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ORIGINAL ARTICLE

Factors associated with chronic musculoskeletal pain in individuals with long-COVID after hospital discharge: cross-sectional study

Fatores associadas à dor crônica musculoesquelética em indivíduos com COVID-longa após alta hospitalar: estudo transversal

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Data availability
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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ABSTRACT

BACKGROUND AND OBJECTIVES: Patients hospitalized for COVID-19 have a higher prevalence of pain compared to patients hospitalized for other health conditions. The objective of this study was to identify the frequency and factors associated with the occurrence and intensity of pain in a population discharged from hospital after COVID-19.

METHODS: This is a cross-sectional study. The study recruited 247 participants through social media and telephone contact. Associations between clinical variables were identified using Odds Ratio and logistic regression.

RESULTS: The rate of occurrence of pain after hospitalization for COVID-19 was 87%. Logistic regression showed that female gender (OR= 4.51 95% CI 1.83-11.13), low family income (OR= 4.62 95% CI 1.75-12.22), pain in the acute phase of the disease, mechanical ventilatory support, hospital discharge less than one year ago (OR= 4.62 95% CI 1.73-12.32) and comorbidities (OR= 0.22 95% CI 0.08-0.61) are associated with the occurrence of pain. Female gender (OR = 3.46 95% CI 1.71-7.02), low family income, hospital discharge less than one year ago, longer hospital stay (OR = 1.02 95% CI 1.00-1.03), two or more areas of pain (OR = 2.51 95% CI 1.40-4.52) and mechanical ventilatory support (OR = 0.37 95% CI 0.16-0.84) are associated with pain intensity.

CONCLUSION: The occurrence of pain is high in individuals hospitalized for COVID-19 even 12 months after discharge. Logistic regression models explain 31% of the occurrence of pain and 21% of pain intensity in patients discharged after hospitalization for COVID-19.

KEYWORDS: Musculoskeletal pain, Pain, Patient discharge, Post-acute COVID-19 syndrome.

RESUMO

JUSTIFICATIVA E OBJETIVOS: Pacientes internados por COVID-19 tem maior predominância de dor quando comparados a pacientes internados por outras condições de saúde. O objetivo deste estudo foi identificar a frequência e os fatores associados a ocorrência e intensidade da dor em uma população que recebeu alta hospitalar após a COVID-19.

MÉTODOS: Trata-se de um estudo transversal. Foram recrutados 247 participantes através das mídias sociais e contato telefônico. As associações entre variáveis clínicas foram identificadas por meio da *Odds Ratio* e regressão logística.

RESULTADOS: A taxa de ocorrência de dor após internação hospitalar por COVID-19 foi de 87%. A regressão logística mostrou que sexo feminino (OR= 4,51 95% IC 1,83-11,13), baixa renda familiar (OR= 4,62 95% IC 1,75-12,22), dor na fase aguda da doença, suporte ventilatório mecânico, alta hospitalar há menos de um ano (OR= 4,62 95% IC 1,73-12,32) e comorbidades (OR= 0,22 95% IC 0,08-0,61) estão associadas à ocorrência de dor. O sexo feminino (OR= 3,46 95% IC 1,71-7,02), baixa renda familiar, alta hospitalar há menos de um ano, maior tempo de internação hospitalar (OR= 1,02 95% IC 1,00-1,03), duas ou mais áreas de dor (OR= 2,51 95% IC 1,40-4,52) e suporte ventilatório mecânico (OR= 0,37 95% IC 0,16-0,84) estão associados à intensidade da dor.

CONCLUSÃO: A ocorrência de dor foi elevada em indivíduos hospitalizados por COVID-19 mesmo 12 meses após a alta. Os modelos de regressão logística explicam 31% da ocorrência de dor e 21% da intensidade da dor em pacientes que receberam alta hospitalar após internação por COVID-19.

DESCRITORES: Alta do paciente, Dor, Dor musculoesquelética, Síndrome de COVID-19 pós-aguda.

HIGHLIGHTS

- The rate of occurrence of pain after hospitalization for COVID-19 is considerably high
- Female gender, use of ventilatory support and low family income are associated with greater pain intensity
- Individuals who experienced pain in the acute phase of COVID-19 and had a long period of hospitalization are more likely to have late musculoskeletal pain after discharge

INTRODUCTION

Although the COVID-19 pandemic has ended, many survivors have developed long COVID, which can be defined as the permanence of symptoms for weeks or months after the infection of SARS-CoV-2[1,2]. Among the several symptoms, musculoskeletal pain (MP) has shown a prevalence that can vary between 19 and 71%[3].

