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Biomass consumption and persistent COVID symptoms in patients with moderate and severe SARS-CoV-2 infection

Consumo de biomasa y síntomas de COVID persistente en pacientes con episodio de infección moderada y severa por SARS-CoV-2

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FLJ: Conceptualized the idea, methodology design, data collection, supervised the research team, analyzed and curated the data, and revised the latest version of the manuscript. **JRCC**: Conceptualized the idea, collected data, wrote the first version of the report, and revised the latest version of the manuscript. **AKT**: analyzed and curated the data, revised the latest version of the manuscript. All assume responsibility for what is published.

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SUMMARY

Biomass consumption causes COPD, but it is unknown if it is linked to Post-Acute COVID-19 Syndrome (PACS). ***Objective:*** To examine the association between biomass use and this syndrome in recovered patients from two hospitals in northern Peru. ***Methods:*** A descriptive, cross-sectional, exploratory study was carried out. A questionnaire collected sociodemographic data, respiratory symptoms, and biomass use. ***Results:*** The final sample consisted of 110 participants. PACS was more common in those aged 35-65 (87.8%) and in Piura (89.1%), occurring in 88.1% of 2021 cases; the median time from symptom onset to interview was 82 (IQR = 79-119) weeks; 97/110 (86.3%) developed PACS; of these, 31% had used biomass before COVID-19 ($p = 0.332$). Among patients with PACS, the prevalence of dyspnea, fatigue, and cough was 68.4%, 67.3%, and 45.3%, respectively. After COVID-19, 61.05% used salbutamol and 14.7% used home oxygen. In the final model: having had a tracheostomy ($p = 0.011$), ICU stay ($p = 0.039$), and the mention of "sequelae in the epicrisis" ($p = 0.052$) were associated with PACS; however, biomass use ($p = 0.332$) and years of use ($p = 0.072$) were not. ***Conclusion:*** No link was found between prior biomass use and the development of PACS. The frequency of PACS was high, with dyspnea being the most common symptom.

KEYWORDS: Post-Acute COVID-19 Syndrome, Biomass, COVID-19, respiratory symptoms and signs, Dyspnea.

RESUMEN

El consumo de biomasa produce EPOC, pero se desconoce si se asocia a Síndrome Post Agudo de COVID-19 (SPAC). ***Objetivo***: Explorar la asociación entre el consumo de biomasa y este síndrome en pacientes recuperados de dos hospitales del norte peruano. ***Material y métodos***: Estudio descriptivo transversal, exploratorio. Se aplicó un cuestionario de datos sociodemográficos, síntomas respiratorios y consumo de biomasa. ***Resultados***: El tamaño final muestral fue 110. SPAC fue más frecuente entre 35-65 años (87,8%) y en Piura (89,1%), se halló en el 88,1% de los casos del 2021; la mediana desde el inicio de síntomas hasta la entrevista fue 82 (IQR = 79-119) semanas; 97/110 (86,3 %) desarrollaron SPAC; de estos, 31% habían consumido biomasa antes de la COVID-19 (p = 0,332). En los pacientes con SPAC la frecuencia de disnea, astenia y tos fue 68,4%, 67,3% y 45,3%, respectivamente. El 61,05% usaron salbutamol después del episodio agudo de COVID-19 y 14,7% oxígeno domiciliario; en el modelo final: haber tenido una traqueotomía (p = 0,011), haber estado en la UCI (p = 0,039) y la aparición del término «secuela en la epicrisis» (p = 0,052) se asociaron con SPAC; ni el consumo de biomasa (p = 0,332) ni los años de consumo (p = 0,072) se asociaron con el SPAC. ***Conclusión***: No se encontró asociación entre el consumo previo de biomasa y el desarrollo del SPAC. La frecuencia SPAC fue alta, siendo la disnea, el síntoma más frecuente.

PALABRAS CLAVE: Síndrome Post Agudo de COVID-19, Biomasa, Covid-19, síntomas y signos respiratorios, disnea.

