Rev. Cuerpo Med. HNAAA, Vol 17 (1) - 2024

REVISTA DEL CUERPO MÉDICO HOSPITAL NACIONAL ALMANZOR AGUINAGA ASENJO, CHICLAYO, PERÚ

ISSN | impresa: 2225-5109; Electrónica: 2227-4731

Cross Ref. DOI: 10.35434/rcmhnaaa | OJS https://cmhnaaa.org.pe/ojs

PUBLICACIÓN ANTICIPADA

Publicación anticipada

El Comité Editor de la Revista del Cuerpo Médico Hospital Nacional Almanzor Aguinaga Asenjo aprobó para publicación este manuscrito, teniendo en cuenta la revisión de pares que lo evaluaron y levantamiento de observaciones. Se publica anticipadamente en versión pdf en forma provisional con base en la última versión electrónica del manuscrito, pero sin que aún haya sido diagramado ni se le haya hecho la corrección de estilo. Siéntase libre de descargar, usar, distribuir y citar esta versión preliminar tal y como lo indicamos, pero recuerde que la versión electrónica final y en formato pdf pueden ser diferentes.

Advance publication

The Editorial Committee of the Journal Cuerpo Medico Hospital Nacional Almanzor Aguinaga Asenjo approved this manuscript for publication, taking into account the peer review that evaluated it and the collection of observations. It is published in advance in a provisional pdf version based on the latest electronic version of the manuscript, but without it having been diagrammed or style corrected yet. Feel free to download, use, distribute, and cite this preliminary version as directed, but remember that the final electronic and pdf versions may differ.

Citación provisional /Toledo AK, León-Jimenez F, Cavalcanti S, Vilchez-Barreto P, Reto N, Vega J, Bolivar LM, Rhor EM, Ypanaque J, Silva-Marchan H, Moyano LM, Neuroepidemiology and Science of Life Working Group (NESL). Alta seroprevalencia tras la segunda oleada de infección respiratoria por SARS-COV2 en un pequeño asentamiento de la costa norte de Perú. Rev. Cuerpo Med. HNAAA [Internet]. 1 de abril de 2024 [citado 13 de abril de 2024];17(1). DOI: 10.35434/rcmhnaaa.2024.171.2287

Recibido / 03/12/2023

Aceptado / 04/03/2024

Publicación en Línea / 01/04/2024

High seroprevalence after the second wave of SARS-COV2 respiratory infection in a small settlement on the northern coastal of Peru.

Alta seroprevalencia de la infección respiratoria por SARS-COV2 tras la segunda ola en un pequeño asentamiento de la costa norte del Perú

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Funding:
This project was supported by the Regional Directorate of Health from Tumbes, the Regional Government, the local Government of Tumbes and Universidad Nacional de Tumbes. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Conflict of interest:
I confirm that both myself and my co-author do not have any conflicts of interest to disclose regarding the publication of this research.

Contributed to the development of the present study:

A.K.T: Participó en la revisión y limpieza de la base de datos. También, participó en el análisis estadístico de datos y diseño de gráficos. Redactó el borrador inicial y realizó el levantamiento de observaciones de la versión final.

F.L.J: Concepto y diseño de la metodología. Conducción de la investigación. Revisión de análisis de datos estadísticos. Revisión y corrección del borrador inicial. Revisión de versión final.

S.C.: Conducción de la investigación. Revisión de análisis de datos estadísticos. Revisión y corrección del borrador inicial. Revisión de versión final.

P.V.B: Ingreso de datos a base de datos. Revisión y limpieza de base de datos. Análisis estadístico de datos y diseño de tablas. Revisión y corrección del borrador inicial. Revisión de versión final.

N.R.: Concepto y diseño de la metodología. Conducción de la investigación. Revisión de análisis de datos estadísticos. Revisión y corrección del borrador inicial. Revisión de versión final.

J.V.: Conducción de la investigación. Revisión y corrección del borrador inicial. Revisión de versión final.

L.B: Conducción de la investigación. Revisión y corrección del borrador inicial. Revisión de versión final.

M.R.: Concepto y diseño de la metodología. Conducción de la investigación. Revisión de análisis de datos estadísticos. Revisión y corrección del borrador inicial. Revisión de versión final.

