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SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2. SEROEPIDEMIOLOGY STUDY IN ARGENTINIAN SLUM

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Abstract Most countries in Latin America have already reported thousands of confirmed cases and vulnerable populations are the most affected by the coronavirus disease 2019 (COVID-19) pandemic. Preventive measures such as hygiene, social distancing, and isolation, essential to stop the spread of coronavirus, are difficult to accomplish for vulnerable populations due to their living conditions. Seroepidemiological surveys are assets to measure the transmission for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Until July 1st, the incidence rate of SARS-CoV-2 infection in Barrio Padre Mugica, one of the largest slums in Buenos Aires City, was 5.9%. This study aimed to establish the prevalence of SARS-CoV-2 antibodies immunoglobulin G (IgG) immediately after the outbreak, and to identify neighbourhood, household and individual factors associated with seroconversion. The prevalence based on IgG was 53.4% (95% CI 52.8% to 54.1%). For each polymerase chain reaction (RT-qPCR) confirmed case, nine people tested IgG positive, indicating a high rate of undetected (probably asymptomatic) infections. Hence, the high rate of undiagnosed people suggests that clinical criteria and epidemiological nexus should be considered. The high seroprevalence observed in the context of an intense epidemic in a vulnerable area might serve as a reference to other countries. This study contributes to future decision making by understanding population immunity against SARS-CoV2 and its relation to living conditions and foccus that comprehensive biosocial, household-level interventions are needed.

Key words: poverty areas, COVID 19, seroepidemiologic studies

Resumen ***Estudio seroepidemiológico de enfermedad por Coronavirus 2019 en un barrio de Argentina.*** Muchos países de América Latina han informado miles de casos confirmados y las poblaciones vulnerables son las más afectadas por la pandemia de la enfermedad por coronavirus 2019 (COVID-19). Las medidas preventivas como la higiene, el distanciamiento social y el aislamiento, fundamentales para frenar la propagación del coronavirus, son difíciles de lograr en estas poblaciones debido a sus condiciones de vida. Los estudios seroepidemiológicos son de gran utilidad para medir la transmisión del síndrome respiratorio agudo severo coronavirus 2 (SARS-CoV-2). Hasta el 1 de julio, la tasa de incidencia de la infección por SARS-CoV-2 en el Barrio Padre Mugica, uno de los barrios marginales más grandes de la ciudad de Buenos Aires, era del 5.9%. Este estudio tuvo como objetivo estimar la prevalencia de anticuerpos inmunoglobulina G (IgG) para SARS-CoV-2 inmediatamente después del brote, e identificar factores del barrio, hogar e individuales asociados con la seroconversión. La prevalencia basada en IgG fue del 53.4% (IC del 95%: 52.8% a 54.1%). Para cada caso confirmado por reacción en cadena de la polimerasa (RT-qPCR), nueve personas dieron positivo en IgG, lo que indica una alta tasa de infecciones no detectadas y probablemente asintomáticas. La alta tasa de personas no diagnosticadas sugiere que se deben considerar los criterios clínicos y el nexo epidemiológico. La alta seroprevalencia observada en el contexto de una intensa epidemia en una zona vulnerable podría servir de referencia a otros países. Este estudio contribuye a la toma de decisiones futuras al comprender la inmunidad de la población contra el SARS-CoV2 en su relación con las condiciones de vida y por su enfoque en la necesidad de intervenciones integrales a nivel del hogar.

Palabras clave: áreas de pobreza, COVID 19, estudios seroepidemiológicos

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KEY POINTS

- Evidence before this study: Most COVID-19 seroprevalence studies were carried out on the general population, usually showing low rates of antibodies. Our study is the first detailed seroprevalence evaluation of a highly vulnerable population in a large slum in South America.
- Contribution: This is the first population-based study that presents seroprevalence of antibodies against SARS-CoV-2 with probabilistic sampling on vulnerable populations in an Urban Slum of Buenos Aires City, Argentina. The high seroprevalence observed in the context of an intense epidemic in a vulnerable area might serve as a reference to other countries.

Population serological data are essential for understanding the prevalence of subclinical infections and the population's herd immunity against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1]. Several COVID-19 seroprevalence studies were carried out on the general population showing low rates of antibodies[2-5]. However such evidence has been obtained from cities with different living conditions than the ones prevailing among slum dwellers of Latin American cities and can hardly be extrapolated to them[6].

