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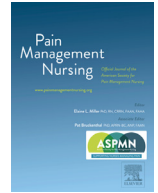
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Original Article

Biopsychosocial Factors Predicting Pain Among Individuals Experiencing the Novel Coronavirus Disease (COVID-19)

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ABSTRACT

Background: Pain is one of the most common symptoms of novel coronavirus disease (COVID-19). Being both a physical and a psychological experience, pain is affected by many factors, including biological, psychological, and social rather than a single variable.

Aims: To determine the effects of biological, psychological, and social factors on pain level among participants experiencing with the COVID-19.

Design: A web-based, retrospective, and descriptive study

Setting: Social media sources such as Facebook, WhatsApp, Instagram, and E-mail

Participants: One hundred forty-nine participants were included.

Methods: Data were collected based on the biopsychosocial model. Pain level was evaluated using the visual analog scale (VAS). The data were analyzed using descriptive, correlational statistics, and structural equation modeling.

Results: The mean age of participants was 32.87 (SD = 11.32) years. The VAS scores were associated with gender ($Z = -2.103, p = .035$), and chronic disease status ($Z = 3.001, p = .003$), and the Chalder Fatigue Scale total score ($\beta = 0.718, p < .001$) associated with biological factors. The Coronavirus Anxiety Scale scores among psychological factors showed a direct impact on the VAS scores ($\beta = 0.583, p < .001$). The Patterns of Activity Measure-Pain total score examined within social factors directly affected the VAS score. The VAS score did not correlate with age, smoking status, hospitalization status, respiratory support, marital status, education level, employment, and income status.

Conclusions: The pain level in COVID-19 participants was determined by biological, psychological, and social factors. Females and participants with chronic illness, anxiety, fatigue, and low physical activity were found to experience high levels of pain. Education and counseling programs for pain management should be comprehensively structured and include anxiety reduction programs, and fatigue management.

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The SARS CoV-2 outbreak that occurred in China in the last months of 2019 has adversely affected the whole world (Akila & Nathan, 2020; Shi et al., 2020). This outbreak was named the new type of COVID-19 by the World Health Organization (WHO) and the WHO declared COVID-19 a global pandemic in March 2020 (Açikgöz & Günay, 2020; Cucinotta & Vanelli, 2020). The prognosis for COVID-19 disease ranges from asymptomatic infection to multiple organ failure with cardiac, renal, hematologic, and neurologic effects (Berlin, Gulick, & Martinez, 2020). Some COVID-19-affected patients may experience Acute Respiratory Distress Syndrome (ARDS), severe viral pneumonia, and multi-organ failure, and these conditions can lead to death (Berlin et al., 2020). Indi-

viduals diagnosed with COVID-19 commonly experience symptoms such as fever, cough, shortness of breath, sputum, diarrhea, muscle pain, fatigue, insomnia, anorexia, and loss of taste and smell (Huang et al., 2020; Mizrahi et al., 2020). In addition to these physical symptoms, patients also suffer from psychosocial problems such as depression, fear, anxiety, and stress (Dubey et al., 2020). Individuals diagnosed with COVID-19 also experience a decrease in physical activity due to severe burden of these symptoms (Tison et al., 2020).

Pain, a common symptom of COVID-19, is defined as an unpleasant bodily sensation or a complex of sensations that cause physical discomfort and emotional distress (Naidu & Pham, 2015). The prevalence of pain in individuals with COVID-19 ranges from 34.7%–92.3%, and studies emphasize that the pain can continue for up to 6 months after infection (Badakhsh et al., 2020; Lacasse et al., 2021). In 45%–75% of cases, COVID-19-related pain is the primary reason for patients presenting to the emergency de-

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partment (Hartnett et al., 2020). In terms of pathophysiology, the inflammation processes are the main factors of COVID-19-related pain (Fara et al., 2020). The inflammatory process activates natural immunity and causes the emergence of pro-inflammatory cytokines (Yi et al., 2020). The impaired immune responses and uncontrolled inflammatory process may cause cytokine storms (Hu et al., 2021). The cytokine storm may induce damage in various tissues such as joints and muscles and trigger pain-related symptoms (El-Tallawy et al., 2020). In addition, the virus causing COVID-19 significantly targets the angiotensin-converting enzyme 2 (ACE2) receptors in the body. ACE2 receptors are present in the muscles, brain, and dorsal horn of the spine. Damage to ACE2 receptors causes hypoxemia, an increase in growth factors, and microvascular changes in cells (Fara et al., 2020). In particular, ACE2 receptors present in the dorsal horn of the spine are influenced by the virus and alter pain communication. All these changes can trigger pain by overexpression in the dorsal root ganglion (Su et al., 2020).

Pain, which is a major symptom of COVID-19, is not only affected by a single variable but also by many physical, social, and cultural characteristics (Lacasse et al., 2021). Therefore, a holistic approach should be adopted in pain assessment and management (Darnall et al., 2017). Accordingly, the biopsychosocial model of pain was adapted to elucidate the multidimensional nature of pain (Gatchel et al., 2020). The model has been identified as the most successful model to date for understanding pain (Gatchel et al., 2020; Miaskowski et al., 2020). The developers of the model argue that each individual is unique, and therefore, biological, psychological, and social factors are necessary for defining subjective pain (Gatchel et al., 2020). The biological factors associated with pain are several, including age, gender, comorbid disease, smoking status, fatigue, and sleep problems (Gatchel et al., 2020). The prevalence of fatigue, one of the biological factors of pain, ranges from 40%–72% in individuals diagnosed with COVID-19 and is one of the most debilitating symptoms of COVID-19 (Carfi et al., 2020; Rudroff et al., 2020). Although fatigue has no universal definition, it is a general feeling of weakness or an unpleasant subjective feeling that can progress from a lack of energy to a feeling of burnout (Micklewright et al., 2017). The assessment of the causes of COVID-19-related fatigue has revealed factors related to the central nervous system (Rudroff et al., 2020). The central nervous system affected by COVID-19 triggers fatigue by causing changes in levels of neurotransmitters such as serotonin and dopamine, decreased neuromuscular irritability, axonal inflammation, and demyelination (Wostyn, 2021).

