Factors related to long COVID in the adult population of Brazil

Fatores relacionados à COVID longa na população adulta do Brasil

Factores relacionados con COVID de larga duración en la población adulta de Brasil

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Abstract

Objective: To analyze the factors related to long COVID in the adult population of Brazil. Methods: Analytical cross-sectional study, web-survey type, with quantitative approach. The sampling was non-probabilistic, of the intentional type, including 228 Brazilian adults who tested positive for COVID-19. Data collection took place through an online questionnaire. To verify the association between qualitative variables, the Chi-square test or Fisher's exact test was used and, in quantitative variables, the Mann-Whitney test was applied with significance of 0.05. Results: It was observed that there was an association of sociodemographic variables with long COVID. A higher mean age was observed among those who persisted symptoms (p=0.041). The family income of those with persistent symptoms was lower than that of individuals without persistence (p=0.005). The practice of physical activity was associated with the non-persistence of symptoms (p=0.024). Arterial hypertension was the most prevalent comorbidity in those with persistent symptoms (5.9%). In the clinical picture of COVID-19 associated with the persistence of symptoms, it is observed: chills (p-value=0.009), headache (p-value=0.0027), cough (p-value=0.000), anosmia (p-value=0.048), ageusia (p-value=0.013), dyspnea (p-value=0.000) and diarrhea (p-value=0.018). The most prevalent long COVID symptom was fatigue (62.89%). Conclusion: Age and income were associated with long COVID. Physical activity was associated with no persistence of symptoms.

Descriptors: COVID-19; Long Covid; Signs and Symptoms; Risk Factors; Brazil.

What is already known on this?
There are debates about the diagnostic criterion for long COVID. The pathophysiology may be associated with oxidative stress, continuous inflammatory and immunological response. Symptoms can be neurological and non-neurological.

What this study adds?
To identify which social groups are prone to long COVID and, consequently, the impact on health and socioeconomic services. It indicates that physical activity is associated with non-persistence of symptoms.
INTRODUCTION

The COVID-19 disease, caused by the SARS-CoV-2 virus, has been a major challenge facing humanity since December 2019 when it emerged in Wuhan, China. From there, it spread around the world and, in March 2020, the World Health Organization (WHO) declared a pandemic of this disease.\(^1\)\(^-\)\(^2\) Among the aspects inherent to the new coronavirus, long COVID stands out. It is a new disease caused by the SARS-CoV-2 virus, has been a major challenge facing humanity since December 2019 when it emerged in Wuhan, China. From there, it spread around the world and, in March 2020, the World Health Organization (WHO) declared a pandemic of this disease.\(^1\)\(^-\)\(^2\)

The most frequently reported symptoms are fatigue, shortness of breath and neuropsychological symptoms, which may be related to residual inflammation (convalescent phase), sequelae of organ damage, non-specific effects of hospitalization (prolonged ventilation) and social isolation.\(^3\)\(^-\)\(^4\)

It was found that adult patients with COVID-19 who underwent evaluation between 10-14 weeks after outpatient recovery had a high incidence for long COVID, about 50%. This included a high level of physical and psychological symptoms presented by patients negatively affecting quality of life.\(^5\)

A study with 3,762 respondents with long COVID from different countries between May and November 2020 showed that only 6.8% recovered after 28 days of illness (they had no more symptoms) and 93.2% still had symptoms at the time of completion of the research.\(^6\)

There is a need for multiprofessional care to these patients due to the complexity of their follow-up. It is necessary to identify the specific needs of each individual and plan a comprehensive and individualized care.\(^8\) Thus, identifying factors related to long COVID will help in the elaboration of appropriate interventions for the disease, in addition to contributing to the planning of resources and public health policies. It is believed that this type of study is necessary to contribute to procedural, technological and political advances in the management of this syndrome.

Given this, the present study aimed to analyze the factors related to long COVID in the adult population of Brazil.
METHODS

This is a cross-sectional and analytical web-survey study with a quantitative approach, following the guidelines of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist.²

The study sample involved 288 participants who answered the online questionnaire allocated in the Google form. Sampling was non-probabilistic, of the intentional type. Adults aged 18 years or older, Brazilians, residing in Brazil and who had tested positive for COVID-19 in the period from March 2020 to the time prior to data collection, in April 2022, were included in the sample. Consequently, those positive for COVID-19 still in the transmissibility phase at the time of collection were excluded, considering the questioning proposed in the form itself if the participants had COVID-19 for more than fourteen days, and those who provided information not consistent with the open questions.

Data collection was carried out through social media with the dissemination of the research and the link to collect responses. An online questionnaire structured with closed questions was used, except for the variables age and income in which the participant was asked the real values. The questionnaire was prepared by the authors, which was standardized and pre-tested.

