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Original article

Neuropsychiatric symptoms associated with post-COVID-19 affectation

Síntomas neuropsiquiátricos asociados con la afectación post-COVID-19

Sintomas neuropsiquiátricos associados às sequelas da COVID-19

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ABSTRACT

Introduction. Post-COVID-19 syndrome is an emerging health problem with significant implications for the quality of life of affected individuals. The objective of this study was to determine the relationship between self-reported acute and post-acute symptoms associated with post-COVID-19 according to gender, age group, vaccination status, and COVID-19 diagnosis in order to define a risk profile. **Methodology.** A prospective inferential study was conducted with a sample of 1,601 Colombians, an ad hoc dichotomous questionnaire of self-reported neuropsychiatric symptoms was designed, and heat maps and probabilistic approaches were used.

Results. Differentiated risk profiles were found: cognitive and emotional manifestations in older adults, physical symptoms in adults, and sensory alterations in younger adults. Vaccination appeared to have a protective effect on some symptoms, whereas having had severe COVID-19 was associated with greater symptom burden. **Discussion.** A dependency exists between acute and post-acute symptoms in tiredness/fatigue, headache, anxiety, and depression, which confirms the prolongation of symptoms. This pattern supports the hypothesis that post-COVID-19 syndrome represents a functional prolongation of acute symptoms, consistent with the definition proposed by the World Health Organization. **Conclusions.** These findings contribute to documenting post-COVID-19 syndrome and highlight the need



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Conceptualization, data collection, drafting, analysis of results, and review.

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cleaning, analysis, writing of results, and review. **FELV.** Data analysis, heat map analysis, and review.

for longitudinal research that incorporates clinical, neuropsychological, and vaccination variables, as well as potential COVID-19 subtypes, is highlighted in order to clarify the mechanisms underlying the persistence of neuropsychiatric symptoms and to guide mental health programs for the most vulnerable groups.

Keywords:

COVID-19; Post- Acute COVID-19 syndrome; Psychic Symptoms; Vaccination; Risk Factors; Fatigue; Mental Health; Cognition; Pandemics.

RESUMEN

Introducción. El síndrome post-COVID-19 es un problema de salud emergente con implicaciones en la calidad de vida de quienes lo padecen. El objetivo de este estudio es determinar la dependencia entre los síntomas autoinformados agudos y postagudos asociados a la afectación post-COVID-19 según género, rango etario, vacuna y diagnóstico COVID-19 para definir un perfil de riesgo. **Metodología.** Estudio prospectivo e inferencial, muestra de 1,601 colombianos, se diseñó un cuestionario *ad hoc* dicotómico de síntomas autoinformados neuropsiquiátricos, se utilizó mapas de calor y perspectivas probabilísticas. **Resultados.** Se hallaron perfiles de riesgo diferenciados: en adultos mayores manifestaciones cognitivas y emocionales; en los adultos síntomas físicos, y en lo jóvenes alteraciones sensoriales. La vacunación parece tener un efecto protector frente a algunos síntomas, contrario al haber tenido COVID-19 severo. **Discusión.**

Existe dependencia entre los síntomas agudos y postagudos en cansancio-fatiga, cefalea, ansiedad y depresión, lo que permite confirmar la prolongación de síntomas; este patrón respalda la hipótesis de que el síndrome post-COVID-19 representa una prolongación funcional de los síntomas agudos, coherente con la definición propuesta por la Organización Mundial de la Salud. **Conclusiones.** Estos hallazgos contribuyen a documentar el síndrome post-COVID-19. Se resalta la necesidad de realizar investigaciones longitudinales que incorporen variables clínicas, neuropsicológicas, de vacunación y posibles subtipos de COVID-19, con el fin de esclarecer los mecanismos que sustentan la persistencia de síntomas neuropsiquiátricos y orientar programas de salud mental para los grupos más vulnerables.

Palabras clave:

COVID-19; Síndrome Postagudo de COVID-19; Síntomas Psíquicos; Vacunación; Factores de Riesgo; Fatiga; Salud Mental; Cognition; Pandemias.

RESUMO

Introdução. A síndrome pós-COVID-19 é um problema de saúde emergente, com implicações na qualidade de vida das pessoas que a sofrem. O objetivo deste estudo é determinar a dependência entre os sintomas autorrelatados agudos e pós-agudos associados às sequelas da COVID-19, segundo género, faixa etária, vacinação e diagnóstico de COVID-19, a fim de definir um perfil de risco. **Metodologia.** Estudo prospectivo e inferencial, com amostra de 1,601 colombianos. Foi elaborado um questionário *ad hoc* dicotómico sobre sintomas neuropsiquiátricos autorrelatados. Foram utilizados mapas de calor e abordagens probabilísticas. **Resultados.** Foram encontrados perfis de risco diferenciados: em idosos, manifestações cognitivas e emocionais; em adultos, sintomas físicos; e em jovens, alterações sensoriais. A vacinação parece exercer efeito protetor sobre alguns sintomas, ao contrário do que se observa em casos de COVID-19 grave. **Discussão.** Existe uma dependência entre os sintomas agudos e pós-agudos, especialmente em relação ao cansaço/fadiga, cefaleia, ansiedade e depressão, o que confirma a persistência dos sintomas. Esse padrão sustenta a hipótese de que a síndrome pós-COVID-19 representa uma prolongação funcional dos sintomas agudos, em consonância com a definição proposta pela World Health Organization. **Conclusões.** Essas descobertas contribuem para documentar a síndrome pós-COVID-19. Destaca-se a necessidade de realizar pesquisas longitudinais que incorporem variáveis clínicas, neuropsicológicas, relacionadas à vacinação e possíveis subtipos de COVID-19, a fim de esclarecer os mecanismos que subjacentes à persistência dos sintomas neuropsiquiátricos e orientar programas de saúde mental voltados aos grupos mais vulneráveis.