Patients hospitalized for COVID-19 have a higher prevalence of pain than patients who have been hospitalized for other health conditions[4,5]. The MP is difficult to manage and involves high costs for the health system, and it is the main cause of years lived with incapacity[6].

There is still no consensus on all the possible factors associated with the presence of post-COVID-19 pain. Systematic reviews have indicated associated factors: female gender, older age, disease severity, comorbidity and poor quality of life. However, some symptoms such as pain in the acute phase of the disease, level of physical activity and income lack evidence. It is worth noting that the evidence have mostly focused on studies with populations from Europe and Asia. Data from South American countries, including Brazil, is scarce[7,8]. This raises a problematic issue, considering that the Brazilian reality in terms of geographical, economic and organizational health policy characteristics differs from the countries of the studied populations. Therefore, evaluation methods and, in the future, interventions should be individualized according to the needs of the Brazilian population.

Since there is still a gap in the literature on the factors associated with the development of pain in patients affected by COVID-19, it is important to investigate the variables that are possibly associated with this dysfunction in these individuals. Some of these patients will develop incapacities as a result of complications after hospitalization. It is not yet known how these dysfunctions will influence functional capacity or their prevalence. In this context, mapping musculoskeletal dysfunctions is essential for defining care guidelines for this patient profile[9].

The present study's objective was to identify the frequency and factors associated with the intensity and occurrence of MP in patients with a history of hospitalization due to COVID-19.

METHODS

This was a cross-sectional observational study approved by the Research Ethics Committee of the Gaffrée and Guinle University Hospital under CAAE number: 52184621.6.0000.5258. The data was presented following the recommendations of the Checklist for Reporting of Survey Studies (CROSS). The study was carried out through telephone interviews with volunteer participants who had been discharged from the Gaffrée and Guinle University Hospital. The authors had access to a list of telephone contacts of patients who had been admitted to the hospital. When contacting the patients, the aim, risks and benefits of the study were explained.

After consenting, the participants answered the questionnaire via a Google forms link (sent via WhatsApp) or a phone call, with the help of the researcher. Social media was also used to send out electronic questionnaires. Users were invited to take part in the study by sending invitation links to COVID-19-related groups on Facebook and WhatsApp. All participants were volunteers and filled in the digital Free and Informed Consent Term (FICT) or gave their verbal consent to take part in the research.

The study established the following inclusion criteria: individuals discharged at least three months after hospitalization for COVID-19; over 18 years old; without any surgical intervention for at least three months prior to the diagnosis of COVID-19; and able to understand the questions posed by the researcher via telephone and electronic questionnaire. Individuals undergoing current cancer treatment; with a history of MP prior to hospitalization for at least one year; and with any type of neurological deficit prior to hospitalization were excluded.

Participants underwent a single interview, during which they answered a structured questionnaire with 13 closed questions. This instrument covered several areas, including sociodemographic features, clinical history, lifestyle, intensity and characteristics of pain and the presence of comorbidities such as hypertension, diabetes, asthma, chronic obstructive pulmonary disease, human immunodeficiency virus, depression, anxiety disorder and heart disease.

In addition, the level of physical activity was assessed by calculating weekly energy expenditure, following the guidelines of the World Health Organization (WHO)[10]. Pain intensity was measured using the Numerical Pain Scale, with a score from zero to 10. The participants used a body map to indicate the affected areas of pain.

When collecting data on comorbidities, examples of diseases were provided, with the option "other" to cover conditions that weren't listed. Family income was categorized into minimum wage bands. Pain intensity was classified as severe (score of 7 to 10) and mild/moderate (score of less than 7). The variables of areas of pain (one or multiple areas) and presence of comorbidities (yes or no) were dichotomized. The remaining questions were answered with "yes/no" answers or by indicating the number of days/years.

Statistical analysis

Sociodemographic, clinical and lifestyle data were presented descriptively. Continuous variables were presented as means and standard deviations (SD) and categorical variables as absolute values and proportions (%). Possible relationships between the clinical variables collected and the presence of pain and pain intensity were assessed. The pain intensity outcome showed a non-normal distribution.

A logistic regression analysis was conducted to investigate possible predictive variables for the outcome presence of pain and pain intensity. The sample calculation was carried out using the G*Power software version 3.1.9 (Heinrich-Heine-Universität, Düsseldorf, Germany). For a reliable model, according to Corrêa et al.[11], with six independent variables to observe at least a small effect size ($f^2 = 0.03$) using an alpha of 0.05 and power of 0.80, the study required a minimum of 208 participants.

