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HEALTH SCIENCES

Prevalence of and risk factors for post-COVID: Results from a survey of 6,958 patients from Brazil

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Abstract: A plethora of prolonged COVID-19 symptoms, or late manifestations has been reported after acute disease and labeled "post-COVID". The aim of this study was to identify the prevalence of and risk factors for post-COVID up to 12 weeks after the onset of acute COVID-19. An electronic survey was conducted to evaluate post-COVID-19 symptoms, disease severity, demographics, and pre-existing diseases. The participants were recruited through 88,648 SMS messages, and post on social media. The associations between variables were explored through multivariate models. From 6,958 respondents with confirmed COVID-19, 753 (10.8%) required hospitalization, and 5,791 (83.2%) exhibited at least one post-COVID manifestation. Hair loss (49.4%), memory loss (40.7%), low attention (37.0%), fatigue (34.2%), anxiety (31.2%), and headache (29.6%) were the most reported post-COVID manifestations. Female sex, myalgia, anosmia, and severe disease were associated with most post-COVID manifestations. Pre-existing depression was associated with the development of neuropsychiatric manifestations. Post-COVID manifestations were identified in most patients following COVID-19 infection, placing a supplementary burden on the healthcare system. Hair loss, fatigue, and neuropsychiatric symptoms were the most prevalent post-COVID manifestations. Female sex, myalgia, anosmia, and more severe disease are risk factors for multiple post-COVID manifestations.

Key words: COVID-19, SARS-CoV-2, post-acute COVID, risk factors, female.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a heterogeneous disease that can manifest through a wide spectrum of severity, and symptom duration. Acute COVID-19 refers to the presence of signs and symptoms of the disease for up to four weeks. To date, no clinical terminology has been established for the persistent symptoms and/or organ dysfunction after acute disease (National Institutes of Health 2022). According to the United States' Centers for Disease Control and Prevention, post-COVID conditions are new, recurring, or ongoing symptoms and clinical findings noticed in the four or more weeks after acute infection and sometimes after initial symptom recovery (Center of Disease Control and Prevention 2021). Conversely, the United Kingdom's National Institute for Health and Care Excellence provides two definitions of post-COVID (a.k.a. long COVID, post-acute COVID-19 sequelae): (1) ongoing symptomatic COVID for people who still have signs and symptoms of COVID-19 from four weeks up to 12 weeks and (2) post-COVID-19 syndrome for those presenting with symptoms for more than 12 weeks after the onset of acute symptoms (Shah et al. 2021). Post-acute sequelae of COVID-19, COVID-19

long-haulers and post-acute, chronic, and long COVID-19 are other terms that have been used in lay press, on social media, and in academic centers (Korompoki et al. 2021, Sudre et al. 2021, Nalbandian et al. 2021, Su et al. 2022).

Post-COVID prevalence varies according to the length of the follow-up period, the hospitalized / non-hospitalized population, the accuracy of self-reporting, and the symptoms examined (Crook et al. 2021). For 90 days after the onset of COVID-19 or hospitalization, estimates of post-COVID have varied from 11.7% in the self-classification participants of the U.K. Coronavirus Infection Survey to at least 45.9% in a sample of 24,255 COVID-19 survivors (Fernández-de-Las-Peñas et al. 2021). Interestingly, a large retrospective study showed that over one third of patients had one or more post-COVID symptoms recorded between three and six months after acute COVID (Taquet et al. 2021).

The most commonly reported post-COVID symptoms are fatigue, headache, dyspnea, cognitive and mental health deficits and conditions, alopecia, and olfactory and gustatory dysfunction (Sudre et al. 2021, Crook et al. 2021, Fernández-de-Las-Peñas et al. 2021, Taquet et al. 2021, Munblit et al. 2021, Kamal et al. 2021, Sigfrid et al. 2021, Mazeto et al. 2022).

Although advances have been made, gaps remain in the current understanding of post-COVID risk factors and their frequency. Female sex has been reported as a strong predictor of post-COVID. Of the pre-existing comorbidities, hypertension, overweight, obesity, asthma, psychiatric conditions, type 2 diabetes, and poor general health were associated with a higher risk of post-COVID (Shah et al. 2021, Su et al. 2022, Munblit et al. 2021, Yong 2021, Tenforde et al. 2020). Moreover, the presence of specific autoantibodies, SARS-CoV-2 RNAemia (viral RNA in blood), and Epstein-Barr virus viremia measured at acute COVID phase could anticipate the development of post-COVID (Su et al. 2022).

Since the onset of the global pandemic, millions of people have been infected by SARS-CoV-2 and survived (National Institutes of Health 2022, Center of Disease Control and Prevention 2021). In this scenario, the number of individuals presenting with persistent symptoms has dramatically increased over time, placing a burden on the healthcare system that will outlast the pandemic (Tempany et al. 2021). To date, vaccination appears to reduce the risk of developing post-COVID symptoms. However, evidence concerning the impact of the immunization program on reducing post-COVID prevalence is still emerging (Antonelli et al. 2022). Nevertheless, the accurate and prompt identification of these symptoms is crucial for the adequate management of patients presenting with such symptoms.