Buenos Aires City (CABA), the capital of Argentina, is a large urban conglomerate in a country of the Southern hemisphere. It has nearly three million inhabitants, of whom approximately 5.7% are a very vulnerable population living within 17 well-defined neighborhoods. In most cases, there are households with scarce potable water and sanitary conditions, poor ventilation, space constraints, and overcrowding, making physical distancing and self-quarantine impractical, thus facilitating the rapid spread of SARS-CoV2 infection[7, 8].

Barrio Mugica is one of the most overcrowded slums with more than 40 000 inhabitants, and almost 1500 people experiencing homelessness[9]. Its first case of SARS-CoV-2 infection, linked to community transmission, was reported four days after the national mandatory quarantine was set on March 19th, 2020. Preventive measures were taught to community-based organizations that provided food assistance, temporary isolation centers for older adults located in churches were set up and an immediate plan for emergency and health care was established in the three medical centers allocated in *Barrio Mugica*. Despite these measures, this slum was the first one in Argentina to become affected by a high number of cases, with a sharp rise of infected people.

On May 5th, 2020, an active policy named Coronavirus Testing Strategy in Argentinian Territory ("DETeCTAr") was set to dampen the spread by testing, diagnosing, and early treating of cases[7]. A crisis planning committee joined weekly to enforce the emergency plan actions related to health access, economic aid and food assistance. Social and health community workers were deployed in active surveillance on cases, and contact tracing. Local sampling for real-time polymerase chain reaction (RT-qPCR) testing was performed, and each positive person, according to clinical severity, was admitted to an out-of-hospital institution (repurposed hotels) or a hospital.

Until July 1st, the COVID-19 incidence rate at *Barrio Mugica* was 5.9% (2949 cases diagnosed by RT-qPCR) and the case fatality rate was 1.5% (44 deaths). In parallel with the mitigation measures, the basic reproductive number (R0) in *Barrio Mugica* decreased from 3.24 to 0.6 in six weeks.

To understand population immunity against SARS-CoV2, on June, 10th, participatory research, the Sero-Covid-POB study, started to detect SARS-CoV2-IgG presence and the housing conditions associated with infection. The final aim of the present study is to contribute to future decision making on control measures in similar neighbourhoods.

Materials and methods

A cross-sectional study for seroprevalence survey was carried out between June 10th and June 26th at *Barrio Mugica.*

Barrio Mugica, a slum with more than 40 000 inhabitants, and almost 1500 people experiencing homelessness is located in a strategic place, next to the main passenger transfer center of the City of Buenos Aires and a few meters from the most sought-after neighborhoods, named Retiro and Recoleta

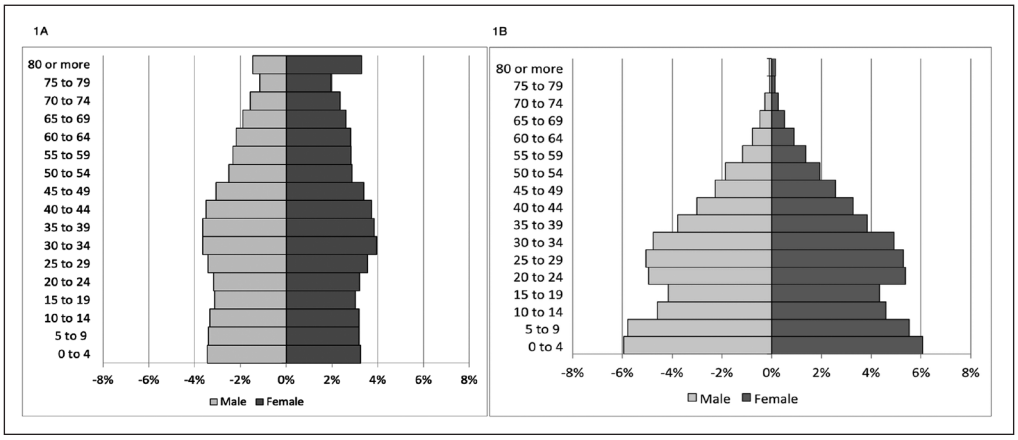
It is a heterogeneous slum, with 10 different areas, each presenting particular cultural and social characteristics, they are: Bajo Autopista, Comunicaciones, Cristo Obrero, Ferroviario, Güemes, Inmigrantes, Playón Este, Playón Oeste, San Martín and YPF.