INTRODUCTION

From March 2020 to early December 2023, the COVID-19 disease has affected 702,137,335 people in the world, with 6,971,929 deaths [1]. In Peru, the number of cases amounts to 4,503,204, with 220,602 deaths. The department of Piura, in northern Peru, is the sixth with the highest positivity for the virus, being higher than the national positivity (14.32% vs. 11.60%). [2]

Even 4 years after the start of the pandemic and having declared its end as a Public Health Emergency of International Concern (PHEIC) on May 5, 2023, cases and deaths continue. For them, the World Health Organization (WHO) has stated that countries must continue to join efforts to understand the evolution of this disease and manage the transition from an emergency phase to a long-term sustained response. [3]

Many of the patients who have suffered from this health problem have systemic manifestations twelve weeks after the infection. This group of demonstrations has been called Long COVID [4]. Its frequency is approximately 10% of severe cases of COVID-19. In the world, there are around 65 million cases of Long COVID, and 200 possible associated symptoms have been reported [5]. Its incidence varies between 10 to 30% in non-hospitalized patients [6,7] and 50 to 70% in hospitalized patients. The greater the severity of the COVID-19 condition (critical/severe), the greater the probability of developing this syndrome. [8]

Chronic obstructive pulmonary disease (COPD) is one of the many comorbidities that have been related to a worse prognosis in acute cases and to pulmonary and extrapulmonary sequelae. According to a meta-analysis of 7 studies with 1,813 COVID-19 patients, COPD patients were more likely to develop severe disease and be admitted to the intensive care unit. [9]

Around the world, the most important risk factor for COPD is smoking. However, in Peru, the consumption of biomass that produces household air pollution has a predominant role [10,11]. Biomass is known as any organic matter, originating from biological processes of animals, plants, and/or their derivatives, spontaneous or provoked, and that can be used as an energy source [12]. The most widely used solid biomass fuels are wood, charcoal, agricultural waste, and manure [13], whose incomplete combustion releases smoke with fine particles that may contain carbon monoxide, nitric oxide, benzenes, and respirable matter particles: PM10 and PM2.5. [14]

About half of the world's population, mainly in developing countries, uses solid biomass [15]. In Africa,

Central America, Southeast Asia and South Asia, more than 90% of rural households use them [16]. According to a 2019 report from the Instituto Nacional de Estadística e Informática (INEI) of Peru, 5 million 700 thousand people in our country consume polluting fuels. In Piura, 31,0% of households consume biomass, while in Trujillo, 23,2%. [17]

Prolonged exposure to this pollutant can produce cell apoptosis, an increase in free radicals and metalloproteinases, as well as a decrease in pulmonary surfactant, phagocytic dysfunction of macrophages, and cell damage [18–20]. The risk is greater in women [21]. During lockdown periods, entire families -including women and children - were continuously exposed to indoor pollutants from biomass cooking and cigarette smoke [22]. Previous studies have shown that both air pollution and smoking increase the risk of severe outcomes in SARS-CoV-1, MERS, and COVID-19, with higher mortality observed in populations from more polluted areas [23]. Given this evidence, it is biologically plausible that chronic biomass exposure may contribute not only to acute severity but also to the persistence of respiratory symptoms after COVID-19.

Chronic exposure to biomass smoke produces long-term pulmonary damage characterized by airway inflammation, oxidative stress, and reduced lung function, which are similar mechanisms to those described in the persistence of respiratory symptoms after COVID-19 infection [24]. Therefore, individuals exposed to biomass may have a greater predisposition to develop post-acute COVID-19 syndrome (PACS), particularly respiratory sequelae such as cough and dyspnea. This biological plausibility supports the need to evaluate whether biomass exposure is associated with a higher frequency of persistent COVID-19 symptoms. It has been seen that biomass consumption impacts the prognosis of patients with COVID-19. In the United States, an increase of just 1 $\mu g/m^3$ in PM2.5 (local concentrations of biomass particulate matter) was associated with 8% increase in the COVID-19 death rate in 2020 [25]. In a prospective study carried out in a hospital of the Ministerio de Salud (MINSA) in Piura, Peru, in 2020, it was found that 17.7% patients with moderate/severe COVID-19 reported history and use of prolonged way of biomass. [26]

It is important that the factors associated with a higher frequency and worse outcome of patients recovered from COVID-19 be evaluated. There is a possibility that the consumption of biomass has an impact on the greater severity of COVID-19, thus generating sequelae. We have not found studies that explore this characteristic in those recovered from COVID-19 in our country. Therefore, this study aimed to evaluate the association between a history of biomass exposure and the persistence of respiratory symptoms compatible with PACS in patients discharged after moderate, severe, or critical COVID-19 in two hospitals in northern Peru during 2022.

