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A Cross-Sectional & Prevalence Study

# Prevalence and Clinical Characteristics of Musculoskeletal Pain in Young Adults with COVID-19: An Observational Cross-Sectional Study from Lanzarote (Canary Island, Spain)

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## Abstract

**Introduction:** Musculoskeletal pain during active Covid-19 infection is a very common symptom in this patient group. Given the lack of studies characterizing pain in young adults with this disease, we set out to identify and characterize musculoskeletal pain in subadults with COVID-19 disease in Lanzarote. **Objective:** Determine the prevalence and characteristics of musculoskeletal pain in young individuals affected by COVID-19 in Lanzarote (Canary Islands, Spain). **Materials and Methods:** A cross-sectional prevalence observational study was carried out in the Covid-19 Monitoring Unit in Lanzarote between February 2022 and March 2022 which were a) males and females, b) aged 18 to 22 years old, c) with confirmed Covid-19 tests and d) no gender restrictions. **Results:** A total of 150 patients were recruited and an ad hoc telephone questionnaire based on the Spanish version of the McGill Pain Questionnaire was administered. The prevalence of musculoskeletal pain was 58% (n=87; men 41 (48.2%); women 46 (51.8%) and its intensity was 4.63 (1.23) Regarding the location of perceived pain, the common anatomical sites of symptoms presentation were right shoulder (n=14, 21.5%), right knee (n=13, 20%) and right leg (n=12, 18.5%). Participants also reported heaviness (23.0%, n=20), numbness (20.7%, n=18) and/or stiffness (17.2%, n=15) followed by thermal changes such as cold (21.2%, n=18), highlighting the presence of stiffness in 43.4% (n=36). On the other hand, 17.2% (n=15) of the respondents reported pain described as fixed, internal, deep compared to 14.9% (n=13) who perceived it as diffuse, fixed, internal and profound. **Conclusions:** The prevalence of musculoskeletal pain was 58.0% in a sample of young people exposed to COVID-19 in Lanzarote (Canary Islands, Spain). Furthermore, respondents generally defined it as an acute attack of low to moderate intensity in various parts of the upper and lower extremities, often accompanied by feelings of tiredness or muscle fatigue.

**Keywords:** Pain, Myalgia, SARS-CoV-2, COVID-19, Lanzarote

## Introduction

The SARS-CoV-2 virus has caused a global pandemic that has deeply affected individuals and entire societies. COVID-19, the disease that is a result of SARS-CoV-2, is primarily known for its respiratory effects. However, recent findings suggest a connection between COVID-19 and musculoskeletal disorders. The most frequent post-acute COVID-19 musculoskeletal symptoms include arthralgias, myalgias and fatigue [1-5].

Although the mechanisms are not fully understood, it has been suggested that the adaptive immune response to SARS-CoV-2 in the respiratory tract may induce systemic inflammation, producing inflammatory factors in distant areas such as the neuromusculoskeletal system [6-8]. To support this hypothesis, recent studies, such as the one conducted by Ramasamy *et al.* (2021) [9], have highlighted the presence of inflammation-mediating substances, including IFN- $\gamma$ , IL-1 $\beta$ , IL-6, IL-17, and TNF- $\alpha$ , that can lead to proteolysis and block muscle cells differentiation.

Additionally, the presence of SARS-CoV-2 has been shown to cause changes in muscle tissue, as evidenced by postmortem patients displaying generalized atrophy with immune cell infiltration and even focal necrosis [1]. The decline in grip strength by 32% and walking distance by 13% during the 6-minute walk test among patients with moderate to severe illness, even after two to three months following their discharge, may be attributed to these mechanisms [2,5,10]. Although they can also be attributed to inactivity during the recovery process [7].

