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ORIGINAL ARTICLE

SARS-CoV-2 in eight municipalities of the Colombian tropics: high immunity, clinical and sociodemographic outcomes

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Background: Serological evaluation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an alternative that allows us to determine the prevalence and dynamics of this infection in populations. The goal of this study was to determine the clinical and sociodemographic dynamics of SARS-CoV-2 infection in a region of the Colombian Caribbean.

Methods: Between July and November 2020, a cross-sectional observational study was carried out in Córdoba, located in northeast Colombia in the Caribbean area. Eight municipalities with the largest populations were chosen and 2564 blood samples were taken. A commercial enzyme-linked immunosorbent assay was used with the recombinant protein antigen N of SARS-CoV-2. The people included in the study were asked for sociodemographic and clinical data, which were analysed by statistical methods.

Results: A seroprevalence of 40.8% was obtained for SARS-CoV-2 in the Córdoba region. In the bivariate analysis, no differences were observed in seropositivity against SARS-CoV-2 for gender or age range ($p>0.05$). Higher seropositivity was found in low socio-economic status and symptomatic patients ($p<0.0001$). A total of 30.7% of the asymptomatic patients were seropositive for SARS-CoV-2, which could be linked to the spread of this infection. In the multivariate analysis, seroconversion was related to poverty and clinical manifestations such as anosmia and ageusia ($p<0.05$).

Conclusions: The high seropositivity in Córdoba is due to widespread SARS-CoV-2 in this population. The relationship between seropositivity and socio-economic status suggests a higher exposure risk to the virus caused by informal economic activities in low-income groups. Clinical manifestations such as anosmia and ageusia could be clinical predictors of infection by the new emergent coronavirus.

Keywords: asymptomatic infections, economic conditions, informal social controls, public health, seroepidemiologic studies, social conditions

Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease of zoonotic origin caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] The virus is an enveloped single-stranded RNA type that belongs to the *Coronaviridae* family.[2] The new coronavirus causes severe pulmonary and extrapulmonary complications, mainly in older adults, individuals with comorbidities and immunosuppressed patients.[3,4] To date (18 May 2021), >164 million cases of COVID-19 have been diagnosed and >3 million deaths have been reported around the world[5] and >3 million cases of COVID-19 and 81 000 deaths have been reported in Colombia.[6] Because the infection can occur asymptomatically in 18–81% of infected people,[7] serological detection of SARS-CoV-2 is an alternative for diagnosing the disease. Serology allows us to determine the actual prevalence and impact of this infection on the population.

Regarding the seroprevalence of SARS-CoV-2, it has been shown that it varies significantly between countries, given that it is dependent on the contagion curve of each region, government management and society's discipline to comply with the standards of self-care. The region of Lombardy, Italy, was heavily hit by this virus and a seropositivity of 23% has been reported,[8] while in South Korea, where massive testing was carried out for SARS-CoV-2 and social discipline is a constant, the seropositivity rate is <1%.[9] Therefore, in developing countries and regions such as the Colombian Caribbean, which is a region with high social inequity, it is likely that there has been greater exposure to this virus and therefore there may be a greater seroprevalence for SARS-CoV-2 compared with regions or countries considered first world.[10]

The objective of this study was to determine the clinical, sociodemographic and community infection dynamics of SARS-CoV-2 in the Colombian Caribbean region.

Methods

Type of study, calculation of sample size and distribution

Between July and November 2020, a cross-sectional observational study was carried out. The study was carried out in the department of Córdoba, with a population of approximately 1 800 000 inhabitants. The department is located in the northwest of Colombia in the Caribbean area. Eight municipalities with the largest populations were chosen and 2564 blood samples were taken from people distributed proportionally from the total population of the selected municipalities. The sample size was calculated based on an estimate of a finite population proportion. A confidence level of 95% and a margin of error of 3% were used. The distribution was thus Monteria, n=1553 (capital of the department); Sahagun, n=220; Lorica, n=147; Tierra Alta, n=133; Montelibano, n=116; Planeta Rica, n=167; San Antero, n=105; and Cereté, n=123.