METHODS

Study design and scope

A cross-sectional descriptive, exploratory study was carried out. The study was carried out in two hospitals in cities on the northern coast of Peru: Hospital Belén in Trujillo with level III-1 complexity and the Hospital de la Amistad Perú Corea Santa Rosa II-2-2 in Piura with level II-1 complexity. Both belong to the Ministerio de Salud de Perú, and provided care to patients with moderate, severe and critical COVID-19 during the pandemic.

Population and sample

The population was: patients discharged from the internal medicine services and/or intensive care unit due to COVID-19 during the period June 2020 to September 2022 with the CIE 10 codes U07.1 and U07.2. In total, this sampling frame consisted of 346 people.

The initial sample size obtained through the OpenEpi application, considering a confidence level of 95%, power of 80%, a percentage of positive exposures (patients with COPD who would develop persistent COVID of 22% and a percentage of unexposed people who would develop persistent COVID of 13%) was 263 for each group, that is, 526 people. These percentages are based on data from the Matsuyama retrospective cohort [27] in Japan. This considers COPD as an exposure factor since no data on biomass was found.

A stratified random sampling by hospital was proposed. However, given the percentage of rejection during the beginning of telephone contact, a census was carried out. All those people who had been hospitalized, whose medical history could be found in the files, who had survived the acute phase, and who responded to telephone calls, were included. No exclusion criteria were considered.

Likewise, a documentary review of clinical history data was carried out (medical history, duration of illness, length of hospitalization, and admission/discharge diagnosis).

Study variables

The dependent variable was the presence of persistent COVID-19 symptoms, defined as at least one respiratory symptom (dyspnea/cough, chest pain) and/or use of medications (inhalers, cough suppressants, mucolytics) from 3 months symptom onset, according to the guidance of the National Institute for Health and Care Excellence (NICE) [4]. The independent variable was biomass consumption. This was operationally defined as staying in a household where food is prepared with firewood and/or charcoal at least once a week, during the four weeks of a month, and for at least 6 months prior to the COVID-19 episode [28]; also whether the patient continued to consume biomass material after hospital discharge (if he had done so before becoming ill), severity of COVID-19, age, sex, duration of illness. COVID-19, time in ICU, arterial hypertension, diabetes mellitus, COPD, tracheostomy, and mechanical and dependent ventilation; also, through the review of medical records, the following variables were defined: COVID pneumonia, Respiratory failure, "Respiratory sequelae", as recorded as present or absent in the medical history.

Instruments and data collection

A structured data collection form was included to collect information from medical history and a checklist of cardiorespiratory and systemic symptoms, use of medication for respiratory symptoms, and previous exposure to biomass. This form was evaluated by expert judgment: one medical epidemiologist, one internist, two pulmonologists, one infectious disease specialist, and one physical therapy and rehabilitation doctor. The questionnaire was administered by telephone from October to December 2022; the telephone calls were made by a final year medical student and a nursing graduate, previously trained via Zoom by the internist in charge of the study. The language used to address the participant, the way the informed consent was presented, and the way the questions were asked were structured. The average interview time was 10 minutes.

Statistical analysis

First, a description of all the variables was made, which included measures of central tendency, dispersion, and absolute and relative frequencies. After this, a bivariate analysis was carried out with the respiratory sequelae as the dependent variable and the others as independent variables, including biomass consumption. Finally, using generalized linear models using Poisson regression with robust variance, a multivariate was performed using the backward technique to determine the adjusted prevalence ratio between history of biomass consumption and respiratory sequelae. Those variables for which a p-value <0.2 was found in the bivariate, and those with clinical plausibility, were also entered into the multivariate model. A significance level of 0.05 and 95% confidence intervals was considered.

Ethical aspects

The project was approved by the Dirección de la Escuela de Medicina and the Comité de Ética of the Universidad César Vallejo of Trujillo, and the Oficina de Apoyo a la Docencia e Investigación of both hospitals. The participants were sent an informed consent form through the WhatsApp application. To ensure confidentiality, all data were anonymized and identified only by codes. Personal identifiers were removed from the database, and access to the information was limited exclusively to the research team. Digital records were stored on password-protected computers, while any physical documents were kept in locked cabinets. In addition, results were presented in aggregate form, preventing the identification of individual participants. Finally, a copy of the final report was delivered to each hospital.