Children and young people have a doubtful role in the transmission of SARS-CoV-2 but their symptoms are usually very mild [11]. In older children and young adults, muscle symptomatology and characteristic findings in the muscle are comparatively more common. Persistent musculoskeletal pain is a common symptom, although it depends on several factors. Musculoskeletal pain is more prevalent in adults than in the youth population in the United States [12]. However, the prevalence of musculoskeletal pain in youth ranges from 4-40% [13]. By contrast, older people tend to have more and longer-lasting pain [14]. The fact that older children and young adults have less obvious symptoms causes their symptoms to be confused with characteristics of adolescence, which delays an accurate diagnosis.

As if all this were not enough, the perception of pain suffered by young people is modulated by patient characteristics, such as the presence of comorbid diseases or medications. Regarding the second factor, younger Spaniards consume more nonsteroidal anti-inflammatory drugs (NSAIDs) than older adults [15]. Drug use among young people, particularly painkillers, has been on the rise since 1993-2003 [16]. These drugs may at least partially explain musculoskeletal pain in young adults. Additionally, immunosuppressants prescribed to reduce the overactive inflammatory response in COVID-19 patients [17] may also impair the painful perception suffered by these young patients, as these drugs are not risk factors in COVID-19 patients [18].

To this we can also add that at the time of carrying out this study, during the first wave of infections, many young people were not yet vaccinated as they were the vaccine group that took the longest to start vaccination, having the greatest risk of contracting the disease [19]. While musculoskeletal pain has been extensively studied in the

elderly population affected by COVID-19 [2,5,7,10] there is a paucity of research on the occurrence and clinical attributes of this pain in young adults and adolescents. Therefore, the current research aimed to determine the prevalence and characteristics of musculoskeletal pain in young individuals who contracted COVID-19 in Lanzarote (Canary Islands, Spain).

## Materials and Methods

### 2.1. Study Design

A cross-sectional observational survey study with consecutive non-probability sampling was carried out to calculate the prevalence and define the characteristics of musculoskeletal pain in patients during the process of active COVID19 infection. The study was conducted from February 1, 2022 to March 31, 2022, at the COVID Unit of the Hospital Dr. José Molina Orosa, Lanzarote (Canary Islands, Spain). All participants were led by researcher M.G. I was contacted by phone. Prior verbal informed consent was obtained before inclusion in the study and recorded in an anonymous database to avoid identification.

### 2.2. Participants

The target group for this study was people who had COVID-19 disease at the time of the information collection test. The inclusion criteria for this study were: 1) Male and female, 2) Aged 18 to 22 years, c) Diagnosed with SARS-CoV-2 and passed a specific test such as RT-PCR (real-time-reverse transcription polymerase chain reaction) or antigen test, and d) Did not exhibit any speech impairment or cognitive changes that would affect understanding of the questionnaire, and e) Did not exhibit any motor speech difficulties or changes in hearing skills that would affect understanding of the questionnaire understanding.

### 2.3. Sample Size Calculation

The sample size was determined by researcher I.M. Calculations were performed using the computational software Calculadora de Grandària Mostral-GRANMO version 7.12 (Municipal Institute of Medical Research, Barcelona, Spain). Sample size calculations were performed on a known population obtained from census data (ISTAC, Government of the Canary Islands). This was determined with a confidence level of 85% and a margin of error of 6%, so a total of 144 subjects represents the ideal sample size. In addition, 5% of participants were included as it was expected that information would be lost on some participants who originally selected to participate in the study.

