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RESEARCH ARTICLE

Clinical manifestations in POST-COVID-19 patients

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Abstract

Background: COVID-19 has significantly impacted the lives of individuals globally, as symptoms can occur in both severe patients requiring intensive care and in patients with mild to moderate symptoms. **Objective:** To evaluate the clinical manifestations after COVID-19 in individuals with and without comorbidities prior to infection by the new coronavirus. **Methods:** This was a cross-sectional observational study with a descriptive and analytical approach. One hundred and thirty-seven participants diagnosed with COVID-19 (3 to 12 months post-infection) of both sexes, aged between 18 and 59 years, underwent a clinical and functional evaluation to identify the late impacts of COVID-19, also known as "long COVID". **Results:** The majority were female (n=103/75.2%) and brown (n=86/62.8%). The most common comorbidities were hypertension (n=19/13.9%) and obesity (n=19/13.9%). The main post-infection symptoms were body pain (n=102/74.5%), cognitive impairment (n=53/38.7%), muscle weakness (n=59/43.1%) and hair loss (n=71/51.8%). There were significant differences between the groups without comorbidities (WCMG) and with comorbidities group (CMG) in mobility ($p=0.03$); labor productivity - presenteeism ($p<0.05$), total impairment at work ($p=0.02$) and impairment in activities of daily living ($p<0.05$); physical functionality ($p=0.01$) and subjective cognitive function ($p<0.05$). In the pulmonary function test, most participants had normal lung function (71.5%). **Conclusion:** Individuals with previous comorbidities have greater impairments in quality of life (mobility domain), rates of work impairment, and physical and cognitive functionality, when compared to patients without previous comorbidities.

Keywords: COVID-19; multimorbidity; quality of life.

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BACKGROUND

COVID-19 significantly impacted the lives of individuals globally, drawing attention for its reach and the speed with which it spread. The confirmation of a new type of virus (SARS-CoV-2) and its subsequent characterization as a global health crisis affected all sectors of society, especially health and economy[1]. Although the new vaccines have drastically reduced new infections and prevented the deaths of thousands of people[2], and the World Health Organization (WHO) has declared the end of the public health emergency, COVID-19 continues to cause fatal infections even in developed countries[3]. In this context, new variants, vaccine updates, and rehabilitation of post-COVID-19 sequelae have been the current focus of public policies to combat SARS-CoV-2[4].

The presence of symptoms even after infection with SARS-CoV-2 can occur both in severe patients, requiring intensive therapy[5], and in patients with mild to moderate symptoms[6]. Among the persistent symptoms, or sequelae, dysfunctions in multiple organs can occur, with both psychosocial and physical impairments[7]. Post-COVID-19 syndrome is characterized by a diverse range of symptoms that affect various organ systems and generally include fatigue, shortness of breath, post-exertional malaise, mental confusion, headaches, nausea, vomiting, anxiety, depression, skin rash, joint pain, and palpitations[8]. Although some studies have investigated the post-COVID-19 repercussions in hospitalized and non-hospitalized patients, there is still little information on these changes in patients with and without pre-existing comorbidities, as well as long periods of post-infection symptoms[9].

Previous studies have shown that the presence of comorbidities is a risk factor for non-recovery post-COVID-19[10]. Exposure to SARS-CoV-2 in individuals with comorbidities, such as diabetes and chronic venous disease, is associated with greater harm to the lungs, heart, kidneys, and liver. The impairment of multiple organs, associated with pre-existing comorbidities, increases the risks of mortality from COVID-19, which demonstrates the vital need for preventive measures and protection for these patients[11]. Although these studies have investigated the persistence of post-COVID-19 symptoms, few have assessed symptoms after six months of infection. Moreover, few studies have compared post-COVID-19 symptoms between patients with and without pre-existing comorbidities after a long post-infection period. In this sense, the evaluation of post-COVID-19 clinical manifestations can provide important information to guide more effective strategies for the prevention and rehabilitation of conditions related to the new coronavirus infection. The objective of the study was to compare the differences in clinical and functional manifestations between individuals with and without pre-existing comorbidities in the post-COVID-19 period.

