



ORIGINAL ARTICLE

Epidemiological and clinical factors associated with persistent post-COVID-19 symptoms in Peruvian adults

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ABSTRACT

Introduction: patients who have suffered from COVID-19 generally recover; however, a proportion continue to present persistent symptoms, making it essential to identify their associated factors.

Objective: to determine the epidemiological and clinical factors associated with persistent post-COVID-19 symptoms in adults.

Methods: an observational, analytical, retrospective, case-control study was conducted at the Ate Vitarte Emergency Hospital in 2021. Through systematic probabilistic sampling, 214 adults discharged after overcoming the acute phase of SARS-CoV-2 infection were selected. Data collection was performed using a validated instrument, and descriptive and inferential statistical methods were applied. Ethical approval was obtained from the hospital's committee.

Results: age between 36 and 65 years ($p < 0,001$), presence of at least one comorbidity ($p = 0,002$), vaccination against COVID-19 ($p = 0,001$), obesity ($p = 0,023$), severe initial COVID-19 ($p < 0,001$), need for oxygen therapy ($p = 0,002$), and ICU admission ($p = 0,005$) were significantly associated with persistent post-COVID-19 symptoms. However, multivariate analysis demonstrated that only age 36–65 years ($p = 0,004$; ORa=4,918) and the presence of at least one comorbidity ($p = 0,010$; ORa=2,738) remained independently associated.

Conclusions: age and comorbidities were the main epidemiological factors linked to persistent post-COVID-19 symptoms in Peruvian adults, reinforcing the need to prioritize clinical follow-up in these groups.

Keywords: Multivariate Analysis; COVID-19; Risk Factors; Post-Acute COVID-19 Syndrome.

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INTRODUCTION

Coronavirus disease (COVID-19) caused by the SARS-CoV-2 virus emerged at the end of 2019 and became a public health emergency of international scope, and was formally characterized as a pandemic by the World Health Organization (WHO) in March 2020.^(1,2,3) Globally, the transmission and lethality dynamics of this pathogen demonstrated marked heterogeneity, with crude mortality rates above 4 % in various regions of the world, recording an incidence of $1,942 \pm 1,309$ cases/million inhabitants, which mainly affected older adults and individuals with pre-existing metabolic or cardiovascular comorbidities.^(4,5,6)

According to international reports, between 10-20 % of survivors who managed to overcome the acute phase of the infection experienced persistent or new-onset clinical manifestations in the medium and long term.⁽⁷⁾ This condition, called by the WHO "Post-COVID-19 Condition" or Long COVID (and clinically recognized as Post-Acute Sequelae of SARS-CoV-2 Infection or PASC),^(8,9,10) represented a complex public health challenge, due to the high prevalence of multisystemic alterations one year after hospital discharge.

This condition was characterized by its marked impact on quality of life, largely motivated by a broad spectrum of symptoms, where chronic fatigue, exertional dyspnea, sleep disorders, persistent cough, and neurocognitive impairment predominate. However, the distribution of these symptoms and their determinants vary according to the geographic and healthcare context. While in the United States it was estimated that 32,6 % of discharged patients manifested persistent symptoms (and 18,9 % develop new symptoms that worsen over time),^(11,12) in the Latin American and Peruvian context, sociodemographic characteristics modulated the risk.

In Latin America, and particularly in Peru, this scenario acquired critical relevance because the country recorded one of the highest per capita mortality rates worldwide during the first pandemic waves.⁽¹³⁾ Despite the broad approach to the topic in the literature, controversies persist regarding the real weight of clinical factors versus baseline epidemiological factors in the development of persistent symptoms in the national context. Specifically, in hospitalized populations with severe conditions, there is uncertainty about whether acute severity markers (such as the requirement for oxygen therapy or admission to Intensive Care Units) maintain an independent association with Long COVID or whether their effect responds to a confounding bias mediated by the patient's age and comorbidities.

In this context, the Ate Vitarte Emergency Hospital was established as the main national reference center for the care of critically ill COVID-19 patients in Peru, turning its cohort into a key epidemiological model to clarify these interactions. In relation to this, precisely identifying the linked factors is therefore fundamental to opportunely stratify the convalescent population, optimize ambulatory follow-up resources, and design focused rehabilitation strategies. Taking this as a reference, the present research was conducted, which aimed to determine the epidemiological and clinical factors associated with persistent post-COVID-19 symptoms in adult patients treated at the Ate Vitarte Emergency Hospital during the year 2021.

