Post-COVID-19 syndrome and obesity: findings in a sample referred for pulmonary rehabilitation

Síndrome pós-COVID-19 e obesidade: achados em uma amostra encaminhada para reabilitação pulmonar

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Abstract

Introduction: Post-COVID-19 condition refers to persistent symptoms following SARS-CoV-2 infection. **Objective:** Investigate the profile of patients with post-COVID-19 condition, classified as obese and non-obese according to body mass index (BMI), and determine whether obese individuals present with worse clinical and functional status. **Methods:** A cross-sectional observational study with adults of both sexes who have a history of hospitalization for SARS-CoV-2 infection and post-COVID-19 condition, referred for pulmonary rehabilitation between August 2020 and October 2022. The data were obtained from physiotherapy assessments. Participants were classified as obese or non-obese, and evaluated in terms of their health history, length of hospital stay, dyspnea during activities of daily living (ADLs), and respiratory muscle strength. **Results:** A total of 54 individuals participated in the study, mostly women, with an average age of 55 years. The majority were obese (75.9%), sedentary, white, and worked in retail or civil construction. There was no association between obesity and the variables hypertension ($p = 0.057$), diabetes ($p = 0.113$), dyspnea ($p = 0.368$), or fatigue ($p = 0.750$). Length of hospital stay ($p = 0.592$), days in the intensive care unit ($p = 0.478$), days on invasive mechanical ventilation (0.075), modified Medical Research Council scale - mMRC ($p = 0.633$), and maximum inspiratory ($p = 0.625$) and expiratory pressure ($p = 0.967$) were not influenced by obesity. **Conclusion:** Although participants with obesity were more likely to require pulmonary rehabilitation due to post-COVID-19 condition, they did not exhibit worse clinical and functional status on assessment of health history, length of hospital stay, dyspnea in activities of daily living, and respiratory muscle strength.

Keywords: Physiotherapy. COVID-19. SARS-CoV-2. Long COVID. Obesity.

Resumo

Introdução: *A síndrome pós-COVID-19 refere-se aos sintomas persistentes após infecção pelo SARS-CoV-2.* ***Objetivo:*** *Investigar o perfil dos pacientes com síndrome pós-COVID-19, classificados conforme o índice de massa corporal (IMC) em obesos e não obesos, e verificar se indivíduos obesos apresentam pior condição clínica e funcional.* ***Métodos:*** *Trata-se de um estudo observacional transversal com adultos de ambos os sexos, com histórico de internação pelo SARS-CoV-2 e síndrome pós-COVID-19, encaminhados para reabilitação pulmonar entre agosto/2020 e outubro/2022. Os dados se originaram de avaliação fisioterapêutica. Os participantes foram classificados em obesos e não obesos, avaliados quanto ao histórico de saúde, período de internação, dispneia às atividades de vida diária e força muscular respiratória.* ***Resultados:*** *Participaram do estudo 54 sujeitos, sobretudo mulheres, com média de idade acima de 55 anos, majoritariamente obesos (75,9%), sedentários, da raça branca, profissionais do comércio e construção civil. Não identificou-se associação significativa entre ser obeso e as variáveis hipertensão (p = 0,057), diabetes (p = 0,113), dispneia (p = 0,368) e fadiga (p = 0,750). As variáveis dias de internamento (p = 0,592), dias de unidade de terapia intensiva (p = 0,478), dias de ventilação mecânica invasiva (0,075), escala do Medical Research Council modificada (p = 0,633), pressão inspiratória máxima (p = 0,625) e pressão expiratória máxima (p = 0,967) não foram influenciadas pela obesidade.* ***Conclusão:*** *Os participantes obesos foram mais propensos a necessitar de reabilitação pulmonar devido à síndrome pós-COVID-19. Entretanto, não apresentaram piores condições clínicas e funcionais na avaliação quanto ao histórico de saúde, período de internação hospitalar, dispneia às atividades de vida diária e força muscular respiratória.*

Palavras-chave: *Fisioterapia. COVID-19. SARS-CoV-2. COVID longa. Obesidade.*

Introduction

After acute SARS-CoV-2 infection, many patients report persistent symptoms, a condition known as post-COVID-19 condition or long COVID. This persistent condition is estimated to be present in one of every ten cases of the disease.[1] Comorbidities such as obesity are among the many risk factors for developing post-COVID-19 condition.[1]