METHODS

Study design

This is a cross-sectional observational study, with a descriptive and analytical approach, conducted from January 2022 to May 2023. Individuals diagnosed with COVID-19 were recruited through social media and printed dissemination in public and private health services in the city of Parnaíba (PI). The minimum sample size was estimated at 86 subjects; however, considering losses due to non-respondents, the estimated sample was 100 individuals. The study was approved by the Research Ethics Committee of the Federal University of Delta do Parnaíba (UFDPar) under nº 5.393.151. All participants signed the Informed Consent Form (TCLE).

Eligibility criteria

Individuals of both sexes, aged between 18 and 59 years, who tested positive for COVID-19 and were registered through the "investigation forms of SG suspected of coronavirus disease 2019 - (B34.2)" by the Epidemiological Surveillance sector of the Municipal Government of Parnaíba (PI) and who were between 3 to 12 months post-COVID-19.

The exclusion criteria were (1) Psychiatric, neurological, or affective-emotional disorders that prevented responding to the sociodemographic questionnaire and clinical assessments; (2) History of pneumonia, flu accompanied by fever, body aches, or diarrhea and anosmia less than 15 days before the assessment; (3) Diagnosis of comorbidity post SARS-COV-2 infection or any treatment for post COVID-19 symptoms.

Evaluations

After agreeing to and signing the ICF, the participants answered the semi-structured questionnaire containing sociodemographic and clinical-functional data. The sociodemographic questions contained data on sex, age, education, self-reported race/color, marital status, and employment. The clinical assessment included data on: physical activity, smoking, alcohol consumption, previous comorbidities, post-infection symptoms, sequelae, need for hospitalization, COVID-19 immunization, number of doses, presence of reinfection by SARS-COV-2, pharmacological and non-pharmacological treatment for pain complaints, as well as the duration, affected region, and factors that alleviate and worsen the pain. Finally, adapted and validated instruments for Brazilian Portuguese were used to characterize the following variables: (1) quality of life, (2) respiratory symptoms, (3) pulmonary capacity, (4) physical function, (5) cognitive function, and (6) overall health perception.

Primary outcome

Quality of life

Quality of life was assessed using the EQ-5D-3L questionnaire, which encompasses five health domains: mobility, self-care, usual activities, pain/discomfort, anxiety/depression. Each dimension has three associated levels of severity, corresponding to no problems (level 1), some problems (level 2), and extreme problems (level 3) experienced or felt by the individual[12].

Secondary outcomes

Productivity and work-related impairment

The impact of the post-COVID-19 period on productivity and work impairment was assessed through the productivity and work activity commitment questionnaire (WACQ). This instrument measures the effect of different health conditions on work productivity, generating scores for absenteeism, presenteeism, absenteeism plus presenteeism, and off-work activity commitment. The questions in the questionnaire refer to the effect of your health problems on your ability to work and perform normal activities; for example, "Are you currently employed (receiving a salary)?", "In the past seven days, how many hours have you missed from work due to your health problems?", "In the past seven days, how many hours have you missed from work for any other reason, such as vacations, holidays, or participating in this study?" among others.

Health problems refer to any physical or emotional issue or symptom. In the questionnaire, the blank spaces are filled in or a number is circled according to the indicated response[13].

Respiratory Symptoms

For the evaluation of respiratory symptoms, the Modified British Medical Research Council (MMRC) questionnaire was used, which assesses the dyspnea index in patients' daily activities. The MMRC consists of only five items, with the patient choosing the item that corresponds to how much dyspnea limits their daily life activities (ADL's). The patient reports their subjective degree of dyspnea by choosing a value between 1 and 5, where (1) "only suffers from shortness of breath during intense exercise"; (2) "suffers from shortness of breath when walking briskly or climbing a slight slope"; (3) "walks more slowly than people of the same age due to shortness of breath or has to stop to breathe even when walking slowly"; (4) "stops to breathe after walking less than 100 meters or after a few minutes"; and (5) "feels so short of breath that they no longer leave the house."[14].

Pulmonary Capacity

Lung capacity was assessed by the Spirometry test. (SP80B, CONTEC MEDICAL SYSTEMS, CHINA). Spirometry is the measurement of voluntary lung volumes and flows. It can be performed during slow breathing or during forced expiratory maneuvers. The test allows for the diagnosis and quantification of ventilatory disorders[5]. All breathing was done through the mouth using a disposable mouthpiece, and the nose remained occluded with a nasal clip during the blowing moment. At the verbal command of the examiner, the participant inhaled all the air through the mouth to the maximum inspiratory capacity and then exhaled all the air in the lungs explosively. All participants received prior familiarization instructions and performed three blows.