Serology

A commercial enzyme-linked immunosorbent assay (ELISA; Eurofins, Madrid, Spain) that uses a recombinant N protein for SARS-CoV-2 was used. The test measures total immunoglobulin G (IgG), IgM and IgA antibodies.[10] The test was previously validated in our laboratory.[11]

Income and socio-economic level of the population

Stratification of the municipalities' socio-economic levels into low, medium and high was carried out based on the guidelines of the Economic Commission for Latin America and the Caribbean.[12]

Analysis of data

For the registration of sociodemographic and clinical characteristics, an evaluation form developed by the Institute for Tropical Biological Research was used. Data were analysed using the Statistical Package for the Social Sciences version 27 (IBM, Armonk, NY, USA). The univariate analysis for the qualitative variables was carried out through the calculation of absolute and relative frequencies. For quantitative variables, measures of central tendency were calculated and the normality of the quantitative variables was determined by applying the Kolmogorov–Smirnov test. Bivariate analysis of the qualitative and quantitative variables was carried out with the Mann–Whitney U test or the Kruskal–Wallis test if the qualitative variable was polytomous. Multivariate analysis was performed through binomial logistic analysis. Significance of the p-value was established at <0.05 for all the analyses carried out. The risk was approximated by calculating the odds ratio (OR) with its respective confidence interval (CI). Also, a heat map was made for the geolocation of the serological data using QGIS version 3.4.15.

Table 1. Description of the sociodemographic and clinical characteristics of the study participants (N=2564), Córdoba, 2020

Characteristics	Values
Female , n (%)	1415 (55.2)
Male, n (%)	1149 (44.8)
Age (years), median (range)	42 (2–98)
Cities, n (%)	
Monteria	1553 (60.6)
Sahagun	220 (8.6)
Montelibano	116 (4.5)
Lorica	147 (5.7)
Tierralta	133 (5.2)
Planeta Rica	167 (6.5)
San Antero	105 (4.1)
Cereté	123 (4.8)
Socio-economic level, n (%)	
Low	1642 (64)
Medium	611 (23.8)
High	296 (11.5)
Symptoms related to COVID-19, n (%)	
Yes	1337 (52.8)
Seroprevalence	1045 (40.8)

Results

Sociodemographic and clinical characteristics

A total of 2564 individuals were evaluated in Córdoba; 55.2% were female, 60.6% lived in Montería and 64% belonged to the low socio-economic level. A total of 52.8% of the participants in this study reported having presented pulmonary or extrapulmonary manifestations related to SARS-CoV-2 infection and, of the samples evaluated, a seroprevalence of 40.8% was observed (Table 1 and Figure 1).

Comparison of seropositivity and geographic area

When comparing seropositivity and detection of antibodies against SARS-CoV-2, it was observed that it was higher in the municipality of Montelibano (52.6%), with a statistically significant difference compared with the other evaluated municipalities (p<0.0001) (Figure 2).