There are strong differences between *Barrio Mugica*'s living conditions and the ones shown in the rest of Buenos Aires City. In *Barrio Mugica*, around 60% of the population inhabits precarious houses, a quarter of them in cramped conditions. Three out of 10 do not have private toilets[9].

Barrio Mugica sociodemographic data show that there is a predominance of the youngest age group, there is a high rate of households with young couples that have children, which represent a strong tendency to overcrowded households[9]. In other words, there are a high number of children and houses with children. Moreover, the number of migrants is higher in *Barrio Mugica* than in the rest of Buenos Aires City, mainly represented by people coming from neighboring countries such as Peru, Bolivia and, Paraguay[9]. Besides, *Barrio Mugica* has a high rate of unemployment, and when gender is considered, women present lower-income and suffer from higher rates of unemployment than men in the same community[9]. Figures 1A and 1B show Buenos Aires City and *Barrio Mugica*'s respective population pyramids. We included all residents above 14 years that consented to the study.

Prevalence positive SARS-CoV2 IgG was the main variable of this study. It was obtained from blood samples collected with a validated Serokit in a capillary tube from a finger prick taken at the doorstep of each person (serological test is explained below). Samples were processed and analyzed at the *Hospital de Niños Dr. R. Gutierrez* Virology laboratory.

Fig. 1.– Population pyramids of Buenos Aires City (A) and Barrio Mujica (B)



The Buenos Aires City population pyramid was constructed with public data of Argentina's 2010 census and the pyramid of Barrio Mugica was constructed with public data of internal 2017 census.

The survey contained the following explanatory variables: age, biological sex; the presence of any related symptom during the past two months before this study was conducted, living, and sharing closed spaces with a confirmed case for COVID-19, number of households in the building and the sector of *Barrio Mugica*. Blood sample collection and epidemiological data were collected and entered in a secure database.

The test COVIDAR IgG, an enzyme-linked immunosorbent assay [ELISA] developed and validated in Argentina (Laboratorio Lemos SRL, Buenos Aires, Argentina), was used to detect antibodies. Performance characteristics of the kit indicate a sensitivity of 75% after 7 days from symptoms onset and more than 90% after 21 days, using RT-PCR as the gold standard. The specificity was near 100% corroborated by studying 200 samples obtained before the pandemic (data in process of publication). The test detects antibodies against two viral antigens, trimeric spike and the receptor-binding domain (RBD) of the spike protein. Viral glycoproteins were expressed in human cells. The test has obtained regulatory approval from Argentina's national drug regulatory agency (ANMAT, National Administration for Drugs, Food and Medical Devices)[10].

A sample size of 406 households was calculated for an estimated seroprevalence of 7% or higher with a precision of 3.5%, accounting for non-response and potential clustering of seropositivity by household (design effect 2).

A two-stage random sampling method was applied where the first level unit was a sector of *Barrio Mugica*; the second level unit was geographical areas determined by the Department of Statistic and Census where thirty houses were selected at this level. People over 14 years old were tested at the front door of their houses. Figure 2 shows an example of a geographical area of one sector the neighbourhood with the 30 houses selected.

The SeroCovid-POB CABA sample dataset was expanded to that of the last census to estimate weighted prevalences. Specifically, we accounted for non-response; projecting the sample to the entire population, and finally calibrating age and sex groups[11]. A choropleth map was performed with QGIS software version 2.18.13.

In the descriptive analysis we used median and interquartile range (IQR) for quantitative data and absolute (n) and relative frequencies (%) for categorical data.

As household members share exposure to SARS-CoV2, the outcome (prevalence of SARS-CoV2 IgG) clustering effect was included in a random-effects logistic regression model (multilevel model) as it includes the variation between clusters explicitly in the likelihood and therefore takes account of intracluster correlation[12-14].

Explanatory variables were fitted in the models according to a) individual level: age and sex; the presence of any related symptom two months before, b) household level: cohabiting with a confirmed case, number of households in the building, and c) the sectors of *Barrio Mugica* were grouped in six ordinal categories according to the level of vulnerability, being *Bajo Autopista* de more deprived sector. A household ID was set for people living together in a household (defined as those who shared income and food) because in some houses there is more than one household sharing a bathroom and kitchen. Odds Ratios (OR) and their confidence intervals 95% (95% CI) from the coefficients obtained in the statistical models were estimated. Free license R software version 4.0.2 was used.