The independent variables were those related to sociodemographic characterization (age, sex, marital status, region of residence, paid activity, monthly family income, receipt of social assistance benefit); lifestyle (practice of physical activity); pre-existing conditions; diagnosis for SARS-CoV-2; characterization of COVID-19; and persistent symptoms. The dependent variable was the persistence of symptoms.

The data were encoded by a data dictionary, and then submitted to statistical processing in the Statistical Package for the Social Science® (SPSS) software, version 20.0. In order to characterize the sample, descriptive statistics such as simple frequency, measures of central tendency and dispersion were performed. The Kolmogorov-Smirnov test was performed to verify the assumption of normality, and a non-normal distribution pattern was found. To verify the association between qualitative variables, the Chi-square test or Fisher's exact test was used and, in quantitative variables, the Mann-Whitney test was applied. For all analyses, a significance level of 0.05 was adopted. The results were discussed in the light of the theoretical framework on the subject.

The study followed all the guidelines of Resolution 466 of December 12, 2012 and was approved by the Research Ethics Committee of the Federal University of Piauí, with opinion number 5,043,434. Therefore, the Informed Consent Form was clear and available in the access link whenever the form was used.

RESULTS

In the study sample, represented by 288 Brazilian adults who tested positive for COVID-19, there was a female prevalence (71.87%), living in the urban area of the municipality (98.61%), with paid activity (79.86%) and partner (51.74%). The persistence of COVID-19 symptoms occurred in 97 participants (33.68%), among them, female sex (25.35%), domiciled in the urban area (32.64%), with paid activity (26.39%) and without partners (18.06%). They showed a statistically significant association with the persistence of symptoms age (p-value=0.041) and income (p-value =0.005) (Table 1).

Table 1. Sociodemographic and economic data related to the persistence of symptoms in Brazilian adults who tested positive for COVID-19. Teresina, Piauí, Brazil, 2022 (n=288).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Persistence of COVID-19 symptoms</th>
<th>TOTAL</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes N (%)</td>
<td>No N (%)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>73 (25.35)</td>
<td>134 (46.53)</td>
<td>207 (71.87)</td>
</tr>
<tr>
<td>Male</td>
<td>24 (8.33)</td>
<td>57 (19.79)</td>
<td>81 (28.13)</td>
</tr>
</tbody>
</table>
It was observed that the mean age of the participants (the youngest was 18 and the oldest 91 years old) with persistent symptoms for COVID-19 ($\chi$41.21 ±15.87) is higher than those in which it did not persist ($\chi$37.09±13.56). The family income of those in whom symptoms persisted ($\chi$6418.92 ± 5723.99) is lower than those in whom symptoms did not persist ($\chi$9463.92±513.50) (Table 1).

Table 2 shows that the physical activity variable (p-value=0.024) also establishes a statistically significant association with the persistence of COVID-19 symptoms, in which 42.71% of the participants who claimed to exercise some physical activity reported not having shown persistence symptoms for more than 14 days.

The variable comorbidities (p-value =0.033) presents a statistically significant relationship with the persistence of symptoms, with individuals who claimed not to have comorbidity prevailing (73.96%). When observing participants who had comorbidities, the majority (14.58%) had no persistence of symptoms. Regarding those who had persistent symptoms, the most prevalent comorbidity was hypertension (5.90%) and the least prevalent was obstructive pulmonary disease (1.39%) (Table 2).

**Table 2 - Association of the practice of physical activity and comorbidities with the persistence of COVID-19 symptoms. Teresina, Piauí, Brazil, 2022 (n=288).**

<table>
<thead>
<tr>
<th>Physical activity</th>
<th>Persistence of COVID-19 symptoms</th>
<th>Total N (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes N (%)</td>
<td>No N (%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>50 (17.36)</td>
<td>123 (42.71)</td>
<td>173 (60.07)</td>
</tr>
<tr>
<td>No</td>
<td>47 (16.32)</td>
<td>68 (23.61)</td>
<td>115 (39.93)</td>
</tr>
</tbody>
</table>
Comorbidities

<table>
<thead>
<tr>
<th>Variables</th>
<th>Persistence of COVID-19 symptoms</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes N (%)</td>
<td>No N (%)</td>
</tr>
<tr>
<td>Fever</td>
<td>61 (21.18)</td>
<td>95 (32.99)</td>
</tr>
<tr>
<td></td>
<td>36 (12.50)</td>
<td>96 (33.33)</td>
</tr>
<tr>
<td>Chills</td>
<td>45 (15.62)</td>
<td>58 (20.14)</td>
</tr>
<tr>
<td></td>
<td>52 (18.06)</td>
<td>133 (46.18)</td>
</tr>
<tr>
<td>Sore throat</td>
<td>51 (17.71)</td>
<td>89 (30.90)</td>
</tr>
<tr>
<td></td>
<td>46 (15.97)</td>
<td>102 (35.42)</td>
</tr>
<tr>
<td>Headache</td>
<td>71 (24.65)</td>
<td>114 (39.58)</td>
</tr>
<tr>
<td></td>
<td>26 (9.03)</td>
<td>77 (26.74)</td>
</tr>
<tr>
<td>Cough</td>
<td>63 (21.88)</td>
<td>82 (28.47)</td>
</tr>
<tr>
<td></td>
<td>34 (11.81)</td>
<td>109 (37.85)</td>
</tr>
</tbody>
</table>

Source: elaboration of the authors (2022).