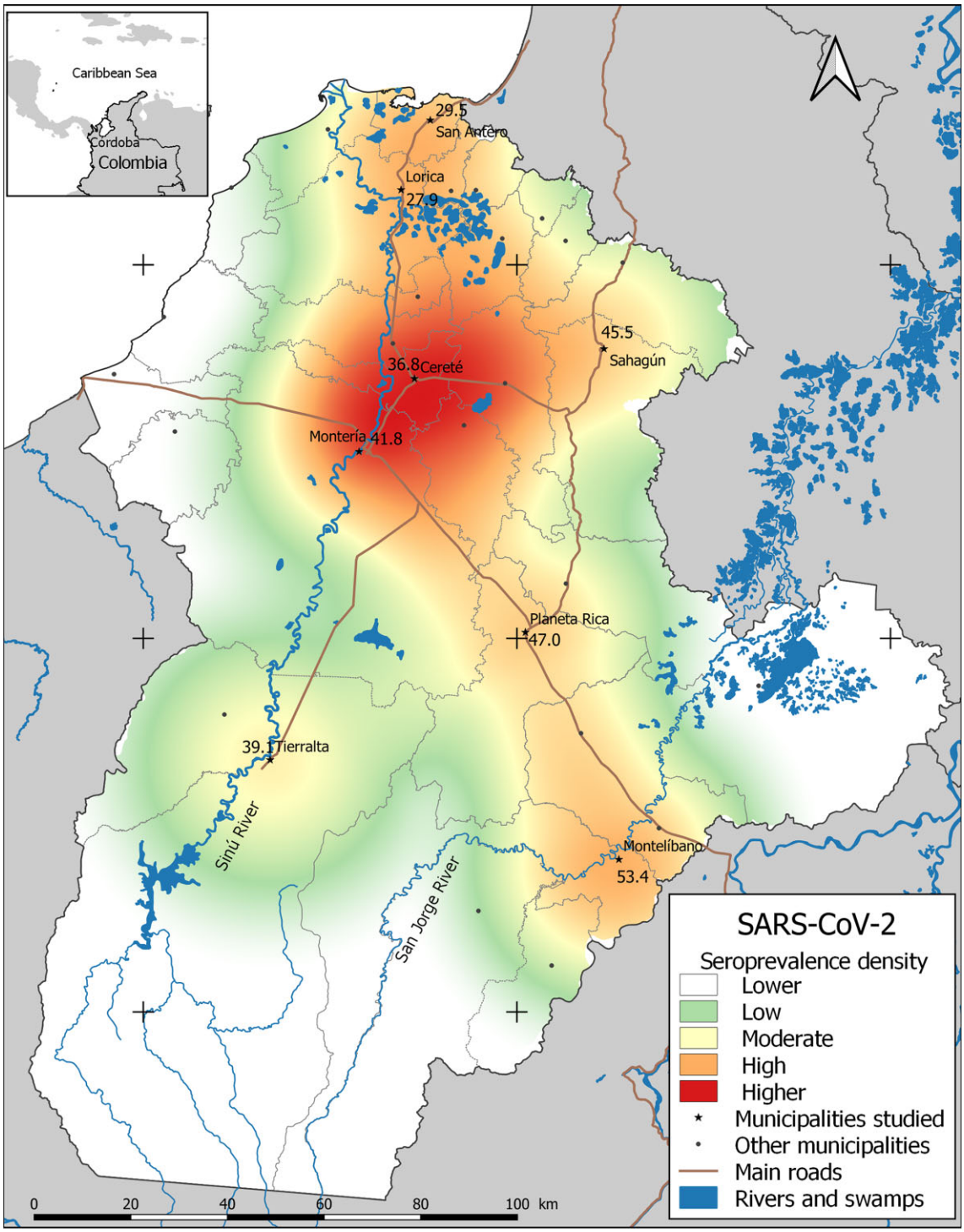

Figure 1. Spatial distribution through a heat map for SARS-CoV-2 infection in Córdoba. A distribution of SARS-CoV-2 cases is observed throughout Córdoba. There is a higher concentration of cases in the central zone that includes Montería, the capital of the state, and Cereté municipalities.