J.Y.: Concepto y diseño de la metodología. Conducción de la investigación. Revisión de análisis de datos estadísticos. Revisión y corrección del borrador inicial. Revisión de versión final.

H.S.: Concepto y diseño de la metodología. Conducción de la investigación. Revisión de análisis de datos estadísticos. Revisión y corrección del borrador inicial. Revisión de versión final.

L.M.M.: Concepto y diseño de la metodología. Conducción de la investigación. Revisión de análisis de datos estadísticos. Revisión y corrección del borrador inicial. Revisión de versión final. Gestión de financiamiento y recursos.

Acknowledgments

We thank the villagers of AAHH Las Flores. LMM and team are grateful to all the regional authorities

from the County Town Hall, the Regional Directorate of Health-Tumbes V Jimenez, and J Arias. We are grateful to the members of the Executive Office of Epidemiology N Julca, and L Arevalo. LMM expresses gratitude to the members of the Grupo de Investigación de la Escuela de Medicina. LMM would like to thanks for the aerial photography to JeanPierre. Angie Toledo is doctoral student in the Epidemiological Research Doctorate at Universidad Peruana Cayetano Heredia under FONDECYT/CIENCIACTIVA scholarship EF033-235-2015 and supported by training grant D43

TW007393 awarded by the Fogarty International Center of the US National Institutes of Health. Neither the FONDECYT/CIENCIACTIVA scholarship nor the training grant D43 TW007393

ABSTRACT

Objective: a) to assess the seroprevalence of SARS-CoV-2 at the end of the second wave; b) to determine the distribution by age group and health determinants associated with seropositivity. **Material and Methodology**: A study performed in a Tumbes' settlement between December 2021–January 2022 sampled individuals over 2 years old from one to every four households. We collected finger-prick blood samples and conducted symptom surveys. **Results:** The adjusted seroprevalence after the second wave increased by twofold (50.15%, 95% CI[45.92–54.40]), compared with the first wave (24.82 %, 95%CI [22.49–27.25]). Females maintained a higher seroprevalence (53.89; 95% CI[48.48-59.23]) vs. 45.49; 95% CI [38.98-52.12], p=0.042) compared to males. Those under 18 years of age had the highest IgG seropositivity: the 12–17 age group during the second wave (85.14%) and the 2–11 age group (25.25%) during the first wave. Nasal congestion and cough were symptoms associated with seropositivity, unlike the first wave. **Conclusions:** The seroprevalence of COVID-19 increased by twofold compared to the initial wave in Tumbes region. Infrastructure constraints, restricted human resources, and supply limitations in healthcare facilities made the Peruvian health system collapse. The epidemiological surveillance network should incorporate mHealth tools for real-time notifiable disease information. Working alongside the community will let us improve interventions for preventing or controlling new pandemics.

Keywords: COVID-19, SARS-CoV-2, seroprevalence, Peru

RESUMEN

Objetivo: a) evaluar la seroprevalencia de SARS-CoV-2 al final de la segunda ola; b) determinar su distribución por grupos de edad y los determinantes de salud asociados a la seropositividad. **Materiales y Método**: Un estudio realizado en un asentamiento humano de Tumbes entre diciembre de 2021 y enero de 2022 muestreó individuos mayores de 2 años en uno de cada cuatro hogares. Se tomó muestras de sangre por punción-digital y se realizó encuestas sintomáticas. Resultados: La seroprevalencia ajustada tras la segunda ola se duplicó (50.15%, IC 95% [45,92-54,40]), comparado con la primera ola (24.82%, IC 95% [22,49-27,25]). Las mujeres mantuvieron una mayor seroprevalencia (53.89; IC 95% [48,48-59,23] vs. 45.49; IC 95% [38,98-52,12], p = 0,042) comparado con los hombres. Los menores de 18 años presentaron mayor seropositividad IgG: el grupo de 12-17 años durante la segunda ola (85,14%) y el grupo de 2-11 años (25,25%) durante la primera ola. Congestión nasal y tos estuvieron asociados a la seropositividad, a diferencia de la primera oleada. **Conclusiones:** La seroprevalencia de COVID-19 se duplicó en comparado con la primera ola en Tumbes. Las limitaciones de infraestructura, los recursos humanos restringidos y las limitaciones de abastecimiento en los establecimientos de salud hicieron colapsar el sistema de salud peruano. La red de vigilancia epidemiológica debería incorporar herramientas de mhealth para obtener información en tiempo real sobre las enfermedades. de declaración obligatoria. Trabajar junto a la comunidad nos permitirá mejorar las intervenciones para prevenir o controlar nuevas pandemias.