Functional Capacity

Physical function was measured through three assessments: (1) isometric grip strength using a dynamometer, (2) post-COVID-19 functionality using the Post-COVID-19 Functional Status Scale (PCFS), and (3) the sitting-rising test (SRT). The assessment of handgrip strength through dynamometry (EMG System/SAS1000V8, Brazil) followed the recommendations of the American Society of Hand Therapists[15]. The participant must remain seated, with shoulders relaxed, elbow flexed at 90°, and forearm in a neutral position[16]. Three attempts were made and the average value of the three grips was used.

The PCFS Scale has six gradation possibilities, where 0: no functional limitation, 1: very mild functional limitations, 2: mild functional limitations, 3: moderate functional limitations, 4: severe functional limitations, 5: Death. It can be applied at hospital discharge and also in outpatient follow-up to assess and monitor functional status[17]. The Sitting-rising test can be performed in practically any location, requiring only 3 or 4 square meters of free space and a flat, non-slippery surface. The instruction given by the evaluator to the evaluated is very simple and straightforward: "Try to sit and stand up without losing your balance, using the fewest supports possible." In the execution of the procedure, the individual stands with their back to a thin mat or carpet placed on the floor immediately behind them and tries to sit down slowly, without using their hands for support and without losing balance.

The measure of the test consists of quantifying how many supports (hands and/or knees or, additionally, hands on the knees or legs) the individual uses to sit down and get up from the ground. Independent scores are assigned for the acts of sitting and standing.

The maximum score is five for each of the two actions, losing half a point for any noticeable imbalance and one point for each support used[18].

Cognitive Function

To assess subjective and objective cognitive function, the Cognitive Failures Questionnaire (CFQ) and the Trail Making Test-Part B (TMT-B) were administered, respectively. The CFQ consists of 25 questions designed to represent cognitive errors in daily life. These questions reflect different aspects of cognitive functioning, including attention, perception, memory, impulsivity, and language. Each question is answered on a frequency scale, ranging from never (0 points) to very frequently (4 points). The total scale ranges from 0 to 100 points. Performance on this scale has been related to affective symptoms, dissociative states, learning difficulties, stress and anxiety, among other aspects of psychopathology and psychological functioning[19].

The TMT-B consists of drawing the alternating path between the numbers 1 to 13 and letters A to M, that is, 1-A, 2-B, 3-C, and so on. Before the execution of the task, a reduced "training sheet" is presented to the subject, and the instructions mentioned above are given. The time is timed until the subject completes the task, and the score is measured by the total seconds used to perform the task[20].

Global Perception

The post-COVID-19 global health perception was assessed using the global perceived effect scale, which evaluates the level of recovery perception of the patient by comparing the onset of symptoms with the last few days. É uma escala numérica de 11 pontos variando de -5 a +5, sendo - 5: extremamente pior; zero: sem modificação; e +5: completamente recuperado, sendo que a maior pontuação representa maior recuperação[21].

Statistical Analysis

Descriptive statistics were used to describe the demographic variables and clinical characteristics of the participants. The Chi-square and Fisher's Exact tests were used to examine the relationships between the groups without and with comorbidities prior to infection with the new coronavirus and the demographic and clinical categorical variables. Mann-Whitney tests were used to verify differences between the groups. The non-parametric Spearman rank correlation (Spearman's rho [r]) was used to evaluate the magnitude of the relationship between the time (months) post-COVID-19 and the variables of physical and cognitive functionality. A significance level of $p < 0.05$ was considered, and the analyses were conducted using IBM SPSS v.20 software for Windows.

RESULTS

One hundred and thirty-seven participants responded to the questionnaire and were included in the study. On average, the participants were evaluated 5.6 (sd = 2.0) months after the diagnosis of COVID-19. The majority were female (n=103/75.2%), brown (n=86/62.8%), employed (n=98/71.5%), single (n=64/46.7%), and had completed high school as their highest level of education (n=48/35.0%). Few participants reported hospitalization during the pandemic (n=3/2.2%). However, 24.8% (n=34) reported reinfection with the new coronavirus. Regarding vaccination, 88.3% (n=121) received a booster dose. The general characteristics of the participants are described in Table 1.