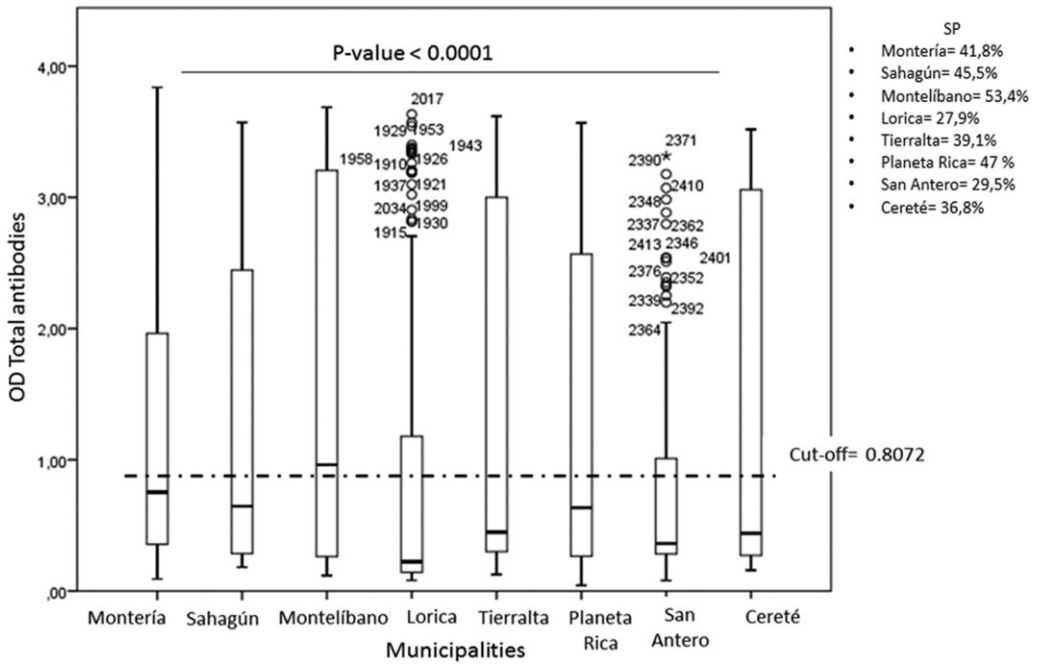

Figure 2. Relationship between the municipalities evaluated with the serological data for SARS-CoV-2. The box is made up of the 25th, 50th (median) and 75th percentiles and extreme values represent outliers. The figure shows high seropositivity in the municipality of Montelibano and an increase in the OD of total antibodies against SARS-CoV-2, which is statistically significant compared with the other municipalities evaluated. *Indicates a statistically significant difference compared with the other groups. SP: seroprevalence.

Relationship of seropositivity for SARS-CoV-2 and age range

Regarding the relationship between seropositivity and age, no statistically significant differences were found when relating seropositivity and total antibody titres against SARS-CoV-2 with the different age groups evaluated ($p>0.05$). However, greater seropositivity and the presence of total antibodies against the virus was observed in individuals who were in the age ranges of 10–14 y (n=45) and 15–19 y (n=100), where seropositivity was 53% and 46%, respectively (Figure 3).

Relationship of seropositivity for SARS-CoV-2 and gender

No statistically significant differences were observed between male (41%) and female (40.6%) serology, nor was there a higher expression of antibody titres against SARS-CoV-2 ($p>0.05$) (Figure 4).

Association of seropositivity for SARS-CoV-2 and socio-economic status

An increase was observed between seropositivity (49.1%) and the total antibody titres in individuals belonging to a low socio-economic level. The difference was statistically significant when compared with individuals from medium and high socio-economic levels ($p<0.0001$) (Figure 5).

Association of seropositivity and medical history related to SARS-CoV-2

Higher seropositivity and antibody titres against SARS-CoV-2 were observed in individuals with a clinical history of pulmonary and extrapulmonary clinical manifestations (49.9%) related to COVID-19 ($p<0.0001$). However, 30.7% of the individuals who reported having no symptoms related to COVID-19 were seropositive (Figure 6).

Relationship of seropositivity for SARS-CoV-2 and the cluster of variables studied

The antecedent of symptoms associated with SARS-CoV-2 in the last 3 months and low socio-economic level stand out from the cluster of variables evaluated. These variables explain within the regression model the increase in seropositivity in the analysed Colombian Caribbean region. Also, these variables are related as a risk factor for an individual to be seropositive for COVID-19 ($p<0.0001$; symptomatic, OR 1.9 [95% CI 1.5 to 2.2]; socio-economic level OR 2 [95% CI 1.7 to 2.3]) (Table 2).