RESULTS

In both hospitals, at the beginning of June 2020 until September 2022 there 346 patients were discharged: 68 in Trujillo and 278 in Piura. The patient selection process is shown in Figure 1.

Regarding the duration of illness, the mean was 3.9 ± 2.68 days, the median hospitalization time was 16.5 (IQR = 8.0 – 152) days, and the median time from the onset of symptoms until the day of the interview (sequela time) was 82 (IQR = 79 – 119) weeks. 110 (100.0%) had more than 4 months since symptom onset; 102/110 (92.72%) had at least one respiratory/non-respiratory symptom (persistent COVID) (Data not shown). Of the 110 patients discharged with moderate to severe/critical COVID-19, 97 (86,3%) developed Post-Acute COVID Syndrome (PACS). PACS was more frequent in patients with severe/critical disease (93.94%) than in those with moderate disease (83.12%), although this difference was not statistically significant (p = 0.072). those patients in whose clinical history appeared "sequel", developed PACS (100.0%). (Table 2**)**

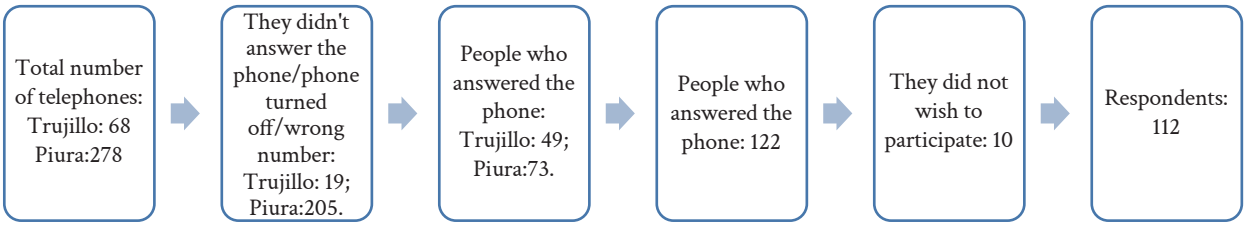

Figure 1. Participant recruitment flowchart.

Only 110/112 had more than 12 weeks since the beginning of symptoms and the interview; so, the final sample size was 110. PACS was more frequent in those aged 35 - 65 years (87.8%) and in patients from Piura (89.1%). Women (85.2%) and men (87.9%) were similarly affected. Regarding education level, the highest proportion was observed in patients with primary education (94.1%). By year of discharge, PACS was reported in 88.1% of cases in 2021. Most patients with hypertension (86.4%) and diabetes mellitus (83.3%) developed PACS, whereas only 15.4% of those with COPD reported this outcome. All patients with tracheostomy presented PACS. (Table 1**)**

In patients with PACS, the frequency of dyspnea, cough and asthenia were: 68.4%, 45.3% and 67.3%, respectively. 61.05% reported having consumed salbutamol after the acute COVID-19 event and 14.7% consumed home oxygen (Table 3). The variables corresponding to the use of biomass appear in Table 4, 30% of the total had consumed biomass before COVID-19, and 31% of the patients with PACS had consumed biomass before COVID-19 (p=0.072). Of the 33 patients with previous use of biomass, 2/33 (6%) reported having a previous diagnosis of COPD.

In the final model only: having had a tracheostomy aPR= 1.2, (CI 95% 1.04 - 1.38; p=0.011), have been in ICU aPR=1.13 (CI 95% 1.0 - 1.27; p=0.039), the term "sequel in epicrisis" aPR= 1.15 (CI 95% 0.99 - 1.34; p= 0.052), were associated with PACS; neither consumption of biomass (p=0.332), nor years of consumption (p=0.072), were associated with PACS. **(**Table 4)

Table 1. Sociodemographic characteristics of patients discharged with moderate/severe/critical COVID-19 from two hospitals in northern Peru, according to the presence of Post-Acute COVID Syndrome (PACS).

