

# Echoes of the pandemic: Contrasting COVID-19 outbreaks in northern Peru

César Johan Pereira-Victorio<sup>1,2</sup>, Virgilio E. Failoc-Rojas<sup>3</sup>, Aldo Alvarez-Risco<sup>4</sup>, Noelia Morocho-Alburquerque<sup>5</sup>, Rubi Plasencia-Dueñas<sup>6</sup>, Alicia Torres-Mera<sup>6</sup>, Víctor J. Vera-Ponce<sup>7</sup>, Shyla Del-Aguila-Arcentales<sup>3</sup>, Jaime A. Yáñez<sup>8</sup>, Mario J. Valladares-Garrido<sup>9,10</sup>

1 *Escuela de Medicina, Universidad Continental, Lima 15046, Peru*

2 *Departamento de Ciencias Médicas, Facultad de Ciencias de la Salud, Universidad Castilla La Mancha, 45600 Talavera de la Reina, Spain*

3 *Universidad San Ignacio de Loyola, Lima, Peru*

4 *Universidad Tecnológica del Perú, Lima, Peru*

5 *Sociedad Científica de Estudiantes de Medicina de la Universidad Nacional de Piura, Piura, Peru*

6 *Sociedad Científica de Estudiantes de Medicina de la Universidad Nacional Pedro Ruiz Gallo, SOCIEM UNPRG, Lambayeque, Peru*

7 *Instituto de Investigación en Ciencias Biomédicas, Universidad Ricardo Palma, Lima, Peru*

8 *Universidad Peruana de Ciencias Aplicadas, Lima, Peru*

9 *School of Medicine, Universidad Continental, Lima, Peru*

10 *Oficina de Inteligencia Sanitaria, Red Prestacional EsSalud Lambayeque, Chiclayo 14008, Peru*

Corresponding author: Virgilio E Failoc-Rojas (virgiliofr@gmail.com)

Received 2 March 2024 ♦ Accepted 18 March 2024 ♦ Published 23 August 2024

**Citation:** Pereira-Victorio CJ, Failoc-Rojas VE, Alvarez-Risco A, Morocho-Alburquerque N, Plasencia-Dueñas R, Torres-Mera A, Vera-Ponce VJ, Del-Aguila-Arcentales S, Yáñez JA, Valladares-Garrido MJ (2024) Echoes of the pandemic: Contrasting COVID-19 outbreaks in northern Peru. *Pharmacia* 71: 1–8. <https://doi.org/10.3897/pharmacia.71.e122087>

## Abstract

Peru reported the second-highest COVID-19 cases in Latin America, after Brazil. The first COVID-19 wave occurred between March–December 2020, and the second occurred between January–September 2021. The differences between these waves remain largely unknown, and there is no comparison between them in Peru. We evaluated the variation in the clinical and epidemiological components of COVID-19-affected patients in both waves in northern Peru by a retrospective study using the clinical follow-up database of Lambayeque and the epidemiological notification form database of NotiWeb. The COVID-19-associated factors during the two waves were determined using simple and multiple regression analysis, and the prevalence ratio (PR) was estimated. During the second wave of COVID-19, there was an increase in cough symptoms in 12.1%, odynophagia in 5.0%, and chills in 16.0% compared with the first wave. The second wave was marked by a higher proportion of affected adolescents and children and a greater percentage of respiratory symptoms than the first wave.

## Keywords

COVID-19, pandemic waves, Peru, epidemiology, infection

## Introduction

The COVID-19 pandemic had many waves (Fan et al. 2021; Buttenschön et al. 2022; Meschiari et al. 2022; Sargin Altunok et al. 2022; Al-Amin et al. 2023). During the first wave,

Peru was the country with the second highest quantity of cases of infection in Latin America, after Brazil (Munayco et al. 2020), and with the highest seroprevalence and transmission (Díaz-Vélez et al. 2021). The regions of Piura and Lambayeque reported the highest case fatality rates (Cruz