METHODS

Study design

An observational, analytical, retrospective, case-control study was conducted at the Ate Vitarte Emergency Hospital, located in the city of Lima, Peru. During the health emergency caused by the SARS-CoV-2 pandemic, this institution was established as the third-level hospital center of national reference for the reception, triage, and specialized medical management of adult patients in critical and intermediate condition due to COVID-19.

Population and sampling frame

Data collection and the symptomatic follow-up period comprised hospital discharges registered between January and December of the year 2021. The population consisted of 1,080 adult patients who received hospital discharge after having overcome the acute phase of SARS-CoV-2 infection whose intrahospital stay period did not exceed 30 days.

Due to the nature of the study (case-control), the sample size was determined using the statistical formula for comparison of proportions in case and control studies with groups of equivalent size (1:1 proportion). An epidemiological reference parameter was taken as a reported prevalence of persistent symptoms of 49,5 % in the post-COVID-19 convalescent population. Setting a confidence level of 95 % ($\alpha = 0,05$), a statistical power of 80 % ($\beta = 0,20$), and a minimum risk estimation to detect equivalent to an Odds Ratio of 2,0, the calculation yielded a minimum sample size of 107 subjects for the case group and 107 for the control group, consolidating a total sample of 214 adult patients.

The sample selection procedure was carried out using systematic probabilistic random sampling, structured from the digitized registry of hospital discharges corresponding to the year 2021. A selection interval of $K = N/n$ ($1080/214 \approx 5$) was calculated, choosing a random start between one and five and subsequently selecting every fifth patient from the list until completing the predefined quota for each group, verifying in each case compliance with the inclusion criteria. For the formation of the groups, the criteria considered were being patients over 18 years of age, with a confirmed diagnosis of COVID-19, who during their intrahospital stay required supplementary oxygen therapy support, managed to overcome the acute condition, obtained medical discharge, and voluntarily agreed to participate in the study.

The case group was made up of patients who actively and documentedly manifested physical or systemic symptoms of new onset or persistent character from the moment of hospital discharge and up to three months after resolution of the acute condition. The controls were patients discharged in the same time window who did not report persistent signs or physical symptoms linked to post-acute syndrome in the same temporal follow-up horizon.

The exclusion criteria comprised patients who died during the hospital stay, with clinical histories with data omissions or incomplete, or who presented severe pre-existing neurological alterations (epilepsy, mental retardation, or cerebral palsy) or psychiatric problems (such as anxiety disorders, dissociative or personality disorders) that could bias the self-report of symptoms, and patients with whom contact could not be established after three attempts on different days.

Procedures and techniques

The independent variables were organized into two dimensions: epidemiological factors (age, biological sex, body mass index, and presence of comorbidities) and clinical factors of the acute condition (initial severity of the infection, time elapsed since recovery, requirement for supplementary oxygen therapy, and need for admission to the Intensive Care Unit). The main dependent variable was persistent post-COVID-19 symptoms, defined as present or absent according to the report of physical manifestations in different systems. For information collection, a standardized form based on the WHO Case Report Form was used,⁽¹⁴⁾ applied through review of electronic clinical histories and structured telephone interviews. Said instrument was validated by experts with an Aiken V coefficient of 0,95 and acceptable internal reliability (Cronbach's Alpha = 0,703).

Statistical analysis

Data processing was performed with the SPSS statistical program version 25,0 for Windows. In the descriptive analysis, categorical and qualitative variables were summarized using absolute frequencies and relative percentages. For the inferential analysis, Pearson's Chi-square test (χ^2) was applied, in the first instance, in order to establish the association between the epidemiological and clinical independent variables and the presence of persistent post-COVID-19 symptoms, calculating crude Odds Ratios (OR) with their respective 95 % confidence intervals. Subsequently, the variables with statistical significance ($p < 0,05$) or clinical relevance were incorporated into a binary logistic regression model using the direct entry method (Enter), estimating adjusted Odds Ratios (aOR) with their 95 % confidence intervals. The goodness of fit of the model was verified with the Hosmer-Lemeshow test and an alpha significance level of 0,05 was set for all inferential tests.