Palavras-chave:

COVID-19; Síndrome de Pós-COVID-19 Aguda; Sintomas Psíquicos; Vacinação; Fatores de Risco; Fadiga; Saúde Mental; Cognição; Pandemias.

Introduction

Long COVID or post-COVID-19 syndrome is an emerging health issue (1) that requires a comprehensive response from health management, public health authorities, and the research community (2) due to its

impact on the mental health, well-being, and quality of life of those affected. However, although symptoms have been reported even in young adults, children, and people who were not hospitalized, there is no consensus on this syndrome's symptoms or its duration, which is why it has not been clearly defined (3,4). Nevertheless, the World

Health Organization (WHO) defines post-COVID-19 as a condition in individuals with a confirmed or probable SARS-CoV-2 infection three months after COVID-19 that cannot be explained by an alternative diagnosis. Symptoms may persist as of the onset of the disease, appear again, or fluctuate or recur over time (5,6).

According to the WHO, between 10% and 20% of the population experiences medium- and long-term effects (6). From an epidemiological perspective, reported rates of incidence and prevalence have ranged from 16% to 87% (7). Similarly, it has been reported that 18% of patients were diagnosed with psychiatric disorders three months after their COVID-19 diagnosis. However, there is little information on the prevalence of cognitive and psychological difficulties following infection (8,9).

It is worth highlighting that previous pandemics revealed a range of neuropsychiatric symptoms, such as mood swings, encephalopathy, and psychosis, which accompanied the viral infection during the acute phase or weeks to months after recovery from the infection, as was the case with SARS (10-13).

Various studies have highlighted the pathological potential of coronavirus and its comorbidities, medical treatments and psychosocial factors related to the onset or exacerbation of symptoms of mental illness health symptoms (14,15). Reviews on the subject have identified neurological and neuropsychological symptoms as the most common (4,7,12,15–17), noting a high prevalence - particularly of insomnia, fatigue, cognitive impairment, depression, and anxiety - in the first six months after infection, impacting the individual's daily functioning (5,18).

Moreover, episodes of confusion, known as “brain fog,” have been reported. These are accompanied by a wide range of psychological symptoms, including disorientation, low energy, difficulty concentrating and finding the right words, tremors, fatigue, phantom smells, and dizziness (19,20). However, research in this area is currently limited (4), so it will likely be years before we have a clearer picture of the cognitive impact and psychological manifestations of COVID-19 (12).

Therefore, describing the neuropsychiatric symptoms associated with COVID-19 is of great epidemiological, clinical, and psychosocial importance in order to design comprehensive treatment plans aimed at rehabilitation, given their potential reversibility (4). This study aims to determine whether there is a correlation between acute self-reported symptoms and post-acute symptoms of post-COVID-19 complications, and to analyze this relationship according to factors such as gender, age group, vaccination status, and type of COVID-19 diagnosis in order to define a risk profile using heat maps or connection networks as alternative methods.

Methodology

Design and sample

The study adopted a quantitative, cross-sectional, and descriptive-inferential approach, using an analytical and observational design based on self-reported COVID-19 symptoms. This allowed the researchers to identify associations, estimate probability patterns, and describe symptom persistence at a single point in time, without establishing causal relationships.

The sample size was determined using stratified random sampling and the Cochran formula (assuming a 95% confidence level and a 5% margin of error), prioritizing adequate statistical power for dependency analyses and the stability of the network models. Furthermore, the sample's high heterogeneity allowed for partial control of confounding or bias variables through stratification by age, gender, disease severity, and vaccination status, thereby reducing the influence of confounders on the interpretation of the results.

A stratified random sample was used, comprising 1,601 Colombian participants aged 18 to 86, of whom 57% identified as male and 43% as female. The age distribution was categorized according to the life stages defined by the Ministry of Health and Social Protection (21): youth (ages 18–26) 28.2%; adulthood (ages 27–59) 65.1%; and older adults (age 60 and older) 6.7%. In terms of level of education, 11.2% reported having completed elementary school, 27.2% secondary, 34% technical or vocational training, 22% undergraduate, and 5.4% postgraduate. With respect to socioeconomic status, 64% were in the low group, 34.3% in the middle group, and 1.7% in the high group (5,6). When it came to health-related variables, 87.1% reported being vaccinated against COVID-19, while 12.9% reported not being vaccinated. Regarding the severity of the illness, 49.4% reported a mild case, 43.8% a moderate case, 6.7% a severe case (including ICU admission), and 1.6% reported having had asymptomatic COVID-19.

Inclusion criteria were: (1) being a Colombian citizen; (2) residing in the country; (3) being at least 18 years of age; (4) having had COVID-19; (5) having persistent neuropsychiatric symptoms within three months of infection; and (6) providing informed consent to participate in the study.