The psychological factors include depression, anxiety, stress, fear, and rumination level of patients (Darnall et al., 2017). Anxiety, one of the psychological factors of pain, is the feeling of mental pressure, worries, and physical health changes, often related to stress (Zis et al., 2017). Moderate to severe anxiety has been observed in patients with COVID-19 (Choi et al., 2020; Peteet, 2020). Factors such as the rapid spread of this disease, risk of death, lack of effective treatment, and permanent damage can increase anxiety in patients with (Peteet, 2020). Disturbing images and news about COVID-19 through the media before encountering the disease may significantly increase the anxiety in individuals after diagnosis (Bendau et al., 2021). Ongoing anxiety causes an increase in the metabolic activity of the body and oxygen consumption and ultimately weakens the immune system.

The social factors comprise race, ethnicity, culture, socioeconomic status, ageism, education level, marital status, employment status, social support, and activity level of the patient (Miaskowski et al., 2020). Studies indicate that approximately 70% of individuals with COVID-19 have a decline in physical activity (Tison et al., 2020; Woods et al., 2020). The quarantine measures

adopted by individuals with COVID-19 also cause social isolation and lead to a sedentary life (Woods et al., 2020). In addition, individuals prefer to avoid physical activity to limit symptoms such as pain, shortness of breath, and fatigue. However, there is no study until now to report the assessment of the factors that affect the pain in participants with COVID-19 based on the biopsychosocial model. Therefore, this study may contribute to a better understanding of pain and related factors on the basis of the biopsychosocial model and in planning appropriate training and interventions according to the needs of participants.

Methods

Aim

This study aimed to examine and evaluate the biopsychosocial factors that affect pain among participants experiencing COVID-19 using a structural equation modeling (SEM) approach. The following research questions were raised in this study:

- What is the mean pain score, measured by VAS self-report, in participants diagnosed with COVID-19 within the previous 8 months?
- What are the biological, psychological, and social factors that impact pain severity in participants diagnosed with COVID-19 within the previous 8 months?
- If effective, how is pain impacted by biological, psychological, and social factors severity in participants diagnosed with COVID-19 within the previous 8 months?

Study Design and Setting

In this study, a retrospective and descriptive study design was used. An anonymous online survey was hosted on the Google Forms survey platform and distributed using social media sources (Facebook, WhatsApp, Instagram, and E-mail). The data were collected in February and March 2021 in Turkey. The institutional review board (IRB) approved the study protocol, and good research practices were followed in this study. The study was conducted and reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist in reporting descriptive and correlational studies.

Participants

The inclusion criteria were: (1) participants diagnosed with COVID-19 disease according to the Ministry of Health criteria based on PCR test and chest tomography results within 8 months of entry into study; (2) aged ≥ 18 years; (3) having the pain severity score ≥ 2 according to the visual analogue scale (VAS); (4) able to access the online survey with a smartphone or a computer; (5) having at least primary level education; and (6) not having cognitive and psychiatric diagnosis (e.g., schizophrenia, bipolar illness, and psychotic illness). Participants who did not agree to participate in the study and those who could not access the online questionnaire were excluded from the study. A snowball sampling technique based on personal links was used to reach potential participants experiencing COVID-19. The sample size of structural equation model studies determines with various rules including 5 or 10 observations per estimated parameter (Wolf et al., 2013). The sample size for the current study was determined according to the N:q rule denoting the ratio of the number of participants (N) versus model parameters (q) (Kline, 2015). The model in this study was seen to consist of 14 parameters and, based on the N:q ratio, the target sample size was calculated to be 140 participants with COVID-19 to perform SEM.

Measurement Tools

In this study, pain was evaluated as the dependent variable utilizing VAS. The independent variables of this study were biological, psychological, and social factors based on the biopsychosocial model.

The dependent variable

Self-reported general body pain was measured using the VAS, which is a widely used tool for clinical pain assessment. The VAS is a scale used to evaluate pain from a score of 0 (no pain) to 10 (the worst possible pain) points, respectively. Higher scores indicate more severe pain. The pain was classified as mild (score 0-3), moderate (score 4-6), and severe (score 7-10). The intra-class correlation coefficient (ICC) of the VAS was 0.99 and was high in the validity and reliability study (Carlsson, 1983).

The independent variables

The following factors within the scope of the biopsychosocial model were evaluated:

Biological Factors: Age, sex (male vs. female), smoking status (current smoker vs. ex-smoker vs. never smoked), chronic conditions (yes vs. no), length of time since COVID-19 diagnosis (<1 month vs. 1-3 month vs. 3-5 month vs. >5 months), hospitalization status (yes vs. no), and respiratory support (yes vs. no) were examined. In addition, the fatigue level of participants was evaluated using the Chalder Fatigue Scale (CFS). The CFS, developed by Chalder et al., (1993) comprises 11 items and is divided into two dimensions, physical and mental fatigue. A four-point Likert-type scale is rated as 0 = less than usual, 1 = no more than usual, 2 = more than usual, and 3 = much more than usual (Chalder et al., 1993). The general fatigue score in this study was obtained from the sum of the scores given to all items. The total fatigue score ranged from 0-33. A scaled score >12 indicates a high severity of fatigue. Adin & Ayhan (2019) reported a change in total item correlation between 0.76 and 0.89 and Cronbach's alpha of 0.89 in the Turkish validity and reliability study (Adin & Ayhan, 2019).