2021), with more than 158,769 and 105,762 cases reported on June 5, 2022, respectively (Ministerio de Salud). Lambayeque reported a seroprevalence of 30% (Díaz-Vélez et al. 2021). During the second wave, Peru ranked fifth in the deaths in Latin America, and the Gamma variant was included (Pacheco-Romero 2021), characterized by a more rapid transmission (Gobierno del Peru 2022a). The major differences in the second wave were in the infected population because it included pregnant women, younger people, and people with fewer comorbidities such as obesity, diabetes, hypertension, and in severity, because the symptoms were generally renal and gastrointestinal, and the time of hospitalization and rates of admission to the ICU and mortality were lower (Vahidy et al. 2020; Iftimie et al. 2021).

The comparison between these two pandemic waves remains largely unknown, and a comparison between the two waves has not yet been performed in northern Peru. Previous studies used a small sample size, with consequently low statistical power and heterogeneity of patients (Iftimie et al. 2021), and were conducted in different geographical areas, due to which the results may vary. The present study evaluated a large sample size, including pregnant women and people of all ages, in addition to considering comorbidities such as diabetes and cardiovascular, renal, pulmonary, and immunological diseases and including simple and multiple regression analysis. This approach will be useful to compare the major characteristics of the infected and hospitalized population in each wave and to better understand the behavior of SARS-CoV-2 and the most vulnerable population (Gobierno del Peru 2022b).

The novelty of the present study is based on the evidence of the impact of the first and second in the country with the highest mortality rates in the world due to COVID-19. It is also a country where vaccines of Chinese origin and a large lockdown of people were initially used. Therefore, the aim of this study was to determine the differences in the characteristics of clinical and epidemiological issues of patients treated in both waves of COVID-19.

## Material and methods

### Design of the study

Current research was analytical, retrospective, cross-sectional which was conducted to evaluate patients with COVID-19 cared at the Regional Hospital of Lambayeque (RHL) in Peru, during the period of COVID-19 health emergency, between both waves: First: March to December 2020 and second: January to September 2021. Lambayeque, a northern region of Peru, is divided into three provinces with a population of 1,197,260 citizens (according to the 2017 Population Census).

### Data source

We used the clinical follow-up database of the RHL Epidemiology Office to obtain preliminary information of

patients with COVID-19. This information was corroborated and incorporated to the epidemiological notification database that was retrieved from the Peruvian Epidemiological Surveillance System (NotiWeb) due to its epidemiological purpose, collects more complete information on the clinical-epidemiological profiles of patients as well as hospitalization and death outcomes. All people with a confirmed diagnosis seen at the RHL were simultaneously reported in the NotiWeb system.

### Population

The patients treated for COVID-19 at the RHL from March 2020 to September 2021. RHL was a level III facility according to the Peruvian Ministry of Health (MINSA), meaning that it has been the largest care center in northern Peru and Lambayeque during the COVID-19 pandemic.

### Selection criteria

The sample included patients with confirmed COVID-19 using routine diagnostic tests (serological/molecular/antigenic). Inclusion of individuals were performed in all patients attended at the RHL, regardless of being new or continuing MINSA users. Patients with no records and incomplete records were eliminated from the study.

### Variables

The outcomes corresponded to clinical and epidemiological characteristics of COVID-19: signs, symptoms, daily number of cases, and death associated with the disease, which were registered at the time of notification. The exposure was the epidemic wave, which corresponded to the waves: March–December 2020 and January–September 2021. The study variables were divided in 1) epidemiological data: sex, age (continuous data), categorized age, presence of comorbidities (cancer, chronic lung disease, diabetes, obesity, cardiovascular disease, HIV), and 2) COVID-19 clinical data: daily number of cases (continuous data), death associated with the disease (no, yes), cough, odynophagia, chills, fever, respiratory distress, nasal congestion, general malaise, diarrhea, nausea/vomiting, headache, irritability, muscle and abdominal pain, pharyngeal exudate, conjunctival infection, seizure, and dyspnea.

