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ORIGINAL ARTICLE

Persistence of symptoms and lung function in mild cases of COVID-19 six months after infection: a cross-sectional study

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ABSTRACT

Objectives: To describe persistent symptoms and lung function in mild cases of COVID-19 six months after infection. **Methods:** Data collection was performed through a semi-structured questionnaire containing information on the participants' demographic and anthropometric data, the disease in the acute phase, and persistent symptoms six months after COVID-19 using spirometry and manovacuometry. **Results:** A total of 136 participants were evaluated, of whom 64% were male, with a mean age of 38.17 ± 14.08 years and a body mass index (BMI) of 29.71 ± 17.48 kg/m^2. The main persistent symptoms reported were dyspnea on exertion (39.7%), memory loss (38.2%), and anxiety (48.5%). Considering lung function, the participants reached 88.87 ± 17.20% of the predicted forced vital capacity (FVC), 86.03 ± 22.01% of the forced expiratory volume in one second (FEV1), and 62.71 ± 25.04% of peak expiratory flow (PEF). Upon manovacuometry, 97.41 ± 34.67% of the predicted inspiratory force (Pimax) and 66.86 ± 22.97% of the predicted expiratory force (Pemax) were observed. **Conclusions:** Six months after COVID-19 infection, a reduction in PEF and MEP was observed. Among the most commonly reported persistent symptoms were fatigue, tiredness with the slightest exertion, anxiety and depression, memory loss, and deficits in concentration.

Keywords: Post-acute COVID-19 Syndrome, Respiratory Function Tests, Dyspnea.

INTRODUCTION

The first cases of the novel coronavirus disease were reported in 2019 (COVID-19) in the city of Wuhan, China. This virus belongs to a family of viruses that cause infections in various systems of the human body. Despite its predilection for the respiratory tract, it also affects the liver, central nervous system, and enteric system in humans. Known for its previously caused outbreaks, the one that began in 2019 was triggered by a strain known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which has high transmissibility, leading to the widespread proliferation of the virus and the emergence of a global pandemic.[1,2]

Among COVID-19 cases, 80% may be asymptomatic or have mild symptoms. Approximately 20% of those infected will require hospitalization, 5% of whom may progress to the need for invasive mechanical ventilation. The disease affects several systems of the human body, leading to complications such as kidney failure, pneumonia, acute respiratory distress syndrome (ARDS), coagulopathies, thromboembolic events, bacterial infections, sepsis, and death.[3]

According to the literature, it is already known that even after recovery, some symptoms can persist, including dyspnea, weakness, and sleep changes, as well as physiological, cardiac, and radiological alterations. These symptoms can persist for months. Post-COVID syndrome is defined as the persistence of symptoms 12 weeks after infection, whether they developed during or after the infection period, and that are not explained by any other diagnosis.[4-6]

Patients who have developed the severe form of the disease are discharged with some degree of physical or emotional impairment, but symptom persistence has also affected those who had the mild form of COVID-19. A survey carried out in the UK with around 3,700 participants found that 92% of those interviewed did not require hospitalization, and, among these, 93% still had persistent symptoms. Among the participants were individuals who had been experiencing symptoms for more than 7 months post-infection.[7,8]

Considering the natural course of the disease, it is expected that some symptoms will persist after recovery. However, it is crucial to identify the most prevalent symptoms reported by the majority of COVID-19 cases, particularly individuals who have had mild cases. Given the virus's preference for the respiratory system, it is also important to investigate potential changes in lung function caused by COVID-19. Therefore, the aim of the present study was to describe persistent symptoms and lung function in individuals with mild cases of COVID-19 six months after infection.

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METHODS

This cross-sectional study was carried out at the Cardiorespiratory Physiotherapy Laboratory of the Federal University of Ceará, in the city of Fortaleza (CE), Brazil. Data collection took place from March to June 2022.

The study included individuals aged 18 and above with a confirmed diagnosis of COVID-19 six months prior, classified as mild according to the recommendations of the Ministry of Health (2020), i.e., those who did not require hospitalization and supplemental oxygen.[6] Participants with any communication or comprehension disorders that hindered their ability to conduct the interview and/or perform respiratory function tests, as well as those with disease reinfection during the data collection period, individuals engaged in regular physical activity, and those who had undergone post-COVID-19 rehabilitation, were excluded from the study (Figure 1).

Initially, the participants completed a semi-structured questionnaire that included information on age, sex, height, weight, drinking and/or smoking habits, the number of vaccinations, COVID-19 recurrence, and any previous lung or heart disease. The second part of the questionnaire focused on the symptoms that persisted after the disease, with the participants' self-reporting regarding the musculoskeletal, neurological, dermatological, cardiovascular, and respiratory systems, as well as their psycho-emotional condition. In addition, the participants provided information on the need for assistance with activities of daily living and the disruption of social, occupational, and leisure activities following COVID-19 infection.