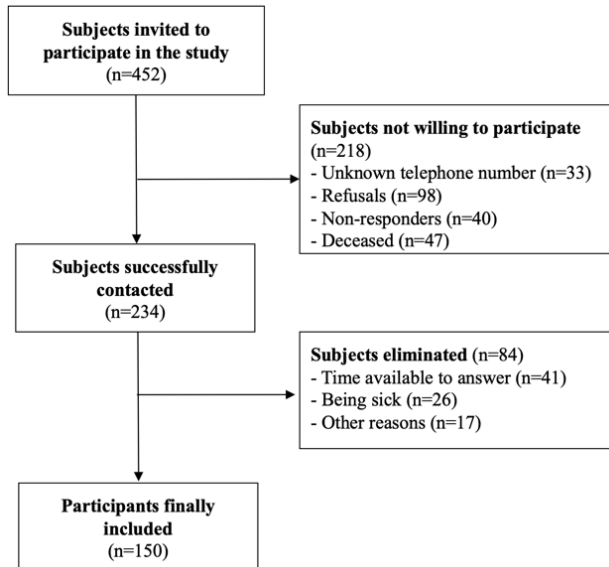
### 2.4. Data Collection Procedure

After assessing eligibility criteria and signing informed consent forms, data collection took place between February 1, 2022, and February 28, 2022. Answers provided by participants via telephone were included in the questionnaire in a standardized form. The data studies developed for this purpose were integrated and able to be captured in an automated database, which facilitated the export and analysis of the collected information.

While answering the questionnaire, the researcher informed the study participants about the purpose and objectives of the work. The

survey was completed after the patient accepted voluntary, anonymous participation in the study. Finally, it should be noted that these data are processed in accordance with Organic Law No. 3/2018 of December 5 on the protection of personal data.

**Figure 1: Flow chart of participants selection**



## 2.5. Instruments

Participants were contacted by telephone were administered the Spanish version of McGill Pain Questionnaire [20]. The questionnaire was developed by Lázaro *et al.* (1994) [20], which was later validated and revised by the same authors and adapted to the specific objectives of this work. In this way, the final questionnaire consisted of two distinct blocks. The first one aimed at analyzing the socio-demographic data of the participants (*age, gender, employment status, academic background, etc.*), the second aimed at asking questions aimed at quantitatively and qualitatively assessing various aspects related to the phenomenon, assessing the participants of pain. In this way, the questionnaire consisted of 59 questions, including 7 open-ended questions, 9 multiple-choice questions, 9 dichotomous questions, and 34 Likert scales (ranging from 1 to 7, with 1 being the lowest and 7 the highest score).

## 2.6. Data Analysis

First, researcher I.A. recorded the results of the assessment tool in an electronic database, while M.G. verified the accuracy of the data by performing double data entry in Microsoft Excel software on the Microsoft Windows 10 operating system. In particular, they check that the data are within the expected range, that participants meet defined sample selection criteria, and that there are no missing data in the imputed information. Secondly, researchers S.M. and I.M. determined frequencies and descriptive statistics of answers provided by questionnaires and calculates quantitative variables of central tendency (mean and median) and dispersion (standard deviation) using the statistical software SPSS v.20 (IBM®, USA). Regarding qualitative variables, absolute frequency and relative frequency are used to describe them. Finally, the results for each survey area were tabulated.

## Results

### 3.1. Demographic Description of the Sample

A total of 150 participants were included of which 47.3% (n=71) were men and 52.7% (n=79) were women. Figure 1. Flow chart of participants selection. The mean age was 19.2 years (SD=0.8). Regarding the academic background of the participants, 22.8% (n=34) completed Compulsory Secondary Education (ESO), 19.5% (n=29) completed the Baccalaureate or COU and 27.5% (n=41) had university education (degree, diploma and/or bachelor's degree, etc.) and 74.7% were employed.

**Table 1: Demographic description of sample**

Category	n (%)
<b>Gender</b>	
Female	79 (52.7%)
Male	71 (47.3%)
<b>Age</b>	
	19.2 (0.8)
<b>Educational level</b>	
<b>No education</b>	
Basic general education / primary education	2 (1.3%)
Secondary education (ESO)	9 (6.0%)
Baccalaureate/COU	34 (22.8%)
FP	29 (19.5%)
Bachelor's degree	11 (7.3%)
	41 (27.5%)
<b>Employment Status</b>	
Active	112 (74.7%)
Unemployed	14 (9.4%)

In order to know the diseases prior to the COVID-19 disease process, 56% (n=84) of the patients did not report a diagnosis of previous disease, while in the remaining group they reported suffering from metabolic (12.7%; n=19), cardiovascular (10.0%; n=15) and respiratory (8.7%; n=13) diseases.