### Procedure

The information from the NotiWeb was compared with the clinical follow-up data by the national identification number as the identification code. Then, a quality review was conducted to detect inconsistent, and incomplete data. Next, a variable called “pandemic wave type” was created considering the clinical and epidemiological profiles according to each wave. It was identified the clinical pattern of each wave.

## Statistical analysis

By Stata v.16.0 the data were analyzed. The calculation of central tendency and dispersion was estimated in the descriptive analysis of numerical variables. Absolute and relative frequencies were calculated. It was conducted the chi-square homogeneity in the bivariate evaluation after evaluation of the expected frequency assumption. To compare the categorical clinical and epidemiological variables between patients attended during both waves was used the Fisher's exact test. After calculating the normal distribution and homoscedasticity, it was conducted the Student's t-test or Mann-Whitney U test. The statistical significance was established as p-values of <0.05. To determine the differences in the characteristics of patients with COVID-19 between both waves, a simple regression analysis was performed considering the exposure of each wave. A Poisson statistical model with log link function and robust variance was used to calculate prevalence ratios (PR) (95% CI).

## Ethical issues

The Ethics Committee of the RHL approved the research protocol, following the ethical guidelines of the Declaration of Helsinki. It was maintained the confidentiality of the patient's information. Non-identifying keys were used to handle and examine the data. The participants completed a informed consent.

## Results

We found 2697 patients in the first wave and 2325 patients in the second wave. Between the two waves, the age group most affected was adult. In both waves (all), there was a slight predominance of male cases over female cases (52.9% vs. 47.1%). Among the most frequent symptoms reported in general were cough (67.3%), respiratory distress (54.6%), and general malaise (58.1%). The mean number of days of disease onset at the time of notification in the first wave was 8.5 days, while in the second wave it was 6.6 days ( $p < 0.001$ ). During the second wave of COVID-19 there was an increase in the symptoms of cough in 12.1% (74.1% vs. 62.0%), odynophagia in 5.0% (37.6% vs. 32.6%), chills in 16.0% (18.9% vs. 2.9%), nasal congestion in 12.7% (23.5% vs. 10.8%), and dyspnea in 13.5% (44.6% vs. 31.1%) compared with the first wave. Fever, malaise, headache, and muscle, abdominal, and chest pain were reported in lower proportions in the second wave (Table 1).

The frequency of having nasal congestion in the second wave was 2.17 times of that in the first wave (PR: 2.17; 95% CI: 1.90–2.49;  $p < 0.001$ ). Similarly, the frequency of chills (PR: 6.54) and pharyngeal exudate (PR: 1.67) was significantly higher in the second wave. Obesity, HIV, cancer, kidney disease, and being pregnant also showed higher frequencies in the second wave (Table 2).

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## Discussion

This study compared the signs and symptoms of COVID-19-affected patients in the first and second waves examined at RHL. In Peru, the second wave developed in a shorter time than the first wave.

## Comparison of findings with previous studies

Our results are comparable to similar studies conducted in different settings. We have observed that adults were the main affected group in both waves, which differs from previous reports in Spain showing that young people were mostly affected during the second wave (Iftimie et al. 2021; Mollinedo-Gajate et al. 2021). This is also different from a study in Denmark reporting no differences of severity in both waves, according to age (Buttenschøn et al. 2022). The present study also showed comorbidities were more frequent in the second wave. This result differs from the outcomes reported in India by Kumar et al. (2021) that showed a lower frequency of comorbidities in the second wave (e.g., hypertension, diabetes, and chronic kidney disease). Mortality due to COVID-19 was lower in the second wave, according to our study. The registry of fewer deaths was also observed in Japan (Saito et al. 2021). In France, patients were no different between both waves in similar age, ICU scores and comorbidities (Contou et al. 2021). Results in Australia showed that activation of blocking measures when the second wave cases indicated exponential growth would be effective to reduce COVID-19 cases (Milne et al. 2021). In Italy, the relaxation of individual behaviors, poor and contradictory communication to the population, and the reopening of schools and businesses made the second wave have been worse (Chirico et al. 2021).