Electronic surveys provide unique opportunities for research in the COVID-19 era. Because of this rapidly evolving infectious disease, conventional methods for obtaining personal and clinical data are not feasible (Watts 2020). The objective of this study was to identify the prevalence of and risk factors for post-COVID symptoms up to 12 weeks after the onset of acute disease on a cohort of laboratory-confirmed SARS-CoV-2-infected individuals who were recruited for a nationwide online survey in Brazil.

MATERIALS AND METHODS

The protocol was approved by the UNESP Institutional Review Board. All subjects consented to study participation and the anonymous publication of their data in a medical journal.

An electronic survey was conducted in Brazil to evaluate acute and post-COVID symptoms. The

participants were recruited between May 3, 2021, and September 30, 2021, through 88,648 SMS messages to registered cellular phones, which were randomized from a countrywide database, and via distinct social media (Facebook, Instagram, WhatsApp, and LinkedIn). The online survey was created in and conducted via Google Forms (https://bit.ly/3tyseVk) and shared with people known to have had COVID-19 (snowball sampling).

The questionnaire comprised baseline demographic and clinical questions related to COVID-19 infection. Individuals with confirmed (by a polymerase chain reaction test, chest computerized tomography, or a serology test) and suspected COVID-19 were invited to complete the questionnaire. The main outcomes were COVID-19 severity (treatment at home, hospitalization, or admission to intensive care units), acute COVID-19 symptoms (fever, cough, dyspnea, myalgia, nausea, vomiting, diarrhea, anosmia, dysgeusia, and arthralgia), and the presence of concomitant diseases (diabetes, hypertension, heart conditions, thyroid disease, or obesity). Additionally, the prevalence of post-COVID findings (symptoms up to 12 weeks after termination of acute disease) was assessed (the appearance or persistence of headaches, alopecia, numbness, dizziness, loss of memory, sadness and/or depression, fear and/or anxiety, arthralgia, fatigue, chest pain, cough, dyspnea, thrombosis, myocardial infarction, or cerebrovascular accident).

Effect sizes were represented as odds ratios (95% confidence interval), which were estimated through hierarchical logistic regression, were adjusted for relevant covariates, including fixed (sex, age, and hospitalization), demographic, comorbid, and (acute COVID) symptomatic covariates (p <0.1 for inclusion). The co-occurrence of post-COVID manifestations was explored through hierarchical cluster analysis (Ward's method) (Frades & Matthiesen 2010). The significance level was set as $p \leq .001$ (two-tailed analysis) (Miola & Miot 2021). The data were analyzed using IBM SPSS v25.

The main analyses were performed on COVID-confirmed cases. Subsequently, a sensitivity analysis that included suspected COVID cases was performed. All results were adjusted for age and sex.

RESULTS

Data from 6,958 respondents with confirmed SARS-CoV-2 infection were analyzed, and their main characteristics are presented in Table I. A preponderance of individuals being female, adult, and educated, as well as self-reporting as white, was observed among the respondents. The most commonly known risk factors for COVID-19 severity presented in this sample were overweight, depression, hypertension, dyslipidemia, and thyroid dysfunction. Of the symptoms experienced during acute COVID-19, myalgia, anosmia, fever, cough, and arthralgia were prevalent. Most respondents had mild COVID-19 and remained at home, whereas 753 respondents (10.8%) were hospitalized. Additionally, 870 respondents without confirmed COVID-19 (suspected cases) were used for sensitivity analysis.

A total of 5,791 respondents (83.2%) exhibited at least one post-COVID symptom up to 12 weeks after the onset of acute disease, and their main characteristics are presented in Table II. Hair loss, memory loss, attention deficits, and fatigue were observed in more than one third of the individuals.

In general, the prevalence of any post-COVID manifestation among the hospitalized patients was 93.6%, whereas this prevalence was 82% in those who were treated at home (p <.001). The prevalence was also higher in females (88.8%

Table I. Main self-reported characteristics of the 6,958 Brazilian individuals with confirmed COVID-19.