Psychological Factors: Anxiety was evaluated within the scope of psychological factors using the COVID-19 Anxiety Scale (CAS). The CAS developed by Lee et al. (2020) assesses COVID-19-related anxiety and consists of five items. Each item of scale is rated on a five-point Likert-type scale ranging from 0 = not at all to 4 = almost every day. A higher score indicates a higher severity of anxiety in individuals with COVID-19 (Lee et al., 2020). The Turkish validity and reliability study of the scale was conducted by Evren et al. (2020) and reported the Cronbach's alpha value between 0.79 and 0.93 (Evren et al., 2020).

Social Factors: Marital status (single vs. married), an education level (primary school vs. high school vs. bachelor's degree vs. master's and doctoral degree), employment (unemployed vs. employed), income status (low vs. moderate vs. high) were evaluated to determine the social factors. Activity level was considered as one of the social factors and assessed with the Patterns of Activity Measures-Pain scale (POAM-P). The POAM-P consists of three subgroups (avoidance, overdoing, and ordering), and a total of 30 questions (Cane et al., 2013). A five-point Likert-like scale ranging from "0 = never" to "4 = always" was used in answering the scale. The total score of the scale is calculated by adding the score given to each item. Higher scale scores indicate decreasing activity levels of the participants. Turkish validity and reliability study conducted by Suygun, & Celenay (2021) and the Cronbach's alpha value was reported to be 0.84-0.94 (Suygun & Celenay, 2021).

Data Collection

The questionnaire was prepared in Google Forms (Google LLC, Mountain View, California, USA) for an online survey to collect data in February 2021. The survey link was forwarded to potential participants using social media platforms, including WhatsApp, Facebook, Instagram, and e-mail. In the first part of the online survey, information about the study was provided. Afterward, all questions in the questionnaire were accessible to the participants who agreed to participate in the study, and they were asked to answer. The online survey took nearly 10-15 min to complete.

Ethical Considerations

This study was approved by the Non-Interventional Clinical Trials Ethics Committee of X University (Approval number: X). The recommendations of the Association of Internet Researchers (AoIR) Ethics Working Committee were utilized in researching the internet. The first part of the online survey contained the study details and an informed consent form. Before participating in the online survey, participants were required to provide consent to participate in the study by ticking the "I have read the information, and I agree to voluntarily participate in the study" box. Informed consent was obtained from each participant with a confirmation button, and the questions were not accessible to those who did not agree to participate in the survey. In the informed consent form, participants were assured of anonymity and they were free to withdraw from the study at any time, and that the data would only be used in the academic field.

Data Analysis

The data were analyzed using SPSS version 25.0 (IBM Corp, Armonk, New York). The normality test carried out using the Kolmogorov-Smirnov test, histogram, and normal Q-Q plot. Descriptive data of participants (age, VAS, CFS, CAS, and POAM-P scores) were described by means and standard deviations (SD). Categorical variables (gender, marital status, smoking status, chronic conditions, hospitalization status, respiratory support, employment, income status, and education level) were presented as frequencies with percentages. The Mann-Whitney *U* test and the Kruskal-Wallis test were used to compare the mean scores of the VAS and categorical variables. In addition, Spearman's correlation coefficient test was used to evaluate correlations between quantitative data (age) and the mean scores of the VAS.

The normal distribution of the study data was confirmed using skewness and kurtosis (Tabachnick et al., 2007). SEM was performed to define direct, indirect, and total effects of fatigue, anxiety, and physical activity on pain level using the AMOS computer program. The structural model of the study was conducted with the path analysis. Path analysis defines the magnitude and importance of causal associations between variables and is a part of multiple regression analysis (Grapentine, 2000). The effect of an independent variable on a dependent variable was shown with a standardized regression coefficient (β) in the path model. In the current study, the independent variables were fatigue, anxiety, and physical activity, whereas the dependent variable was pain level. The critical ratio (CR) value was calculated by dividing an estimate by its standard error. The path parameter was statistically significant if the CR was >1.96 for a regression weight (Hox & Bechger, 1998). For all analyses, the level of statistical significance was specified as $p < .05$. In addition, measurement equations were created using a maximum likelihood solution to estimate the VAS scores (dependent parameter) with the CFS, CAS, and POAM-P (in-

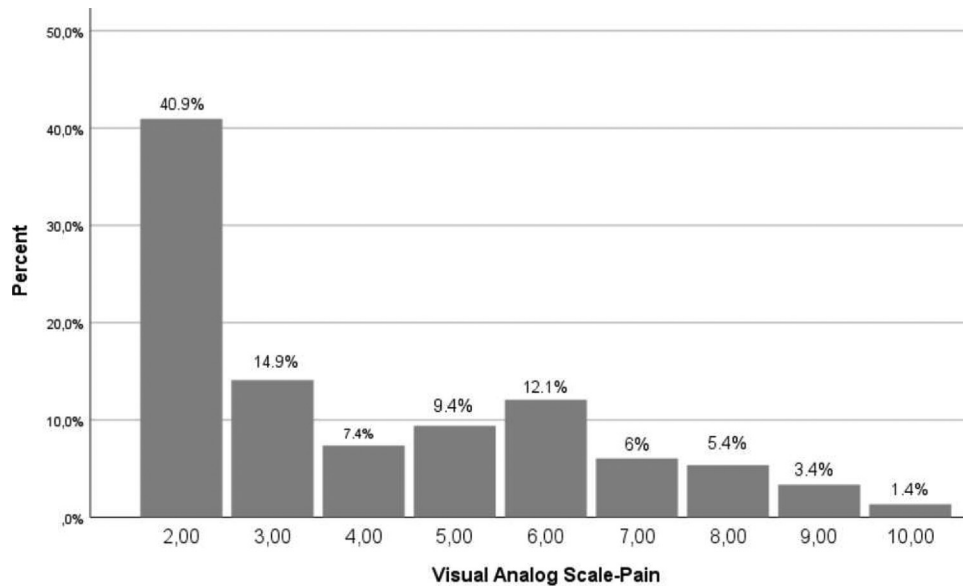


Figure 1. The distribution of pain scores.