The differences observed in our study may be related to characteristics of the population and the epidemic waves in northern Peru. In general, there were more adult patients and a slightly higher frequency of comorbidities. However, vaccination rates were present during the second wave, which could have protected patients from severity and deaths in this region (Valladares-Garrido et al. 2022). This can be reflected in an increasing infection rate due to predominant variants of concern like the Beta and Lambda variants, but without presenting fatal outcomes. Recognizing this pattern may help better understand the behavior of the outbreaks and provide resources efficiently to control the costs to the health care system in northern Peru.

**Table 1.** Clinical and epidemiological characteristics according to the pandemic wave.

Variables	Waves		p*
	First Wave (n = 2697) n (%)	Second Wave (n = 2325) n (%)	
Age (years)**	46.54 ± 24.86	44.00 ± 21.75	<0.001
Age (categorized)			<0.001
Child/Adolescent	94 (3.5)	284 (12.2)	
Young	248 (9.2)	216 (9.3)	
Adult	1360 (50.4)	1109 (47.7)	
Older adult	995 (36.9)	716 (30.8)	
Sex			<0.001
Female	1332 (49.4)	1032 (44.4)	
Male	1365 (50.6)	1293 (55.6)	
Daily number of cases***	11 (8–17)	12 (8–16)	0.686
Deceased			<0.001
No	1181 (55.2)	1253 (67.4)	
Yes	959 (44.8)	607 (32.6)	
SIGNS AND SYMPTOMS			
Cough			<0.001
No	1021 (38.0)	547 (25.9)	
Yes	1664 (62.0)	1562 (74.1)	
Odynophagia			<0.001
No	1794 (67.4)	1279 (62.5)	
Yes	869 (32.6)	769 (37.6)	
Nasal congestion			<0.001
No	2374 (89.2)	1537 (76.5)	
Yes	287 (10.8)	471 (23.5)	
Respiratory distress			0.489
No	1226 (45.8)	945 (44.8)	
Yes	1449 (54.2)	1163 (55.2)	
Fever			<0.001
No	1347 (50.3)	1297 (63.0)	
Yes	1330 (49.7)	761 (37.0)	
Chills			<0.001
No	2586 (97.2)	1632 (81.3)	
Yes	76 (2.9)	375 (18.9)	
General malaise			<0.001
No	1033 (38.5)	976 (46.3)	
Yes	1647 (61.5)	1134 (53.7)	
Diarrhea			0.558
No	2423 (90.9)	1785 (90.4)	
Yes	243 (9.1)	190 (9.6)	
Nausea			0.543
No	2523 (94.9)	1866 (94.5)	
Yes	136 (5.1)	109 (5.5)	
Headache			0.279
No	2156 (80.8)	1643 (82.0)	
Yes	513 (19.2)	360 (18.0)	
Irritability			0.767
No	2606 (98.1)	1919 (98.0)	
Yes	51 (1.9)	40 (2.0)	
Muscle pain			<0.001
No	2119 (79.5)	1685 (84.7)	
Yes	547 (20.5)	305 (15.3)	