Association between the cluster of clinical manifestations of COVID-19 and a positive serological test for SARS-CoV-2

The presence of neurological manifestations of the upper respiratory tract, such as anosmia and ageusia, increases the probability of infection by SARS-CoV-2 by five times ($p<0.0001$, OR 4.8 [95%

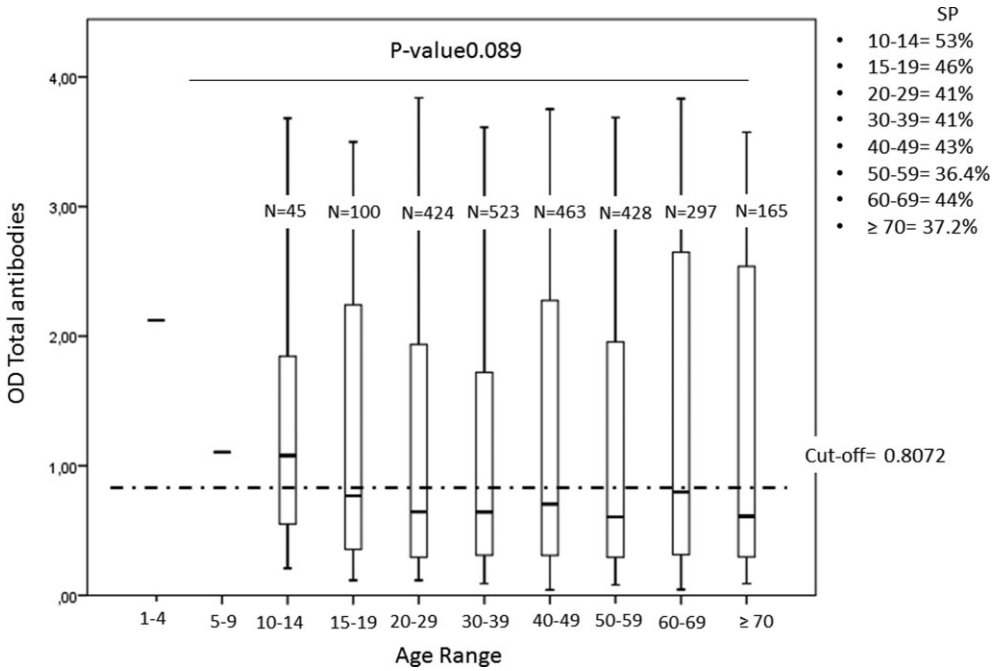

Figure 3. The relationship between the age ranges was evaluated against the serological data for SARS-CoV-2. In this box-and-whisker plot it is observed that despite having a higher seropositivity and OD of total antibodies against SARS-CoV-2 in the age groups of 10–14 y and 15–19 y, this difference is not statistically significant when compared with the other age groups. SP: seroprevalence.

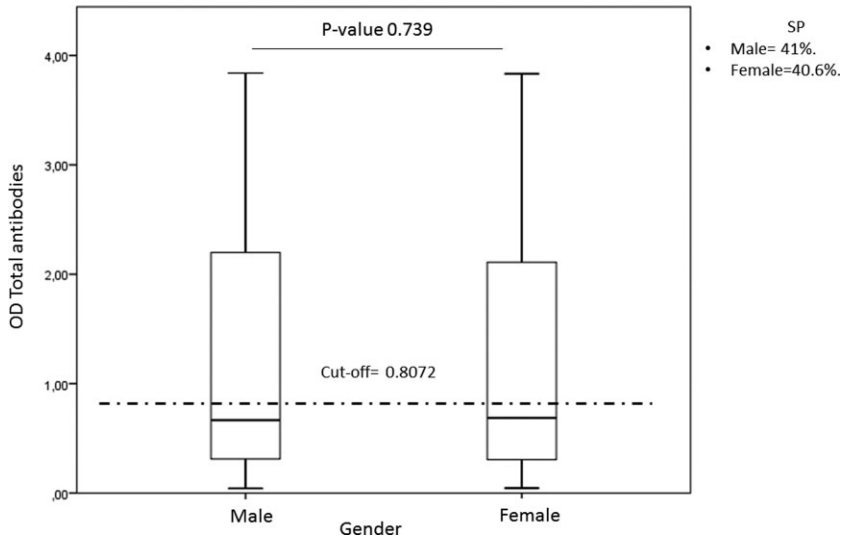

Figure 4. Relationship between gender and serological data for SARS-CoV-2. It is observed that there is no differences in the seropositivity or the OD of total antibodies against SARS-CoV-2 between men and women. SP: seroprevalence.