Table 1. General characteristics of the participants

Variables n (%)	All (n=137)	WCMG (n=88)	CMG (n=49)	p SC vs CC
Sex				
Female	103 (75,2)	71 (80,7)	32 (65,3)	**0,04***
Male	34 (24,8)	17 (19,3)	17 (34,7)	
Age (years)	38,0 (27,0-47,5)	36,5 (24,0-45,0)	40,0 (30,5-48,0)	0,05
Race				
White	38 (27,7)	26 (29,5)	12 (24,5)	0,64
Brown	86 (62,8)	55 (62,5)	31 (63,3)	
Black	13 (9,5)	7 (8,0)	6 (12,2)	
Yellow	-----	-----	-----	
Marital Status				
Single	64 (46,7)	44 (50,0)	20 (40,8)	0,41
Married	58 (42,3)	36 (40,9)	22 (44,9)	
Divorced	14 (10,2)	8 (9,1)	6 (12,2)	
Widower	1 (0,7)	-----	1 (2,0)	
Ocupation				
Employed	98 (71,5)	58 (65,9)	40 (81,6)	0,18
Estudent	22 (16,1)	18 (20,5)	4 (8,2)	
From home	5 (3,6)	3 (3,4)	2 (4,1)	
Unemployed	12 (8,8)	9 (10,2)	3 (6,1)	
Education				
Incomplete Elementary School	4 (2,9)	1 (1,1)	3 (6,1)	0,19
Complete Elementary	2 (1,5)	-----	2 (4,1)	
Incomplete High School	2 (1,5)	2 (2,3)	-----	
High School Graduate	48 (35,0)	33 (37,5)	15 (30,6)	
Superior	46 (33,6)	30 (34,1)	16 (32,5)	
Post-Graduation	35 (25,5)	22 (25,0)	13 (26,5)	
Smoking				
Yes	8 (5,8)	3 (3,4)	5 (10,2)	0,13
No	129 (94,2)	85 (96,6)	44 (89,8)	
Alcohol Consumption				
Yes	50 (36,5)	27 (30,7)	23 (46,9)	0,06
No	87 (63,5)	61 (69,3)	26 (53,1)	
Physical Activity				
Pre-infection				
No Physical Activity	53 (38,7)	33 (37,5)	20 (40,8)	0,84
< 150 min/week	18 (13,1)	11 (12,5)	7 (14,3)	
> 150min/week	66 (43,8)	44 (50,0)	22 (44,9)	
Physical Activity				
Post-infection				

No Physical Activity	59 (43,1)	39 (44,3)	20 (40,8)	
< 150 min/week	18 (13,1)	10 (11,4)	8 (16,3)	0,71
> 150min/week	60 (43,8)	39 (44,3)	21 (42,9)	

Note: WCMG: Without comorbidities prior to infection with the new coronavirus; CMG: With pre-existing comorbidities. Categorical data expressed in absolute frequency (n) and relative frequency (%). Continuous data expressed in terms of median and interquartile range (25-75). The association between the participants' characteristics and the WCMG and CMG groups was examined using Pearson's Chi-square* and Fisher's Exact** tests. Differences between the WCMG and CMG groups were examined using the Mann-Whitney U test*** ($p < 0.05$).

In Table 2, it can be observed that the diagnosis of hypertension and obesity was present in 13.9% (n=19), while diabetes Mellitus was only in 5.8% (n=8), chronic heart disease in 4% (n=4), and chronic kidney disease in 0.7% (n=1). Among the mentioned clinical characteristics, 88% (n=100) of the participants did not have other associated comorbidities. The most frequent persistent symptoms were body pain, muscle weakness, hair loss, cognitive deficit, and pulmonary dysfunction (Table 3).

Table 2. Clinical characteristics of the participants

Variables n (%)	All (n=137)	Without Comorbidities (n=88)	With Comorbidities (n=49)
Arterial Hypertension			
Yes	19 (13,9)	-----	19 (38,8)
No	118 (86,1)	88 (100)	30 (61,2)
Diabetes Mellitus			
Yes	8 (5,8)	-----	8 (16,3)
No	94,2 (129)	88 (100)	41 (83,7)
Cancer			
Yes	-----	-----	-----
No	137 (100)	88 (100)	49 (100)
Obesity			
Yes	19 (13,9)	-----	19 (38,8)
No	118 (86,1)	88 (100)	30 (61,2)
Chronic Heart Disease			
Yes	4 (2,9)	-----	4 (8,2)
No	133 (97,1)	88 (100)	45 (91,8)
Chronic Kidney Disease			
Yes	1 (0,7)	-----	1 (2,0)
No	136 (99,3)	88 (100)	48 (98,0)
Others			
Yes	10 (7,3)	-----	10 (20,4)
No	127 (92,7)	88 (100)	39 (79,6)

Note: Categorical data expressed in absolute frequency (n) and relative frequency (%).