Palabras clave: COVID-19, SARS-CoV-2, seroprevalencia en segunda ola-Perú

INTRODUCTION

Due to a lack of hospital capacity, critical oxygen supply, political unrest, and a fragmented healthcare system, Peru experienced high rates of morbidity and mortality during the first and second catastrophic waves (1–3). Prevalence rates on the first wave ranged from 20.8% to 72% (1,2,4,5). Without the option of massive vaccination, a disastrous second wave was expected unless the health system responded adequately. On December 17th, 2021, in the Tumbes district, close to 93% of the population over 18 years old and seniors had received the first dose of the Sinopharm and Pfizer COVID-19 vaccine. 75% of the population between the ages of 12 and 17 was vaccinated, while no one under the age of 12 had been immunized (6). The first wave hit Peru in March 2020, peaked in August, and declined in December 2020 (7). The second wave started in January, with the highest number of infections and deaths decreasing in June 2021. Throughout a significant portion of the second wave, the number of daily infections consistently exceeded the number of daily recoveries.

The peak was observed during week 54, specifically from March 22nd to 28th, with an average of 9,079 new infections and 8,727 recoveries per day (8,9). The highest attack rate (6.96) was for 30- to 59-year-olds, followed by 6.56 for adults aged 60 and above. (9). During this same period, Tumbes had the seventh highest cumulative attack rate (5.29), compared with the national average of 4.84. The Tumbes case fatality rate rose from 3.54% to 9.40% on May´s last day of 2021. Peru was fifth in the world for deaths per 100,000 people (10), behind the United States, Brazil, India, and Mexico (2,9). In April 2021, during the peak of cases, the Tumbes region had three hospitals, 17 beds in the ICU, and 20 mechanical ventilators (11).

In 2020, COVID-19 outbreaks in the Amazonian cities of Manaus and Iquitos were explosive, and by the conclusion of the first wave, herd immunity was predicted (70% seroprevalence). However, compared to the first wave, the second one had an even higher death rate. In Manaus, severe acute respiratory illness deaths doubled from 4,971 to 8,949 between the first and second waves. Remarkably, Iquitos had a three to four times greater per capita death rate during the epidemic's peak compared to Manaus (12). Lambayeque region was impacted by two waves of COVID-19 between March 2020 and September 2021. In comparison to the first wave, the second wave's peak was marginally smaller. There were notable distinctions between the two waves, with the second wave exhibiting a higher proportion of chronic illness cases and older individuals (13).

A cross-sectional study conducted in a rural village of Tumbes (Puerto Pizarro) on the final days of the first wave found an adjusted seroprevalence of 24.82% (14) where being a woman [28.03%, p=0.002], water storage [PR 1.37, p=0.034], and symptoms such as fever, general discomfort, cough, nasal congestion, respiratory distress, headache, anosmia, and ageusia being variables associated with a positive antibody rapid-test of Sars-cov-2 (14,15). Taking full advantage of the regional program of active surveillance of the Tumbes Government (GORE) and Regional Directorate of Health (DIRESA) (16), we conducted a cross-sectional study in a human settlement named AAHH Las Flores (n = 781 population): a) to assess the seroprevalence of SARS-CoV-2 at the end of the second wave, b) to determine the distribution by age group, and health determinants associated with residents over 2 years old.

Materials and methods

Ethical considerations

Approval for the study protocol and consent forms was obtained from the institutional review boards of Universidad Peruana Cayetano Heredia and the Regional Directorate of Health (DIRESA, Spanish acronym) in Tumbes. To ensure comprehension, illiterate individuals were included by having the IC and survey read aloud to them. All participants provided written informed consent (IC) in the presence of a witness. For minors, both the minor and their parents or legal guardians provided written informed consent.