Despite being preventable, obesity, a chronic non-communicable disease characterized by excess body fat, is a global epidemic. Data indicate that global obesity in adults has more than doubled since 1990[2] and the global prevalence of overweight and obesity is forecast to exceed 57% by 2030.[3]

Obesity is a known risk factor for several other diseases, including cardiovascular and thromboembolic diseases, diabetes, infections, acute lung injury, and dyslipidemia, and an important risk factor for the worsening of COVID-19.[4-6]

Research indicates that individuals with obesity had a worse prognosis following COVID-19 infection, with a greater risk of hospitalization, intensive care unit (ICU) admission, need for ventilatory support, morbidity, and mortlaity.[7-9]

In Latin America, when compared to normal weight individuals, people with obesity and COVID-19 were 113 and 74% more likely to require hospital and intensive care, respectively, and had a 48% greater chance of dying.[3]

As such, obesity combines risk factors for both chronic and infectious diseases, such as COVID-19. This highlights two major global health concerns, namely the growing prevalence of individuals with obesity and the increased risk of severe outcomes in this population when infected with SARS-CoV-2.[10] Moreover, the multisystemic disturbances present in obesity (hormonal, metabolic, and a persistent pro-inflammatory state) may be associated with post-COVID-19 condition because the body remains in an inflamed state.[11]

As such, this study aimed to investigate the profile of patients with post-COVID-19 condition, classified as obese and non-obese according to body mass index (BMI), and determine whether obese individuals exhibit worse clinical and functional status.

Methods

This is a cross-sectional observational study with a convenience sample of adults with post-COVID-19 condition referred for pulmonary rehabilitation between August 2020 and October 2022.

After discharged, adults who were hospitalized at the Hospital de Clínicas Complex of the Federal University of Paraná (CHC-UFPR), with a confirmed clinical

diagnosis of COVID-19, continued regular follow-up at a specific outpatient clinic for patients with post-COVID-19 condition. Those who experienced persistent physical and respiratory complaints, with no other probable causes, and who were clinically diagnosed with post-COVID-19 condition by a physician, were referred for pulmonary rehabilitation. It is important to note that all referrals were made at least four weeks after the onset of acute infection, meaning that the study was conducted at the CHC-UFPR physiotherapy outpatient clinic. At their first physiotherapy visit, patients were informed of the study and invited to participate in the initial assessment. Prior to assessment, they were advised of the study procedures and objectives, and that participation was voluntary. The research was approved by the institutional Research Ethics Committee (CAAE: 47158821.6.0000.0096, protocol number 4.805.035) and all participants provided written informed consent.

Inclusion criteria were a history of hospitalization with a positive test, age > 18 years, both sexes, and a a medical referral for physiotherapy follow-up. Individuals who lacked complete information about their hospital stay or were unable to perform respiratory muscle strength training (manuvacuometry) were excluded.

Thus, the necessary data were obtained from physiotherapy assessments. Data were collected using a form developed by the researchers, including sociodemographic and anthropometric information, medical history (lifestyle habits, comorbidities, persistent com-plaints), relevant details about hospitalization for COVID-19, degree of dyspnea during activities of daily living (ADLs), and respiratory muscle assessment. All the evaluations were conducted on the same day during participants' first visit to the physiotherapy clinic.

All the participants were evaluated by one of the researchers from the study, previously trained for this purpose. Although some of the items on the form can be self-assessed, all the data were obtained and recorded by one of the researchers to prevent potential bias due to participants' varying education levels. Information related to hospitalization for COVID-19 was retrieved from the patient's medical records to ensure an accurate account of the hospital stay.

According to World Health Organization (WHO) recommendations, individuals were classified as physically inactive prior to COVID-19 infection when they did not engage in at least 150 minutes of moderate-intensity or 75 minutes of vigorous aerobic activity per week.[12] To that end, the following questions were asked: "Did you engage in physical activity before COVID-19 infection?". If so: "What activity?"; "How often and for how long?".