The following independent variables were assumed for the model: gender, mechanical ventilatory support, presence of pain in the acute phase of the disease, time since hospital discharge, comorbidity and family income; and as a dependent variable, the presence of pain after hospital discharge. In the model with pain intensity as the dependent variable, the independent variables were gender, mechanical ventilatory support, length of post-hospital discharge, number of areas of pain, length of hospital stay and family income.

The Odds Ratio was used to identify associations for categorical variables. The distribution of data for the primary outcome was assessed using the Shapiro-Wilk test. The data was analyzed using the JASP software, Version 0.17.0, with a significant level of 5%.

RESULTS

A total of 247 participants were included in the study. The mean age was 44±10.5 years old, the mean years of study was 13±3.1 years. The average time from hospital discharge to the time of collection was 404±227.6 days, the average length of stay was 25±32.4 days and the average time of invasive mechanical ventilation was 20±13.6 days. The average pain intensity indicated by the Numerical Pain Scale was 5±3 points, and the number of pain areas was 2±1.. The regions with pain complaints were head and neck (23%), trunk (51%), right upper limb (28%) and left upper limb (24%) and right lower limb (44%) and left lower limb (45%). The demographic and clinical characteristics of the participants are shown in Table 1.

Significant associations were identified between the presence of post-COVID-19 pain and several factors, including female gender, shorter hospital discharge time, presence of comorbidities, pain in the acute phase of COVID-19 and low family income. Women had a higher probability of post-hospitalization pain from COVID-19 compared to men (OR = 1.37; 95% CI 0.60-2.13). Individuals discharged from hospital after less than a year were more likely to have pain than those discharged after more than a year (OR=1.21; 95% CI 0.39-2.02). The presence of comorbidities was associated with a lower probability of pain (OR=-1.34; 95% CI -2.27- -.41). Individuals who reported pain during the acute phase of COVID-19 were more likely to have persistent pain (OR=1.12; 95% CI 0.34-1.91). Individuals with lower family income were more likely to have post-hospitalization pain from COVID-19 compared to those with higher income (OR=1.06; 95% CI 0.24-1.87).

An exploratory logistic regression analysis was carried out to identify the factors associated with the presence of pain. The model included the presence of pain as a dependent variable and the following independent variables: gender, time since hospital discharge, presence of comorbidities, pain in the acute phase of COVID-19, family income and mechanical ventilatory support. The model showed statistical significance (Nagelkerke R2=0.319; p<0.001).

The following variables were associated with the presence of pain: (1) female gender - women were 4.51 times more likely to report pain (OR=4.51; 95% CI 1.83-11.13); (2) low family income - individuals with low family income were 4.62 times more likely to report pain (OR=4.62; 95% CI 1.75-12.22); (3) time since hospital discharge of less than one year - individuals with less than one year since hospital discharge were 4.62 times more likely to report pain (OR=4.62; 95% CI 1.73-12.32); (4) presence of comorbidities - individuals with comorbidities were 0.22 times less likely to report pain, indicating a protective effect (OR=0.22; 95% CI 0.08-0.61).

A significant association was found between post-COVID-19 pain intensity, female gender and the number of pain areas reported. Women had significantly higher levels of pain intensity compared to men (OR=1.31; 95% CI 0.66-1.96). In addition, individuals with complaints of pain in multiple regions (more than one) had higher levels of pain intensity compared to those with less than two affected regions (OR=1.16; 95% CI 0.61-1.71).

An exploratory logistic regression analysis was carried out to identify factors associated with pain intensity. The model included pain intensity as the dependent variable and gender, time to hospital discharge, family income, length of stay, number of pain areas and use of mechanical ventilation as independent variables. The model showed statistical significance (Nagelkerke R2=0.218; p<0.001). Results revealed that female gender (OR=3.46; 95% CI 1.71-7.02), longer length of stay (OR=1.02; 95% CI 1.00-1.03) and greater number of pain areas (OR=2.51; 95% CI 1.40-4.52) were associated with greater pain intensity. In opposition, the use of mechanical ventilation was associated with lower pain intensity (OR=0.37; 95% CI 0.16-0.84), indicating a protective effect.

Table 1. Sociodemographic and clinical characteristics.