Instruments and Variables

A self-administered, dichotomous, *ad hoc* survey on COVID-19-associated symptoms was designed based on the neuropsychiatric symptoms reported in the studies by Piore and Hampshire et al. (19–20), specifically regarding episodes of confusion, known as brain fog (disorientation,

low energy, difficulty focusing and finding words) and other neuropsychiatric symptoms reported in studies of COVID-19 involving hospitalized and non-hospitalized individuals, such as loss of taste and smell, depression, anxiety, tremors, and headaches, among other symptoms. Therefore, the items in the survey refer to the following symptoms: headaches, anosmia (complete loss of smell), hyposmia (partial loss of smell), ageusia (complete or partial loss of taste), confusion, disorientation, lack of energy, tremors, difficulty finding words, sadness/depression, worry/anxiety, tiredness/fatigue, phantom smells, and vertigo (17) during the acute and post-acute stages of COVID-19 (symptoms that persisted three months after infection, according to the definition of the WHO) (5,6).

From a psychometric perspective, the survey exhibited adequate characteristics, as indicated by Cronbach's and McDonald's statistics, both of which were greater than 0.828. This suggests good reliability and validity based on confirmatory factor analysis and the chi-square statistic as a measure of fit. Two dimensions related to acute symptoms and another related to post-acute symptoms were confirmed (p -value < 0.001). First, the necessary assumptions were assessed using Bartlett's sphericity test and the KMO measure of sampling adequacy, whose values confirmed the appropriateness of factor analysis. Together, these properties confirm that the items measure the domains they are intended to measure and provide sufficient statistical evidence to support using the instrument in characterizing self-reported symptoms associated with COVID-19.

The survey was also supplemented with a sociodemographic questionnaire and questions related to COVID-19, which collected information on age, gender, educational level, socioeconomic status, COVID-19 vaccination, and the severity of the COVID-19 diagnosis (mild, moderate, or severe; Intensive Care Unit [ICU]).

Data collection and ethical considerations

This study was conducted between May and December 2021. Participants' data was collected online using an open-ended Google Forms survey. This study adhered to the ethical standards for conducting research involving human subjects, the Declaration of Helsinki, and the ethical principles of psychology in Colombia, in accordance with the Code of Ethics and Bioethics of the Colombian College of Psychologists (Law 1090 of 2006). Consequently, it included virtual informed consent, confidentiality, and anonymity in handling information exclusively for research purposes. In accordance with Resolution 8430 of 1993 of the Colombian Ministry of Health, this was a risk-free research project. No interventions are performed on participants.

Analysis

For this study, sociodemographic variables and variables related to COVID-19 served as categorical and nominal independent variables. In accordance with the proposed model, association between the independent and dependent variables (acute and post-acute symptoms) was evaluated, as well as the influence the two groups of independent variables had on the symptoms.

For the dependency analysis, the chi-square test was used in contingency tables with two classification criteria, comparing acute symptoms with post-acute symptoms, using the p -value as the decision criterion and a significance level of 5%. In addition, a post-acute index (risk profile) was defined from a probabilistic perspective, serving as a statistical measure of the likelihood that a generally undesirable event will occur in the future. Furthermore, risk was categorized in the traditional manner: low [0; 0.33], medium [0.33; 0.66], high [0.66; 0.90], and absolute risk [0.90; 1.00], taking into account that risk implies the presence of one or more factors that increase the probability of adverse consequences (12). The statistical analyses were performed using the JAMOVI statistical software, version 1.2.27.

The network analysis was organized into three levels, each with a similar internal structure. The marginal analysis strategy involved temporal conditioning, meaning reports of acute self-reported symptoms and symptoms reported three months later (post-acute) were considered. By mapping the networks that represent each interaction, the networks with the most connections were identified, indicating a greater number of similarities among symptoms. Methodologically, the analysis of the number of interactions was based on the degree divergence method (Hamming distance) and similarity measures. In this way, the closer the value is to zero, the greater the similarity between the networks. Heat maps were used for visualization, with blue representing similarity and red representing greater dissimilarity.

The analyses of the variables were based on cross-sectional and longitudinal (temporal) comparisons, with the letter G representing the graphs or networks in question in the female group (G1 acute and G2 post-acute), male (G3 acute and G4 post-acute), and being vaccinated (G5 acute and G6 post-acute) and not vaccinated (G7 acute and G8 post-acute). In the case of diagnostic categories, there was mild COVID-19 (G9, G13, and G15 acute), moderate (G11 acute and G12 post-acute), asymptomatic (G13 acute and G14 post-acute), and severe (G15 acute and G16 post-acute).

Results

First, we present the descriptive results and dependency relationships for both acute and post-acute symptoms in the study population, followed by an analysis incorporating the factors of gender, age group, vaccination status, and type of COVID-19 diagnosis. It concludes with the profiles at highest risk of developing post-acute symptoms and with the degree divergence method (Hamming distance) and similarity measures for network analysis.

Table 1 presents both descriptive data on self-reported acute and post-acute symptoms and analyses of the dependencies among these symptoms in the study population. With respect to the descriptive data, it was found that, of the 14 acute symptoms, ageusia, headaches, anosmia, lack of energy, fatigue, and hyposmia were the most commonly reported, whereas difficulty finding words and phantom smells were reported less frequently.

Table 1. Descriptive statistics and dependency analysis of self-reported acute and post-acute symptoms in the study population (n=1,601).