**Table 2: Illnesses prior to the COVID-19 disease process.**

Category	n (%)
<b>No previous illnesses</b>	
	<b>84 (56.0%)</b>
<b>With previous illnesses</b>	
Metabolic	66 (44.0%)
Cardiovascular	19 (12.7%)
Respiratory	15 (10.0%)
Ocular	13 (8.7%)
Urorenal	5 (3.3%)
Neurological	4 (2.7%)
Rheumatic	3 (2.0%)
Trauma	1 (0.7%)
Digestive	2 (1.3%)
Allergy	1 (0.7%)
Psychiatric	1 (0.7%)
	2 (1.3%)

Regarding to taking medication, 56.55% (n=82) of the patients indicated that they do not take any medication prior to the COVID-19 disease process, while the remaining 43.45% (n=63) reported taking medication on a regular basis before suffering from COVID-19, in which antihypertensive drugs (8%), anticholesterol (6%) and antidepressants (6%) are the pharmaceutical species that reach the highest consumption.

**Table 3: Consumption of drugs prior to the COVID-19 disease process classified by pharmaceutical agents.**

Category	n (%)
No	82 (54.7%)
Yes	57 (38.0%)
Antihypertensive	12 (8.0%)
Anti-cholesterol	9 (6.0%)
Antidepressant	9 (6.0%)
Antidiabetic	6 (4.0%)
Analgesic	6 (4.0%)
Bronchodilator	5 (3.3%)
Antithyroid	3 (2.0%)
Alpha-blocker	2 (1.3%)
Contraceptive	2 (1.3%)
Antiglaucoma	2 (1.3%)
NSAIDs	1 (0.7%)
Antacid	1 (0.7%)
Antiallergic	1 (0.7%)
Antihistamine	1 (0.7%)
Insulin	1 (0.7%)
Antiglycemic	1 (0.7%)
Anti-asthma	1 (0.7%)
Antiarrhythmic	1 (0.7%)
Antiplatelet	1 (0.7%)
Anxiolytic	1 (0.7%)
Progesterone	1 (0.7%)
Corticosteroid	1 (0.7%)

Regarding the vaccination status of the participants against COVID-19, 54% (n=81) of the patients 40% (n=60) said they had received only the 2nd dose, 1% (n=1) reported being vaccinated with a single dose and 5% (n=8) not being vaccinated. Among those who were unvaccinated or those who did not have the booster schedule, 55.7% (n=34) reported that it was due to organizational reasons of the health system, 26.2% (n=16) for individual reasons (beliefs, fear, etc.), 11.5% (n=7) for work reasons (studies, jobs, etc.), and 6.6% (n=4) because they had the disease previously or at the time they were scheduled to be vaccinated.

## 3.2. Main Findings

### 3.2.1. Prevalence of Musculoskeletal Pain Disorders

The point prevalence of musculoskeletal pain disorders was 58.0% (n=87), while the rest of the sample (42.0%; n=63) reported not suffering from pain. If we perform a detailed analysis, 56.7% (n=85) of the respondents manifested musculoskeletal pain along with other symptoms such as fatigue, tiredness, etc.