dependent parameter) scores. In this context, measurement equations were structured as follows:

- Dependent variable = $\beta \times$ (independent variable) + standard error

Results

Descriptive Characteristics of the Participants

The power of the study was reached by a total of 149 participants diagnosed with COVID-19 between February and March 2021. The average age of participants was 32.87 (SD = 11.32) years. The majority of participants were female (75.2%) and had a bachelor's degree (61.7%). Nearly half the number of participants (49%) were married. Moreover, 61.1% of participants had moderate-income, and 62.4% of them were employed; most of the participants (75.8%) never smoked, and 18.1% were current smokers; 24.2% of participants had at least one chronic disease (asthma [4%], hypertension [2.7%], type II diabetes mellitus [2%], and nearly half of them (49.7%) had the length of time since COVID-19 diagnosis ranging from 3-5 months. Among the participants, 9.4% of participants were hospitalized for COVID-19, and 6% received respiratory support (Table 1). The mean total score of VAS was 4.04 (SD = 2.23) points (Fig. 1). Normal distribution assumptions were provided in this study due to Kurtosis and Skewness values are between -1.5 and +1.5.

Effects of Biological Factors on Pain

The VAS scores correlated with the gender of the participants and were significantly higher in female participants ($Z = -2.103$, $p = .035$). VAS scores were also found to be significantly higher in those participants with a chronic disease ($Z = 3.001$, $p = .003$). However, the VAS scores did not show a significant association with age ($r = 0.107$, $p = .194$), smoking status ($F = 0.535$, $p = .765$), hospitalization status ($Z = 0.183$, $p = .855$), and respiratory support ($Z = 1.031$, $p = .302$) (Table 2). In addition, the CFS scores were evaluated in the scope of biological factors. The mean total score was 17 points (SD = 7.65), indicating a high severity in fatigue. The VAS score was directly and positively affected by CFS total score

($\beta = 0.718$, $p < .001$) (Table 3). An equation was created to calculate VAS scores (dependent parameter) using the CFS scores based on the maximum probability solution (Fig. 2). The specified measurement equation is:

$$\text{Pain (VAS)} = (0.72) \text{ Fatigue (CFS)} + (0.036) \text{ error}$$

Effects of Psychological Factors on Pain

The CAS scores were evaluated within the scope of psychological factors. The mean CAS score was 4.65 (SD = 3.81). The CAS scores directly influenced the VAS scores ($\beta = 0.583$, $p < .001$) (Table 3). An equation was created to determine VAS scores (dependent variable) with CAS scores utilizing the maximum probability solution (Fig. 2). The specified measurement equation is:

$$\text{Pain (VAS)} = (0.58) \text{ Anxiety (CAS)} + (0.063) \text{ error}$$

Effects of Social Factors on Pain

The VAS score did not indicate any significant relationship with marital status ($Z = -1.877$, $p = .060$), education level ($F = 2.521$, $p = .471$), employment ($z = -1.338$, $p = .181$), and income status ($F = 4.408$, $p = .110$) (Table 2). Then, the POAM-P scores of the participants were assessed within the social factors. Participants had an average POAM-P score of 77.99 (SD = 14.45), indicating a low level of physical activity. The VAS score was directly affected by POAM-P total score ($\beta = 0.380$, $p < .001$) (Table 3). An equation was created to calculate VAS scores (dependent parameter) using the POAM-P scores based on the maximum probability solution (Fig. 2). The specified measurement equation is:

$$\text{Pain (VAS)} = (0.38) \text{ Physical activity (POAM-P)} + (0.014) \text{ error}$$

Discussion

One of the most common symptoms experienced by individuals diagnosed with COVID-19 is pain which is manifested due to conditions such as an increase in pro-inflammatory cytokines and damage to the ACE2 receptors. Studies have found that the pain experienced by individuals with COVID-19 is moderate (El-Tallawy et al., 2020; Lacasse et al., 2021). Lacasse et al. (2021) conducted a study on individuals with COVID-19 who experienced

Table 1
Descriptive Characteristics of the Patients (N = 149)

	Characteristic	n	%	Mean	SD
Biological factors	Age (year) (min:19, max: 78)			32.87	11.32
	Sex				
	Female	112	75.2		
	Male	37	24.8		
	Smoking status				
	Current smoker	27	18.1		
	Ex-smoker	9	6.1		
	Never smoked	113	75.8		
	Chronic conditions				
	Yes	36	24.2		
	No	113	75.8		
	Length of time since COVID-19 diagnosis				
	<1 month	11	7.4		
	1-3 months	30	20.1		
	3-5 months	74	49.7		
	>5 months	33	22.1		
	Hospitalization status				
	Yes	14	9.4		
	No	135	90.6		
Respiratory support					
Yes	9	6.0			
No	140	94.0			
	Fatigue (CFS Total Score) (min:1.00, max: 33.0)			17.0	7.65
Psychological factors	Anxiety (CAS Total Score) (min:0.00, max:16.0)			4.65	3.81
Social factors	Marital status				
	Married	73	49.0		
	Single	76	51.0		
	Education level				
	Primary school	13	8.7		
	High school	25	16.8		
	Graduate	92	61.7		
	Postgraduate	19	12.8		
	Employment				
	Unemployed	56	37.6		
	Employed	93	62.4		
Income status					
Low	26	17.4			
Moderate	91	61.1			
High	32	21.5			
	Activity level (POAM-P Total Score) (min:30.00, max:117.00)			77.99	14.45
Pain level	VAS (min:1.00, max:10.00)*			4.04	2.33