Subsequently, a respiratory assessment was conducted, comprising an evaluation of respiratory muscle strength by manovacuometry and pulmonary function by spirometry. Both inspiratory and expiratory respiratory muscle strength were measured. In order to determine the value obtained for each individual, each maneuver was performed three times, with the highest result considered the best. If a learning effect was observed, the procedure could be repeated up to five times. The parameters for comparison were based on values suggested for the Brazilian population.[9,10]

Data on forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), and peak expiratory flow (PEF) were collected via spirometry. The test was carried out using the FVC maneuver, which was performed three times, with the best result being considered. Similar to manovacuometry, the maneuver could be repeated up to five times if the evaluator noticed a learning effect. The predicted values for each participant were determined using Pereira's formula (2007), which is validated for the Brazilian population.[11]

All data were structured and analyzed using IBM SPSS Statistics software, version 20. Descriptive analysis was performed on the aforementioned data, and the results were expressed as means and standard deviation, frequencies, and percentages.[12]

This study was approved by the Research Ethics Committee involving human beings of the Federal University of Ceará (CAAE No. 64780022.1.0000.5054), in accordance with Resolution 466/12 of the National Health Council (CNS).

RESULTS

Demographic, anthropometric, and clinical data related to the period of COVID-19 infection

The analysis included 135 individuals who had confirmed COVID-19 six months prior to the evaluation period. The sample had a mean age of 38.10 ± 14.12 years, a BMI of 29.72 ± 17.54 kg/m^2, and 63.7% were men. Among the participants, 29.6% had experienced COVID-19 more than once. Of those included in the study, 11% had a history of previous lung disease, including asthma, and 14% had a history of previous heart disease. In addition to the data characterizing the sample, Table 1 shows the symptoms reported during the acute COVID-19 infection, with the most prevalent being dyspnea, fever, cough, and body pain.

Respiratory muscle strength and lung function six months after COVID-19 infection

With regard to the maximum inspiratory pressure (MIP), the participants obtained a mean of 84.14 ± 49.37 cm/H_2O, representing 97.41 ± 34.67% of the predicted value. The mean maximum expiratory pressure (MEP) was 89.44 ± 29.49 cm/H_2O, and 66.86 ± 22.97% of the predicted level was achieved. The spirometry results showed a mean FVC of 3.40 ± 0.95 L, corresponding to 88.87 ± 17.20% of the predicted

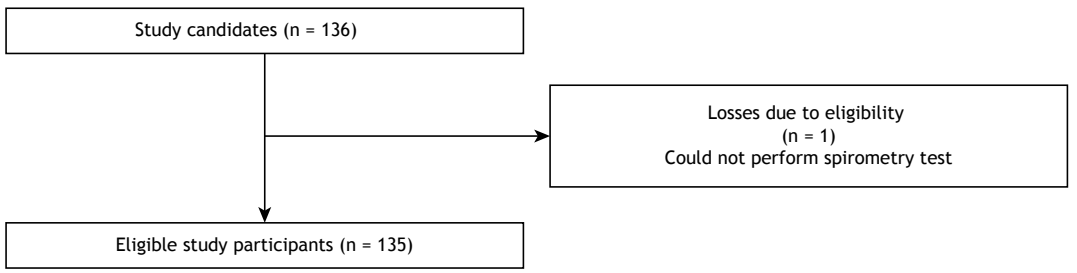

Figure 1. Flowchart of study sample selection.

Table 1. Demographic, anthropometric, and clinical data related to the period of COVID-19 infection. Fortaleza (CE), 2022.

Variables	N = 135
Age, years (mean ± SD)	38.10 ± 14.12
Body Mass Index (weight/height²) (BMI)	29.72 ± 17.54
Male sex, n (%)	86 (63.7)
Smoking, n (%)	10 (7.4)
Alcoholism, n (%)	55 (40.7)
Previous lung disease, n (%)	15 (11)
Previous heart disease, n (%)	19 (14)
COVID-19 more than once, n (%)	40 (29.6)
Symptoms related to the acute period of COVID-19 infection	
Fever, n (%)	79 (58.5)
Dyspnea, n (%)	100 (74.1)
Fatigue, n (%)	40 (29.6)
Sore throat, n (%)	38 (28.1)
Runny nose, n (%)	36 (26.7)
Cough, n (%)	74 (54.8)
Body pain, n (%)	72 (53.3)

value, and a mean expired volume of 2.70 ± 0.92 L, reaching 86.03 ± 22.01% of the predicted value. The mean PEF was 4.57 ± 2.25 L/min, corresponding to 62.71 ± 25.04% of the expected value. Table 2 shows the results of the respiratory assessment.