**Table 4: Prevalence of painful disorders of musculoskeletal origin among COVID-19 exposed young adult from Lanzarote (Canary Island, Spain).**

Category	n (%)
Yes	87 (58.0%)
Yes, you have musculoskeletal pain exclusively	2 (1.3%)
Yes, you have musculoskeletal pain and other symptoms associated with the disease	85 (56.7%)
No	63 (42.0%)
Has no musculoskeletal pain	3 (2.0%)
He does not have musculoskeletal pain, but he does have other symptoms associated with the disease	60 (40.0%)

### 3.2.2. Adapted Questionnaire Spanish Version of the McGill Pain Questionnaire

The data obtained showed that the mean value of pain perception was 4.63 (1.23). The majority of patients 89 (58.7%) reported pain before infection with illness caused by SARS-CoV-2. On the contrary, it is noteworthy that almost half of the respondents reported continued pain even after the infectious process 62 (41.3%). Only 10.7% of those affected (n=16) seemed to experience this much increase in pain, while the remaining participants either reported no pain-related symptoms or answered negatively to the question 134 (89.3%). A total of 64 (76.2%) of participants reported increased pain associated with the characteristic respiratory symptoms of the disease. Only 23.8% of the respondents reported no pain during the infection.

43 (51.8%) participants reported current musculoskeletal pain. Contrary to these results, half of the respondents were unaware of the procedure, indicating that in 48.5% of cases they were not currently experiencing pain. Among the sample who reported experiencing pain before but not during the disease course, pain lasted an average of  $1.96 \pm 1.09$  days. Finally, 87 (58.0%) patients interviewed admitted to having taken or continued to take painkillers. The most common medications included paracetamol 72 (48.3%), followed by ibuprofen 5 (3.4%).

#### 3.2.2.a Localization of Pain

Regarding musculoskeletal pain in the right upper limb, 48 (56.5%) of the analyzed sample reported suffering no musculoskeletal pain, while 10 (11.8%) reported bothersome musculoskeletal pain. In the left upper extremity, 50 (58.8%) respondents reported no musculoskeletal pain, while 9 (10.6%) reported tolerable pain. Data collected for the right lower extremity showed that 40 (46.5%)

participants experienced no pain at all, while 17 (19.8%) rated the pain as uncomfortable. Moreover, data regarding musculoskeletal pain in the left lower extremity, 36 (41.9%) reported no pain in this area and 18 (20.9%) reported discomfort. According to the data, a total of 46 (54.1%) patients said they did not experience cervical musculoskeletal pain, and 11.8% (n=10) reported unpleasant pain.

Survey data showed that 59.3% (n=51) had no musculoskeletal back pain, while 11 (12.8%) reported severe back pain. Regarding lumbar musculoskeletal pain, 37.2% (n=32) reported no pain and 13 (15.1%) participants reported unpleasant pain. 75.6% (n=62) of the subjects had no pain in the chest area, while 6 (7.3%) reported severe pain in this muscle area. 76.6% (n=36) of patients experienced no abdominal pain, compared with 10.6% (n=5) of patients who experienced discomfort and only 2 (4.3%) of patients who experienced severe abdominal pain.

In summary, the main sites of musculoskeletal pain was the upper extremity, such as the right shoulder (n=14, 21.5%), followed by the right knee (n=13, 20%) and right leg (n=12, 18.5%). In contrast, the least pain was reported in the neck region (n=4, 6.1%) and shoulder girdle region (n=1, 1.5%).

### 3.2.2.b Characteristics of Pain

According to the analyzed data, 71.3% (n=62) reported never feeling musculoskeletal pain, such as pulsation or palpitations, while 6.9% (n=6) reported experiencing this pain occasionally or often. Survey data showed that 86.2% (n=75) of people had never experienced pain such as tremors, compared with 8.0% (n=7) who frequently reported this pain. A total of 73.3% (n=63) of participants answered they had never experienced whiplash-related pain, while 10.5% (n=9) said they often experienced this pain.

The data obtained showed that 57.6% (n=49) did not experience pain-related thermal sensations. However, 21.2% (n=18) reported that their relevant body areas were very cold and had musculoskeletal pain. 65.9% (n=56) reported no sensation of heat in the painful area, while 8.2% (n=7) reported an unpleasant sensation of heat in the area.