Variables	Yes	No
Post-COVID pain	215 (87%)	32 (13%)
Body pain in the acute phase of the disease	195 (78%)	52 (22%)
Comorbidities	140 (56%)	99 (44%)
Physically active	89 (36%)	158 (64%)
Use of IMV	92 (37%)	155 (63%)
Gender	182 F (73%)	65 M (27%)
Family income	203 (C/D/E) (82%)	44 (A/B) (18%)
Pain intensity	111 (≥ 7) (45%)	136 (< 7) (55%)
Number of areas of pain	151 (less than 2) (61%)	96 (less than 2) (39%)

IMV = invasive mechanical ventilation; F = Female, M = Male; Family income A/B = from 10 to 20 minimum wages in 2022; C/D/E = from zero to 10 minimum wages in 2022.

DISCUSSION

The present findings indicate a high frequency rate of MP in patients hospitalized for COVID-19. Some differences were found in the models of the dependent variables. In the model in which the dependent variable is the occurrence of pain, it was observed that the variables gender, time of hospital discharge, presence of comorbidities, pain in the acute phase of COVID-19, family income and mechanical ventilatory support explain 31% of this outcome. In the model in which the dependent variable is pain intensity, the variables gender, time since hospital discharge, family income, length of stay, number of areas of pain and mechanical ventilatory support were found to explain 21% of the outcome.

The high frequency of pain found in the present study may be due to the form of recruitment. Individuals in social networks who are more engaged and with post-COVID-19 sequelae are probably more likely to participate in research. However, this percentage is in line with other studies that have studied this same outcome in patients with long COVID. Murat et al.[12] reported a prevalence of pain of 69.3%, and the study[3] reported 71.6%. In a study published by the present group of authors with a sample of 195 patients, 57% had MP after COVID-19. In addition, it was observed that length of stay in the intensive care unit and length of invasive mechanical ventilation were associated with pain intensity in patients with post-COVID pain[13]. This finding is in line with the present study, which identified mechanical ventilation support as a protective variable for pain intensity.

As for predictive variables, some studies have found similar associations between female gender and the presence of pain. The study[5] found a 26.4% difference between females and males for the presence of pain. Karaarslan et al.[14] showed that female patients were more likely to develop fatigue, myalgia and arthralgia at three and six months post-COVID.

To date, the income variable has not been widely explored in relation to post-COVID pain. Nevertheless, there are studies showing that low income is associated with chronic MP[15,16]. The study[17] reported from a Brazilian sample that patients with severe COVID-19 had a lower average income than patients with mild and moderate COVID-19. Another study in a Brazilian sample showed that patients with lower incomes had higher mortality rates[18]. The study[19] carried out with a sample of 939 individuals from Thailand found that low monthly income was associated with the development of long-term symptoms, including post-COVID pain. It is possible that income could be associated with other variables that have not been investigated, since people on low incomes are more prone to obesity, lower quality of life and difficulty in accessing healthcare in Brazil[20].

Interestingly, the absence of comorbidities was another factor associated with the presence of pain in this study and was an important variable in the multivariate analysis model. One possible hypothesis is that the pharmacological treatment used for some of the comorbidities present in the sample also interferes with the pain modulation system in these patients. Another possibility is that patients with these conditions received more intensive care during and after hospitalization[21-25].

A limitation of the study is that the lack of information on the degree of severity of comorbidities found makes it difficult to interpret the data. Because the data was collected by self-report, it's not possible to guarantee that the participants were formally diagnosed by a health professional. However, the study contributes to discussions about post-COVID-19 pain, as well as identifying associations that can be better explored in the future.

CONCLUSION

The frequency of pain was high in individuals who have been hospitalized for COVID-19 even after 12 months of discharge. Female individuals, with lower family income, who experienced pain during the acute phase of the COVID-19 infection, who required mechanical ventilatory support and were discharged from the hospital less than a year before are more likely to report late MP. Individuals who are female, who were discharged from the hospital less than a year before, with a lower family income, with a longer period of hospitalization and with more than one area of pain are more likely to have higher levels of pain intensity. Treatment measures should be implemented in this population to prevent or minimize pain associated with COVID-19.

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AUTHORS' CONTRIBUTIONS

Igor da Silva Bonfim: Statistical Analysis, Data Collection, Conceptualization, Resource Management, Project Management, Research, Methodology, Writing - Preparation of the Original, Writing - Review and Editing, Software, Supervision, Validation, Visualization
Leandro Alberto Calazans Nogueira: Methodology, Writing - Review and Editing
Ney Armando Meziat-Filho: Methodology, Writing - Review and Editing
Renato Santos de-Almeida: Statistical Analysis, Funding Acquisition, Data Collection, Conceptualization, Resource Management, Project Management, Research, Methodology, Writing - Preparation of the Original, Writing - Review and Editing, Software, Supervision, Validation, Visualization
Arthur de Sá Ferreira: Statistical Analysis, Writing - Review and Editing