Variable		Values
Sex, n (%)		
	Female	4,867 (69.9)
	Male	2,091 (30.1)
Age-group, n (%)		
	< 30 years-old	1,482 (21.3)
	31-60 years-old	4,653 (66.9)
	> 60 years-old	823 (11.8)
Education level, n (%)		
	Fundamental	174 (2.5)
	High school	922 (13.3)
	University	5,862 (84.2)
Skin color, n (%)		
	White	5,043 (72.5)
	Non-white	1,915 (27.5)
Body composition, n (%)		
	Euthrophic / thin	3,830 (55.0)
	Heavy	2,653 (38.1)
	Obese	475 (6.8)
Tobacco smoking, n (%)		
	Ever	1,711 (24.6)
	Never	5,247 (75.4)
Comorbidities, n (%)		
	Depression	1,400 (20.1)
	Hypertension	1,216 (17.5)
	Dyslipidemia	970 (13.9)
	Thyroid disease	818 (11.8)
	Diabetes	477 (6.9)
	Lung disease	397 (5.7)
	Liver disease	225 (3.0)
	Heart disease	208 (3.0)
COVID-19 treatment, n (%)		
	At home	6,205 (89.2)
	Hospitalization	473 (6.8)
	Intensive care unit	280 (4.0)
Acute COVID-19 symptoms, n (%)		
	Myalgia	5,149 (74.0)
	Anosmia	4,665 (67.0)
	Cough	3,899 (56.0)
	Fever	3,672 (52.8)
	Arthralgia	3,539 (50.9)
	Nausea / Diarrhea	3,092 (44.4)
	Dyspnea	2,967 (42.6)

vs. 70.3%, p <.001), the obese (87.6% vs. 81.7%, p <.001), those with severe dyspnea (97.1% vs. 75.9%, p <.001), those with anosmia (85.2% vs. 79.3%, p <.001), those with severe myalgia (93.6% vs. 68.7%, p <.001), those with pre-existing depression (91.9% vs. 81.1%, p <.001), those with thyroid disorders (90.1% vs. 81.3%, p <.001), and those with lung disease (89.9% vs. 82.8%, p <.001). Nevertheless, skin color, education, diabetes, dyslipidemia, hypertension, and smoking were not associated with post-COVID occurrence. These results were confirmed in the sensitivity analysis.

Additionally, certain post-COVID manifestations co-occurred in a similar pattern (Figure 1). Attention and memory loss; depression and anxiety; and chest pain, thrombosis, and dyspnea were particularly interconnected.

The multivariable analysis revealed different patterns of risk factors for each post-COVID manifestation (Table III). Female sex, myalgia, anosmia, and severe disease (i.e., disease that required hospitalization) were associated with most post-COVID manifestations. Pre-existing depression was associated with the development of neuropsychiatric manifestations. Chest pain, cough, and dyspnea were associated with acute pulmonary symptoms. Additionally, thrombotic events followed more severe disease. All of these associations were confirmed by the sensitive analysis, which included the 870 participants with unconfirmed COVID-19.

DISCUSSION

This study evidenced a high prevalence of post-COVID manifestations following acute disease. Moreover, certain risk factors make it possible to stratify the risks of post-COVID symptoms that reinforce the need for an active screening in the follow-up period. It is important to recognize post-COVID as a potential public health problem

Table II. Main self-reported characteristics of the 5,791 Brazilian individuals with confirmed COVID-19, who reported post-COVID symptoms.

Variable		Values
Sex, n (%)*		
	Female	4,322 (74.6)
	Male	1,469 (25.4)
Age-group, n (%)*		
	< 30 years-old	1,207 (20.8)
	31-60 years-old	3,912 (67.6)
	> 60 years-old	672 (11.6)
Education level, n (%)*		
	Fundamental	129 (2.2)
	High school	801 (13.8)
	University	4,861 (83.9)
Skin color, n (%)*		
	White	4,185 (72.3)
	Non-white	1,606 (27.7)
Body composition, n (%)*		
	Euthrophic / thin	3,129 (54.0)
	Heavy	2,246 (38.8)
	Obese	416 (7.2)
Tobacco smoking, n (%)*		
	Ever	1,424 (24.6)
	Never	4,367 (75.4)
Comorbidities, n (%)*		
	Depression	1,286 (22.2)
	Hypertension	1,034 (17.9)
	Heart disease	184 (3.2)
	Dyslipidemia	829 (14.3)
	Thyroid disease	737 (12.7)
	Diabetes	406 (7.0)
	Lung disease	357 (6.2)
	Liver disease	201 (3.5)
COVID-19 treatment, n (%)*		
	At home	5,086 (87.8)
	Hospitalization	437 (7.5)
	Intensive care unit	268 (4.6)
Post-COVID-19 symptoms, n (%)**		
	Hair loss	3,435 (49.4)
	Memory loss	2,835 (40.7)
	Low-attention	2,571 (37.0)
	Fatigue	2,378 (34.2)
	Anxiety	2,172 (31.2)
	Headache	2,057 (29.6)
	Depression / Unhappiness	1,740 (25.0)
	Arthralgia	1,371 (19.7)
	Dizziness / Vertigo	1,351 (19.4)
	Cough	1,279 (18.4)
	Dyspnea	939 (13.5)
	Acral numbness	940 (13.5)
	Chest pain	910 (13.1)
	Thrombotic event / infarction	49 (0.7)

***Percentile of 5,791 individuals who reported post-COVID symptoms; ** Percentile of 6,958 individuals with confirmed COVID-19.**

and quantify its burden on individuals' quality of life and impact on the healthcare system. Whether considering a four-week or a 12-week threshold for defining post-COVID, a plethora of prolonged symptoms with different degrees of severity has been reported.