Participants were classified into two groups based on their BMI, calculated using weight and height, with BMI > 30 kg/m^2 considered obese and the remainder non-obese. Subdivision into different degrees of obesity also followed the BMI criteria, with BMI between 30 and 34.9 kg/m^2 categorized as class I, 35 to 39.9 kg/m^2 class II, and > 40 kg/m^2 class III.[13] Weight and height were measured on a Welmy® digital electronic balance equipped with a stadiometer, and participants wearing light clothing.

Dyspnea during ADLs was evaluated using the modified Medical Research Council (mMRC) scale, with participants rating their degree of dyspnea from 0 to 4, as follows: 0 = breathlessness only on strenuous exercise; 1 = breathlessness when walking quickly on level ground or up a gentle slope; 2 = walking slower than others of the same age on level ground due to breathlessness or stopping for breath when walking at own pace; 3 = short of breath after walking a few minutes or 90 to 120 meters on level ground; 4 = too breathless to leave the house or breathless when dressing or undressing.[14] This scale was applied only once by reading and explaining each item and the response options to participants, who then selected the degree of dyspnea that best reflected their current condition.

Respiratory muscle strength was evaluated using a handheld manometer to obtain maximal inspiratory (MIP) and expiratory pressure (MEP), which represent the greatest pressure that can be generated against a closed system. To measure MIP, participants first exhaled to reach their residual volume, then immediately sealed their lips around the mouthpiece and performed a maximal inspiratory effort against the occluded mouthpiece, whereas for MEP they initially inhaled until total lung capacity, followed by a maximal expiratory effort.[15] Individuals were given detailed instructions on the procedures and allowed to ask questions before the test. The test was performed using a handheld analog manometer (Murenas®, range -150 +150 cm H_2O). Participants performed three to five maneuvers with no air leakage, each sustained for two seconds, with a 1-minute rest between attempts. At least two reproducible maneuvers (values differing by no more than 10%) were required and the highest value obtained was recorded.

Statistical analysis

The data were tabulated and analyzed in Jamovi statistical software (version 2.3.21). Results are presented as mean and standard deviation, absolute and relative frequency, or median and interquartile range, depending on the nature of the variable. Data normality was assessed using the Shapiro-Wilk test, intergroup diffeences by the nonparametric Mann-Whitney test, based on variable assumptions and non-normal distribution, and categorical variables with the chi-square test. Significance was set at $p < 0.05$ for all the tests.[16]

Results

A total of 87 individuals visited the physiotherapy center for post-COVID-19 pulmonary rehabilitation, 58 of whom agreed to take part in the study. Four were excluded, leaving a final study sample of 54 participants (Figure 1).