Area and study population

The settlement "AAHH Las Flores," which has a population of 781 individuals, is located in the Pampa Grande Population Center in the district and province of Tumbes. It is situated 2.5km away from the town center and lacks proper infrastructure, with unpaved streets and no continuous access to safe drinking water (17). The population is of a homogeneous mestizo ethnicity. According to the last national census, the population of this settlement was 721 individuals, with a total of 184 households. Also, 94.5%, had access to potable water and 95.1% had access to sewage disposal (18).
The Pampa Grande health facility was staffed by six physicians, six nurses, six midwives, one pediatrician, and six nursing technicians. It provides 24/7 service and has an ambulance for emergency transportation (19).

Study design and sampling

A cross-sectional analytical approach was used to invite and enroll individuals over than 2 years and above (n=781 pop) through a door-to-door intervention conducted between December 2021 and the first day of January 2022. This intervention took place after the second wave and a few weeks before the start of the third wave.

The sampling, recruitment process, censuses, and rapid antibody testing for COVID-19, were described elsewhere (14,15). Briefly, the regional directorate of Health-Tumbes and the Center for Global Health collaborated to conduct a nominal census with block-numbered homes. Individuals over the age of two who stayed in the village at least three nights per week and consented to sign the informed consent form were eligible to participate. The study included 781 individuals who met these criteria. Non-medical field workers collected blood samples via finger prick and explained the results of the lateral flow test to everyone surveyed. Clinical signs suggestive of COVID-19 disease were evaluated in accordance with WHO criteria (20). Trained physicians from the study team evaluated participants with respiratory symptoms, and data was entered into the Notiweb and SISCOVID databases for follow-up by the healthcare system. The COVID-19 Clinical Epidemiological Investigation format was used to identify symptoms experienced within the previous 14 days, as recommended by the Peruvian Ministry of Health (21).

A census previously validated by the Center for Global Health in epidemiological population-based investigations was used in this study (22,23). Comorbidities were determined as the existence of at least one of the following medical disorders: hypertension, diabetes, hepatic disease, renal disease, lung disease, asthma, obesity, neurological problems, HIV, cancer, or tuberculosis (24).

Definitions and operationalization of variables

The seroprevalence of SARS-CoV-2 was determined by dividing the number of participants who tested positive for IgG, IgM, or both in a lateral flow test by the total number of participants. The variables: sex, "type of family", rooms per person , water supply and water storage were describe in a previously research (14). "Latrines/don't have" and "other and restrooms," which are designated as places with a toilet, sink, network connection, and drainage, are the two categories for the variable for hygienic services (14). Visual examination was used to confirm the factors related to the water supply, water storage, and hygiene services. A lateral flow test was declared positive when IgG, IgM, or both findings were observed.

Statistical analysis

The SARS-CoV-2 seroprevalence ratios in Las Flores settlement were aimed to be estimated by performing descriptive statistics and binomial family generalized linear models with a logarithmic link function, while controlling for other variables, such as age, sex, type of family, water storage, and basic hygienic services at home. Household clustering was accounted for by using robust sandwich-type standard errors. Each variable was evaluated for inclusion in the final model using the log likelihood ratio. 95% confidence intervals (CIs) were reported, and statistical significance was set at $P < 0.05$. The seroprevalence was adjusted for the test's reported sensitivity (99.03%) and specificity (98.65%). The statistical analysis was performed using Stata v 17.0 software (College Station, Texas 77845, USA).

RESULTS

A total of 580/781 (74.26%) individuals older than 2 years old agreed to participate. Female participants were 59.83 % (347/580). The overall participants' mean age was 28.80±19.36 years. MINSA stratification mean ages were from: 2 to 11 years (mean 6.83±2.81), 12 to 17 years (mean 14.53±1.81), 18 to 29 years (mean 23.60±3.23), 30 to 59 years (mean 44.00±7.98) and older than 60 years (mean 67.84±6.80). Most people lived in single families 391/580 (67.41 %), had access to public potable water 342/580 (58.97%) for 02-04 hours per day and 454/580 (78.28 %) had access to hygienic services.