SD = standard deviation; min = minimum; max = maximum; CFS = Chalder Fatigue Scale; CAS = Coronavirus Anxiety Scale; POAM-P = Patterns of Activity Measure-Pain; VAS = visual analogue scale

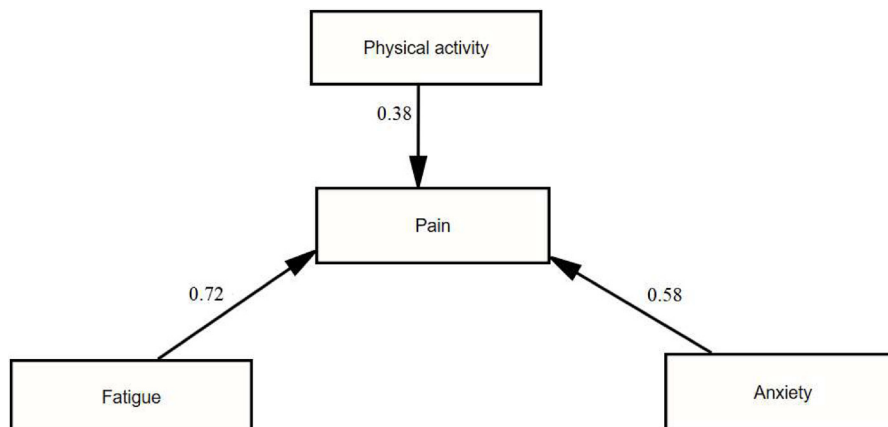


Figure 2. Results of the path analysis.

Table 2
Comparison of Pain by Variables from the Biopsychosocial Model (n = 149)

Dimension	Characteristic	VAS	
		Mean (SD)	Test statistics
Biological factors	Age (year)		r = 0.107 ^a p = .194
	Gender		
	Female	4.52 (0.23)	Z = -2.103 ^b
	Male	2.37 (0.29)	p = .035
	Smoking status		F = .535 ^c
	Current smoker	3.21 (0.39)	p = .765
	Ex-smoker	3.98 (1.12)	
	Never smoked	3.06 (0.21)	
	Chronic conditions		Z = -3.001 ^b
	Yes	2.65 (0.19)	p = .003
	No	4.27 (0.46)	
	Length of time since COVID-19 diagnosis	4.18 (0.88)	F = 2.789 ^c
	<1 month	2.96 (0.42)	p = .425
	1-3 months	2.90 (0.27)	
	3-5 months	3.05 (0.36)	
>5 months			
Social factors	Hospitalization status		Z = -0.183 ^b
	Yes	3.35 (0.70)	p = .855
	No	3.01 (0.19)	
	Respiratory support		Z = -1.031 ^b
	Yes	3.55 (0.64)	p = .302
	No	3.01 (0.19)	
	Marital status		Z = -1.877 ^b
	Married	3.72 (0.24)	p = .060
	Single	3.38 (0.28)	F = 2.521 ^c
	Education level		p = .471
	Primary school	4.06 (0.60)	
	High school	3.80 (0.51)	
	Graduate	4.05 (0.23)	
	Postgraduate	3.90 (0.59)	
	Employment		Z = -1.338 ^b
Unemployed	3.33 (0.32)	p = .181	
Employed	3.50 (0.23)		
Income status		F = 4.408 ^c	
Low	3.42 (0.42)	p = .110	
Moderate	3.15 (0.24)		
High	3.14 (0.39)		

VAS = visual analogue scale; SD = standard deviation.

^a Spearman correlation test.

^b Mann-Whitney U test.

^c Kruskal-Wallis test.

Table 3
The Effect of Fatigue, Anxiety, and Physical Activity on Pain (n = 149)

Independent variables	Path	Dependent variables	β	SE	P value	Critical ratio	Direct effect	Indirect effect	Total effect
CFS total score	→	VAS	0.718	0.036	<0.001	7.655	0.718	0.000	0.718
CAS total score	→	VAS	0.583	0.063	<0.001	6.640	0.583	0.000	0.583
POAM-P total score	→	VAS	0.380	0.014	<0.001	4.756	0.380	0.000	0.380

CAS, Coronavirus Anxiety Scale; CFS, Chalder Fatigue Scale; POAM-P: Patterns of Activity Measure-Pain; VAS, Visual Analogue Scale

SE: Standard error, β: a standardized regression coefficient

pain for >3 months due to COVID-19 and observed the pain intensity of 6.13 in such patients. Accordingly, in the current study, individuals with COVID-19 reported moderate pain with a pain intensity of 4.04. This moderate level of pain experienced by individuals with COVID-19 is due to the varying nature of the disease. Overall, the pain levels of individuals with COVID-19 are moderate, as some are asymptomatic, and others experience severe symptom burden. Pain is affected by many factors due to its versatile nature. Therefore, as with other diseases, pain in COVID-19 is a significant symptom that must be addressed in a multifaceted way. This study was the first to assess the effects of the biological, psychological, and social factors based on the biopsychosocial model on pain level in individuals with COVID-19 using an SEM approach. The findings

of this study indicate that the biological, psychological, and social factors influence the pain severity.