SARS-CoV-2 was detected in most body tissues, and it induced a complex systemic immune response that could lead to inflammatory and thrombotic phenomena in several organs and systems, which, in turn, led to highly heterogeneous clinical manifestations of acute COVID (Criado et al. 2021). In our study, myalgia; anosmia; cough; fever; arthralgia; nausea, vomiting, or diarrhea; and dyspnea were the most frequently self-reported symptoms. Interestingly, a prospective observational study showed that more than five different symptoms in the first week of illness were the strongest predictors of post-COVID manifestations (Sudre et al. 2021). In this sample, myalgia and severe disease (i.e., disease that required hospitalization) were associated with most of the post-COVID manifestations, resulting in a greater inflammatory response leading to tissue damage and prolonged symptoms.

Most of our respondents had mild COVID-19. In this sample, alopecia, memory loss, attention deficits, fatigue, anxiety, headache, depression, arthralgia, vertigo, cough, and dyspnea were among the most common symptoms. These features were similar to those found by other studies in the same follow-up time (Fernández-de-Las-Peñas et al. 2021, Chopra et al. 2021). In particular, half of our respondents reported hair effluvium, which is higher than the 20% earlier described (Garrigues et al. 2020). Hair loss is the most common post-COVID manifestation, and evidence can be found to suggest multiple mechanisms and diagnoses. Dystrophic anagen effluvium can justify earlier cases, but acute telogen effluvium, whose onset is typically

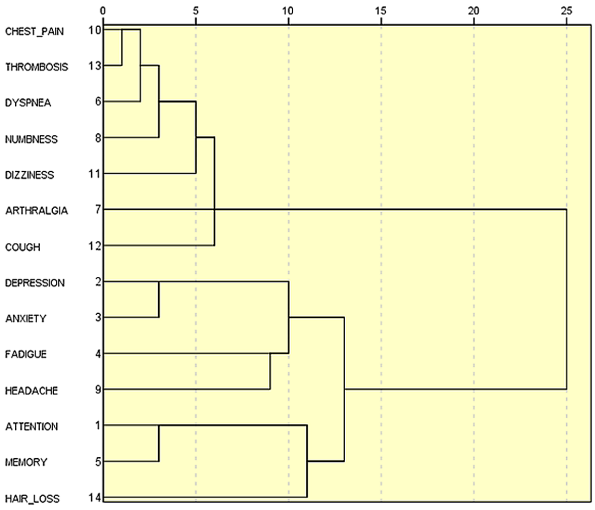

Figure 1. Dendrogram (Ward´s method) of the manifestations of post-COVID syndrome in 5,791 individuals.

triggered after three months, diffuse alopecia areata, and pressure alopecia due to long periods of immobility cannot be differentiated across self-report surveys (Abrantes et al. 2021, Perry et al. 2021, Capalbo et al. 2021, Ramos et al. 2022, Miola et al. 2022).

In our study, females were at high risk of post-COVID. Similarly, Taquet et al. (2021) also reported a preponderance of post-COVID symptoms in females, even in those of a younger age and with relatively mild illness (Taquet et al. 2021). Interestingly, of our respondents, all age groups showed a predisposition to post-COVID. The effect of age on longer illness is still debated (Shah et al. 2021). Conversely, the elderly population and males are predisposed to more severe acute COVID (Center of Disease Control and Prevention 2021, Munblit et al. 2021, Yong 2021, Tenforde et al. 2020, Giagulli et al. 2021, Miot et al. 2021).

We found that pre-existing depression affected 20.1% of our respondents and was considered a risk factor for the development of cognitive deficits and memory loss. Depression also co-occurred with other post-COVID symptoms, such as fatigue, headache, and anxiety.

Table III. Odds ratios (95% CI) from the final multivariable models of the factors associated with the occurrence of the main manifestations of post-COVID syndrome (*n* = 6,958). **p* ≤.001.