Self-reported symptom	% No post-acute / total acute	% Yes post-acute / total acute	Analysis
Confusion No acute symptom	98.8%	1.2%	Of the individuals who did not self-report acute confusion, 1.2% reported it as a post-acute symptom, whereas 18% of those who did self-report acute confusion also reported it post-acutely; the association was significant (χ^2 Test =163, df 1 and p-valor <0.001).
Acute symptom present	82%	18%	
Disorientation No acute symptom	99.2%	0.8%	Of those who did not report disorientation as an acute symptom, 0.8% reported it post-acutely. In contrast, 18% of those who reported this symptom acutely also reported it post-acutely; the association was significant (χ^2 Test =184, df 1 and p-valor <0.001).
Acute symptom present	82%	18%	
Lack of energy No acute symptom	90%	10%	Among individuals who did not present lack of energy as an acute symptom, 10% reported it post-acutely; among those who did report lack of energy acutely, 39% also reported it post-acutely; the association was significant (χ^2 Test =89.8, df 1 and p-valor <0.001).
Acute symptom present	61%	39%	
Word-finding difficulty No acute symptom	99.1%	0.83%	Among individuals who did not report difficulty naming words, 0.83% reported it post-acutely; among those who did report this difficulty acutely, 25% also reported it post-acutely; the association was significant (χ^2 Test =258, df 1 and p-valor <0.001).
Acute symptom present	75%	25%	
Fatigue/tiredness No acute symptom	91%	9%	Among individuals who did not report fatigue/tiredness, 9% reported it post-acutely; among those who did report this symptom acutely, 42% also reported it post-acutely; the association was significant (χ^2 Test =134, df 1 and p-valor <0.001).
Acute symptom present	58%	42%	
Depressive symptoms (sadness/depression) No acute symptom	98%	2.2%	Among those who did not report depressive/sadness symptoms, 2.2% reported them post-acutely; among those who reported this symptom acutely, 33% also reported it post-acutely; the association was significant (χ^2 Test =312, df 1 and p-valor <0.001).
Acute symptom present	67%	33%	
Anxiety symptoms (worry/anxiety) No acute symptom	96%	4%	Among those who did not report worry/anxiety symptoms, 4% reported them post-acutely; among those who reported this symptom acutely, 38% also reported it post-acutely; the association was significant (χ^2 Test =322, df 1 and p-valor <0.001).
Acute symptom present	62%	38%	
Phantom smells No acute symptom	97%	3.0%	Among those who did not indicate phantom smells, 3.0% reported them post-acutely; among those who reported phantom smells as an acute symptom, 29% also reported them post-acutely; the association was significant (χ^2 Test =225, df 1 and p-valor <0.001).
Acute symptom present	71%	29%	
Vertigo No acute symptom	98%	1.8%	Among those who did not report vertigo, 1.8% reported it post-acutely; among those who reported vertigo acutely, 31% also reported it post-acutely; the association was significant (χ^2 Test =313, df 1 and p-valor <0.001).
Acute symptom present	69%	31%	
Headache No acute symptom	95%	5.4%	Among those who did not report acute headache, 5.4% reported it post-acutely; among those who reported acute headache, 40.2% also reported it post-acutely; the association was significant (χ^2 Test =94.0, df 1 and p-valor <0.001).
Acute symptom present	60%	40%	

Anosmia (complete loss of smell) No acute symptom	98%	2.0%	Among those who did not report anosmia as an acute symptom, 2.0% reported it post-acutely; among those who reported anosmia acutely, 15% also reported it post-acutely; the association was significant (χ^2 Test =78.3, df 1 and p-valor <0.001)
Acute symptom present	85%	15%	
Hyposmia (partial loss of smell) No acute symptom	91%	9%	Among those who did not report hyposmia, 8% reported it post-acutely; among those who reported this symptom acutely, 24% also reported it post-acutely; the association was significant (χ^2 Test =67.3, df 1 and p-valor <0.001).
Acute symptom present	76%	24%	
Ageusia (loss of taste) No acute symptom	97.4%	2.5%	Among those who did not report ageusia, 2.5% reported it post-acutely; among those who reported it acutely, 16% also reported it post-acutely; the association was significant (χ^2 Test =60.7, df 1 and p-valor <0.001).
Acute symptom present	84%	16%	
Tremors No acute symptom	99.2%	0.8%	Among those who did not indicate tremors as an acute symptom, 0.8% reported them post-acutely; among those who reported tremors acutely, 20% also reported them post-acutely; the association was significant (χ^2 Test =189, df 1 and p-valor <0.001).
Acute symptom present	80%	20%	

Source: prepared by the authors.

Similarly, the most common post-acute symptoms were headaches, fatigue, lack of energy, hyposmia, and anosmia, with anxiety symptoms also being reported in this group. Difficulty finding words and disorientation were observed less frequently, as with the acute symptoms.

In the analysis of dependency relationships, individuals who did not exhibit acute symptoms, such as fatigue, hyposmia, headaches, anxiety symptoms, ageusia, phantom smells, and anosmia, did exhibit these symptoms as post-acute symptoms. In addition, fatigue, headaches, lack of energy, anxiety, depression, dizziness, and acute phantom smells, were also reported as post-acute symptoms.

Furthermore, in the descriptive analysis of acute and post-acute symptoms in the study population (Table 2), based on the variables of age group, COVID-19 vaccination, and type of COVID-19 diagnosis, as shown in Table 3, the same acute and post-acute symptoms, such as lack of energy, fatigue, headaches, anosmia, and ageusia, were found across all analysis variables. However, males had higher percentages compared to females across all variables, and in the case of the type of COVID-19 diagnosis variable, the severe category did not show high percentages for headaches compared to the mild and moderate categories.

Table 2. Descriptive statistics by gender, age group, COVID-19 vaccination status, and COVID-19 diagnosis severity.