We analyzed biological factors such as age, gender, chronic illness, smoking status, duration of diagnosis, hospital stay, and fatigue in terms of their effects on pain. Although Lacasse et al. (2021) determined that some factors such as age, smoking status, and hospitalization have a significant impact on pain, our study findings reveal no significant relationship between pain and the above-mentioned factors. This difference may be due to the discrepancy between other factors affecting pain, such as the individuals' chronic illness and fatigue severity. Chronic diseases lead to a more severe course of COVID-19 infection by weakening the immune system and causing damage to ACE2 receptors and the

renin-angiotensin-aldosterone system (RAAS) (Su et al., 2020). Indeed, this study revealed that the presence of chronic disease exacerbates pain in COVID-19 disease. Similar to these findings, earlier studies have reported that comorbid diseases influence pain levels in individuals with COVID-19 (Lacasse et al., 2021). Moreover, our study determined that gender is another biological factor impacting pain in individuals experiencing COVID-19. In contrast with this finding, Fallon et al. (2020) stated that there is no direct relationship between pain and gender in COVID-19 disease (Fallon et al., 2020). However, it has been emphasized in the literature that women experience more severe pain than men when they suffer from chronic diseases (Fallon et al., 2020). Although the reason for this has not been clarified yet, it may be because the hormonal balance in women is more sensitive in perceiving symptoms and a lower pain threshold of women than that of men (Boerner et al., 2018). Fatigue is another biological factor that affects pain level in individuals experiencing COVID-19. We observed that participants with high fatigue levels experienced severe pain levels and that fatigue has a direct effect on pain levels in participants experiencing COVID-19. Zou et al. (2020) conducted a study with elderly individuals diagnosed with COVID-19 and found that pain and fatigue were interrelated (Zou et al., 2020). Fatigue is among the primary biological factors to increase pain and plays an important role in pain pathophysiology (Moldofsky & Patcai, 2011; Wostyn, 2021). In addition, fatigue increases negative illness perception in individuals, and this leads to disease-related symptoms, including pain, shortness of breath, and insomnia. Individuals suffering from fatigue are unable to suppress long-term pain, have trouble coping with it, and consequently experience greater pain (Miaskowski et al., 2020; Nijrolder et al., 2010). It has been reported that fatigue may increase pain due to stimulation in the central nervous system and changes in the expression of neurotransmitters, including serotonin and dopamine (Clauw et al., 2020; Townsend et al., 2020).

In this study, anxiety was evaluated as a psychological factor within the scope of the BPS model. In individuals experiencing COVID-19, anxiety and pain are two closely related symptoms (Pimentel et al., 2020). The literature on COVID-19 states that anxiety can increase pain due to respiratory and endocrine events, weakened immune system, accelerated oxygen demand, and escalated muscle tension (Parizad et al., 2021; Pimentel et al., 2020). On the other hand, in a study conducted with individuals with COVID-19, Fallon et al. (2020) reported that patients with chronic pain experienced more anxiety than those in the non-pain group (Fallon et al., 2020). Individuals with anxiety experience excessive muscle tension, and this condition especially triggers muscle pain by causing physiological stimulation. In this context, anxiety is emphasized as a factor that increases pain severity and the perceived disease burden (Lumley et al., 2011; Miaskowski et al., 2020). In other words, it is a cyclic phenomenon; as anxiety increases pain, pain also triggers anxiety. Furthermore, the results of this study revealed that participants with anxiety experienced more pain.

One of the most important social conditions that affect individuals experiencing COVID-19 is the decline in physical activity due to both the symptoms of the disease and the quarantine requirements in its treatment. Therefore, according to the BPS model, the activity level examined in this study was found to be one of the social factors affecting pain severity in participants. Reduced physical activity and pain are two strongly interrelated symptoms in COVID-19 (Tison et al., 2020). Quarantine procedures and symptoms such as pain, fatigue, weakness, and anxiety due to COVID-19 cause a decline in physical activity (Woods et al., 2020). Physical activity improves immune function in chronic systemic inflammation and various diseases while strengthening the immune system reduces the symptoms, such as pain associated with COVID-19

(Bourdas & Zacharakis, 2020). It also supports individuals in terms of psychosocial aspects and reduces symptoms of depression and anxiety (Callow et al., 2020). Studies emphasize that physical and psychosocial aspects of pain can be affected by physical activity (Fallon et al., 2020; Feter et al., 2020). Compatible with the studies on COVID-19, this study revealed that a decrease in physical activity increased pain severity in participants.

Strengths and Limitation

The present study had a number of strengths. First, this study described the impact on pain of the physical, psychological and social factors using SEM. Second, this study is the first to examine all aspects of pain in participants with COVID-19 and provides important contributions to the literature. Third, anxiety directly caused by COVID-19 was evaluated in this study using CAS. However, the study also had some limitations. The sample of the study consisted of a young population, and, therefore, before generalizing the results, it should be tested, especially in the context of an older population. In addition, some participants may have had trouble remembering the symptoms they experienced, as data were collected months after their COVID-19 diagnosis. Finally, to observe changes in pain levels over time, longitudinal data are needed.

Conclusions

To conclude, pain levels in participants experiencing COVID-19 are associated with biological, psychological, and social factors according to the biopsychosocial model. Pain intensity was higher in women and participants with chronic diseases. Participants experiencing COVID-19 with fatigue and anxiety experienced higher pain levels. In addition, low physical activity level was found to increase pain in participants experiencing COVID-19. This study shows that the “biopsychosocial model” is a useful guide in the evaluation of pain, and additional studies are needed to evaluate whether it can predict all factors related to COVID-19-related pain.

Clinical Implications

The current study emphasized that health professionals should consider that pain level is affected by the combination of various factors such as gender, chronic disease, fatigue, anxiety, and physical activity. The education and counseling programs for pain management should be comprehensively structured and also include reduction programs for anxiety, fatigue, and physical activities.

Declaration of Competing Interest

None.

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References

- Açikgöz, Ö., & Günay, A. (2020). The early impact of the Covid-19 pandemic on the global and Turkish economy. *Turkish Journal of Medical Sciences*, 50(S1-1), 520–526.
- Adin, R. M., & Ayhan, C. (2019). *Turkish Adaptation of Chalder Fatigue Scale and Investigating Its Psychometric Properties in Young Adults*. Hacettepe University Master of Science thesis, Ankara, Turkey.
- Akila, K., & Nathan, S. (2020). A Review Study On Relationship Among Covid-19 And Pneumonia. *European Journal of Molecular & Clinical Medicine*, 7(7), 5476–5480.