CI 3.6 to 6.3]). Also, another clinical manifestation that is associated with a greater risk of infection by this new virus is fever, which increases the risk of being seropositive against SARS-CoV-2 by almost two times (p<0.0001, OR 1.9 [95% CI 1.5 to 2.5]) (Table 3).

Discussion

The present study showed a seroprevalence of 40.8%, which is high compared with other studies in countries strongly affected by SARS-CoV-2, such as Italy, the USA and Peru, where

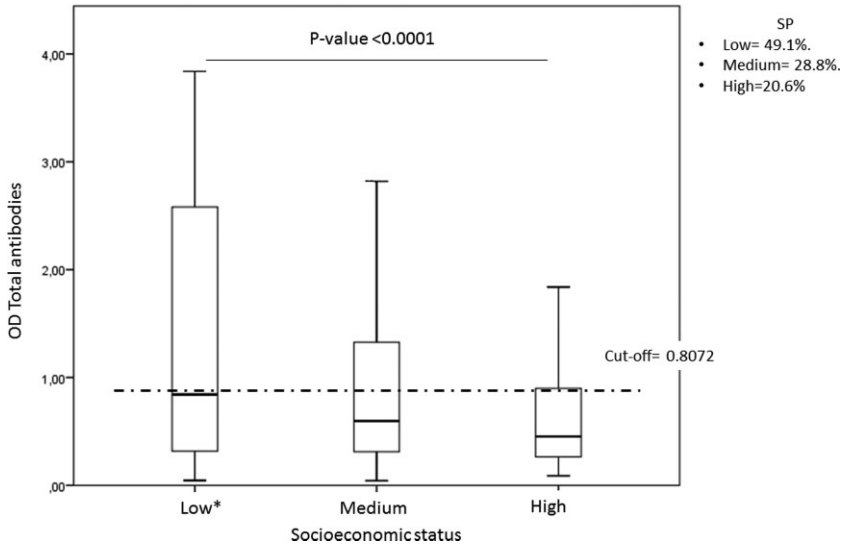

Figure 5. Association of income level and serological data for SARS-CoV-2. High seropositivity can be observed in individuals of low socio-economic stratus and with increased OD of total antibodies. The results are statistically significant when compared with individuals of medium and high socio-economic levels. *Indicates a statistically significant difference compared with the other groups. SP: seroprevalence.

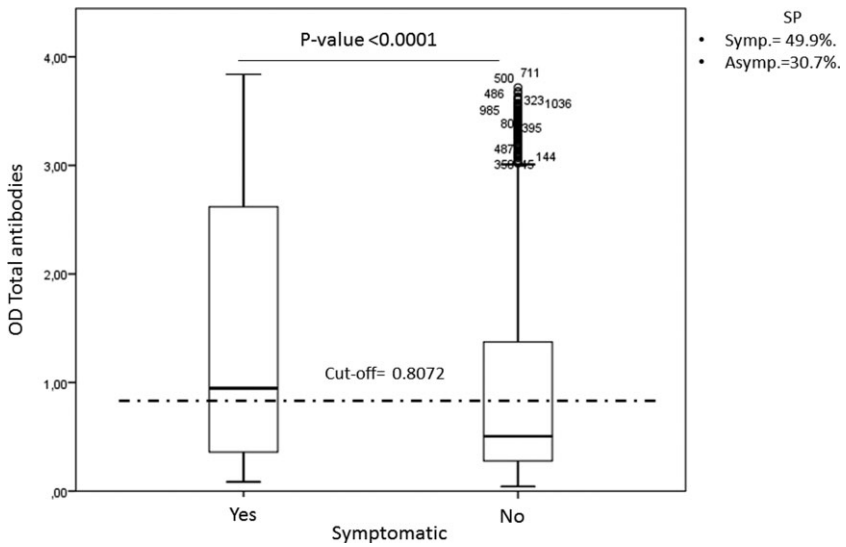

Figure 6. Relationship of the presence of clinical manifestations related to SARS-CoV-2 infection and the presence of a positive serological test for SARS-CoV-2. Higher seropositivity and OD of total antibodies are observed in individuals with clinical manifestations related to SARS-CoV-2 infection. Asymptomatic individuals had a seropositivity of 30.7%. SP: seroprevalence.