Variables	Waves		p*
	First Wave (n = 2697) n (%)	Second Wave (n = 2325) n (%)	
Abdominal pain			0.001
No	2546 (95.6)	1917 (97.4)	
Yes	116 (4.4)	51 (2.6)	
Chest pain			<0.001
No	2361 (88.7)	1831 (92.6)	
Yes	300 (11.3)	147 (7.4)	
Anosmia			<0.001
No	2656 (99.9)	1930 (98.7)	
Yes	1 (0.04)	26 (1.3)	
Ageusia			<0.001
No	2657 (100.0)	1933 (98.9)	
Yes	0 (0.0)	21 (1.1)	
Pharyngeal exudate			0.012
No	2615 (98.4)	1919 (97.4)	
Yes	42 (1.6)	52 (2.6)	
Conjunctival infection			0.510
No	2636 (99.2)	1935 (99.0)	
Yes	21 (0.8)	19 (1.0)	
Seizure			0.067
No	2650 (99.7)	1948 (99.4)	
Yes	7 (0.3)	12 (0.6)	
Dyspnea			<0.001
No	1838 (68.9)	1155 (55.4)	
Yes	830 (31.1)	931 (44.6)	
COMORBIDITIES			
Cardiovascular disease			<0.001
No	2332 (87.5)	1671 (83.3)	
Yes	332 (12.5)	336 (16.7)	
Diabetes			0.015
No	2412 (90.7)	1768 (88.5)	
Yes	247 (9.3)	229 (11.5)	
HIV			0.016
No	2655 (99.9)	1948 (99.6)	
Yes	2 (0.1)	8 (0.4)	
Chronic kidney disease			<0.001
No	2586 (97.2)	1862 (93.3)	
Yes	74 (2.8)	133 (6.7)	
Pulmonary disease			0.666
No	2636 (99.2)	1945 (99.3)	
Yes	22 (0.8)	14 (0.7)	
Cancer			<0.001
No	2629 (98.8)	1890 (96.1)	
Yes	31 (1.2)	76 (3.9)	
Obesity			<0.001
No	2640 (99.3)	1815 (92.0)	
Yes	19 (0.7)	159 (8.1)	
Pregnancy			0.001
No	2579 (97.1)	1890 (95.3)	
Yes	78 (2.9)	94 (4.7)	

\* p-value obtained by chi-square test

\*\* Mean and standard deviation; p-value obtained by Student's t-test.

\*\*\* Median and 25<sup>th</sup>-75<sup>th</sup> percentile; p-value obtained by Mann-Wh.

## Difference between both waves

Males were the most affected in both waves, a pattern like the national and international records of patients infected with COVID-19 (Balacchi et al. 2021; Zeiser et al. 2022). This could be explained by the theory that androgens such as testosterone promote SARS-CoV-2 infection through the activation of a transmembrane protease (TMPRSS2) (Baughn et al. 2020; Lukassen et al. 2020; Matsuyama et al. 2020; Ragia and Manolopoulos 2020; Wambier and Goren 2020; Abbasi et al. 2021).

The average age of patients was slightly lower in the second wave. This difference has also been found in other countries such as India (Kumar et al. 2021), Germany (Graichen 2021), Japan (Saito et al. 2021), South Korea (Seong et al. 2021), and Iran (Jalali et al. 2020). In Peru, the predominant variants during the second wave were Lambda (C37 or the Andean variant) and Beta (B.1.351) (Aguilar-Gamboa et al. 2021) due to their greater transmissibility, which displaced other variants, specifically Gamma (P.1) that was concentrated in Lambayeque (Ministerio de Salud 2021a). It has been observed that the Gamma variant affects a greater

**Table 2.** Simple regression analysis of the clinical and epidemiological variations of patients with COVID-19 treated at the Regional Hospital of Lambayeque during both waves.

Characteristics	Pandemic wave		
	Simple regression		
	PR	95% CI	p*
Age (categorized)			
Child/Adolescent	3.50	2.79–4.40	<0.001
Young	1.01	0.85–1.20	0.908
Adult	0.95	0.89–1.00	0.054
Older adult	0.83	0.77–0.90	<0.001
Deceased			
Yes	0.92	0.90–0.94	<0.001
Cough			
Yes	1.20	1.15–1.24	<0.001
Odynophagia			
Yes	1.15	1.06–1.24	<0.001
Nasal congestion			
Yes	2.17	1.90–2.49	<0.001
Respiratory distress			
Yes	1.02	0.97–1.07	0.489
Fever			
Yes	0.74	0.70–0.80	<0.001
Chills			
Yes	6.54	5.15–8.32	<0.001
General malaise			
Yes	0.87	0.83–0.92	<0.001
Diarrhea			
Yes	1.06	0.88–1.26	0.558
Nausea			
Yes	1.08	0.84–1.38	0.543
Headache			
Yes	0.94	0.83–1.06	0.280
Irritability			
Yes	1.06	0.71–1.60	0.768
Muscle pain			
Yes	0.75	0.66–0.85	<0.001
Abdominal pain			
Yes	0.59	0.43–0.82	0.002
Chest pain			
Yes	0.66	0.55–0.80	<0.001
Anosmia			
Yes	1.38	1.33–1.44	<0.001
Ageusia			
Yes	1.41	1.39–1.42	<0.001
Pharyngeal exudate			
Yes	1.67	1.12–2.50	0.013
Conjunctival infection			
Yes	1.23	0.66–2.28	0.511
Seizure			
Yes	2.32	0.92–5.89	0.076
Dyspnea			
Yes	1.43	1.33–1.54	<0.001
Cardiovascular disease			
Yes	1.34	1.17–1.55	<0.001
Diabetes			
Yes	1.23	1.04–1.46	0.015
HIV			
Yes	5.43	1.15–25.56	0.032
Chronic kidney disease			
Yes	2.40	1.81–3.17	<0.001
Pulmonary disease			
Yes	0.86	0.44–1.68	0.666
Cancer			
Yes	3.32	2.19–5.02	<0.001
Obesity			
Yes	11.27	7.03–18.08	<0.001
Pregnancy			
Yes	1.61	1.20–2.17	0.001