- Bendau, A., Petzold, M. B., Pyrkosch, L., Maricic, L. M., Betzler, F., Rogoll, J., Rogoll, J., Große, J., Ströhle, A., & Plag, J. (2021). Associations between COVID-19 related media consumption and symptoms of anxiety, depression and COVID-19 related fear in the general population in Germany. *European Archives of Psychiatry and Clinical Neuroscience*, 271(2), 283–291.
- Berlin, D. A., Gulick, R. M., & Martinez, F. J. (2020). Severe Covid-19. *New England Journal of Medicine*, 383(25), 2451–2460.
- Boerner, K. E., Chambers, C. T., Gahagan, J., Keogh, E., Fillingim, R. B., & Mogil, J. S. (2018). Conceptual complexity of gender and its relevance to pain. *Pain*, 159(11), 2137–2141.
- Cane, D., Nielson, W. R., McCarthy, M., & Mazmanian, D. (2013). Pain-related activity patterns: measurement, interrelationships, and associations with psychosocial functioning. *Clinical Journal of Pain*, 29(5), 435–442.
- Carfi, A., Bernabei, R., & Landi, F. (2020). Persistent symptoms in patients after acute COVID-19. *JAMA*, 324(6), 603–605.
- Carlsson, A. M. (1983). Assessment of chronic pain. I. Aspects of the reliability and validity of the visual analogue scale. *Pain*, 16(1), 87–101.
- Chalder, T., Berelowitz, G., Pawlikowska, T., Watts, L., Wessely, S., Wright, D., & Wallace, E. P. (1993). Development of a fatigue scale. *Journal of Psychosomatic Research*, 37(2), 147–153.
- Choi, E. P. H., Hui, B. P. H., & Wan, E. Y. F. (2020). Depression and anxiety in Hong Kong during COVID-19. *International Journal of Environmental Research and Public Health*, 17(10), 3740.
- Clauw, D. J., Häuser, W., Cohen, S. P., & Fitzcharles, M.-A. (2020). Considering the potential for an increase in chronic pain after the COVID-19 pandemic. *Pain*, 161(8), 1694–1697.
- Cucinotta, D., & Vanelli, M. (2020). WHO declares COVID-19 a pandemic. *Acta Bio Medica: Atenei Parmensis*, 91(1), 157–160.
- Darnall, B. D., Carr, D. B., & Schatman, M. E. (2017). Pain psychology and the biopsychosocial model of pain treatment: Ethical imperatives and social responsibility. *Pain Medicine*, 18(8), 1413–1415.
- Dubey, S., Biswas, P., Ghosh, R., Chatterjee, S., Dubey, M. J., Chatterjee, S., Lahiri, D., & Lavie, C. J. (2020). Psychosocial impact of COVID-19. *Diabetes & Metabolic Syndrome*, 14(5), 779–788.
- El-Tallawy, S. N., Nalamasu, R., Pergolizzi, J. V., & Gharibo, C. (2020). Pain management during the COVID-19 pandemic. *Pain and Therapy*, 9(2), 453–466.
- Evren, C., Evren, B., Dalbudak, E., Topcu, M., & Kutlu, N. (2020). Measuring anxiety related to COVID-19: A Turkish validation study of the Coronavirus Anxiety Scale. *Death Studies*, 1–7.
- Fallon, N., Brown, C., Twiddy, H., Brian, E., Frank, B., Nurmikko, T., & Stancak, A. (2020). Adverse effects of COVID-19-related lockdown on pain, physical activity and psychological well-being in people with chronic pain. *British Journal of Pain*, 15(3), 357–3689.
- Fara, A., Mitrev, Z., Rosalia, R. A., & Assas, B. M. (2020). Cytokine storm and COVID-19: A chronicle of pro-inflammatory cytokines. *Open Biology*, 10(9), Article 200160.
- Feter, N., Caputo, E. L., Doring, I. R., Leite, J. S., Cassuriaga, J., Reichert, F. F., Cozzensa da Silva, M., & Rombaldi, A. J. (2020). Longitudinal study about low back pain, mental health, and access to healthcare system during COVID-19 pandemic: Protocol of an ambispective cohort. *medRxiv*. <https://doi.org/10.1101/2020.07.22.20160309>.
- Gatchel, R. J., Ray, C. T., Kishino, N., & Brindle, A. (2020). The biopsychosocial model. In L. Cohen (Ed.), *The Wiley encyclopedia of health psychology* (pp. 1–8). Hoboken, NJ: Wiley-Blackwell.
- Grapentine, T. (2000). Path analysis vs. structural equation modeling. *Marketing research*, 12(3), 14–20.
- Hartnett, K. P., Kite-Powell, A., DeVies, J., Coletta, M. A., Boehmer, T. K., Adjemian, J., & Gundlapalli, A. V. (2020). Impact of the COVID-19 pandemic on emergency department visits—United States, January 1, 2019–May 30, 2020. *MMWR. Morbidity and Mortality Weekly Report*, 69(23), 699–704.
- Hox, J. J., & Bechger, T. M. (1998). An introduction to structural equation modeling. *Family Science Review*, 11, 354–373.
- Hu, B., Huang, S., & Yin, L. (2021). The cytokine storm and COVID-19. *Journal of Medical Virology*, 93(1), 250–256.
- Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., ... Gu, X. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*, 395(10223), 497–506.
- Kline, R. B. (2015). *Principles and practice of structural equation modeling*. Guilford Press.
- Lacasse, A., Pagé, M. G., Dassié, L., Sourial, N., Janelle-Montcalm, A., Dorais, M., & Moor, G. (2021). Impact of the COVID-19 pandemic on the pharmacological, physical, and psychological treatments of pain: Findings from the Chronic Pain & COVID-19 Pan-Canadian Study. *Pain Reports*, 6(1), e891.