Variables	Hair loss	Memory loss	Low-attention	Fatigue	Anxiety	Headache	Depression
Hospitalization	1.6 (1.3-2.0)*	1.5 (1.2-2.8)*	1.4 (1.1-1.7)*	2.5 (2.0-3.0)*	1.6 (1.3-1.9)*	0.9 (0.7-1.1)	1.3 (1.1-1.6)
Female sex	7.9 (6.9-9.1)*	2.4 (2.1-2.7)*	2.3 (2.0-2.6)*	1.5 (1.3-1.7)*	1.8 (1.6-2.0)*	2.3 (2.0-2.6)*	2.0 (1.8-2.4)*
Age > 60	0.9 (0.7-1.1)	0.8 (0.7-1.0)	0.7 (0.6-0.9)*	1.5 (1.2-1.9)*	0.7 (0.5-0.9)*	0.5 (0.4-0.6)*	0.9 (0.7-1.1)
Smoking	-	-	-	-	1.1 (1.0-1.3)	-	-
Lung disease	1.0 (0.8-1.3)	1.1 (0.9-1.4)	1.2 (1.0-1.5)	1.0 (0.8-1.2)	1.1 (0.9-1.3)	1.2 (1.0-1.6)	-
Hypertension	-	1.2 (1.1-1.4)*	-	1.3 (1.2-1.6)*	1.2 (1.0-1.4)	-	1.1 (1.0-1.3)
Diabetes	-	-	-	-	-	-	1.3 (1.1-1.7)
Liver disease	-	-	-	1.4 (1.0-1.8)	1.4 (1.0-1.8)	-	1.5 (1.1-2.0)
Depression	1.2 (1.1-1.4)*	1.6 (1.4-1.8)*	1.7 (1.5-1.9)*	-	2.8 (2.4-3.2)*	1.4 (1.2-1.6)*	2.7 (2.4-3.1)*
Dyslipidemia	1.2 (1.0-1.4)	-	1.3 (1.1-1.6)*	1.2 (1.0-1.4)	-	-	-
Heart Disease	-	-	-	1.5 (1.1-2.1)	-	1.5 (1.0-2.0)	-
Fever	1.3 (1.1-1.5)*	-	1.2 (1.1-1.4)*	1.2 (1.1-1.4)*	-	-	1.2 (1.0-1.4)
Dyspnea	2.0 (1.7-2.5)*	2.3 (1.9-2.8)*	2.2 (1.8-2.6)*	2.1 (1.8-2.6)*	2.2 (1.8-2.6)*	1.7 (1.4-2.0)*	2.2 (1.8-2.7)*
Anosmia	1.2 (1.1-1.4)*	1.4 (1.3-1.6)*	1.3 (1.2-1.5)*	1.1 (1.0-1.3)	1.2 (1.0-1.3)	1.1 (1.0-1.3)	1.3 (1.1-1.4)*
Myalgia	1.7 (1.5-2.0)*	2.0 (1.7-2.3)*	2.2 (1.9-2.6)*	3.5 (3.0-4.1)*	1.6 (1.4-1.9)*	3.0 (2.5-3.5)*	1.7 (1.4-2.0)*
Nausea / Diarrhea	1.3 (1.1-1.4)*	1.4 (1.2-1.5)*	1.3 (1.1-1.4)*	1.3 (1.2-1.5)*	1.5 (1.3-1.6)*	1.4 (1.2-1.6)	1.4 (1.2-1.5)*
Variables	Arthralgia	Vertigo	Cough	Dyspnea	Numbness	Chest Pain	Thrombotic event
Hospitalization	1.3 (1.0-1.6)	1.3 (1.0-1.6)	1.1 (0.8-1.3)	0.9 (0.7-1.1)	1.2 (1.0-1.5)	1.1 (0.9-1.4)	4.1 (2.2-7.9)*
Female sex	1.6 (1.4-1.9)*	1.7 (1.4-2.0)*	1.1 (1.0-1.3)	1.1 (0.9-1.3)	1.5 (1.2-1.8)*	1.4 (1.2-1.7)*	1.1 (0.6-2.1)
Age > 60	1.9 (1.5-2.5)*	0.9 (0.7-1.2)	1.5 (1.1-1.9)*	1.0 (0.7-1.3)	1.4 (1.0-1.8)	0.7 (0.5-1.0)	3.0 (0.9-9.8)
Smoking	1.2 (1.0-1.3)	-	-		1.1 (1.0-1.3)	-	-
Lung disease	1.2 (1.0-1.6)	1.2 (0.9-1.5)	-	1.6 (1.1-2.2)*	1.2 (0.9-1.6)	1.0 (0.8-1.3)	-
Hypertension	1.2 (1.1-1.5)	1.3 (1.1-1.5)*	1.1 (0.8-1.3)		1.2 (1.0-1.5)	-	-
Diabetes	1.2 (0.9-1.5)	-	-		1.3 (1.0-1.7)	-	-
Liver disease	1.6 (1.1-2.1)*	-	1.2 (0.9-1.7)	1.4 (1.1-2.0)	-	-	-
Depression	1.3 (1.1-1.5)*	1.6 (1.4-1.9)*	-	1.3 (1.1-1.6)*	1.5 (1.3-1.8)*	-	-
Dyslipidemia	-	-	1.2 (1.0-1.4)		-	-	-
Heart Disease	-	1.8 (1.3-2.5)*	-		1.7 (1.2-2.4)*	1.9 (1.3-2.7)*	-
Fever	0.8 (0.7-1.0)	-	-	1.0 (0.8-1.2)	-	-	2.3 (1.1-4.5)
Dyspnea	1.6 (1.3-2.0)*	1.9 (1.5-2.4)*	1.5 (1.2-1.9)*	33.6 (25.4-44.5)*	2.0 (1.6-2.6)*	4.0 (3.2-5.2)*	-
Cough	-	1.1 (1.0-1.3)	12.7 (10.2-15.8)*		-	1.2 (1.0-1.4)	
Anosmia	-	1.2 (1.1-1.4)*	-	1.1 (1.0-1.4)	-	1.2 (1.0-1.4)	-
Myalgia	7.9 (6.3-10.0)*	2.5 (2.0-3.0)*	1.3 (1.1-1.6)*	1.5 (1.2-1.9)*	2.8 (2.3-3.5)*	2.1 (1.7-2.7)*	-
Nausea / Diarrhea	1.2 (1.0-1.3)	1.7 (1.5-1.9)*	-	1.3 (1.1-1.5)*	1.4 (1.2-1.6)*	1.3 (1.1-1.5)*	0.6 (0.3-1.0)