Table 3. Main symptoms after infection with the new coronavirus

Variables n (%)	All (n=137)	WCMG (n=88)	CMG (n=49)	*P* SC vs CC

Pain				
Yes	102 (74,5)	63 (71,6)	39 (79,6)	0,30
No	35 (25,5)	25 (28,4)	10 (20,4)	
Cognitive Deficit				
Yes	53 (38,7)	33 (37,5)	20 (40,8)	0,70
No	84 (61,3)	55 (62,5)	29 (59,2)	
Pulmonary Dysfunction				
Yes	52 (38,0)	36 (40,9)	16 (32,7)	0,34
No	85 (62,0)	52 (59,1)	33 (67,3)	
Muscle Weakness				
Yes	59 (43,1)	36 (40,9)	23 (46,9)	0,49
No	78 (56,9)	52 (59,1)	26 (53,1)	
Dysphagia				
Yes	12 (8,8)	5 (5,7)	7 (14,3)	0,11
No	125 (91,2)	83 (94,3)	42 (85,7)	
Hair Loss				
Yes	71 (51,8)	43 (48,9)	28 (57,1)	0,35
No	66 (48,2)	45 (51,1)	21 (42,9)	
Alteration of Smell				
Yes	12 (8,8)	8 (9,1)	4 (8,2)	0,99
No	125 (91,2)	80 (90,9)	45 (91,8)	
Alteration of Taste				
Yes	9 (6,6)	4 (4,5)	5 (10,2)	0,28
No	128 (93,4)	84 (95,5)	44 (89,8)	

Note: Categorical data expressed in absolute (n) and relative (%) frequency. The association between the participants' characteristics and the SC and CC groups was examined using the Pearson Chi-square* and Fisher's Exact** tests ($p < 0.05$).

In the assessment of quality of life, there was a significant association between the mobility domain and the presence of pre-existing comorbidities (p=0.03), indicating that people with comorbidities may be more likely to have some mobility limitations than those without comorbidities (table 4). The impairments in work productivity and activities of daily living (ADL's) resulting from their health condition were described in Table 5, where a significant difference was observed between the groups for presenteeism ($p<0.05$), total work impairment (p=0.02), and impairment in ADL's ($p<0.05$). These differences indicate that participants with pre-existing comorbidities may have a reduction in workload or daily activities due to their health problems.

Table 4. Quality of life post-COVID-19

EQ-5D-3L	n (%)

Domains		
Mobility	Level 1	116 (84,7)
	Level 2	21 (15,3)
	Level 3	-----
Care Personal	Level 1	129 (94,2)
	Level 2	7 (5,1)
	Level 3	1 (0,7)
Activities Habituals	Level 1	93 (67,9)
	Level 2	41 (29,9)
	Level 3	3 (2,2)
Pain/ Discomfort	Level 1	38 (27,7)
	Level 2	81 (59,1)
	Level 3	18 (13,1)
Anxiety/ Depression	Level 1	46 (33,6)
	Level 2	67 (48,9)
	Level 3	24 (17,5)

Note: EQ-5D-3L: Euroqol quality of life questionnaire with five dimensions and three levels. Level 1: No problems; Level 2: Some problems; Level 3: Severe problems.

Table 5. Losses in work productivity and daily living activities

Escale (0-100%)	All (n=137)	Whithout Comorbidities (n=88)	Whith Comorbidities (n=49)	*Z*	*P* WCMG vs CMG
Absenteeism	0,0 (0,0-0,0)	0,0 (0,0-0,0)	0,0 (0,0-0,0)	-0,013	0,99
Presenteeism	0,0 (0,0-40,0)	0,0 (0,0-37,5)	20,0 (0,0-50,0)	-2,887	**<0,05**
Total harm to work	0,0 (0,0-38,0)	0,0 (0,0-19,7)	0,0 (0,0-50,0)	-2,294	**0,02**
Harm to ADLs	0,0 (0,0-50,0)	0,0 (0,0-37,5)	40,0 (0,0-60,0)	-2,934	**<0,05**

Note: WCMG: Without comorbidities prior to infection with the new coronavirus; CMG: With pre-existing comorbidities. ADL's: Activities of Daily Living. WPAI-GH Questionnaire: Work Productivity and Activity Impairment – General Health. High scores indicate prolonged sick leave or disability and decreased productivity. Values expressed in terms of median and interquartile range (25-75). Differences between the WCMG and CMG groups were examined using the Mann-Whitney U test ($p < 0.05$).