Variable	With PACS	Without PACS
	n (%)	n (%)
Age (Years)		
< 35	19 (20.0%)	2 (13.3%)
35-65	65 (68.4%)	9 (60.0%)
> 65	11 (11.6%)	4 (26.7%)
Origin		
Trujillo	38 (40.0%)	8 (53.4%)
Piura	57 (60.0%)	7 (46.6%)
Sex		
Women	45 (47.4%)	8 (53.4%)
Men	50 (52.6%)	7 (46.6%)
Education level		
Superior/technical	22 (23.15%)	3 (12.0%)
Secondary	44 (46.31%)	9 (17.0%)
Primary	16 (16.84%)	1 (5.9%)
Initial	2 (2.1%)	0 (0.0%)
No instruction	10 (10.52%)	2 (16.7%)
No data	1 (1.05%)	0 (0.0%)
Year of discharge		
2020	20 (21.05%)	5 (33.33%)
2021	74 (77.89%)	10 (66.66%)
2022	1 (1.05%)	0 (0,0%)
Comorbidities		
Hypertension	17 (17.89%)	2 (13.31%)
Diabetes mellitus*	14 (14.89%)	3 (20.0%)
COPD	2 (2.1%)	10 (66.6%)
Procedures		
Tracheostomy	3 (100.0%)	0 (0,0%)
ICU	18 (100.0%)	0 (0,0%)

COPD: chronic obstructive pulmonary disease; ICU: intensive care unit.
*data was not recorded for 01 patient with Diabetes

Table 2. Clinical severity of COVID-19, frequency of pneumonia, respiratory failure, sequelae, in patients with PACS.

	With PACS	Without PACS	*p-value*
Covid-19 Severity			
Moderate	64 (67.4%)	13 (86.7%)	Ref.
Severe/Critical	31 (32.6%)	2 (13.3%)	0.072
COVID-19 Pneumonia			
No	18 (18.94%)	1 (6.67%)	Ref.
Yes	77 (81.05%)	14 (93.33%)	0.109
Respiratory failure			
No	81 (85.26%)	13 (86.6%)	Ref.
Yes	15 (15.78%)	2 (13.3%)	0.882
"Sequel" appears in epicrisis			
No	91 (95.78%)	15 (100.0%)	Ref.
Yes	4 (4.21%)	0 (0.0%)	<0.001

Table 3. Frequency of symptoms and use of medications in patients with PACS (N=95).

	n (%)
1. Symptoms	
Dyspnea	65 (68.4%)
Cough	43 (45.3%)
Asthenia	64 (67,3%)
Abnormal Appetite	47 (49.5%)
Insomnia	54 (57.5%)
2. Medication use	
Salbutamol	37 (38,95%)
Ipratropium Bromide	15 (15.8%)
Salmeterol/ fluticasone	6 (6.3%)
Dextromethorphan	17 (17.9%)
Ambroxol	11 (11.6%)
N acetyl cysteine	12 (12.6%)
Home oxygen therapy	14 (14.7%)

Table 4. Description of variables related to biomass in the total number of participants.

Variables	n	%	Post Acute COVID Syndrome		
			n	%	*p value**
Previous consumption					
No	77	70.0	64	83.1	Ref.
Yes	33	30.0	31	93.9	0.072
Years of consumption (N=33)					
1 -10	19	57.58	18	94.7	Ref.
10 - 20	8	24.24	7	87.5	0.587
>20	6	18.18	6	100.0	0.325
Days per week (N=33)					
1 a 3	11	33.3	11	100.0	Ref.
4 a 7	22	66.7	19	86.4	0.164
Post-COVID consumption					
No	79	71.8	66	83.5	Ref.
Yes	31	28.2	29	93.5	0.101
"I knew it was harmful before infected"					
No	4	3.6	3	75.0	Ref.
Yes	106	96.4	92	86.7	0.618

*Logistic regression p

Table 5. Bivariate and multivariate analysis with clinical and biomass variables.