	Gender		Age Group			COVID-19 vaccination status		COVID-19 diagnosis severity		
	Female	Male	Youth	Adulthood	Older adult	Yes	No	Mild	Moderate	Severe
Self-reported symptoms / variables	n=913	n= 688	n=451	n= 1043	n= 107	n=1394	n=207	n=791	n= 702	n=108
	57%	43%	28.2%	65.1%	6.7%	87.1%	12.9%	49.4%	43.8%	6.7%
Confusión Acute	12%	15%	12%	12%	16%	12%	14%	25%	14%	19%
Post-acute	3%	4%	2%	3%	4%	3%	3%	6%	3%	5%
Disorientation Acute	11%	15%	11%	12%	14%	12%	14%	9%	14%	19%
Post-acute	3%	3%	2%	3%	3%	2%	4%	1%	3%	6%
Lack of energy Acute	51%*	67%*	52%*	49%*	40%*	49%*	52%*	54%*	47%*	24%
Post-acute	32%*	42%*	28%*	32%*	41%**	32%*	31%*	24%	37%*	45%*
Word-finding difficulty (difficulty naming words) Acute	6%	8%	8%	7%	7%	7%	7%	6%	7%	11%

Post-acute	2%	3%	1%	2%	6%	2%	2%	2%	2%	5%
Fatigue/tiredness Acute	45%*	59%*	48%*	44%*	36%	45%*	44%*	47%*	44%*	22%
Post-acute	35%*	47%*	28%*	34%*	43%**	33%*	34%*	26%*	38%*	44%*
Depressive symptoms (sadness/depression) Acute	20%*	26%*	18%*	19%*	13%	18%*	19%*	14%*	21%*	23%
Post-acute	9%	12%	6%	9%	18%	9%	7%	6%	5%	17%
Anxiety symptoms (worry/anxiety) Acute	23%*	31%*	22%*	23%*	21%	22%*	25%*	19%*	26%*	26%
Post-acute	14%	19%	13%	14%	18%	14%	15%	11%	16%	23%
Phantom smells Acute	12%*	15%*	12%*	11%*	10%	11%*	12%*	9%*	13%*	15%
Post-acute	5%	6%	5%	5%	3%	5%	5%	4%	5%	6%
Vertigo Acute	19%*	25%*	15%*	19%*	18%	18%*	16%*	5%*	19%*	18%
Post-acute	8%	11%	6%	8%	15%	1%	8%	5%	9%	17%
Headache Acute	52%*	69%*	52%*	52%*	54%*	51%*	58%*	53%*	53%*	30%
Post-acute	37%*	49%*	35%	35%*	33%*	36%*	29%*	32%*	37%*	41%*
Anosmia (complete loss of smell) Acute	53%*	71%*	55%*	52%*	41%*	51%*	58%*	49%*	55%*	43%
Post-acute	9%	12%	9%	10%	7%	9%	8%	10%	8%	8%
Hyposmia (partial loss of smell) Acute	33%	44%*	36%	34%	33%	34%	36%	96%	34%	25%
Post-acute	12%	16%	13%	10%	10%	0%	14%	9%	13%	13%
Ageusia (loss of taste) Acute	58%*	77%*	59%	57%*	49%*	57%*	56%	21,9%	60%	47%
Post-acute	11%	15%	12%	10%	11%	11%	12%	22%	12%	10%
Tremors Acute	27%	27%	25%	28%	26%	27%	62%	22%	33%	20%
Post-acute	6%	7%	6%	28%	10%	27%	62%	22%	33%	20%

Note: %=percentage; * acute symptoms $\geq 40\%$;

* post-acute symptoms that exceed half of the acute percentage;

** increase in the percentage of presenting the post-acute symptom compared with the acute symptom.

Source: prepared by the authors.

In the case of the acute symptoms of hyposmia, it was present in 96% of individuals diagnosed with mild COVID-19. However, this same post-acute symptom, along with anosmia and ageusia, showed a marked decline in the post-acute group across all variables, while symptoms, such as lack of energy, fatigue, and headaches, persisted in over half of the post-acute cases across all variables.

On the other hand, regarding the age group variable, older adults showed a slight increase in the percentage of the post-acute symptom of fatigue, while, with respect to the vaccination status variable, it was the post-acute symptom of headaches among those who were unvaccinated.

However, when analyzing the relationship between acute symptoms that persisted into the post-acute phase and the study factors, significant associations were found for all factors, specifically for the gender factor: women were more likely to experience the post-acute symptoms of confusion, disorientation, difficulty finding words, fatigue, headaches, hyposmia, and ageusia, while men reported a lack of energy, phantom smells, vertigo, anosmia, and tremors. Both genders were likely to experience anxiety symptoms.

With respect to the age group factor, significant associations were found in youth with phantom smells, hyposmia, and

ageusia; difficulty finding words, symptoms of depression, symptoms of anxiety, and tremors were found in older adults; and headaches, fatigue, lack of energy, hyposmia, and ageusia were found in adults.

Table 3. Dependency analysis of self-reported acute and post-acute symptoms by gender, age group, COVID-19 vaccination status, and COVID-19 diagnosis severity.