Furthermore, 46.0% (n=40) reported no numbness in the musculoskeletal painful area, while 20.7% (n=18) reported discomfort in the painful area. The results obtained showed that 90.8% (n=79) of the respondents did not perceive the pain as pinching, while only 3.4% (n=3) expressed this sensation in an unpleasant way at the site of pain.

Moreover, stiffness was absent in 50.6% (n=44) of the matched patients, whereas in the sample, 17.2% (n=15) experienced an unpleasant sensation in the painful area. According to the data collected, 78.2% (n=68) reported no cramping, while only 5.7% (n=5) reported that cramping in the painful area was bothersome. 83.9% (n=73) of adolescents generally had no cramping sensation at the painful site, whereas only 5.7% (n=5) experienced unpleasant sensations. 82.8% (n=72) reported no cramping sensation or just a disturbing feeling in the painful area 4.6% (n=4).

58.6% (n=51) did not feel anxious while 12.6% (n=11) of respondents reported a strong feeling of discomfort. Stinging was absent in 66.7% (n=58) and manifested in a disturbing manner in the painful area in 9.2% (n=8). 69.0% (n=60) of the respondents did not

experience a tingling sensation, but the remaining 31% of the respondents experienced a tingling sensation, of which 10.3% (n=9) expressed it in an unpleasant way at the painful site. 72.4% (n=63) of respondents experienced no tingling sensation, compared with 10.3% (n=9) who defined tingling as a rather stinging sensation.

57.5% (n=50) had a general, intense sensation of needle tip pressure, and 13.8% (n=12) expressed this sensation in an unpleasant way at the site of pain. 33.3% (n=29) reported that strong attraction was not dominant, while 23.0% (n=20) expressed feelings of musculoskeletal pain in an unpleasant way. 86.2% (n=75) did not experience a tearing sensation due to gravity, compared with 6.9% (n=6) who experienced musculoskeletal pain.

A total of 69.0% (n=60) of respondents reported no tightness, while 11.5% (n=10) reported tightness in areas associated with musculoskeletal pain. 47.1% (n=41) reported tightness in painful areas of the musculoskeletal system, while 14.9% (n=13) experienced significant tightness.

### 3.2.2.c Typology of Pain

17.2% (n=15) described the pain as fixed, internal and deep, while 14.9% (n=13) described it as diffuse, fixed, internal and deep. Regarding the assessment of musculoskeletal pain severity, the results showed that 43.4% (n=36) of respondents had muscle pain compared to those who had no sensation (18.1%, n=5).

However, it is striking that 13.4% (n=11) reported dizziness accompanied by musculoskeletal pain. 34.5% (n=30) of patients with musculoskeletal pain did not have fatigue, while 21.8% (n=19) had maximum fatigue during episodes of musculoskeletal pain. 21.8% (n=19) of patients rated the sensation as annoying, slightly higher than the 20.7% (n=18) of patients complaining of pain-related fatigue who rated it as severe.

According to the data obtained, 74.7% (n=65) of patients did not experience pain-induced sadness or anxiety, while only 25.4% (n=22) of those who did experience these symptoms.

## Discussion

The aim of this study was to estimate the prevalence and characterize musculoskeletal pain in young people affected by COVID-19 disease in Lanzarote (Canary Islands, Spain). Our hypothesis was that the prevalence of musculoskeletal pain (58%) would be higher in younger adults following SARS-CoV-2 infection when compared to other complications.

Based on our own results, it is evident that musculoskeletal pain is a prevalent disorder after contract COVID-19 among younger inhabitants in Lanzarote. The development of this affection can be attributed to various factors. One of the main determinants is that the global health of young patients is better than that of their older equivalents. This is because they are less susceptible of comorbidities and have lesser consumption of drugs that can potentially cause musculoskeletal pain. Another contributing factor is the increased incidence of the disease among this age group, which is partially due to lower vaccination rates at the time of the recruitment. While prevalent in younger individuals, the effects may not be as apparent, leading to delayed diagnosis and treatment, potentially exacerbating the individual's overall health status.

