VAS score does not change at 3 and 4 months.

As a result of the Kolmogorov-Smirnov test, which was carried out to determine whether the scores of the participants from the EQ-5D-3L quality of life scale changed over time, it was found that the data did not show normal distribution ($p<.05$). Findings related to the analysis are shared in Table XIV.

A significant difference was found between the groups as a result of the Friedman test, which was carried out to examine whether the scores of the participants from the EQ-5D-3L quality of life scale changed in the 3rd and 4th months from the first measurement ($\chi^2=19.419$, $p<0.05$). When the averages of the rows were examined, it was seen that the first measurement score was the highest, while the score decreased in the 3rd month and remained the same in the 4th month.

The Kolmogorov-Smirnov test was also used to determine whether the VAS scores of the participants from the EQ-5D-3L quality of life scale changed over time, it was found that the data did not show normal distribution ($p<0.05$). Findings related to the analysis are shared in Table XV.

A significant difference was found between the groups as a result of the Friedman test, which was carried out to examine whether the VAS scores of the participants from the EQ-5D-3L quality of life scale changed in the 3rd and 4th months from the first measurement ($\chi^2=18.167$, $p<0.05$). When the averages of the rows were examined, it was seen that the first measurement score was the highest, while the score decreased in the 3rd month and remained the same in the 4th month.

Ultimately, the Kolmogorov-Smirnov test was carried out to determine whether the scores of the participants from the international physical activity questionnaire (UFAA) changed over time, and it was found that the data did not show normal distribution ($p<0.05$). Findings related to the analysis are shared in Table XVI.

The Friedman test was used to examine whether the scores of the participants from the International Physical Activity Questionnaire changed in the 3rd and 4th months from the first measurement; there was no significant difference between the groups in the vigorous activity score ($\chi^2=2.000$, $p>0.05$), while the moderate activity ($\chi^2=12.286$, $p<0.05$), walking ($\chi^2=10.333$, $p<0.05$), sitting ($\chi^2=11.143$, $p<0.05$) and total score ($\chi^2=12.071$, $p<0.05$) groups. It was found that there was a significant difference between moderate activity, walking, and total scores; the first measurement score was higher than the 3rd and 4th month scores. The lowest score in sitting score was obtained in the first measurement.

Discussion

While the pain score was high in the first measurement compared to the VAS pain scale score, it decreased in the 3rd month and remained stable in the 4th month. Post-COVID functional status scale scores remain the same at 3 and 4 months. The MMRC dyspnea score remains the same at 3 and 4 months. While muscle strength increased at 4 months compared to 3 months, walking speeds did not change. The S-LANSS pain scale score remains the same at 3 and 4 months. L VAS score does not change at 3 and 4 months. According to the EQ-5D-3L quality of life scale score, while the score was higher in the first measurement, it decreased in the 3rd month and remained the same in the 4th month. Based on the VAS score from the EQ-5D-3L quality of life scale, first measurements were high, however, the scores decreased in the 3rd month and remained stable in the 4th month. Considering the physical activity scores, it was seen that the intense activity score did not change over time. Second, considering the activity, walking, and total scores, the score obtained in the first measurement is higher than the measurements taken in the 3rd and 4th months. In the sitting score, the score taken in the first measurement is higher than in the 3rd and 4th months.

Prevalence of pain symptomatology in post-COVID-19 survivors and post-COVID-19 pain sufferers using a validated self-report questionnaire. This is the first cohort study to investigate almost 25% of previously hospitalized COVID-19 survivors exhibited post-COVID-19 pain. In our study, the prevalence of pain was determined by the method of Oguz-Akarsu et al21 with a self-reported phone call. In our patient sample, the pain prevalence was 25% in survivors of COVID-19. Current prevalence data of symptoms related to pain in COVID-19 survivors (25%) is higher than the nationwide prevalence of reported pain symptoms (6.9%) in persons with chronic pain, which contributes to COVID-19 pain-related pain[22] supporting the expected increase in prevalence. The neuroinvasive potential of the SARS-CoV-2 virus, which explains the presence of neuropathic pain symptoms in COVID-19 survivors, may be explained by the high expression of angiotensin-converting enzyme-2 (ACE2) receptors detected in nervous system cells, including neurons and microglia. In addition, storms associated with SARS-CoV-2 cytokine and interleukin may promote the development of chronic pain by sensitizing peripheral and central pain pathways[23,24]. In such a scenario, the SARS-CoV-2 virus may trigger different mechanisms that lead to the development of predisposed neuropathic pain in individuals. However, the role of ACE2 receptors on peripheral small-fiber sensory neurons is still unknown[25-27].

Precision medicine implies that patient education, management, and treatment must be tailored to each patient's pain phenotype, such as neuropathic pain associated with anxiety or kinesiophobia. The application of telemedicine for the management of factors can be effectively applied to the management of post-COVID pain[28-30].

Limitations

Finally, the present study has some limitations. First, the current results may only apply to previously hospitalized, mild to moderate COVID-19 victims. Actually, critically ill survivors of COVID-19 also exhibit post-COVID-19 pain symptoms[24]. Possibly, the prevalence of neuropathic pain may be higher in severely ill patients.

Conclusions

The presence of pre-existing symptoms prior to SARS-CoV-2 infection may be a risk factor for the development of neuropathic pain. Post-COVID pain is neuropathic in almost 25% of individuals.

Post-COVID pain has also been classified as nociplastic pain, although this indicates that it includes symptomatology. Post-COVID pain is likely to consist of a complex disorder involving different mechanisms simultaneously.

Ethics Approval
Ethical approval was taken from Gazi Yaşargil Training and Research Hospital (date: 03.09.2021, number: 871).

Informed Consent
All patients were informed in detail about the study and signed the informed patient form.

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Conflict of Interest
The authors have nothing to disclose.

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