\*p-values by generalized linear models, Poisson distribution family, logarithmic link function and robust variance.

proportion of people aged >65 years, whereas the Lambda variant affects more children and adolescents (Instituto de Salud Pública de Chile 2021). Restriction measures implemented during the first wave became less strict during the second wave, which resulted in younger people resuming their work activities (Hoogenboom et al. 2021), and even without having received immunization against COVID-19, they were more exposed to SARS-CoV-2 infection. Furthermore, early-care-seeking among younger people may have resulted in greater access to health services, leading to a relative increase of cases in young people during the second wave compared with the first wave (Kumar et al. 2021). Another explanation may be that older adults, being more vulnerable, died during the first wave, generating a shift to a younger group during the second wave (Hoogenboom et al. 2021).

In the second wave, the prevalence of COVID-19 infection in children was 250% higher than that in the first wave (PR: 3.50; 95% CI: 2.79–4.40), whereas the prevalence in older adults decreased by 17% (PR: 0.83; 95% CI: 0.77–0.90) compared to that in the first wave. These findings could be due to the start of vaccination in older adults (as of April 26, 2021), which protected against COVID-19 in second wave (that lasted until the end of December 2021 approximately), and consequently, the pediatric population remaining unvaccinated was affected in a greater proportion.

## Signs and symptoms between both waves

In second wave, the incidence of respiratory signs and symptoms such as cough (PR: 1.20; 95% CI: 1.15–1.24), dyspnea (PR: 1.43; 95% CI: 1.33–1.54), nasal congestion (PR: 2.17; 95% CI: 1.90–2.49), and abnormal pulmonary auscultation (PR: 2.73, 95% CI: 2.32–3.21) was significantly increased compared to that in the first wave. This finding is different from an Italian study in which during the first wave, the proportion of cases with dyspnea (71.7% vs. 37.1%, OR: 4.29) and cough (45% vs. 22.8%, OR: 2.76) was higher in the second wave (Bongiovanni et al. 2021). This could be due to better recording of information by the epidemiological surveillance system of the epidemiological surveillance center of MINSA, better training and awareness for data capture by frontline staff, and lower patient demand, which facilitated data recording by the health personnel. Compared with the beginning of the pandemic, in which cough, respiratory distress, malaise, odynophagia, and diarrhea were the most frequent symptoms of SARS-CoV-2 positivity, we recognized that during the second wave, positivity was more frequent in males, and cough, odynophagia, and malaise were significantly lower compared with the first wave. Respiratory distress and diarrhea were frequent in both waves of the pandemic (Vera-Ponce et al. 2021).