Persistent symptoms six months after COVID-19 infection

In the self-report, the most frequently persistent symptoms were respiratory, observed in 80% of the sample, with 40% of the participants reporting tiredness upon slight exertion. The second-highest prevalence of persistent symptoms was psychological, reported by 75.6% of the assessed participants, with anxiety present in 48.1% of the reports. Memory loss was described by 37.8% of the participants, contributing to the 74.8% who persisted with neurological symptoms, making it the third most affected system.

The persistence of symptoms in the integumentary system was described by 57.8% of the participants in our study, with hair loss being the most common symptom, present in 32.6% of the reports from this group. Regarding the musculoskeletal system, 53.3% of the participants reported persistent symptoms, with muscle fatigue/weakness mentioned in 23.7% of the reports, followed by myoarticular pain in 23%. Palpitation was reported by 22.2% of the participants, contributing to the 44.4% who reported persistent cardiovascular symptoms.

Among the study participants, 20% required assistance with instrumental activities of daily living after the acute phase of the disease, and 34.8% discontinued social, occupational, and/or leisure activities due to the persistent symptoms. The aforementioned data is shown in Table 3.

DISCUSSION

Our findings from the respiratory assessment indicate that the parameters of FVC, FEV1, and MIP were within the normal range, while MEP and PEF were lower than expected six months after COVID-19. The most commonly reported persistent symptoms following infection included tiredness upon slight exertion, anxiety, and memory loss. The participants also reported the need for assistance with basic and instrumental activities of daily living after recovering from the disease, and the absence of social, occupational, and/or leisure activities due to persistent symptoms.

The persistence of symptoms for more than 12 weeks is characterized as post-COVID-19 syndrome. A cohort study was conducted with participants who were not hospitalized due to COVID-19, and a follow-up was carried out one year after infection to assess the persistence of symptoms. Among the 336 participants, 156 (47%) reported symptom persistence. The cohort summarized the symptoms of the acute phase of COVID-19 infection, and the results were similar to those found herein, with the most prevalent symptoms in that phase being fatigue, fever, body pain, cough, runny nose, and dyspnea.[12]

In analyzing respiratory muscle strength, it was observed that the MEP reached a predicted level, implying a functional diagnosis of expiratory muscle weakness. This reduction may be attributed to the loss of muscle strength caused by the inflammatory process of COVID-19 and the persistence of symptoms, particularly muscle fatigue, a symptom reported in our sample. This finding may also explain the reduction in PEF, which is influenced by expiratory muscle strength.[13-15]

As for the MIP, our sample performed better than expected. Another finding that may be related to the above is the overweight status according to the BMI. Previous studies have reported a positive relationship between body weight and MIP, relating the isometric length of different muscle groups to weight – a phenomenon known as the 'muscularity effect'. In this

Table 2. Respiratory muscle strength and lung function of study participants six months after COVID-19 infection. Fortaleza (CE), 2022.

Respiratory muscle strength	Achieved (mean ± SD)	Expected % (mean ± SD)
MIP (cm/H_2O)	84.14 ± 49.37	97.41 ± 34.67
MEP (cm/H_2O)	89.44 ± 29.49	66.86 ± 22.97
Lung Function	**Achieved (mean ± SD)**	**Expected % (mean ± SD)**
FVC (L)	3.40 ± 0.95	88.87 ± 17.20
FEV1 (L)	2.70 ± 0.92	86.03 ± 22.01
PEF (L/min)	4.57 ± 2.25	62.71 ± 25.04

SD: Standard Deviation; MIP: Maximum Inspiratory Pressure; MEP: Maximum Expiratory Pressure; FVC: Forced Vital Capacity; FEV1: Forced Expiratory Volume in the first second; PEF: Peak Expiratory Flow.

Table 3. Persistent COVID-19 symptoms six months after infection. Fortaleza (CE), 2022.

Persistent symptoms after the COVID-19 infection period	
Cardiovascular	60 (44.4)
Palpitation	30 (22.2)
Chest pain	2 (1.5)
SAH	5 (3.7)
Palpitation and SAH	23 (17.0)
Respiratory	108 (80)
Minor fatigue	54 (40)
Fatigue on medium exertion	26 (19.3)
Tiredness upon heavy exertion	23 (17)
Persistent cough	3 (2.2)
Dermatological	78 (57.8)
Hair loss	44 (32.6)
Dermatitis	15 (11.1)
Hair loss and dermatitis	18 (13.3)
Musculoskeletal	72 (53.3)
Myoarticular pain	31 (23)
Muscle fatigue/weakness	32 (23.7)
Pain and fatigue and muscle weakness	8 (5.9)
Neurological	101 (74.8)
Memory loss	51 (37.8)
Concentration deficit	7 (5.2)
Memory loss and concentration deficit	40 (29.6)
Paresthesia of limbs	3 (2.2)
Psychological	102 (75.6)
Anxiety	65 (48.1)
Depression	9 (6.7)
Anxiety and depression	22 (16.3)
Irritability or stress	7 (5.2)
Activity and participation after COVID-19 infection	
Required help with self-care activities after COVID-19	27 (20)
Stopped performing activities (work, sports, and/or leisure) after COVID-19	47 (34.8)