Seroprevalence

Anti-SARS-CoV-2 antibodies were detected in 292/580 (50.34 %) participants: 282 IgG reactive, 8 IgM/IgG reactive, and 2 IgM reactive. After adjusting for sensitivity (99.03%) and specificity (98.65%), the calculated adjusted seroprevalence was 50.15 % (95% CI: 45.92 - 54.40). Women had a slightly higher adjusted seroprevalence compared to men (53.89 [95% CI: 48.48 - 59.23] vs. 45.49 [95% CI: 38.98 - 52.12], p=0.042). No other demographic characteristics were associated with SARS-CoV-2 lateral flow test seropositivity (Table 1).

Table 1. Seroprevalence adjusted for participant characteristics and associated factors from first and second COVID-19 wave.

	First wave					Second wave				
Sociodemographic characteristic	**Total (N=1391) n (%)**	**Seropositive (N=356) n (%)**	**Adjusted seroprevalence**	**PR* (95%IC)**	**p-value**	**Total (N=580) n (%)**	**Seropositive (N=292) n (%)**	**Adjusted seroprevalence**	**PR* (95%IC)**	**p-value**
Sex										
Female	742 (53.34)	213 (59.83)	28.03 (24.83 - 31.41)	Ref.		347 (59.83)	187 (53.89)	53.89 (48.48 - 59.23)	Ref.	
Male	649 (46.66)	143 (40.17)	21.11 (18.03 - 24.45)	0.76 (0.63 - 0.91)	**0.002**	233 (40.17)	105 (45.06)	45.49 (38.98 – 52.12)	0.84 (0.70 - 0.99)	**0.042**
Type of family										
Single family	1322 (95.04)	343 (96.35)	25.19 (22.87 - 27.62)	Ref.		391 (67.41)	197 (50.38)	50.64 (45.57 - 55.70)	Ref.	
Multi-family	69 (4.96)	13 (3.65)	17.39 (9.32 - 28.41)	0.82 (0.60 - 1.12)	0.217	189 (32.59)	95 (50.26)	50.79 (43.44 - 58.12)	1.00 (0.83 - 1.19)	0.979
Rooms per person†										
≤ 1	967 (72.06)	217 (70.68)	21.59 (18.94 – 24.42)	Ref.		345 (59.48)	180 (52.17)	52.46 (47.05 - 57.84)	Ref.	
> 1	375 (27.94)	90 (29.32)	23.19 (18.85 – 27.95)	0.96 (0.78 – 1.18)	0.681	235 (40.52)	112 (47.66)	48.09 (41.54 - 54.67)	0.91 (0.82 - 1.02)	0.116
Water supply										
non-shared connection	1287 (92.52)	338 (94.94)	25.49 (23.12 - 27.96)	Ref.		342 (58.97)	168 (49.12)	49.42 (44.00 - 54.85)	Ref.	
shared connection	104 (7.48)	18 (5.06)	16.35 (9.82 - 24.88)	0.84 (0.71 - 1.11)	0.309	238 (41.04)	124 (52.10)	52.52 (45.97 - 59.01)	1.06 (0.89 - 1.26)	0.509
Water storage										
No	91 (6.54)	17 (4.78)	17.58 (10.40 - 26.98)	Ref.		2 (0.34)	1 (50.00)	100.00 (15.81 – 100.00)	Ref.	
Yes	1300 (93.46)	339 (95.22)	25.31 (22.97 - 27.76)	1.37 (1.02 - 1.83)	**0.034**	578 (99.66)	291 (50.35)	50.69 (46.54 - 54.84)	1.00 (0.25 - 4.03)	0.992
Hygienic services										
Other and restroom	1109 (79.73)	294 (82.58)	25.79 (23.24 - 28.47)	Ref.		454 (78.28)	224 (49.34)	49.56 (44.87 - 54.26)	Ref.	
Latrine / don't have	262 (5.97)	62 (17.42)	22.90 (17.95 - 28.47)	0.94 (0.83 - 1.08)	0.391	126 (21.72)	68 (53.97)	54.76 (45.65 - 63.64)	1.09 (0.89 - 1.34)	0.394

Adjusted seroprevalence estimated considering the sensitivity (99·03%) and specificity (98·65%) of the diagnostic test. 95%IC: 95% confidence interval. p-values were calculated using glm, fam (bin) link (log). * Adjusted for house. † Missing values

As illustrated in Fig 1, the age groups with the highest prevalence of IgG seropositive were from 12 to 17 years (85.14%), from 30 to 59 years (59.80 %) and older than 60 years (55.81%). On the other hand, more than 80% of seropositive patients were asymptomatic in all age groups (Figure 2).