VARIABLES	cPR (IC95%)	VIF	*p value*	aPR (IC95%)	VIF (m)	*p value*
Days of illness	0.99 (0.97-1.01)	1	0.77			
Hospitalization time	1.00 (1.00-1.002)	1	**0,002**	1.0 (0.99-1.0)	1.6	0.148
Sequel time*	0,99 (0,99 - 1,00)	1	0,106	0.99 (0.99-1.0)	1.14	0.404
Disease Severity	1.01 (0.98-1.29)	1	**0.072**	1.01 (0.81-1.26)	1.87	0.875
ICU**	1.13 (1.00-1.27)	1	**<0.001**	1.13 (1.0-1.27)	2.34	**0.039**
COPD***	0.96 (0.73-1.25)	1	0.749			
Diabetes	0.94 (0.74-1.19)	1	0.65			
Tracheostomy	1.16 (1.07-1.25)	1	**<0.001**	1.2 (1.04-1.38)	1.52	**0.011**
COVID Pneumonia	0.89 (0.77-1.02)	1	0.109	0.96 (0.78-1.20)	1.7	0.773
Respiratory Insufficiency	1.01 (0.82-1.24)	1	0.882			
"Sequel in epicrisis"	1.16 (1.07-1.25)	1	**<0.001**	1.15 (0.99-1.34)	1.3	**0.052**
Mechanical Ventilation	1.16 (1.07-1.25)	1	**<0.001**	0.95(0.73-1.23)	2.14	0.706
Biomass consumption	1.13 (0.98-1.29)	1	**0.072**	1.09 (0.99-1.0)	1.78	0.332
Years of consumption	1.0 (1.00-1.00)	1	**0.003**	1.00 (0.99-1.0)	1.82	**0.073**

*: weeks; **: Intensive care unit; ***: Chronic obstructive pulmonary disease; aRP= adjusted prevalence ratios;

DISCUSSION

According to the results, no association was found between having consumed biomass and the years of consumption and having symptoms of persistent COVID. This could have several explanations. One of them could be the insufficient sample size. There was a significant rejection percentage: 67.63%. This would explain the non-representative size and design of the sample. In fact, there is a selection bias because in both cities a stratified randomization could not be carried out, which was ideal. Another possibility is the underreporting and diagnosis of COPD in our health system. In different studies, it has been found that COPD is an associated factor for PACS; however, no studies have been found that biomass consumption is. Another possibility is actually a non-association. Although it is true to have previous COPD, it increases the risk of severe/critical disease (9,29) and therefore, having more sequelae a direct association. It's debatable. Subramanian et.al (30), in a cohort of 486,149 patients with mild COVID, found that patients with COPD had an HR of 1.55 (CI 95% 1.47-1.64) for developing persistent COVID; Likewise, it was found that those who smoked and ex-smokers had an HR= 1.12, (CI 95% 1.08-1.15) and 1.08, (CI 95% 1.05-1.11), respectively; however, this data is from non-hospitalized patients. However, in Peru, the consumption of biomass that produces household air pollution has a predominant role. [10,11]

31% of the patients with PACS had consumed biomass before COVID. A previous biomass consumption of 29.46% was found, by León et.al. [26], in the Piura Hospital in the first wave. According to the INEI (Instituto Nacional de Estadística e Informática), in Piura, 31.0% of households consume biomass, and in Trujillo, 23.2%. In some districts, this reality exceeds 80%, with people living in rural areas being 4 times more exposed [17]. We do not have data on the origin (urban/rural) of the participants, which could partly explain the not-so-high frequency. Another interesting fact is that 96.4% knew that it was harmful to their health before the COVID-19 episode, and 27.6% continued consuming biomass after recovering from the acute phase; that is, they did not consider it a pulmonary-damaging agent. Likewise, during the pandemic, it was observed in different countries that populations already aware of cooking with other, less toxic fuels returned to the consumption of biomass, confinement being one of the key factors [31]. The motivation to continue consumption could be not being able to have access to improved stoves, overcrowding, and a lack of knowledge about it.

Having been in the ICU and having had a tracheostomy was associated with PACS. This result is similar to that found by Laurent et al. [32] in 2021, in which one year after discharge, 65% reported dyspnea. However, it is higher than that found by Mallik et al. [33], who, in a systematic review of 12 studies with 4,828 patients, found that only 39.5% of people reported dyspnea and 47% sleep disturbances. Possible differences in the severity of the condition and the limitations of the patients in our study, who were unable to obtain a bed in the ICU, could explain these differences.