Table 6 shows the results of the tests conducted to assess functional capacity, perception of post-COVID-19 recovery, and cognitive function. There were significant differences in the sitting tests (p=0.01) and in subjective cognitive function (p<0.05). When the groups were compared, participants in the comorbidity group (CC) had more difficulty sitting on the floor without support and their subjective cognitive function was impaired, showing changes in attention, perception, memory, impulsivity, and language.

Table 6. Post-COVID-19 functional and cognitive capacity

Variables	All (n=137)	Whithout Comorbidities (n=88)	Whith Comorbidities (n=49)	*Z*	*P* SC vs CC
Handgrip Strength (Kgf)	12,9 (9,3-18,7)	12,5 (8,7-17,0)	13,3 (9,9-21,3)	-1,004	0,32
Sitting Test (0-5)	4,5 (4,5-5,0)	4,5 (4,5-5,0)	4,5 (4,0-5,0)	-2,443	**0,01**
Lift Test (0-5)	4,0 (3,5-4,5)	4,5 (3,6-4,5)	4,0 (3,0-4,5)	-1,892	0,06
Functional Status (0-5)	1,0 (1,0-2,0)	1,0 (1,0-2,0)	1,0 (0,0-2,0)	-0,210	0,83
Subjective Cognitive Function (0-100)	42,0 (31,0-56,0)	39,0 (30,2-53,0)	47,0 (39,0-63,0)	-2,774	**<0,05**
Objective Cognitive Function (seconds)	116,0 (80,5-179,0)	112,0 (81,2-162,7)	132,0 (77,0-201,0)	-0,786	0,43
Global Perception of Recovery (-5 to +5)	0,0 (-2,0-4,0)	0,5 (-2,0-3,7)	-2,0 (-2,0-4,0)	-0,604	0,55

Notes: WCMG: Without comorbidities prior to infection with the new coronavirus; CMGC: With prior comorbidities. Low scores indicate worse levels of functionality for the sit-to-stand tests and functional status. High scores for dyspnea indicate worse dyspnea. High scores indicate worsening of subjective and objective cognitive function. Values expressed in terms of median and interquartile range (25-75). Differences between the SC and CC groups were examined using the Mann-Whitney U test ($p < 0.05$).

The assessment of the participants' pulmonary function conducted through spirometry showed that the majority of participants had a negative predictive value (71.5%), that is, a normal pulmonary function test. Only 28.5% of the evaluated participants showed changes in pulmonary function, with 16.1% showing mild restrictive changes and only 12.4% showing other pulmonary changes. There were no significant differences in pulmonary capacity between the groups (Table 7).

Finally, the exploratory analysis, described in Table 8, demonstrated significant correlations between the variable work impairment (presenteeism) and post-infection time (p=0.04) in the group without comorbidities. In the group with pre-existing comorbidities, there was a significant correlation between the variables lift tests (p=0.04), subjective cognitive function (p=0.02), dyspnea (p=0.02), and the post-infection period.

Table 7. Post-COVID-19 lung capacity

Espirometry	All (n=137)	Whithout Comorbidities (n=88)	Whith Comorbidities (n=49)	*P* SC vs CC
Negative Predictive Value	98 (71,5)	60 (68,2)	38 (77,6)	0,51
Mild Obstructive and Mild Restrictive	9 (6,6)	7 (8,0)	2 (4,1)	
Mild Obstructive and Severe Restrictive	-----	-----	-----	
Moderate Obstructive and Moderate Restrictive	1 (0,7)	1 (1,1)	-----	
Moderate Obstructive and Severe Restrictive	1 (0,7)	1 (1,1)	-----	
Moderately Severe Obstructive and Severe Restrictive	-----	-----	-----	
Severe Obstructive and Mild Restrictive	1 (1,1)	1 (1,1)	-----	
Moderate Obstructive and Mild Restrictive	-----	-----	-----	
Mild Restrictive	22 (16,1)	13 (14,8)	9 (18,4)	
Mild Obstructive and Moderate Restrictive	5 (3,6)	5 (5,7)	-----	

Note: SC: Without comorbidities prior to infection with the new coronavirus; CC: With pre-existing comorbidities. Categorical data expressed in absolute (n) and relative (%) frequency. The association between the participants' characteristics and the SC and CC groups was examined using Fisher's Exact Test ($p < 0.05$).