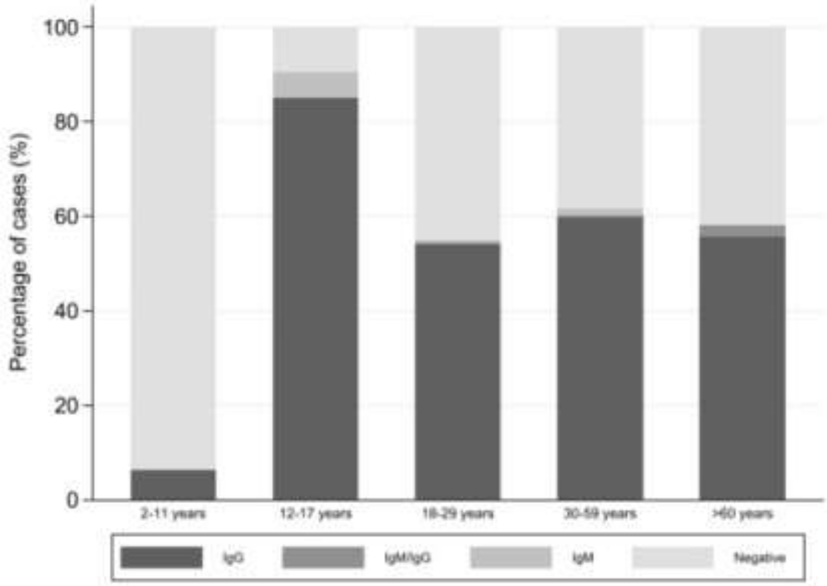

Fig 1. Seronegative and seropositivity from first and second COVID-19 wave.

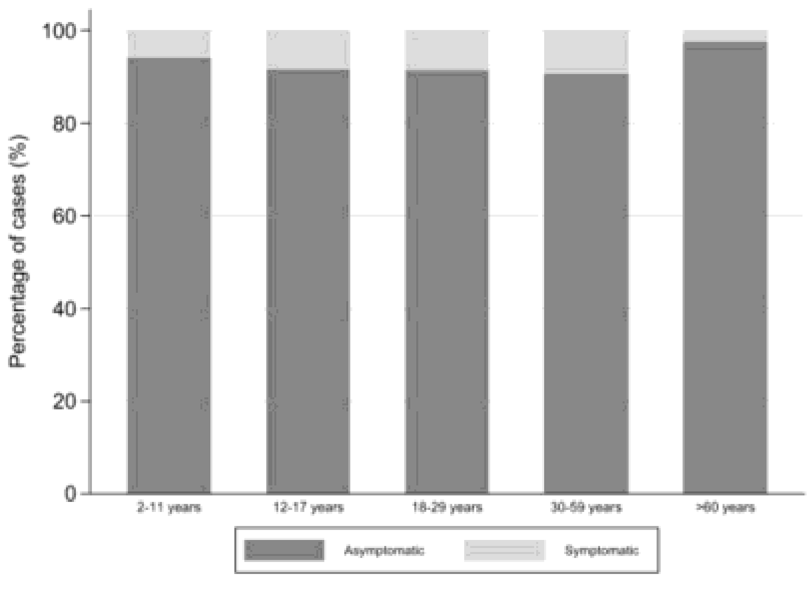

Fig 2. Symptomatic and asymptomatic cases in the seropositive population from first and second COVID-19 wave.

In a bivariate analysis, symptoms such as cough (PR: 1.74; 95% CI: [1.27 - 2.38], p=0.001) and nasal congestion (PR: 0.60, 95% CI: [0.36 - 0.99], p=0.045) were associated with SARS-CoV-2 seropositivity. Both symptoms were associated with seropositivity in a multiple analysis (PR: 4.15, 95% CI: [1.90 - 9.07], p<0.001) and (PR: 0.41; 95% CI: [0.20 - 0.84], p=0.014) (Table 2).