SAH: Systemic Arterial Hypertension (Brazilian Guidelines on Systemic Arterial Hypertension).

case, the positive relationship is attributed to a greater amount of lean mass in the respiratory muscles.[16,17]

A Brazilian study carried out with individuals who did not require hospitalization due to COVID-19, and which also assessed pulmonary function, yielded results that were consistent with our findings. No pulmonary function disorders were observed when analyzing FVC and FEV1. One explanation for this may be that these were mild cases of COVID-19 that did not require support with positive pressure and supplementary oxygen. Despite the normal FVC and FEV1 findings, it is noteworthy that this did not exempt the patients from experiencing persistent symptoms, primarily respiratory, which can lead to functional impairment, affecting activity and participation.[18]

Patients who have not been hospitalized for COVID-19 exhibit persistent symptoms similar to those who have required hospitalization due to the disease. Cohort studies carried out with patients who required hospitalization during the acute phase and were evaluated 12 weeks after infection yielded similar results to the present study regarding the most prevalent

persistent symptoms reported by patients who did not require hospitalization, assessed 24 weeks after the disease: fatigue, dyspnea, and pain. Follow-up is crucial to ascertain the impact of these symptoms on non-hospitalized patients, enabling the provision of adequate care for those in need.[18,19]

A cohort comprising 958 individuals who were not hospitalized for COVID-19 investigated persistent symptoms between the sixth and eighth month after infection, reporting body pain in 13% of participants and hair loss in 5%, results that corroborate our findings. The mechanisms of the post-acute conditions of COVID-19 are not fully understood, but body pain and hair loss may be influenced by the excessive release of pro-inflammatory cytokines during the infectious period. Both symptoms may be impacted by the direct effects of the viral condition, social isolation, and the psychosocial state during post-COVID-19 recovery.[4,14]

Another cohort study conducted by Titze-de-Almeida et al. (2022), with patients who were not hospitalized, also assessed psycho-emotional symptoms, finding a prevalence of anxiety in 36.9% of the sample, corroborating our findings, in which psychological symptoms such as anxiety and depression were among the main persistent symptoms. Proportional values regarding symptoms related to difficulty concentrating and memory loss, as well as their persistence for more than five months after infection, were also found in both studies. Mental disorders have a multifactorial origin and can be triggered by environmental factors, such as the COVID-19 pandemic. Contracting the disease and the persistence of symptoms lead to a state of chronic stress that can impact basic cognitive processing, favoring deficits in memory and concentration.[20-22]

In our study, the participants faced limitations in performing activities of daily living after COVID-19 infection; i.e., some required assistance with these activities following infection. During self-reporting, the participants often expressed feeling the impact of symptoms, but did not consider it important to seek rehabilitation because they perceived such limitations as normal post-COVID-19. Some degree of physical limitation and the impact on the mental health of individuals after the course of an illness are expected, especially in those who already had some underlying condition. However, the potential consequences of these physical and psycho-emotional symptoms, such as an increased risk of mortality from clinical diseases, should not be overlooked.[23,24]

The literature is still limited regarding the follow-up of patients who have not required hospitalization due to COVID-19 infection but continue to experience persistent symptoms affecting their functionality, and consequently, their activity and participation. A strong point of this study is the significant number of mild cases of the disease in the sample, with respiratory muscle strength and lung function assessments conducted 6 months after recovery from the infection. Additionally, the symptoms were reported taking into account the perceptions of each individual. To the best of our knowledge, this is the second Brazilian study to evaluate lung function in patients who had COVID-19 and were not hospitalized, and the first to measure respiratory muscle strength in this population.

As a limitation, we acknowledge the absence of laboratory tests to explore possible correlations between biomarkers, persistent symptoms, and lung function.

After six months of recovery from COVID-19, individuals who did not require hospitalization due to the disease exhibited altered lung function, with reduced PEF, and respiratory muscle weakness, with reduced MEP.

Respiratory symptoms were the most persistent, particularly fatigue on exertion. In addition to respiratory symptoms, there were frequent reports of anxiety, depression, difficulty concentrating, and memory deficits, even six months after the disease. It is important to carry out studies on the impact of the persistence of these symptoms to understand their potential limitations in aspects of daily life, functionality, and quality of life.

AUTHOR CONTRIBUTIONS

BGS: data collection, writing, and descriptive analysis; ICS: writing and translation; RFC: data collection and writing; ERNR: data collection and writing; TRR: data collection and writing; JGSA: data collection and writing; EDBP: writing; NGC: data collection, writing, descriptive analysis, and translation.

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