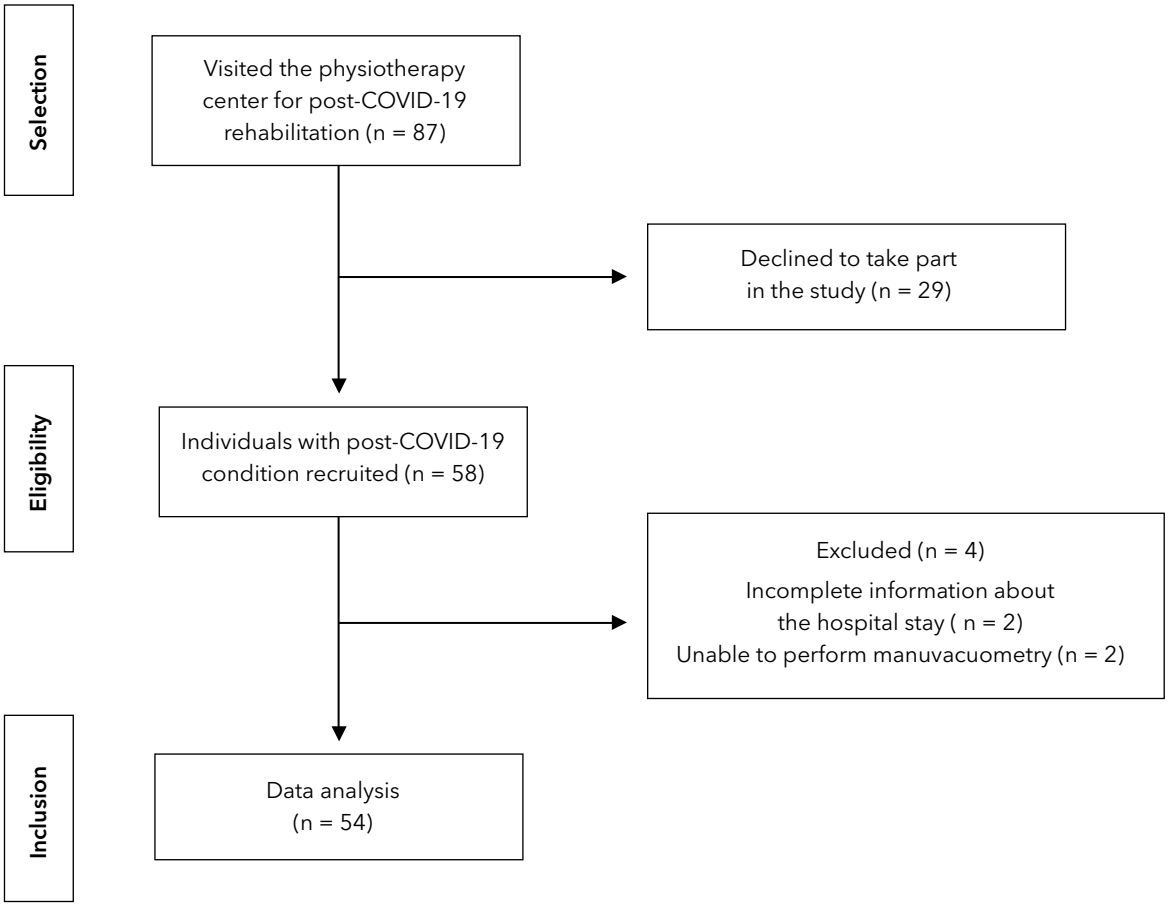

Figure 1 - Flowchart of data collection.

The sample consisted of 54 participants with post-COVID-19 condition, primarily women, with an average age of 55 years, mostly white, obese, and sedentary, from the retail and civil construction sectors. The length of hospital stay for SARS-CoV-2 infection varied from three to 66 days, ICU stay from zero to 57 days, and invasive mechanical ventilation (IMV) duration from 0 to 49 days. Of those investigated, 37 (68.51%) required ICU care and 26 (48.14%) IMV. The remaining epidemiological data for the sample are described in Table 1.

Table 1 - General data on the study participants (n = 54)

General Data	n (%)
Age (years), mean + SD	55.3 + 10.5
Women	29 (53.7)
Men	25 (46.3)
Body mass index (kg/m^2), mean + SD	32.6 + 4.54
Race	
White	50 (92.6)
Brown	2 (3.7)
Black	1 (1.8)
Indigenous	1 (1.8)
Profession (Sector)	
Retail	9 (16.7)
Civil construction	9 (16.7)
Homemaker	8 (14.8)
Service provider	8 (14.8)
Retired	6 (11.1)
Health	5 (9.2)
Cleaning and maintenance	4 (7.4)
Administration and technology	3 (5.5)
Agriculture	1 (1.8)
Transport	1 (1.8)
Hospitalization, median (IQR)	
Hospital stay in days	20.5 (12.3 – 26.8)
Days in intensive care unit	9 (0 – 19.8)
IMV duration in days	0 (0 – 14.5)
Comorbidities	
Obesity	41 (75.9)
Systemic hypertension (SH)	29 (53.7)
SH in obese individuals	25 (46.3)
SH in non-obese individuals	4 (7.4)
Diabetes	13 (24.1)
Diabetes in obese individuals	12 (22.2)
Diabetes in non-obese individuals	1 (1.9)
No comorbidities	8 (14.8)
Complaints	
Dyspnea	36 (66.7)
Dyspnea in obese individuals	26 (48.2)
Dyspnea in non-obese individuals	10 (18.5)
Fatigue	27 (50.0)
Fatigue in obese individuals	20 (37.0)
Fatigue in non-obese individuals	7 (13.0)
Sedentary before COVID-19 infection	32 (59.3)
Obese and sedentary before C19i	22 (40.8)
Non-obese and sedentary before C19i	10 (18.5)

Note: SD = standard deviation; IMV = invasive mechanical ventilation; QR = interquartile range; C19i = COVID-19 infection.