Table 2. Self-reported symptoms seropositive and seronegative participants from first and second COVID-19 wave.

	First wave								Second wave							
Covid-19 symptoms	**Positives** n=356		**Negatives** n=1035		**PR (CI 95%)**	***p-value****	**PRA (CI 95%)**	***p-value*****	**Positives** n=288		**Negatives** n=292		**PR (CI 95%)**	***p-value****	**PRA (CI 95%)**	***p-value******
	yes	no	yes	no					yes	no	yes	no				
Fever	34	322	42	993	1.89 (1.44 - 2.48)	<0.001	1.29 (0.84 - 1.98)	0.254	0	288	0	292	1.00	-	-	-
General Discomfort	28	328	42	993	1.67 (1.23 - 2.26)	0.001	-	-	0	288	1	291	1.00	-	-	-
Cough	53	303	63	972	2.00 (1.60 - 2.50)	<0.001	1.78 (1.24 - 2.57)	0.002	6	282	1	291	1.74 (1.27 - 2.38)	0.001	4.15 (1.90 - 9.07)	< 0.001
Sore Throat	39	317	126	909	0.95 (0.71 - 1.27)	0.716	-	-	1	287	2	290	0.67 (0.13 - 3.33)	0.624	-	-
Nasal congestion	21	335	38	997	1.46 (1.03 - 2.09)	0.036	1.08 (0.67 - 1.75)	0.742	11	277	25	267	0.60 (0.36 - 0.99)	0.045	0.41 (0.20 - 0.84)	0.014
Respiratory Distress	18	338	12	1023	1.64 (1.04 - 2.56)	0.031	0.99 (0.53 - 1.88)	0.999	0	288	0	292	1.00	-	-	-
Diarrhea	3	353	12	1023	0.81 (0.29 - 2.23)	0.676	-	-	0	288	0	292	1.00	-	-	-
Sickness	3	353	4	1031	1.73 (0.73 - 4.10)	0.209	-	-	0	288	0	292	1.00	-	-	-
Headache	22	334	37	998	1.54 (1.09 - 2.17)	0.014	-	-	0	288	0	292	1.00	-	-	-
Irritability	2	354	5	1030	1.15 (0.35 - 3.74)	0.811	-	-	0	288	0	292	1.00	-	-	-
Anosmia	7	349	9	1026	1.78 (1.01 - 3.14)	0.046	-	-	-	-	-	-	-	-	-	-
Ageusia	9	347	7	1028	2.31 (1.48 - 3.61)	<0.001	1.57 (0.78 - 3.15)	0.202	-	-	-	-	-	-	-	-

** p-value were calculated with glm, fam(bin) link(log)*

*** p-value were calculated glm, fam(bin) link(log), adjusted by anosmia, fever, cough, respiratory distress and nasal congestion*

**** p-value were calculated glm, fam(bin) link(log), adjusted by cough, and nasal congestion*

DISCUSSION

In the second wave, a higher COVID-19 prevalence was reported globally compared to the first wave. In Peru, it grew by 100 percent between November 2020 (first wave) and December 2021 (second wave). This research group conducted two population-based studies in the Tumbes Region, revealing the same trend (24.82% vs. 50.15%) (S1 Fig), contradictory to Regional Directorate of Health Tumbes reported (6.11%) (16). This numbers were similar to reported in Italy, which had a seroprevalence of over 50% in the second wave (25), and higher than Japan, which doubled its caseload (26). Seroprevalence increased as more people were infected with the virus and its different variants that could escape vaccination (27) and the immunity generated by contagion from the asymptomatic to the uninfected (28). In addition, these variants resulted in variations in transmissibility, disease severity, risk of reinfection, diagnostic failures, natural immunity, vaccination efficacy, and treatment. Persistent community transmission in regions with a higher vaccination rate or history of infection may indicate the presence of a variant capable of evading the immune response (29). The new variants began to appear in the world at the end of 2020, right at the end of the first study, as variants of interest (VOI) and variants of concern (VOC) according to the WHO; the Delta variant began to circulate in October 2021 and could be the variant that explains this high seroprevalence (30). According to a weekly report from the INS, in Peru, at the end of August 2021, the delta variant corresponded to 40% of the samples, gamma was 37%, lambda was 17%, and the mu variant was 5% (31). In Tumbes, in the 20–30-year-old group. From January to November 2022, omicron (n = 463) and delta (n = 125) variants were identified (32).