seropositivity was 23%, 1.82% and 20.8%, respectively.[8,13,14] In China and South Korea, which were the initial epicentres of this infection, the seroprevalence data did not exceed 5%.[9,15] This percentage could be related to their capacity to carry out massive sampling against SARS-CoV-2 and the social discipline of its population. China and South Korea's results contrast with ours because there is little adherence to compliance with health measures in controlling the epidemic in the Colombian Caribbean population. Also, cultural customs and low income promote overcrowding, poor sanitary conditions and informal economic activities with greater exposure to the virus. However, our finding is lower than that reported in Manaus, Brazil, with a seropositivity of 76%.[16] A study recently published by us showed high seropositivity in Montería (55.3%), Córdoba's department capital. Although there are cross-reactions between SARS-CoV-2 and endemic arboviruses in the population studied, the high seroprevalence found confirms the novel coronavirus's great infectious capacity.[17] The socio-economic characteristics of the studied population allow us to infer that the infection rate can be considered high.

In the age groups of 10–14 y and 15–19 y, high seropositivity of 53% and 46%, respectively, was found. These findings are similar to those reported in Sweden, where increased

Table 2. Multivariate analysis among the cluster of variables evaluated with the probability of being seropositive for SARS-CoV-2

Clinical variables	Seropositivity	
	p-Value	OR (95% CI)
Symptomatic	<0.0001	1.9 (1.5 to 2.2)
Socio-economic level	<0.0001	2 (1.7 to 2.3)
Gender	0.66	1 (0.87 to 1.2)
Municipality	0.31	1 (0.97 to 1.1)
Age range	0.53	1 (0.97 to 1.1)

Table 3. Multivariate analysis of the cluster of clinical manifestations associated with COVID-19 with the probability of being seropositive for SARS-CoV-2

Clinical variables	Seropositivity	
	p-Value	OR (95% CI)
Anosmia/ageusia	<0.0001	4.8 (3.6 to 6.3)
Fever	<0.0001	1.9 (1.5 to 2.5)
Dyspnoea	<0.96	0.73 (0.51 to 1.05)
Headache	0.29	1.1 (0.9 to 1.4)
Shortness of breath	0.022	0.6 (0.4 to 1)
Cough	0.68	1.9 (1.5 to 2.5)
Diarrhoea	0.99	0.9 (0.7 to 1.4)
Nausea/vomiting	0.39	0.82 (0.55 to 1.2)
Myalgia	0.21	2.1 (1.7 to 2.6)

seropositivity for SARS-CoV-2 was observed in children and adolescents. However, the rate of seropositivity in this group of young Swedes did not exceed 7%.[18] In comparison, in the Colombian Caribbean youth, the rate of seropositivity was >45%, which is curious considering that Sweden did not implement quarantines and the use of masks was not mandatory in its population. This high infection rate among young people would also explain the high seropositivity observed in individuals >60 y of age. Older adults were locked down in Colombia, therefore the primary source of infection could be associated with interactions with symptomatic and asymptomatic carriers of the virus, who usually are <20 y of age.[7] However, our results in the young population should be confirmed in further studies since this population represented only 5.6% of the studied sample.