Most participants referred for pulmonary rehabilitation exhibited some degree of obesity, and fewer than one quarter had a BMI lower than 30 kg/m^2, considered non-obese. Obesity was also more prevalent among women, with class II obesity only observed in female participants, as shown in Table 2.

Table 2 - Frequency and classification of obesity among participants (n = 54) according to body mass index (BMI)

BMI - Based classification	n (%)
Obese	41 (75.9)
Women	25 (46.3)
Men	16 (29.6)
Class I obesity	26 (48.1)
Women	16 (29.6)
Men	10 (18.5)
Class II obesity	12 (22.2)
Women	6 (11.1)
Men	6 (11.1)
Class III obesity	3 (5.6)
Women	3 (5.6)
Men	0 (0.0)
Non-obese	13 (24.1)
Women	4 (7.4)
Men	9 (16.7)

The frequency of hypertension and diabetes and persistent dyspnea and fatigue in the study sample were presented in Table 1. However, the chi-square test showed no significant association between being obese and the variables hypertension ($x^2 = 3.62$; $p = 0.057$), diabetes ($x^2 = 2.51$; $p = 0.113$), dyspnea ($x^2 = 0.811$; $p = 0.368$) and fatigue ($x^2 = 0.101$; $p = 0.750$).

In intergroup comparison (obese and non-obese), although the median for length of hospital stay, days in the ICU and IMV duration was greater among obese individuals, there was no statistically significant difference. Additionally, no statistically significant inter-group difference was observed between degree of dyspnea during ADLs (mMRC) and respiratory muscle strength (MIP and MEP) (Table 3).

In the obese group, 18 (43.9%) individuals showed a reduction in MIP and 12 (29.3%) in MEP, while these variables declined in 4 (30.8%) and 4 (30.8%) of their non-obese counterparts, respectively.

Table 3 - Comparison between obese and non-obese individuals according to the study variables (n = 54)

Variable	Group (n)	Median	25th percentile	75th percentile	p*
Hospital stay in days	Obese (41)	21	10	32	0.592
	Non-Obese (13)	17	14	24	
Days in the ICU	Obese (41)	10	0	21	0.478
	Non-Obese (13)	8	1	10	
IMV duration in days	Obese (41)	8	0	15	0.075
	Non-Obese (13)	0	0	5	
mMRC	Obese (41)	2	1	3	0.633
	Non-Obese (13)	2	2	2	
MIP	Obese (41)	80	60	110	0.625
	Non-Obese (13)	85	80	92	
MEP	Obese (41)	90	60	112	0.967
	Non-Obese (13)	85	72	100	

Note: Data presented as median, 1st and 3rd percentile. ICU = intensive care unit; IMV = invasive mechanical ventilation; mMRC = modified Medical Research Council dyspnea scale; MIP = maximal inspiratory pressure; MEP = maximal inspiratory pressure. *Mann-Whitney test.

Discussion

The present study demonstrated that individuals referred for post-COVID-19 rehabilitation due to persistent physical and/or respiratory symptoms were predominantly women. Indeed, other studies suggest that recovery from long COVID is slower in women,[17] which could explain the smaller number of men in the population investigated. A possible explanation found in the literature is that women are at greater risk than men of persistent impairment of pulmonary diffusion capacity following SARS-CoV-2 infection.[18]

The sample analyzed indicated that even younger adults may be susceptible to prolonged symptoms. This finding differs from other studies in which only advanced age was associated with prolonged symptoms after SARS-CoV-2 infection.[18,19] After analysis and given the large number of participants in the present study who required ICU care and IMV, it is believed that in this case disease severity may have been a key factor in long-term symptoms even in middle-aged adults.

Sedentary behavior is known to be directly related to severe cases of COVID-19 and obesity.[3] Along with poor nutrition, the absence of physical exercise leads to insulin resistance, which can compromise the immune response.[3] In the present study, most participants were sedentary prior to contracting the virus.