Neurological and psychological symptoms are commonly associated with both acute and post-COVID. The occurrence of neuropsychiatric manifestations such as anxiety, insomnia and post-traumatic stress syndrome in post-COVID patients may correspond to a phenotype of post-COVID 19 neurological syndrome (Rubiano-Buitrago et al. 2022). Among the known causes of the neurological manifestations that SARS-CoV-2 infection results in are the involvement of the overproduction of cytokines and immune cell hyperactivation, the hypoxia that is secondary to COVID-19 pulmonary disease, and the reduced perfusion to the brain, which is partly caused by the cardiovascular compromise resulting from the disease (Jesuthasan et al. 2021). The mechanisms of post-COVID headache are still controversial; it can be caused by sustained inflammatory response and/or persistent trigeminovascular damage caused by either the virus itself or local inflammation of the endothelium (Caronna et al. 2021). Moreover, it is known that the pandemic has had a negative effect on the population's mental health. Quarantines, isolation, social distancing, post-traumatic stress, and treatments may

contribute to the appearance or worsening of neurological and psychological symptoms in people recovering from acute COVID (Crook et al. 2021, Fernández-de-Las-Peñas et al. 2021, Duran & Erkin 2021, Xie et al. 2021).

Other investigations also revealed the co-occurrence of post-COVID symptoms, (Sudre et al. 2021, Taquet et al. 2021, Munblit et al. 2021) which corroborates the existence of a "long COVID syndrome," with symptoms co-occurring and appearing over time. The causes of post-COVID are yet to be fully elucidated. Persistent chronic tissue inflammation, autoimmunity, coronavirus tissue reservoirs that remain after acute infection, hormonal imbalance, and non-specific effects resulting from hospitalization or prolonged ventilation are among the main hypotheses (Su et al. 2022, Yong 2021, Anaya et al. 2021, Moreno-Pérez et al. 2021). Individuals with post-COVID are particularly heterogeneous: those with organ damage following hospitalization/intensive care unit admission, those with moderate acute phase of COVID-19 but persistent organ damage or even individuals with a plethora of occasionally remitting-relapsing symptoms such as fatigue, neurological dysfunctions, weakness, or chronic pain (Korompoki et al. 2021).

In our study, persistent chest pain, cough, and dyspnea were associated with acute pulmonary symptoms. During acute COVID-19, the respiratory system is the most critically affected system. Post-acute COVID-19 complications include secondary pulmonary infections, thromboembolism, hypertension, function test disorders, and pulmonary fibrosis (Korompoki et al. 2021). Among previously hospitalized COVID-19 patients with normalized inflammatory biomarkers and persistent dyspnea, 40% remained hypocapnic and more than half still had pulmonary interstitial involvement after three months of acute illness. In particular, an association between a persistent cough and the presence of bronchiectasis and consolidation in a follow-up chest screening was also described (Mumoli et al. 2021).

Besides post-COVID-19 neurological syndrome, other specific organ specific post-COVID 19 syndromes have been described. A cardio-renal post-COVID-19 illness including increased circulating concentrations of NT-proBNP, a biomarker of impaired cardiac function and prognosis, and Factor VIII, indicating hemostasis pathway activation was recently reported (Morrow et al. 2022).

Among our respondents, overall post-COVID symptoms were more prevalent in females, the obese, those with pre-existing lung disease, and those with intense acute COVID symptoms. Other studies found similar results (Shah et al. 2021, Sudre et al. 2021, Kamal et al. 2021, LaVergne et al. 2021). Although the association between more severe acute illness and post-COVID manifestations is still debated, in our study, hospitalization was associated with most post-COVID manifestations. Interestingly, in a longitudinal study, individuals who had moderate and severe COVID-19 were equally as likely to develop post-COVID (LaVergne et al. 2021). Hence, individuals with comorbidities, especially hospitalized individuals, should be advised to attend follow-up appointments with a healthcare provider after termination of acute illness and/or their discharge from hospital.

Certain limitations, which are inherent to this method, with regard to the self-report questionnaire affected our study. The asked items were developed specifically for this study. The overall study predominantly represented highly educated white females, aged between 30 and 50 years, rather than a representative sample of the general population. Moreover, recall bias could not be ruled out, and we could not ascertain the vaccination status of the

whole sample. Nevertheless, the study, whose inferential results were compared to those of the international series, comprised a large Brazilian sample of COVID-19-proven patients. The prevalence of post-COVID among the fully vaccinated and in those who have been infected by less pathogenic SARS-CoV-2 variants (e.g., Omicron) warrants further investigation (Ledford 2021).