Síntomas auto informados/variables		Gender		Age group			COVID-19 vaccination status		COVID-19 diagnosis severity		
		Female	Male	Youth	Adulthood	Older adult	Yes	No	Mild	Moderate	Severe
Confusion	Acute	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 005
	Post-acute	**21.1%	15.1%	17.1%	18.8%	19%*	18.3%	18.9%**	18.4	19.8%**	19.2%
Disorientation	Acute	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 008	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 006
	Post-acute	**19.2%	16.7%	18%	18.18%*	16.7%	17.4%	21%*	10.7%	20.2%**	23%
Lack of energy	Acute	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 013	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 008
	Post-acute	38.6%	**39.4%	35.2%	39.3%*	50.6%	39.1%**	37.5%	30.9%	44%*	65.3%
Word-finding difficulty	Acute	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001
	Post-acute	**27%	23%	12.8%	27%	46.2%*	23%	25%**	21.2%	25.8%	29.4%**
Fatigue/tiredness	Acute	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 009	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 005
	Post-acute	**44.1%	40%	26%	43.6%*	54.1%	42.1%	43.8%*	35.8%	46%*	66.7%
Depressive symptoms	Acute	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001
	Post-acute	31.6%	34.1%	36.7%	32.3%	57.6%**	33.4%**	27.2%	29.6%	32.9%	41.8%**
Anxiety symptoms (worry/anxiety)	Acute	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001
	Post-acute	**38%	**38%	36.8%	38%	46.3%**	38.3%*	37.3%	36.8%	37.6%	47.1%**
Phantom smells	Acute	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 006	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001
	Post-acute	28.4%	**30.1%	31.2%*	28.9%	21.4%	28.8%	31.4%**	30.4%**	28%	27.2%
Vertigo	Acute	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001
	Post-acute	30.1%	**32.3%	26.9%	30.7%	45.7%*	30.9%	32.6%**	26%	31.5%	48.6%**
Headache	Acute	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 087	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 006
	Post-acute	**41.2%	38.2%	40.1%	40.3%**	37.6%	41.2%**	34%	37.6%	41.2%*	57.9%
Anosmia (complete loss of smell)	Acute	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 004	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001
	Post-acute	14.7%	**15.8%	14.2%	15.7%**	13.7%	16%*	12.3%	17.3%**	13%	16.4%
Hyposmia (partial loss of smell)	Acute	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 010	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 135
	Post-acute	**26.3	21.1%	26.1%*	22.9%	23.9%	23.4%	27.1%**	20%	27.1%**	34.1%
Ageusia (loss of taste)	Acute	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 034	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 161
	Post-acute	**16.1%	15.7%	18%*	14.9%	18%	15.6%	17.7%*	15.9%	16.6%**	17.7%
Tremors	Acute	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 001	Sig, 047	Sig, 001	Sig, 001	Sig, 001
	Post-acute	19.1%	**20.2%	5.5%	19.2%	28.2%**	20.4%**	9.7%	16.9%	18%	45%**

Note: Sig.=Significance; %=percentage; * or ** significant relationships.

Source: prepared by the authors.

Regarding the vaccination factor, being vaccinated was associated with low energy, symptoms of depression, anxiety, headaches, and tremors, while not being vaccinated was associated with the remaining self-reported symptoms. In mild COVID-19 diagnoses, there were significant associations with phantom smells and anosmia. In the severe category were difficulties finding words, sadness and anxiety, vertigo, and tremors, while the remaining self-reported symptoms were associated with the moderate diagnosis category.

Finally, with respect to network analysis, it was found that the interaction between gender and COVID-19 diagnosis results in significant differences in network similarity between the two genders, with distances ranging from 1.05 to 1.70 for mild and severe cases for both acute and post-acute self-reported symptoms (Figure 1). When it comes to gender and vaccination status (G18 and G20 networks, distance 1.11; and G22 and G24 networks, distance 1.07), it can be interpreted that the symptoms and their prevalence were profoundly altered over time. This result is consistent across both genders.