Upon closer examination of the prevalence within this particular group of ages, it is important to note that the estimations provided in this research are relatively small compared to later periods of SARS-CoV-2 pandemic in Lanzarote. This may be due to some subjects gradually receiving full vaccination and additional booster vaccines at enrollment, transforming the exposed group into a non-susceptible group. Therefore, prevalence should be interpreted cautiously as it can only be limited to the progression of the pandemic at a specific time and place.

When analyzing the clinical presentation of musculoskeletal pain, it appears that younger individuals experience a moderate intensity of pain with an average of 4.63. If we look at it by gender, it was observed that a greater proportion of women were affected by this pain compared to men, which corroborates previous findings by Fernández-De-las-peñas *et al.* (2022) [4].

In a thorough analysis of the evolution of the symptoms, more than half of respondents (56.7%) reported experiencing pain-related complaints during the course of the infection. Additionally, 10% of participants stated that they continued to experience musculoskeletal pain after recovering from illness caused by SARS-CoV-2. These findings are consistent with those of Fiala *et al.* (2022), who found that musculoskeletal pain persists even years after recovery from COVID-19 [21].

Regarding the location of pain, it is worth noting that in younger was randomly located in different areas of the upper limb, such as the right shoulder (n=14, 21.5%) or the lower limb, such as the right knee (n=13, 20%) or the right leg (n=12, 18.5%). According to the study by Wang *et al.* (2020) [3], the lower limbs are the most common site of pain due to deconditioning processes that occur during recovery. The cause of this musculoskeletal pain is uncertain, but it is possible that it is associated with COVID-19-induced sarcopenia [22,23]. This condition may be a result of either the virus itself or the secondary hyperinflammatory response that can cause muscle atrophy [1].

In reference to the characteristics of pain, our findings indicated that 17.2% of the participants who were interviewed experienced a distinctive point-like sensation. This ache was described as being unchanging, originating from within, and located deeply within the body. During interviews, a considerable proportion of subjects (43.4%) expressed that they feel pain in the form of stiffness. In addition, nearly half of the subjects (49.4%) reported experiencing pain as a sensation of heaviness. In our opinion, these characteristics are close to those of nociceptive and/or neuropathic pain. According to Ramasamy *et al.* (2021) [9], it is possible to suggest that pain might arise due to the impact of viruses on nerve tissue, which in turn causes demyelination. In contrast, pain could be explained as a result of cytotoxic T lymphocytes effect, which are a key cell group in the adaptive immune response against COVID-19 in young adults. [24]. Although this hypothesis needs to be studied further, our findings suggest that neuropathic pain may be a result of an altered immune response to SARS-CoV-2.

In contrast, pain could be explained as a result of cytotoxic T lymphocytes effect, which are a key cell group in the adaptive immune response against COVID-19 in young adults. Along these

lines, the presence of anxiety-related symptoms reached 25.4% (n=22) of the respondents, while disgust was annoying in 21.8% (n=19) and quite annoying in 20.7% (n=18). This finding implies the need for early detection of mood disorders that may co-occur during pain as part of the COVID-19 recovery process.

## Conclusions

Among a sample of young individuals infected by COVID-19 in Lanzarote (Canary Islands, Spain) the prevalence of musculoskeletal pain was 58%. Additionally, approximately 10.7% continued to experience persistent pain even after months of recovering from the disease. Most patients present with musculoskeletal pain characterized by a sudden and severe onset of mild to moderate intensity, with a fixed, internal and deep location in various regions of the upper and lower limbs. This is usually accompanied by feelings of tiredness or fatigue in the muscles. Additionally, character changes may be related to feelings of disgust, sadness or fear.

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**Ethical Consideration:** Not Applicable

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