*Chi-square test or Fisher’s exact test, with significance of 0.05

The clinical manifestations of COVID-19 associated with the persistence of symptoms were: fever (p-value=0.045), chills (p-value=0.009), headache (p-value=0.0027), cough (p-value=0.000), anosmia (p-value=0.048), ageusia (p-value=0.013), dyspnea (p-value=0.000) and diarrhea (p-value=0.018). It is observed that among the individuals who reported dyspnea and diarrhea, the majority (13.19%) had persistent symptoms. Those who had the persistence, it was observed that in the acute phase of the disease there was a prevalence of the following symptoms: headache (24.65%), cough (21.88%) and fever (21.18%); compared to those who had the least prevalence were diarrhea (13.19%), dyspnea (13.19%) and chills (15.62%) (Table 3).

Table 3. Association of the clinical picture with the persistence of COVID-19 symptoms. Teresina, Piauí, Brazil, 2022 (n=288).
Among the 97 participants who stated the persistence of symptoms, there was a higher prevalence of the following symptoms in long COVID, considering non-neuropsychiatric and neuropsychiatric symptoms: fatigue (62.89%; 61/97); headache (52.58%; 51/97); cough (50.52%; 49/97); anxiety (47.42%; 46/97); and muscle and/or joint pain (44.35%; 43/97).

DISCUSSION

In this research, it was observed that the frequency of the epidemiological profile of participants with long COVID is characterized by higher prevalences in females, in those who had paid activity and had no partners. In addition, there was an association with higher mean age and lower family income in relation to those who did not have long COVID.

Regarding the results presented, there is a lower rate of persistence of symptoms of long COVID when compared to other studies. In Fars Province (Iran), a survey of 4,681 participants identified persistent symptoms of COVID-19 in 2,915 patients (62.3%).\(^{(10)}\) In Italy (Milan), a sample of 301 eligible patients presented a frequency of 81% of persistence of at least one symptom after one year of the acute phase of the disease.\(^{(11)}\) However, a survey conducted in London with a small sample of 49 participants identified a frequency of 20% of symptoms after the acute phase of COVID-19 among participants.\(^{(12)}\) In the studies, regardless of the quantity of the sample, the prevalence of persistence of symptoms can be considered high.

In the sociodemographic characterization, the literature indicates that the female sex has a significant association (p<0.05) with the persistence of symptoms,\(^{(13-14)}\) which was not found in this research. The most persistent symptoms in women were dyspnea, fatigue, chest pain and palpitations. This analysis suggests the importance of assessing the implementation of assistance according to gender, aiming at early and individual treatments.\(^{(15)}\)

Regarding income, this study identified that individuals with lower incomes had a significant association with the prevalence of symptoms. It is noteworthy that during the COVID-19 pandemic, the isolation proposed by health agencies was not followed appropriately by all audiences. People in vulnerable economic conditions had low adherence to this practice in order to avoid loss of income, thus putting themselves at greater risk of contracting the disease.\(^{(16)}\)

In addition, it was observed in this study that the economically active population was the most impacted by the sequelae of COVID-19. It is known that with the beginning of the pandemic, Brazil entered...
The persistence of COVID-19 symptoms associated with age stands out, in which the increase in the age group is due to higher prevalences. In France, a survey conducted with 231 participants six months after the onset of the disease showed that the mean age was 53 years. In patients evaluated after 3 months of the disease had a mean age of 52 years. Higher prevalence of symptom persistence is also found in a population with a median age of 62 years. The older population was the age group that suffered the most when contracting the disease. The aging process that affects the immune system and weakens organic functions are factors that may be conditioned to complications from COVID-19 and the repercussion of symptoms.

A variable associated with the non-persistence of symptoms of COVID-19 was to practice physical activities. Physical exercises help in strengthening the immune system, stimulates anti-inflammatory responses, action of defense cells, improves the cardiovascular system, quality of life and physical conditioning. It is a practice that can be applied with varied audiences such as the older adults, people who have had or lived with cancer and overweight individuals.