The delta variant generated a lower response to mRNA vaccines (Pfizer-BioNTech and Moderna NIH), viral vectors (Oxford-AstraZeneca) (33), as well as inactivated viruses (Sinopharm-Beijing) (34). On December 19, 2022, the coverage with three doses of vaccines in Tumbes was as follows: 55.1% for adolescents, 77.15 % for young persons, 77.9 % for adults, and 82.5 % for the elderly. Indicative of adequate coverage, the majority of doses were distributed by Pfizer (56%), AstraZeneca (19.7%), Sinopharm (17%), and Moderna (7.2%) (35). In addition, the WHO classified the omicron variant as concerning on November 26, 2021. Although the classic public health restriction measures may be effective against the new variants, they are less effective in terms of infectivity; on the other hand, herd immunity achieved with a previous variant might not be helpful (30). We acknowledge the potential role of mass vaccination and post-vaccination immunological responses in the observed rise in seroprevalence during the second wave.

Seroprevalence in the second wave (53.89 [48.48-59.23]) was higher compared to other Reports of the second wave in Peru, where there were no gender differences (2,16), similar in France (Corsica) (36); our numbers were lower compared to the Democratic Republic of the Congo (74.3% vs. 68.3%; p = 0.021) (37), Kashmir, India (86.21 [85.86-86.55](38) and slightly higher compared to Delhi, India (52.42,OR 1.16[1.10-1.23],p<0.001)(39). A possible explanation for this increased seroprevalence in women is that they were the ones caring for positive cases at home (40); there are more female health workers than male health workers (nurses, nurse technicians, and midwives) (41); women purchase supplies in stores and markets, and this overexposure could lead to an increase in COVID-19 infection.

There were many possible explanations for the only statistically significant clinical manifestations in this second wave (cough and nasal congestion): the new variants sacrificed their virulence for their infectious capacity, so we observed in the delta variant there was some variability in clinical expression compared to the original virus strain (42); people gained more knowledge about COVID-19 on the second wave, may have contributed to the increased prevalence of clinical manifestations.

One of the limitations of this research is the sample size and the fact that the study was conducted in a single settlement, limiting the generalizability of the findings to other regions of Peru. The limited availability of rapid tests, which have lower sensitivity and specificity compared to PCR tests; and finally, the study did not collect data on participants' vaccination status; this information was obtained from reports of the Ministry of Health. With persistent IgG seropositivity, it is recommended that follow-up be conducted to detect COVID-19 sequelae related to the presence of pulmonary lesions, mental health issues and, the implementation of an application-based surveillance system in our country. Many systematic reviews and meta-analyses revealed that 62.2% of asymptomatic patients had tomographic abnormalities, indicating that they are a potential source of transmission (43)

Our research has several implications for Peru's public health policy. First, the high seroprevalence indicates that a substantial portion of the population may already be infected, indicating the need to increase vaccine coverage. The significance of targeted vaccination campaigns to safeguard younger age groups with a higher seroprevalence is emphasized by the study's findings. Given the higher seroprevalence in females, there may be gender-specific differences in exposure to the virus that need further investigation.

This study shows a higher prevalence of SARS-CoV-2 antibodies after the second wave of COVID-19 in Tumbes, with a huge prevalence of IgG in individuals younger than 17 years old, more than 80% of seropositive patients were asymptomatic in all age groups. The findings suggest that a significant portion of the population was exposed to the virus and developed antibodies, highlighting the importance of continued efforts to control the spread of new variants of the virus through massive campaigns of vaccination.

Footnotes

The statements contained in this document are those of the authors and should not be construed as official points of view of the Universidad Cesar Vallejo, Universidad Nacional de Tumbes, or other organizations mentioned.

A preprint has previously been published Toledo et.al 2023 (44).

Supporting information

S1 Fig. Enrollment and seroprevalence flowchart of the first and second wave of COVID-19 in two Tumbes settlements. Created with BioRender.com

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S1 Figure. Enrollment and seroprevalence flowchart of the first and second wave of COVID-19 in two Tumbes settlements.