Post-COVID manifestations were identified in most patients following COVID-19 infection, placing a supplementary burden on the healthcare system. Hair loss and neuropsychiatric symptoms were the most prevalent post-COVID manifestations. Female sex, myalgia, anosmia, and more severe disease are risk factors for multiple post-COVID manifestations that require attention during patient follow-ups.

REFERENCES

ABRANTES TF, ARTOUNIAN KA, FALSEY R, SIMÃO JCL, VAÑÓ-GALVÁN S, FERREIRA SB, DAVIS TL, RIDENOUR W, GOREN A, TOSTI A & WAMBIER CG. 2021. Time of onset and duration of post-COVID-19 acute telogen effluvium. J Am Acad Dermatol 85: 975-976.

ANAYA JM ET AL. 2021. Post-COVID syndrome. A case series and comprehensive review. Autoimmun Rev 20: 102947.

ANTONELLI M ET AL. 2022. Risk factors and disease profile of post-vaccination SARS-CoV-2 infection in UK users of the COVID Symptom Study app: a prospective, community-based, nested, case-control study. Lancet Infect Dis 22: 43-55.

CAPALBO A, GIORDANO D, GAGLIOSTRO N, BALAMPANOS CG, PERSECHINO F, ORRÙ F & PERSECHINO S. 2021. Alopecia areata in a COVID-19 patient: A case report. Dermatol Ther 34: e14685.

CARONNA E, ALPUENTE A, TORRES-FERRUS M & POZO-ROSICH P. 2021. Toward a better understanding of persistent headache after mild COVID-19: Three migraine-like yet distinct scenarios. Headache 61: 1277-1280.

CENTER OF DISEASE CONTROL AND PREVENTION. 2021. Evaluating and Caring for Patients with Post-COVID Conditions: Interim Guidance. Available at https://pesquisa.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/resource/pt/grc-747269.

CHOPRA V, FLANDERS SA, O'MALLEY M, MALANI AN & PRESCOTT HC. 2021. Sixty-Day Outcomes Among Patients Hospitalized With COVID-19. Ann Intern Med 174: 576-578.

CRIADO PR, MIOT HA, PINCELLI TPH & FABRO AT. 2021. From dermatological conditions to COVID-19: Reasoning for anticoagulation, suppression of inflammation, and hyperbaric oxygen therapy. Dermatol Ther 34: e14565.

CROOK H, RAZA S, NOWELL J, YOUNG M & EDISON P. 2021. Long covid-mechanisms, risk factors, and management. BMJ 374: n1648.

DURAN S & ERKIN O. 2021. Psychologic distress and sleep quality among adults in Turkey during the COVID-19 pandemic. Prog Neuropsychopharmacol Biol Psychiatry 107: 110254.

FERNÁNDEZ-DE-LAS-PEÑAS C, PALACIOS-CEÑA D, GÓMEZ-MAYORDOMO V, FLORENCIO LL, CUADRADO ML, PLAZA-MANZANO G & NAVARRO-SANTANA M. 2021. Prevalence of post-COVID-19 symptoms in hospitalized and non-hospitalized COVID-19 survivors: A systematic review and meta-analysis. Eur J Intern Med 92: 55-70.

FRADES I & MATTHIESEN R. 2010. Overview on techniques in cluster analysis. Methods Mol Biol 593: 81-107.

GARRIGUES E ET AL. 2020. Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. J Infect 81: e4-e6.

GIAGULLI VA, GUASTAMACCHIA E, MAGRONE T, JIRILLO E, LISCO G, DE PERGOLA G & TRIGGIANI V. 2021. Worse progression of COVID-19 in men: Is testosterone a key factor? Andrology 9: 53-64.

JESUTHASAN A, MASSEY F, MANJI H, ZANDI MS & WIETHOFF S. 2021. Emerging potential mechanisms and predispositions to the neurological manifestations of COVID-19. J Neurol Sci 428: 117608.

KAMAL M, ABO OMIRAH M, HUSSEIN A & SAEED H. 2021. Assessment and characterisation of post-COVID-19 manifestations. Int J Clin Pract 75: e13746.

KOROMPOKI E ET AL. 2021. Epidemiology and organ specific sequelae of post-acute COVID19: A narrative review. J Infect 83: 1-16.

LAVERGNE SM ET AL. 2021. A longitudinal SARS-CoV-2 biorepository for COVID-19 survivors with and without post-acute sequelae. BMC Infect Dis 21: 677.

LEDFORD H. 2021. Do vaccines protect against long COVID? What the data say. Nature 599: 546-548.