The study was approved by the institutional review board of the *Hospital de Niños Dr. R. Gutierrez*. Oral informed consent was obtained from every participant. The study protocol was registered in *clinicaltrials.gov*. Identifier: NCT04472078.

The National and local Ministries of Health provided medical supplies for the survey and for the virology laboratory to perform the ELISA test for SARS-COV2 antibodies detection.

The National Research Council (CONICET) provided the serokits test COVIDAR IgG.

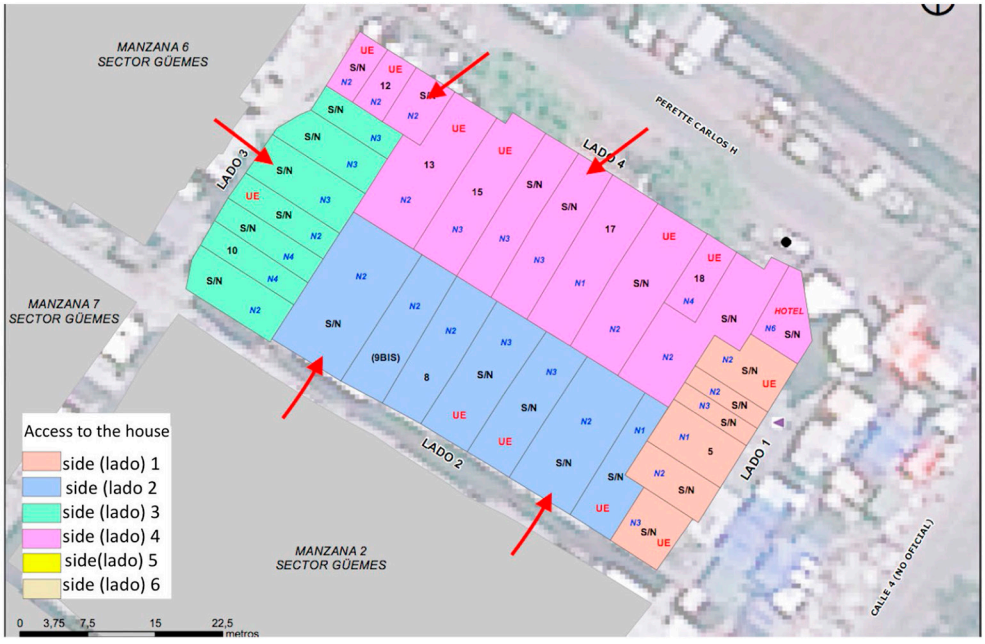
None of the funding sources provided economical support for the data collection, statistical analysis, or were used to write the manuscript, or to submit it for publication.

The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

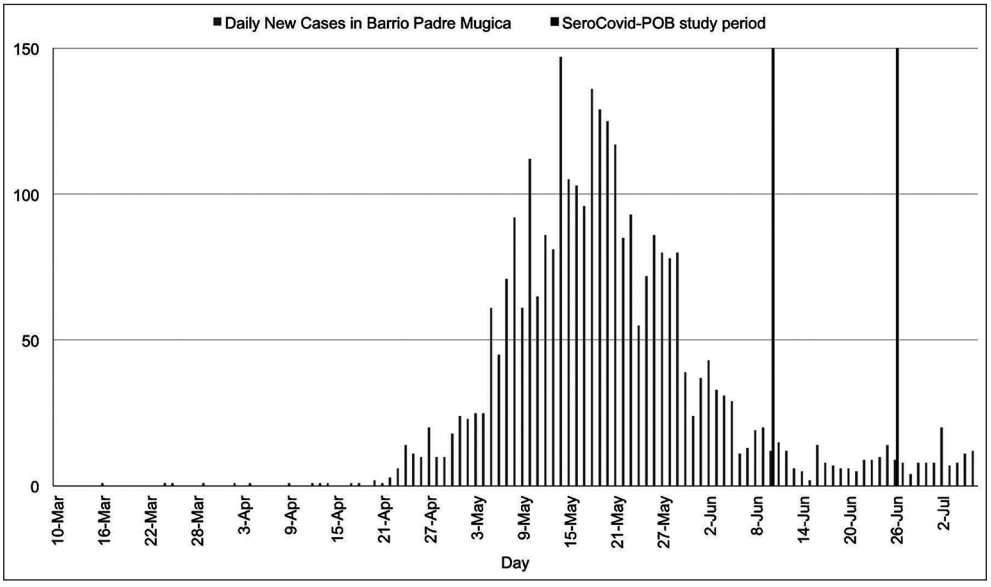
The study was carried out immediately after the number of confirmed COVID-19 cases flattened, between June 10th to June 26th. Figure 3 shows COVID-19 incident cases at *Barrio Mugica* and the period of the SeroCovid-POB study (June 10th to June 26th).