Regarding participants without comorbidities, the longer the post-infection period, the fewer the work-related impairments in the workplace. In contrast, among participants with pre-existing comorbidities prior to COVID-19, the longer the time post-infection, the more difficulty they had performing physical functions, such as getting up from the ground without support (lower test scores); greater changes in cognitive functioning, including attention, perception, memory, impulsivity, and language; and they also exhibited more severe dyspnea symptoms. In the other variables, no significant correlations were observed.

Table 8. Correlation between Functionality, Work Impairment, and Time Post-Infection

Without Comorbidities	Physical and Cognitive Functionality		
	R	*P*	95% IC
Muscle Strength	-0,05	0,65	-0,26 a 0,17
Sitting Test	0,02	0,88	-0,20 a 0,23
Standing Test	-0,04	0,70	-0,25 a 0,18
Subjective Cognitive Function	0,07	0,48	-0,14 a 0,28
Objective Cognitive Function	-0,17	0,10	-0,38 a 0,04
Dyspnea	0,12	0,28	-0,10 a 0,32
	Workplace Injury		
Absenteeism	-0,15	0,17	-0,35 a 0,07
Presenteeism	-0,22	**0,04**	-0,41 a -0,00
Total Work Impairment	-0,18	0,08	-0,38 a 0,03
Impairment in ADLs	-0,07	0,50	-0,28 a 0,14
With Comorbites	Physical and Cognitive Functionality		
	R	*P*	95% IC

Muscle Strength	0,02	0,87	-0,27 a 0,31
Sitting Test	-0,21	0,14	-0,47 a 0,08
Standing Test	-0,30	**0,04**	-0,54 a -0,01
Subjective Cognitive Function	0,32	**0,02**	0,04 a 0,56
Objective Cognitive Function	0,05	0,71	-0,24 a 0,34
Dyspnea	0,34	**0,02**	0,06 a 0,58
	Workplace Injury		
Absenteeism	0,01	0,92	-0,27 a 0,30
Presenteeism	0,04	0,80	-0,25 a 0,32
Total Work Impairment	0,00	0,98	-0,28 a 0,29
Impairment in ADLs	-0,11	0,47	-0,38 a 0,19

Note: The magnitude of the relationship between the variables was tested using the Spearman correlation test ($p < 0.05$).

DISCUSSION

The main findings of this study demonstrate significant clinical and functional impairments months post-COVID-19, regardless of the presence of pre-existing comorbidities. Moreover, individuals with pre-existing comorbidities exhibited greater impairments in quality of life (mobility domain), work indices, daily living activities, physical and cognitive functionality. Moreover, there was a higher prevalence of women regardless of the presence of previous comorbidities, with hypertension and obesity being the most prevalent conditions. Consistent with our findings, Saad et al. (2021) in their longitudinal study with 102 confirmed cases of COVID-19 in home isolation, reported in Berlin (Germany), that 37% of patients who presented with more than one symptom up to 60 days after COVID-19 reported comorbidities, with obesity being the most common. In addition, the female sex was also the most prevalent[22].

In the study by Subramanian et al. (2022), 53.8% were overweight or obese. The baseline BMI in the overweight or obese range was also associated with an increased risk of persistent symptoms, with those having a BMI greater than 30 kg/m² experiencing a relative 10% increase in the risk of reporting long COVID symptoms compared to those with a BMI of 18.5–25 kg/m² [23].

The most frequent persistent symptoms post-infection in the present study were body pain, cognitive deficit, muscle weakness, and hair loss. In longitudinal prospective studies, these symptoms were also found by other researchers, in addition to fatigue, physical slowness, impaired sleep quality, joint edema, dyspnea, memory loss, and slowed thinking[24]. The authors also identified that the number of persistent symptoms was higher in those with pre-existing comorbidities.