Still on the practice of physical activity, a study with 30 participants between 25-45 years diagnosed with COVID-19, had the proposal to apply a series of aerobic exercises, which culminated in physical activity enabling the increase of leukocytes, lymphocytes and immunoglobulin after two weeks of intervention. The practice of physical activity is able to reduce the risk of severe COVID-19 (p=0.02). It is noteworthy that as a consequence of COVID-19, some individuals had their physical activities affected; research carried out with patients one year after the diagnosis of the disease, showed that after physical exertion there was a worsening of persistent symptoms.

In the context of pre-existing health conditions, a study in France showed that more than half of the patients had at least one comorbidity; others in Italy presented hypertension as the most prevalent comorbidity, which is associated with the need for follow-up after discharge of patients infected with Sars-CoV-2. In the analysis of this study, it appears that more than a third of the participants who had symptoms for a longer time had comorbidities, with hypertension being the most prevalent.

In addition to hypertension, other pre-existing diseases were found to follow for six months the post-discharge of patients who had COVID-19, they are diabetes and cardiovascular disease. A prospective observational study in India, with 1234 participants, which demonstrated comorbidities as a risk factor for the development of long COVID, had a higher prevalence in diabetes mellitus, followed by hypertension and hypothyroidism.

With regard to symptomatology, presenting five or more symptoms in the acute phase of COVID-19 is almost three times more likely to report persistent symptoms compared to other symptomatic patients, according to a cohort study from Zambia. This same study brings as most prevalent COVID-19 symptoms: cough, rhinorrhea, headache, fatigue and fever. In the report that is presented, it was possible to associate up to eight symptoms of COVID-19 with long COVID, and of these, headache, fever and cough prevailed among the participants.

Several studies report the persistence of physical and/or psychic symptoms for weeks. A significant proportion of patients hospitalized for COVID-19 reported a high proportion of symptoms associated with COVID-19 up to four months after hospital discharge, being the most prevalent symptoms in the acute phase, fever, cough and dyspnea; and the most prevalent symptoms in the persistence phase, cough, arthralgia and myalgia phase. However, the highlight of this study was fatigue, a symptom that directly affects the quality of life of the individual, which is also observed in other studies.

In addition, in this research, the prevalence of anxiety as a neuropsychiatric symptom is observed (47.42%). A two-way cohort study conducted in China showed that after six months of the acute phase, 23% (367/1617) of patients reported anxiety or depression. Also, according to an analysis with the objective of evaluating psychiatric symptoms in patients who had COVID-19 infection, 18.4% of patients were considered with probable anxiety, according to the Hospital Anxiety and Depression Scale (HADS).

As limitations of the study, one can list the choice of sampling method, which, due to the adoption of a non-probabilistic sampling, it was not possible to guarantee a proportion of representativeness among the participants by Brazilian region, although participants from all regions were included. Thus, it is not...
possible to statistically state that the findings behave equally. In addition, the study was not developed with the purpose of evaluating regional differences related to long COVID.

The sample size also prevented a better analysis of the prevalent symptoms. Thus, it is suggested, for future research, that the sample calculation be considered that expands the possibility of generalization at the national level, in addition to conducting investigations on Brazilian regions, in order to provide specific data with a more detailed approach to each territory.

Despite this gap, this study allows an important overview, by providing information that can contribute to the elaboration of public policies and protocols to care for the portion of the population affected by COVID-19 that presents the persistence of its symptoms. Finally, the research can serve as a parameter for further investigations.

CONCLUSION

When analyzing the factors related to long COVID in the adult population of Brazil, it was found that age and income were statistically associated with long COVID. Older individuals have a higher prevalence of persistence of symptoms as well as those with lower income. The practice of physical activity was associated with non-persistence of symptoms.

Thus, the study can help in the early identification of the public more susceptible to long COVID and, thus, contribute to the design of preventive measures and therapeutic guidelines. It will be possible to develop resource management strategies, protocols with diagnostic criteria and develop more robust studies that deal with the impact of the disease and, thus, improve the quality of life of society.

CONTRIBUTIONS

Contributed to the conception or design of the study/research: Araújo ADDG, Carvalho JM, Galiza FT, Silva FJJ, Vieira CP. Contributed to data collection: Araújo ADDG, Carvalho JM, Galiza FT, Silva FJJ, Vieira CP. Contributed to the analysis and/or interpretation of data: Araújo ADDG, Carvalho JM, Galiza FT, Silva FJJ, Vieira CP. Contributed to article writing or critical review: Araújo ADDG, Carvalho JM, Galiza FT, Silva FJJ, Vieira CP, Silva EF. Final approval of the version to be published Araújo ADDG, Carvalho JM, Galiza FT, Silva FJJ, Vieira CP, Silva EF.

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Factors related to long COVID in the adult...