MAZETO IFS, BROMMONSCHENKEL CC, MIOLA AC, MULLER RAMOS P, CARVALHO DOS SANTOS D & MIOT HA. 2022. Ultrastructural evidence for anagen hair follicle infection with SARS-CoV-2 in early-onset COVID-19 effluvium. J Eur Acad Dermatol Venereol 36: e865-e867.

MIOLA AC, FLORENCIO LC, BELLINI RIBEIRO ME, ALCANTARA GP, MULLER RAMOS P & MIOT HA. 2022. Early-onset effluvium secondary to COVID-19: Clinical and histologic characterization. J Am Acad Dermatol 86: e207-e208.

MIOLA AC & MIOT HA. 2021. P-value and effect-size in clinical and experimental studies. J Vasc Bras 20: e20210038.

MIOT HA, IANHEZ M & RAMOS PM. 2021. Self-reported cutaneous manifestations in 1,429 Brazilian COVID-19 patients. J Eur Acad Dermatol Venereol 35: e172-e173.

MORENO-PÉREZ O ET AL. 2021. Post-acute COVID-19 syndrome. Incidence and risk factors: A Mediterranean cohort study. J Infect 82: 378-383.

MORROW AJ ET AL. 2022. A multisystem, cardio-renal investigation of post-COVID-19 illness. Nat Med 28: 1303-1313.

MUMOLI N, BONAVENTURA A, COLOMBO A, VECCHIÉ A, CEI M, VITALE J, PAVAN L, MAZZONE A & DENTALI F. 2021. Lung Function and Symptoms in Post–COVID-19 Patients: A Single-Center Experience. Mayo Clin Proc Innovations Quality & Outcomes 5: 907-915.

MUNBLIT D ET AL. 2021. Incidence and risk factors for persistent symptoms in adults previously hospitalized for COVID-19. Clin Exp Allergy 51: 1107-1120.

NALBANDIAN A ET AL. 2021. Post-acute COVID-19 syndrome. Nat Med 27: 601-615.

NATIONAL INSTITUTES OF HEALTH. 2022. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. Available at https://www.covid19treatmentguidelines.nih.gov/.

PERRY T II, ROSEN H, PETTIT C & TRINIDAD JC. 2021. Pressure-induced alopecia due to proning in COVID-19. Dermatol Ther 34: e14764.

RAMOS PM, IANHEZ M, DE CASTRO S, TALHARI C, CRIADO PR & MIOT HA. 2022. Post-COVID-19 hair loss: prevalence and associated factors among 5,891 patients. Int J Dermatol 61: e162-e164.

RUBIANO-BUITRAGO JD, RAHIRAN-RAMIREZ AF, PENA-VARGAS DM, PAEZ-RINCON LA & LOZADA-MARTINEZ ID. 2022. Post-COVID 19 neurological syndrome: Are we facing a neuropsychiatric phenotype? J Clin Neurosci 97: 106-107.

SHAH W, HILLMAN T, PLAYFORD ED & HISHMEH L. 2021. Managing the long term effects of covid-19: summary of NICE, SIGN, and RCGP rapid guideline. BMJ 372: n136.

SIGFRID L ET AL. 2021. Long Covid in adults discharged from UK hospitals after Covid-19: A prospective, multicentre cohort study using the ISARIC WHO Clinical Characterisation Protocol. Lancet Reg Health Eur 8: 100186.

SU Y ET AL. 2022. Multiple Early Factors Anticipate Post-Acute COVID-19 Sequelae. Cell 185: 881-895.

SUDRE CH ET AL. 2021. Attributes and predictors of long COVID. Nat Med 27: 626-631.

TAQUET M, DERCON Q, LUCIANO S, GEDDES JR, HUSAIN M & HARRISON PJ. 2021. Incidence, co-occurrence, and evolution of long-COVID features: A 6-month retrospective cohort study of 273,618 survivors of COVID-19. PLoS MED 18: e1003773.

TEMPANY M ET AL. 2021. The potential impact of post-COVID symptoms in the healthcare sector. Occup Med (Lond) 71: 284-289.

TENFORDE MW ET AL. 2020. Symptom Duration and Risk Factors for Delayed Return to Usual Health Among Outpatients with COVID-19 in a Multistate Health Care Systems Network - United States, March-June 2020. MMWR Morb Mortal Wkly Rep 69: 993-998.

WATTS G. 2020. COVID-19 and the digital divide in the UK. Lancet Digit Health 2: e395-e396.

XIE M, WANG X, ZHANG J & WANG Y. 2021. Alteration in the psychologic status and family environment of pregnant women before and during the COVID-19 pandemic. Int J Gynaecol Obstet 153: 71-75.

YONG SJ. 2021. Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. Infect Dis (Lond) 53: 737-754.

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Author contributions

HAM conceived the study. All authors participated in the design of the study. HAM performed the statistical analysis. All authors performed the acquisition of data and its analysis. CT drafted the manuscript. PRC, CCSC, PMR and MI helped to draft the manuscript. All authors read and approved the final manuscript.