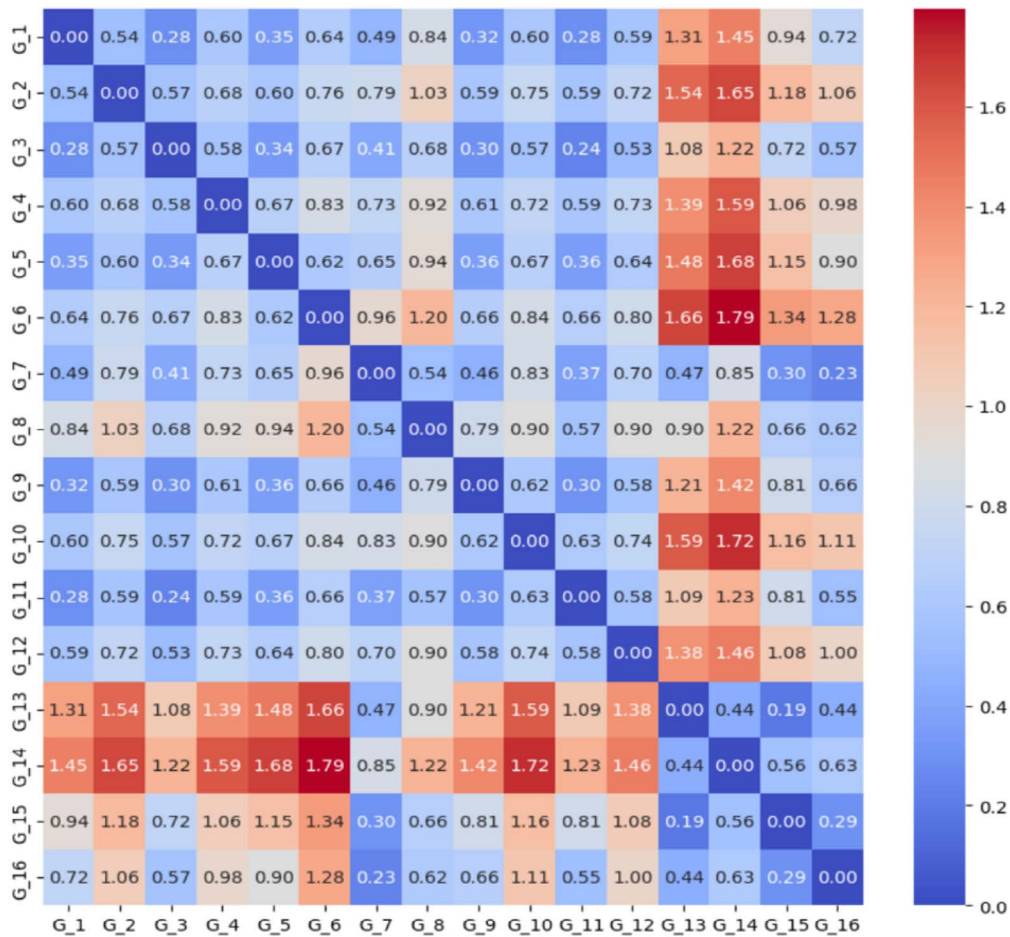


Figure 1. Heat map comparing connection networks.
Source: prepared by the authors.

Figure 1 shows a comparison of the G1 and G3 networks with a similarity score of 0.28. For the G2 and G4 networks, the score is 0.68, which means the “acute” measurement indicates a high degree of similarity between the networks. Therefore, it can be concluded that gender does not produce significant differences in the configuration of the connections or in the type of symptoms present. In the case of the G2 and G4 network

comparison, there is an increase in the quantification - nearly double the previous value -, which means the number of connections is reduced by a factor of 2.4 compared to the “acute” phase. Therefore, they share fewer similar symptoms. This leads us to conclude that gender is a significant factor in “post-acute” measurements. Therefore, the symptoms only differed between men and women in the “post-acute” reports.

The comparison between connection networks G1 and G2 illustrates the behavior of connections over time for females, and the G3 and G4 networks for males. The quantification for the first case is 0.54, while it is 0.58 for the second. This means the number of connections remains stable. Therefore, time is not a factor that produces significant differences in terms of connections.

When comparing networks G5 and G7, their similarity score is 0.65. Conversely, the score for networks G6 and G8 is 1.20. The latter is highlighted in red, indicating how dissimilar the symptoms are between vaccinated and unvaccinated individuals in the “post-acute” time period. Therefore, vaccination status results in significant differences in the “post-acute” time period. In percentage terms, there is a decrease of nearly 50% in the number of connections.

When comparing the G5 and G6 networks, as well as for G7 and G8 networks, the resulting quantification for the first case is 0.62, while it is 0.54 for the second. This means the number of connections remains virtually the same. It indicates that the interconnections between symptoms are similar regardless of whether or not a person is vaccinated.

A comparison was made of the G13, G9, G11, and G15 networks, positioned in the statements made before diagnosis, and the G14, G10, G12, and G16 networks, for after diagnosis for symptoms SS, Lv, Md, and Sv, respectively. It is also noted that the greatest dissimilarity is observed between SS and Lv and Md. Regarding “post-acute” symptoms, the greatest distances are found between SS and Lv and Md. In this way, it can be observed that individuals with an Sv level exhibit symptoms similar to those who reported no symptoms. Comparing the connection networks G13 and G14 for SS, G9 and G10 for Lv, G11 and G12 for Md, and finally, G15 and G16 for Sv, the following respective distances are obtained: 0.44, 0.62, 0.58, and 0.29, suggesting a similarity between the networks that identify the transition between “acute” and “post-acute” phases.

In summary, the most common acute symptoms were headaches, fatigue, lack of energy, hyposmia, anosmia, and ageusia, while difficulties finding words, phantom smells, and vertigo occurred less frequently. A significant proportion of those who experienced symptoms during the acute phase continued to report them during the post-acute phase, particularly fatigue, headaches, lack of energy, anxiety and depression, dizziness, and phantom smells. It is noteworthy that even some individuals who did not report certain symptoms during the acute phase did develop them later on, which reinforces the idea that post-COVID-19 syndrome is not merely a linear

extension of the initial symptoms, but may involve new manifestations over time.

When considering sociodemographic and clinical characteristics, it was observed that these acute and post-acute symptoms were distributed relatively consistently across the different groups, with symptoms such as lack of energy, fatigue, headaches, anosmia, and ageusia being particularly prevalent across all categories of gender, age group, vaccination status, and type of diagnosis. However, some notable differences were identified: men tended to report higher percentages of symptoms across several categories, older adults experienced more persistent fatigue, and the persistence of post-acute headaches was more pronounced among those who were unvaccinated. Overall, symptom dependency and symptom network analyses suggest that the transition from the acute to the post-acute phase is accompanied by a reorganization of symptoms, with specific risk profiles associated with gender, age, vaccination status, and the severity of the initial illness, underscoring the need for tailored clinical monitoring in these groups.

Discussion

This study found that acute self-reported symptoms associated with smell and taste - hyposmia, anosmia, and ageusia - decreased significantly during the post-acute phase, suggesting that these symptoms are characteristic of the infection stage and initial diagnosis of COVID-19, as has been reported in previous literature (19–23).

Furthermore, a significant association was found between acute and post-acute self-reported symptoms, particularly fatigue, headaches, anxiety, and depression. This pattern confirms the persistence of symptoms beyond the acute phase and supports the hypothesis that post-COVID-19 syndrome represents a functional continuation of the initial symptoms. This is consistent with the definition proposed by the WHO (5,6).