In the present study, participants with pre-existing comorbidities showed impairments in mobility; work productivity and daily living activities; physical functionality, especially in the act of sitting, and in subjective cognitive function, such as memory, perception, and language. Consistent with the symptoms found in the present study, more than half of the post-COVID-19 patients (65%) included in the registry of the study by Chudzik et al. (2022), reported the persistence of symptoms up to three months after the resolution of the disease, with the most common symptoms being chronic fatigue, cough,

headache, and a set of neurological symptoms known as mental confusion[25]. According to Chudzik et al. (2022), the severity of the disease, the duration of symptoms, and female sex increased the risk of long COVID. With obesity being an independent risk factor for persistent chronic fatigue.

Many authors have raised hypotheses of mechanistic processes to explain the association between certain risk factors, including female sex. For example, it has been suggested that hormones may play a role in perpetuating the hyperinflammatory state of the acute phase of COVID-19, even after recovery. Furthermore, a stronger production of IgG antibodies was reported in female individuals during the acute phase, which could contribute to the perpetuation of the disease manifestations[26].

Crema et al. (2022), reported in their study that all participants showed impairments in quality of life, with the most affected domains being physical aspects, functional capacity, and social aspects[27]. Taking into consideration all the symptoms that persisted post-COVID-19 reported by the participants of the present study, it is believed that the quality of life, especially impaired mobility, is due to symptoms of body pain, cognitive deficit, and muscle weakness, which directly affect the participants' daily living activities.

In the assessment of cognitive function, participants with comorbidities showed changes in attention, perception, memory, impulsivity, and language. When cognitive impairments were compared with the time post-COVID-19, it was observed that the longer the time post-infection, the greater the difficulty in performing subjective cognitive functions. Guesser et al. (2022), demonstrated that out of 11 articles included in their review, 10 showed alterations in the cognitive function of patients who had COVID-19, including dysfunctions related to attention, concentration, memory, language, executive functions, and processing speed[28]. Raman 2021 conducted a case-control study with 58 adults, where it was observed that the COVID-19 group showed cognitive changes related to executive and visuospatial domains compared to the controls[29]. Theoretically, SARS-CoV-2 can infiltrate neurons, interrupting the production of proteins and mitochondria, leading to brain degeneration months or years after the infection[30]. The virus infects cells through the ACE2 receptor, which is mainly found in the cerebral cortex, amygdala, and brainstem, potentially explaining the deficits in cognitive functions observed in research, such as attention, which is regulated by the brainstem[31]. Taken together, current evidence indicates that COVID-19, regardless of the presence of comorbidities, significantly affects cognitive function. Moreover, the presence of pre-existing comorbidity can result in greater functional impairments, both physical and cognitive.

In the present study, the results of the spirometry tests did not show statistical differences between the groups. This result may be related to the fact that only three participants (2.2%) reported hospitalization during the pandemic, meaning they developed mild symptoms of the disease with minimal pulmonary involvement. Patients with severe disease generally present signs and symptoms of viral pneumonia and may progress to situations of severe acute respiratory syndrome (SARS), acute heart failure, acute kidney injury, sepsis, or shock[32]. With pulmonary alterations, there is the onset of hypoxemic respiratory failure and changes in pulmonary compliance.

Finally, participants with pre-existing comorbidities showed a reduction in workload or daily activities due to their health problems. In a cohort study of COVID-19

survivors in China, 88% returned to work at the 12-month follow-up visit. However, 24% were unable to return to the same level of work as before COVID-19[33]. Persistent symptoms after returning to work can result in a reduction in overall well-being, difficulty in performing previously accomplished tasks, loss of concentration, and decreased work performance, in addition to economic and social impacts[34]. Thus, the persistent symptoms reported by the participants in this study may have directly influenced the reduction in work productivity. The present study corroborates the results previously found in the literature, demonstrating that changes in overall functionality directly lead to changes in the quality of life of post-COVID-19 patients, especially those with pre-existing comorbidities.

CONCLUSION

The results of the present study indicate that the main clinical manifestations post-COVID-19, even three to twelve months after infection with the new coronavirus, regardless of the presence of pre-existing comorbidities, were pain, cognitive deficit, muscle weakness, and hair loss. However, individuals with pre-existing comorbidities exhibit greater impairments in quality of life (mobility domain), work-related indices, and physical and cognitive functionality.

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