Current research shows that during the second wave, there was a significant increase in the number of patients with comorbidities in general. This is a different finding from an Indian study that found that patients examined in

the second wave had a lower percentage of comorbidities (45.9% in the second wave vs. 55.9% in the first wave) (Kumar et al. 2021). The proportion of cases with cardiovascular illness (12.5% vs. 16.7%; PR: 1.34), diabetes mellitus (9.3% vs. 11.5%; PR: 1.23), obesity (0.7% vs. 8.1%; PR: 11.27), and chronic kidney disease (2.8% vs. 6.7%; PR: 2.40) was increased during the second wave. This finding coincides with a multicenter study from Spain, Andorra, and Ireland, which reported that patients in ICU for COVID-19 during the second wave had a higher proportion of comorbidities such as diabetes mellitus (20.9% vs. 26.7%;  $p < 0.001$ ), obesity (32.2% vs. 42.3%;  $p < 0.001$ ), and chronic kidney disease (4.6% vs. 6.8%;  $p = 0.005$ ) (Carbonell et al. 2021).

Another study in Mexico during the second wave reported 5.4% of cases of chronic kidney disease (Puicón-Suárez et al. 2022). However, this is different from a study in India that reported that the proportion of patients with cardiovascular disease (6.9% vs. 4.2%;  $p < 0.001$ ), diabetes mellitus (26.5% vs. 21.5%;  $p < 0.001$ ), and chronic kidney disease (3.9% vs. 3.3%;  $p = 0.03$ ) decreased during the second wave (Kumar et al. 2021). This could be because prevention measures were stricter in the first wave so that patients with comorbidities could have greater prevention during the first wave than during the second wave. It could also be a consequence of better identification of patients with comorbidities due to the implementation of citizen surveillance strategies of high-risk populations and/or people with comorbidities, which was established in the plan for a potential second wave by COVID-19 in the Ministry of Health of Peru in December 2020 (Ministerio de Salud 2021b).

In this study, the proportion of cases with HIV (0.1% vs. 0.4%; PR: 5.43), cancer (1.2% vs. 3.9%; PR: 3.32), and pregnancy (2.9% vs. 4.7%; PR: 1.61) increased between waves. One Indian study corroborates the increase in the proportion of cancer cases (1.8% vs. 1.9%;  $p = 0.5$ ), although not significant (Kumar et al. 2021). However, another Indian study did find a significant increase (2% vs. 5.9%;  $p < 0.001$ ) (Kumar et al. 2021). Similarly, a multicenter study conducted in Europe identified that in the second wave, the proportion of cases with overall immunosuppression increased (4.2% vs. 8.3%;  $p < 0.001$ ) compared to that in the first wave (Carbonell et al. 2021).

## Public health significance

Genomic surveillance is limited in developing countries; therefore, the findings of this study could be useful for epidemiological follow-up and for understanding the differences between both waves. Continuous epidemiological surveillance could help to be prepared for a possible fourth

wave concerning the management of COVID-19 and prioritizing treatment for the most vulnerable population.

## Limitations and strengths

Current research has important limitations. Initially, a possible measurement bias existed during data collection due to different registration personnel. Moreover, our results reflect the profile of patients in the first and second waves from a single hospital in Peru. Hence, there could be a selection bias, where these findings do not represent the characteristics of patients with COVID-19 in the entire country, and there could also be significant differences concerning other regions of the country. Additionally, the comparison of clinical and epidemiological characteristics lacks detailed information on variants of concern. In future studies, a robust statistical difference may be achieved adjusting the regression analysis by relevant factors like age and sex. Despite these limitations, the strength of this study is that the sample size is large and obtained from a reference hospital for COVID-19 care, meaning that data have been captured from patients residing in not only Chiclayo but also the entire northern Peruvian macro region. This allows an adequate comparison and description of the pandemic waves.

## Conclusion

The presentation of the second wave may have been different from the first wave. It was observed that in the second wave, there was a higher proportion of young people, including children, adolescents and young adults, who were affected compared to the first wave, while adults and young adults accounted for a lower percentage. In addition, during the second wave of COVID-19 in Lambayeque, Peru, there was a higher proportion of respiratory symptoms, such as cough and shortness of breath. Comorbidities such as cardiovascular disease, diabetes, HIV, chronic kidney disease, cancer, obesity, and pregnancy showed higher percentages among COVID-19 cases seen during the second wave, with a statistically significant difference.

## Conflict of Interest

The authors declare that the research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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