Ethical aspects

The present research was conducted in strict compliance with the bioethical principles enunciated in the Declaration of Helsinki (2024), for medical research in human beings. The study protocol, the data collection form, and the verbal consent procedure were evaluated and formally approved by the Research Ethics Committee of the Ate Vitarte Emergency Hospital. The principle of autonomy was guaranteed through the request for verbal informed consent from each participant prior to the beginning of the telephone call. The confidentiality and anonymity of personal information were safeguarded through an alphanumeric coding system in the database, restricting direct access to the information only to the principal investigator through encrypted storage.

RESULTS

The study included a total of 214 adult patients, equally distributed into 107 cases with persistent post-COVID-19 symptoms and 107 controls who did not develop said condition. In the general population evaluated, patients aged between 36 and 65 years predominated (74,8 %), followed by the male sex (57,9 %). Regarding immunization status, 93,5 % of the subjects had received the COVID-19 vaccine, and of this group, 51,5 % had more than three doses. Likewise, 30,4 % of the participants registered at least one comorbidity at the time of the study.

In relation to the initial clinical profile of SARS-CoV-2 infection, 47,2 % of the patients were overweight. Additionally, 51,5 % experienced the disease in its severe form, 76,2 % required supplementary oxygen therapy, and 30,4 % needed admission to the Intensive Care Unit (ICU). Finally, 63,9 % of the sample managed to overcome the acute phase of the disease after a period of 30 days or more.

The preliminary bivariate analysis identified that the epidemiological factors significantly associated with the presence of persistent symptoms were age ($p<0,001$; $OR=3,518$), the presence of comorbidities ($p=0,002$; $OR=2,596$), and having the vaccination schedule ($p=0,001$; $OR=14,660$). Among the clinical factors, significant associations were found with obesity ($p=0,023$; $OR=1,920$), the initial extreme severity of the disease ($p<0,001$; $OR=4,062$), the requirement for oxygen therapy ($p=0,002$; $OR=2,765$), and the need for ICU admission ($p=0,005$; $OR=2,360$).

When introducing the variables into the binary logistic regression model for multivariate adjustment, it was demonstrated that the epidemiological factors maintained a statistically significant association ($p<0,05$). As observed in Table 1, the 36-65 age group increased the probability of manifesting persistent symptoms compared with those under 35 years of age ($aOR=4,918$; 95 % CI: 1,688-14,328; $p=0,004$). Similarly, suffering from at least one comorbidity increased said probability ($aOR=2,738$; 95 % CI: 1,268-5,914; $p=0,010$).

Table 1. Epidemiological factors associated with persistent post-COVID-19 symptoms.

Epidemiological factors		Coefficient β	aOR	95 % IC		P Value
				Inferior	Superior	
Age	≤ 35 years	Ref.	0	0	0	0
	36 to 65 years	1,593	4,918	1,688	14,328	0,004
	> 65 years	0,748	2,113	0,408	10,952	0,373
Sex	Female	Ref.	0	0	0	0
	Male	-0,248	0,780	0,368	1,657	0,518
Comorbidities	Presents some comorbidity	1,007	2,738	1,268	5,914	0,010
vaccination	Has COVID-19 vaccination	1,774	5,897	0,667	52,149	0,111

Notes: aOR (adjusted Odds Ratio); 95 % CI (95 % confidence intervals)

On the other hand, the multivariate analysis confirmed the absence of statistically significant associations between the clinical factors evaluated and the development of persistent post-COVID-19 symptoms ($p>0,05$), as detailed in Table 2.

Table 2. Clinical factors associated with persistent post-COVID-19 symptoms.

Clinical factors		Coefficient β	aOR	95 % IC		P Value
				Inferior	Superior	
Body Mass Index	Normal	Ref.	0	0	0	0
	Overweight	-0,410	0,664	0,212	2,080	0,482
	Obesity	0,094	1,098	0,335	3,601	0,877
Initial severity of COVID-19	Asymptomatic	Ref.	0	0	0	0
	Mild	-0,490	0,313	0,050	7,520	0,978
	Moderate	0,077	1,080	0,029	39,614	0,967
	Severe	1,052	2,864	0,077	106,386	0,568
Time since overcoming the disease	< 30 days	Ref.	0	0	0	0
	$\geq$ 30 days	-0,505	0,603	0,257	1,417	0,246
Oxygen therapy	Did not require	Ref.	0	0	0	0
	Requirement for oxygen therapy	-0,973	0,378	0,115	1,244	0,109
ICU admission	Did not require	Ref.	0	0	0	0
	Requirement for ICU admission	-0,007	0,993	0,405	2,430	0,987

Notes: aOR (adjusted Odds Ratio); 95 % CI (95 % confidence intervals)

DISCUSSION

The present study evaluated the factors associated with persistent post-COVID-19 symptoms, demonstrating through a multivariate analysis that age 36 to 65 years and the presence of at least one comorbidity constitute the main independent predictors for the development of this condition in the hospitalized population analyzed.