The frequency of 86.4% of PACS is higher than that found in the literature: Davis et.al. [34], in 2021, in 3,762 patients from 56 countries, found 65.2%, Taquet et.al. [35], in 273,618 medical records, found 57% in 6 months, and Huang et.al. [8], in 1,773 histories, 63% at 6 months. One possibility is the inclusion only of moderate/severe/critical patients (71% had pneumonia), unlike these studies with mild patients. The other possibility is that there is measurement bias due to telephone interviews; the participants may have confused the questions with those from the acute episode. Also, previous consumption of biomass could produce respiratory symptoms (undiagnosed COPD) and make it difficult to determine the presence of PACS. Finally, other intercurrent respiratory viruses could confuse interpretation. Despite the small sample size, it could correspond to a consequence of the sequel of the initial picture.

We must also mention that in this study, some associated factors previously described as predictors of persistent COVID could not be corroborated. Notarte et.al. [36], in a systematic review, found that being a woman, having previous lung disease, diabetes, and obesity were associated with this problem of health. One possibility is the sample size of our study or a different behavior of the risk factors tested. It is a reason for investigation.

In a recent cohort study, Danesh et.al. [37], have described two clusters in patients with PACS: a group with predominance of neuro-psychiatric manifestations and another with respiratory manifestations: this last group has been hospitalized more frequently ($p = 0.046$), has more comorbidities ($p=0.019$) and more respiratory sequelae ($p< 0.001$), results similar to our study. This approach can allow health care to be managed, depending on the cluster to which people belong.

In the RECOVER study [38], a prospective cohort of 9,764 patients (8,646 infected with COVID-19 and 1,118 uninfected), from the United States and Puerto Rico, (16% Latino/Hispanic), was analyzed for the presence of 37 COVID persistent symptoms; it was found that "post-exertional discomfort" (28% vs 7%; aOR= 5.2 (CI 95% 3.9-6.8) and fatigue (38% vs 17%; aOR=2.9 (CI 95% 2.4-3.4), were associated with persistent COVID. These values are lower than those of our study, but again, we must mention the severity of our patients and the difference in sample size of this cohort. In our study, we found that dyspnea and asthenia were the most frequent symptoms.

The Peruvian health system collapsed during the pandemic (39). We believe that these figures can give a rough idea of what this system will have to face in the future as a result of this health problem.

This study has several limitations; Firstly, because the sample size was not achieved, a census procedure was carried out, selecting the entire population, which may have induced a selection bias, in addition to the problem of the high frequency of rejection. Ideally, to search for an association, 526 people interviewed in both hospitals would have been needed, which could not be achieved since the population size was only 346, and those who responded were 112. However, this is an exploratory study. Another limitation is that it is difficult to distinguish the presence of previous respiratory symptoms (due to the use of biomass) from those caused by PACS. Respiratory symptoms were not investigated before the acute phase, and this may create confusion.

Likewise, for the diagnosis of respiratory symptoms in persistent COVID, no validated questionnaire was found in the literature, only checklists, so we opted to create one with experts. Yang [40], in a systematic review of 291 studies, found that in 175 (60%), the diagnosis was made in a follow-up cohort from the acute phase; in the rest, through operational definitions; In this second group, in 51% of studies the authors themselves established an operational definition, different from those of international public health organizations, showing heterogeneity in their diagnosis.

However, this approach, in a country with alarming morbidity and mortality figures during the first two waves and before the vaccine implementation, and a poor health system, gives us a global idea of the potential impact of the pandemic. These results can allow an approximation of what a hospitalized patient could be in in the medium to long term and facilitate the management of human and logistical resources.

We must mention that a previously validated questionnaire for biomass consumption was not found. Ortiz-Quintero et.al. [28], in a review on biomass and COPD, consider that 10 years of exposure to biomass or more than 60 hours-year increases the risk. In this regard, we must comment that the definition taken in our study exceeds the cited definition in number of hours-year (24 hours*1 day week*4 weeks* 6 months). Furthermore, the exact quantity and quality of fuel is very difficult to define operationally. We must also note that in different systematic reviews, the definition of exposure time is variable [29,41]. Bachelet et.al. [42] in a review study, points out that there are currently no studies of adequate quality on PACS in its clinical and epidemiological aspects, in Latin America. which highlights the need to generate local information.

We conclude that no association was found between biomass consumption and respiratory sequelae and that the frequency of symptoms related to persistent COVID was very high; dyspnea and asthenia were the most frequent symptoms.

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