- Lee, S. A., Mathis, A. A., Jobe, M. C., & Pappalardo, E. A. (2020). Clinically significant fear and anxiety of COVID-19: A psychometric examination of the Coronavirus Anxiety Scale. *Psychiatry Research*, 290, Article 113112.
- Lumley, M. A., Cohen, J. L., Borszcz, G. S., Cano, A., Radcliffe, A. M., Porter, L. S., Schubiner, H., & Keefe, F. J. (2011). Pain and emotion: A biopsychosocial review of recent research. *Journal of Clinical Psychology*, 67(9), 942–968.
- Miaskowski, C., Blyth, F., Nicosia, F., Haan, M., Keefe, F., Smith, A., & Ritchie, C. (2020). A biopsychosocial model of chronic pain for older adults. *Pain Medicine*, 21(9), 1793–1805.
- Micklewright, D., Gibson, A. S. C., Gladwell, V., & Al Salman, A. (2017). Development and validity of the rating-of-fatigue scale. *Sports Medicine*, 47(11), 2375–2393.
- Mizrahi, B., Shilo, S., Rossman, H., Kalkstein, N., Marcus, K., Barer, Y., ... segal, E. (2020). Longitudinal symptom dynamics of COVID-19 infection. *Nature Communications*, 11(1), 6208.
- Naidu, R. K., & Pham, T. M. (2015). Pain management. In P. K. Sikka, S. T. Beaman, & J. A. Street (Eds.), *Basic clinical anesthesia* (pp. 265–296). New York: Springer.
- Nijrolder, I., van der Windt, D. A., Twisk, J. W., & van der Horst, H. E. (2010). Fatigue in primary care: Longitudinal associations with pain. *Pain*, 150(2), 351–357.
- Parizad, N., Goli, R., Faraji, N., Mam-Qaderi, M., Mirzaee, R., Gharebaghi, N., ... Haghghi, M.-M. (2021). Effect of guided imagery on anxiety, muscle pain, and vital signs in patients with COVID-19: A randomized controlled trial. *Complementary Therapies in Clinical Practice*, 43, Article 101335.
- Peteet, J. R. (2020). COVID-19 anxiety. *Journal of Religion and Health*, 59(5), 2203–2204.
- Pimentel, M. A., Redfern, O. C., Hatch, R., Young, J. D., Tarassenko, L., & Watkinson, P. J. (2020). Trajectories of vital signs in patients with COVID-19. *Resuscitation*, 156, 99–106.
- Rudroff, T., Fietsam, A. C., Deters, J. R., Bryant, A. D., & Kamholz, J. (2020). Post-covid-19 fatigue: Potential contributing factors. *Brain Sciences*, 10(12), 1012.
- Shi, Y., Wang, G., Cai, X.-p., Deng, J.-w., Zheng, L., Zhu, H.-h., ... Chen, Z. (2020). An overview of COVID-19. *Journal of Zhejiang University-Science B*, 21(5), 343–360.
- Su, S., Cui, H., Wang, T., Shen, X., & Ma, C. (2020). Pain: A potential new label of COVID-19. *Brain, Behavior, and Immunity*, 87, 159–160.
- Suygun, E. T., & Celenay, S. T. (2021). Turkish translation of the patterns of activity measure-pain in patients with chronic low back and neck pain: Validity and reliability. *Pain Management Nursing*. [https://www.painmanagementnursing.org/article/S1524-9042\(21\)00023-0/fulltext](https://www.painmanagementnursing.org/article/S1524-9042(21)00023-0/fulltext).
- Tison, G. H., Avram, R., Kuhar, P., Abreau, S., Marcus, G. M., Pletcher, M. J., & Olgin, J. E. (2020). Worldwide effect of COVID-19 on physical activity: A descriptive study. *Annals of Internal Medicine*, 173(9), 767–770.
- Townsend, L., Dyer, A. H., Jones, K., Dunne, J., Mooney, A., Gaffney, F., ... Conlon, N. (2020). Persistent fatigue following SARS-CoV-2 infection is common and independent of severity of initial infection. *PLoS One*, 15(11), Article e0240784.
- Wolf, E. J., Harrington, K. M., Clark, S. L., & Miller, M. W. (2013). Sample size requirements for structural equation models: An evaluation of power, bias, and solution propriety. *Educational and Psychological Measurement*, 73(6), 913–934.
- Woods, J. A., Hutchinson, N. T., Powers, S. K., Roberts, W. O., Gomez-Cabrera, M. C., Radak, Z., ... Ji, L. L. (2020). The COVID-19 pandemic and physical activity. *Sports Medicine and Health Science*, 2(2), 55–64.
- Wostyn, P. (2021). COVID-19 and chronic fatigue syndrome: Is the worst yet to come? *Medical Hypotheses*, 146, Article 110469.
- Yi, Y., Lagniton, P. N., Ye, S., Li, E., & Xu, R.-H. (2020). COVID-19: what has been learned and to be learned about the novel coronavirus disease. *International Journal of Biological Sciences*, 16(10), 1753–1766.
- Zis, P., Daskalaki, A., Bountouni, I., Sykioti, P., Varrassi, G., & Paladini, A. (2017). Depression and chronic pain in the elderly: links and management challenges. *Clinical Interventions in Aging*, 12, 709–720.
- Zou, S., Liu, Z.-H., Yan, X., Wang, H., Li, Y., Xu, X., ... xiang, Y.-T. (2020). Prevalence and correlates of fatigue and its association with quality of life among clinically stable older psychiatric patients during the COVID-19 outbreak: A cross-sectional study. *Globalization and Health*, 16(1), 119.