Differences were observed in risk profiles across the life cycle: mood and cognitive symptoms predominated among older adults, physical symptoms were the most common among adults, and sensory disturbances were more prevalent among young people. These differences may be linked to psychological, social, and physiological factors associated with age. In older adults, these symptoms may be related to aging processes, comorbidities, and neuroinflammatory mechanisms (8,9,16,24). In young people, sensory disturbances may be associated with transient impairment of the epithelium and peripheral neurochemical pathways (20,22). In adults, the persistence of physical symptoms may be due to a sustained systemic response following infection (9,16,25).

In terms of gender, it was observed that males exhibited a higher frequency of physical and sensory symptoms, while females had a higher proportion of emotional and cognitive symptoms during the post-acute period. This could be explained by hormonal and psychosocial factors, as well as by differences in emotional reactivity during the pandemic (8,22,26). However, both genders demonstrated a high risk of persistent symptoms, particularly those related to anxiety.

With respect to the COVID-19 diagnosis variable, differences were found that were consistent with the severity of the condition. In mild cases, sensory symptoms such as anosmia and phantom smells were observed most frequently; in severe cases, patients experienced difficulties finding words, sadness and anxiety, dizziness, and tremors; while moderate cases accounted for the highest number of post-acute symptoms. This is consistent with studies indicating that hospitalized patients or those with more severe symptoms tended to experience persistent neuropsychiatric sequelae (8,27,28).

Regarding the vaccination factor, significances were found both in vaccinated and unvaccinated individuals, particularly when it comes to symptoms, such as fatigue, depression, anxiety, headaches, and tremors. Although the data suggests that vaccination may have a protective effect against certain symptoms, this study did not include information on vaccination schedule or booster doses. These factors have been identified as being important for reducing the likelihood of long-term symptoms (29). Therefore, it is recommended for future research to incorporate these variables.

Although this study did not find a dependent relationship for symptoms associated with brain fog (confusion, difficulty finding words, and disorientation), it did demonstrate a higher likelihood of these symptoms occurring in the post-acute phase among women, in the adult and older adult groups, and in moderate and severe cases of COVID-19. This is consistent with research that has documented the presence of these symptoms in patients with neurological or neuropsychological sequelae following infection (12,16,20). Therefore, it is recommended for these individuals to be monitored, including neurocognitive and affective assessments.

Network analysis revealed differences in the similarity of symptom patterns based on gender, COVID-19 diagnosis, and vaccination status. It was found that the networks involving vaccinated and unvaccinated individuals showed significant changes in the number of connections during the post-acute period, suggesting a significant shift in the pattern of symptoms. With respect to gender, it was observed that differences between the networks became more apparent in post-acute symptoms, suggesting that

time may influence the differentiation of patterns between men and women.

Although this study provides evidence regarding the persistence of neuropsychiatric symptoms and the risk profiles associated with post-COVID-19 syndrome, questions remain to be answered, particularly regarding type of vaccine, virus variants, medical comorbidities, and possible subtypes of post-acute COVID-19 (22,29). In addition, the study acknowledges the presence of methodological limitations, such as the use of self-reported symptoms, the lack of diagnostic confirmation via PCR, the absence of medical records, and the inability to identify reinfections or complete vaccination schedules. However, these findings help document post-COVID-19 syndrome and highlight the need for longitudinal studies that incorporate clinical, neuropsychological, and vaccination-related variables, in order to guide mental health programs for the most vulnerable groups.

Conclusions

The results of this study reveal a correlation between acute and post-acute self-reported symptoms of COVID-19, with symptoms such as fatigue, headaches, anxiety, and depression persisting in the post-acute period. In addition, distinct risk profiles were identified: cognitive and emotional symptoms were predominant among older adults; physical symptoms, such as fatigue, exhaustion, and headaches, were predominant among adults; and sensory disturbances related to smell and taste were predominant among young people. Similarly, certain symptoms, such as fatigue, dizziness, and difficulty finding the right words, were associated with a higher risk of long-term symptoms, with variations based on gender, age group, and the severity of the COVID-19 diagnosis.

It was observed that sensory symptoms - hyposmia, anosmia, and ageusia - tend to decrease significantly after the acute phase, suggesting that they are primarily associated with the initial stage of the infection. In contrast, neuropsychiatric symptoms were more common in women and older adults and may be linked to a more severe clinical condition. On the other hand, vaccination appeared to offer some protection against certain symptoms, although this study did not examine the type of vaccine or the dosing schedule in detail.

These findings help us understand post-COVID-19 syndrome as a multifactorial condition in which biological, emotional, and cognitive factors interact, manifesting themselves differently depending on the individual and clinical characteristics of the population. The findings also emphasize the need for longitudinal studies that incorporate clinical, neuropsychological, and vaccination-related

variables, as well as potential COVID-19 subtypes, in order to clarify the mechanisms underlying the persistence of neuropsychiatric symptoms and guide mental health programs targeting the most vulnerable groups in the post-pandemic period.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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Ethical responsibilities

Protection of people and animals: Given its nature, this study is considered to be risk-free.

Data confidentiality: The authors declare that they have followed the ethical principles of psychology in Colombia, in accordance with the Code of Ethics and Bioethics of the Colombian College of Psychologists, Law 1090 of 2006, which includes virtual informed consent, confidentiality, and anonymity in the handling of information, exclusively for research purposes.

Right to privacy and informed consent: The authors have obtained virtual informed consent from the subjects referred to in the article.

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