Regarding gender, no significant differences in seropositivity were found in this study between men and women. These data are consistent with seroprevalence studies conducted in China and Switzerland, in which no differences were found when comparing seropositivity between men and women.[15,19] However, since there are no differences in the infection rate regarding gender, it is essential to note that SARS-CoV-2 infection tends to be more severe in men, as women tend to develop innate and adaptive immune responses that are more effective against SARS-CoV-2.[20] Also, female oestrogen action has been related to a reduction in the expression of angiotensin-converting enzyme 2 (ACE2) receptors. ACE2 is the key for internalization of the virus at the lung parenchyma level, which reduces the risk of a systemic condition in women.[20] However, there is a similar infection rate between genders and the immune response is variable between individuals. The development of severe forms of the disease are not limited by the gender of the individual infected with SARS-CoV-2.

Our results showed increased seropositivity against SARS-CoV-2 in individuals of low socio-economic status. These findings are similar to those at the community level in inhabitants of urban slums of Buenos Aires, Argentina, who have a high seroprevalence of 53.4% in the most deprived areas.[21] The high seropositivity found in vulnerable populations are related to economic and social factors that have been previously discussed.

Moreover, the presence of symptoms related to COVID-19 in participants of this study demonstrated greater seropositivity to SARS-CoV-2 in individuals who had presented pulmonary and extrapulmonary clinical manifestations compatible with this infection in the last 3 months. However, it is essential to mention that 29.2% of the individuals reported as asymptomatic for COVID-19 were seropositive. The percentage of asymptomatic individuals is a possible way of spreading SARS-CoV-2 infection in the community since it has been shown that asymptomatic and presymptomatic patients can present more prolonged infections and a higher viral load.[22] Therefore public health policies from the government should focus on detecting these individuals to limit the spread of the disease.

In the multivariate analysis, the present study allowed us to confirm that belonging to a low socio-economic stratum and having symptoms was strongly linked to seropositivity. Among the symptoms, this analysis showed that neurological alterations of the upper respiratory tract, such as anosmia and ageusia, are strongly related to seropositivity against SARS-CoV-2. A study carried out in London found that the only predictive symptom of seropositivity was anosmia, thus the UK government has added anosmia as a symptom that requires self-isolation.[23] In Europe, the prevalence of anosmia and ageusia is high in patients with SARS-CoV-2 and they are becoming key symptoms for the early diagnosis of infection.[24,25]

Our work has also had some limitations. One is that the population groups by age range in this work are not homogeneous. Therefore extrapolation of these results becomes complex for the general population. The ELISAs used are based on detecting total antibodies against SARS-CoV-2, which prevented us from evaluating the type of antibodies detected and making an inference if the individual had an active or past infection.

In conclusion, the present study found high seropositivity in Córdoba, which is associated with the high dissemination of this new virus and a probable community immunity in this region of the Colombian Caribbean. However, it is not yet clear how long the antibodies confer protection in individuals. On the other hand, we observed that the population with low income presents a greater risk of infection by SARS-CoV-2. Clinically, the upper respiratory tract (anosmia, ageusia) can be considered pathognomonic of COVID-19. Therefore health authorities must redouble their efforts to control this infection in the most vulnerable populations by improving hygiene and sanitary conditions and the performance of clinical, molecular and serological screenings.

This would promote the detection and isolation of those newly infected by SARS-CoV-2. This is vital due to the circulation of a new variant of SARS-CoV-2 from the UK.[26] It is crucial to continue with the population's serological and molecular studies since this will provide information on how long those already infected maintain immunity against the virus and the proportion of reinfection cases.

Authors' contributions: SM, EG and HS-C designed the study. AF-M, JB and HS-C evaluated study participants. The lab protocol was standardized (serology) and performed by RR, EG, YB, VC, YL, BG, MB and KG. HS-C performed the data analysis. HS-C and EG wrote the manuscript. Critical review was performed by JM, AC, ML, CM-B, GA and EB-T. SM directed the research. All authors read and approved the manuscript.

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Competing interests: None declared.

Ethical approval: The research was carried out following the international ethical standards given by the World Health Organization and the Pan American Health Organization, supported by the Declaration of Helsinki, and national legislation, resolution number 008430 of 1993 of the Ministry of Health of Colombia. This work was endorsed by the ethics committee of the Institute for Tropical Biological Research.

Data availability: The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation, to any qualified researcher.

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