With regard to obesity, evidence indicates that the chronic proinflammatory state of this condition overlaps and exacerbates the underlying pathogenic mechanisms of COVID-19 through the following factors: dysregulated immune responses, chronic inflammation and oxidative stress, exacerbation of the cytokine storm and cellular hypoxia, endothelial dysfunction, hypercoagulability, overactivation of the renin-angiotensin-aldosterone system, increased expression of the angiotensin-converting enzyme 2 (ACE2) receptor in adipose tissue, and associated cardiometabolic comorbidities.[20-22]

The heightened chronic inflammatory state in individuals with obesity following SARS-CoV-2 infection may be a key factor in explaining the persistence of long-term symptoms, given the potential involvement of multiple systems and tissues. A study with 88 obese and 176 non-obese patients approximately 7 months after hospital discharge found that obesity was associated with a larger number of long-term post-COVID-19 symptoms.[23] These findings support those of our study, in which over 75% of the sample consisted of obese participants. This suggests that individuals with obesity experience greater long-term post-COVID-19 impairment and more frequently require physiotherapy rehabilitation. It should also be noted that, as previously indicated, obesity was more prevalent

among female participants, demonstrating that obese women may be at greater risk of prolonged physical symptoms.

The combination of obesity, hypertension and diabetes is commonly associated with more severe SARS-CoV-2 infection.[24-26] Although the findings indicate that over 50% of the sample was also hypertensive and more than 24% diabetic, the presence of hypertension or diabetes alongside obesity was not statistically significant when compared to the non-obese group.

In chronic long COVID patients, dyspnea and fatigue are listed as the most common persistent complaints.[27-29] This pattern is reinforced by our findings, whereby persistent dyspnea and fatigue were also frequently reported by both obese and non-obese participants.

Different investigations have found that patients with comorbidities, particularly obesity, exhibited more severe hospital-related outcomes, such as longer hospital and ICU stays and extended mechanical ventilation, as well as more critical clinical outcomes.[30-32]

However, in the present study, the data that came closest to statistical significance in intergroup comparison were those regarding the duration of IVM. This may be due to the sample size and the fact that most obese participants were classified in class I. As such, additional studies with larger samples and comparisons across higher obesity classes are needed.

Obesity may also compromise respiratory function through mechanisms such as increased mechanical demand on the respiratory system, ventilation-perfusion mismatch, respiratory muscle fatigue, and reduced ventilatory capacity and respiratory muscle strength.[7,33]

In the analysis of perceived dyspnea during ADLs, the median score on the mMRC scale was 2, indicating that participants reported walking slower than others of the same age due to breathlessness or stopping for breath when walking at their own pace on level ground, with no intergroup difference. Respiratory muscle strength, assessed via MIP and MEP, showed no association with anthropometric measures, as observed in other studies.[34]

Fortunately, following vaccination, the number of patients referred for post-COVID-19 pulmonary rehabilitation declined significantly, which limited the sample size. As such, all the findings should be critically analyzed and interpreted with care, particularly due to the small sample size.

Finally, the correlation between two major health problems, namely COVID-19 and obesity, clearly indicates that global health policies must acknowledge scientific evidence and, beyond simply mitigating the spread of SARS-CoV-2, invest in interventions capable of reducing the alarming obesity rates to protect the population from the aggravation of multiple health conditions, including infectious diseases.

Conclusion

Although participants with obesity were more likely to require pulmonary rehabilitation due to post-COVID-19 syndrome, they did not exhibit worse clinical and functional status on assessment of health history, length of hospital stay, dyspnea in activities of daily living, and respiratory muscle strength.

The post-pandemic period will undoubtedly continue to place significant demands on health systems, particularly in regard to long-term manifestations. In this respect, the perspectives of different healthcare professionals within multidisciplinary teams are essential in establishing strong correlations and addressing outstanding concerns.

Authors' contributions

All the authors were responsible for the study's conception, design, data analysis, and interpretation. ADBL, ILA and AIBT drafted and revised the manuscript, and HRAB, RHSG and AAM critically reviewed its content. All the authors approved the final version.

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