In relation to the age factor, it was found that the 36 to 65 age group increased almost five times the probability of manifesting persistent symptoms compared with those under 35 years of age. Although at a descriptive level local authors such as Mauricio Trelles et al.,⁽¹³⁾ evidenced a higher prevalence of sequelae in similar age ranges (36 to 59 years), at a global level a multifactorial susceptibility curve has been described. This vulnerability in mature and productive age could be explained by a less efficient cellular immune response compared with young people, added to a potentially higher initial viral load and slower-resolving tissue inflammatory processes. Likewise, these findings are consistent with what was reported by Fumagalli et al.,⁽¹¹⁾ who identified mature age as a determining factor in the persistence of long-term clinical manifestations.

On the other hand, the presence of comorbidities doubled the risk of developing post-COVID-19 syndrome (aOR=2,738). This result is consistent with the technical criteria of the National Institute of Health of Peru,⁽¹⁵⁾ and with the results offered by De la Calle Castro et al.,⁽¹⁶⁾ Pathophysiologically, patients with chronic antecedents such as diabetes mellitus, cardiovascular conditions, or pre-existing pneumopathies suffer a deleterious synergistic interaction between SARS-CoV-2 and a basally compromised immune system. This condition not only perpetuates a residual systemic proinflammatory state, but also alters tissue homeostasis and reduces post-acute infection organ resilience, prolonging the functional recovery time.^(17,18)

A relevant methodological finding was the loss of statistical significance of critical clinical variables (such as ICU admission, obesity, and the requirement for oxygen therapy) when transitioning from the bivariate analysis to the multivariate adjusted model. Although authors such as Boglione et al.,⁽¹⁹⁾ Iqbal et al.,⁽²⁰⁾ and Mahmud et al.,⁽²¹⁾ firmly associate the severity of the acute condition with post-COVID-19 syndrome, in our sample said association was diluted. This phenomenon can be attributed to a confounding effect or biological collinearity, where clinical severity variables are intrinsically subordinated to the presence of previous comorbidities and advanced age.

Consequently, when introducing the binary logistic regression model, the statistical weight was predominantly absorbed by the baseline epidemiological factors. It is not ruled out that the sample size may have limited the statistical power necessary to discriminate the independent impact of these clinical variables in the final model.

Finally, limitations inherent to the methodological design are recognized. The memory bias derived from telephone follow-up, together with the retrospective collection of data in a single care center, restricts the possibility of generalizing the results to populations with different demographic profiles or clinical management patterns. However, the use of an instrument endorsed by the WHO and formally validated contributes solidity to the measurement process and credibility to the data obtained. However, it is important to point out that the internal validity of the study depends on the design set, the selection of participants, the quality of the measurement, the control of possible confounding factors, and the statistical analysis, so it cannot be inferred solely from the content validation and the internal consistency of the questionnaire.

CONCLUSION

The study conducted evidenced that age between 36 and 65 years and the presence of comorbidities are the main epidemiological factors independently associated with the persistence of post-COVID-19 symptoms in Peruvian adults, while clinical variables related to the acute phase showed association in the bivariate analysis but lost significance in the multivariate model, which suggests that their effect is conditioned by baseline epidemiological characteristics. Taken together, these findings reinforce the need to prioritize the follow-up and rehabilitation of these groups.

Conflicts of interest

It is declared that there are no conflicts of interest.

Financial information

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Author contributions

NJPY: participated in the conceptualization; formal analysis; research; methodology; project administration; writing-elaboration of the original draft, as well as its review and editing.

RVA: participated in the conceptualization; data curation; methodology; supervision; visualization; writing-elaboration of the original draft, as well as its review and editing.

Data availability

The data used are confidential according to the consent voluntarily provided by the participants; the information collected is confidential and will not be shown to any person outside the study. Likewise, the data obtained are used for research purposes and their subsequent publication. They are stored in Word Office 365; authorization from the authors is required to access them. You may contact us through the email that will be provided below: nielspomayaymi@gmail.com

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