Fig. 2.– Example of a geographical area of one sector the neighbourhood Barrio Mugica used in SeroCovid-POB study



This figure is an example of block four in the Güemes sector of Barrio Mugica. The colors depict the different sides to access to the houses. The purple triangle shows the first house, and the black dot is the last house of the block. The selection interval in this block was every 15 houses. The red arrows indicate the selected houses. The blue numbers are the number of floors in each house and the red legend UE shows if there is any economic activity or store in the house. The black numbers are the numbers assigned to each house, when there is no number it is shown S/N

Fig. 3.– COVID-19 Incident cases - Barrio Mugica, Buenos Aires, Argentina. SeroCovid-POB study (June 10th to June 26th)



Grey lines represent incident cases since the detection of the first confirmed case and black lines show the period when the SeroCovid-POB study was carried out

A total of 460 houses were visited, having a response rate of 73%. A total of 398 houses were included, in which 577 households (families) lived. Out of them, 873 people accepted to be tested at their house's doorstep. The median age was 38 years (IQR 28-49) and 499 (57.2%) were women. Seventy-two people (16.8%) reported being symptomatic and 489 houses shared bathrooms and kitchens (55.3%). Table 1 shows the descriptive characteristics of the sample according to *Barrio Mugica*'s sector.

The weighted SARS-CoV2 IgG seroprevalence was 53.4% (95% CI 52.8%-54.1%). Prevalence among males was 51.5% (95%CI 50.6-52.4) and for women 55.3% (95% CI 54.4-56.2). Sex and age-group specific prevalence is shown in Figure 4.

The SARS-CoV2 IgG seroprevalence according to Barrio Mugica's every sector is shown in Figure 5.

We have found strong evidence of within-household clustering effect (rho = 0.52; 95% CI 0.36-0.67; LRT 43.8 p-value < 0.001). We did not find an association between being symptomatic and a positive result in the serological assay (OR 1.01; 95% CI 0.54-1.87).

An association between being IgG positive and living with a RT-qPCR confirmed COVID-19 case was found (OR 2.13; 95% IC 1.17-3.85). Living in the *Bajo Autopista* sector of the neighborhood had the highest risk of infection (OR 30.39 95% CI 5.50-168.0). Other variable associations are shown in Table 2.

TABLE 1.– *Characteristics of the sample according to Barrio Mugica's sector of residence*

	Bajo Autopista	Comunica-ciones	Cristo Obrero	Ferro-viario	Güemes	Inmigran-tes	Playón Este	Playón Oeste	San Martin	YPF
Houses surveyed, n	12	23	52	28	46	27	49	79	45	37
Households surveyed, n	15	29	66	41	109	34	63	113	54	53
People, n	29	41	97	69	171	45	88	173	77	83
Age, median (IQR)	34	40	37	34	39	40	39	37	38	40
	(25-40)	(29-52)	(29-45)	(26-45)	(29- 53)	(26-47)	(29- 47)	(27-50)	(28- 49)	(27-53)
Women, n (%)	19	24	65	38	96	22	59	91	42	43
	(65.5)	(58.5)	(67.0)	(55.1)	(56.1)	(48.9)	(67.0)	(52.6)	(54.5)	(51.8)
Symptoms, n (%)	10	5	13	12	23	0	18	20	17	9
	(34.5)	(12.2)	(14.4)	(17.4)	(13.5)	(0.0)	(20.5)	(11.6)	(22.1)	(10.8)
Population density	2995	1253	5640	3059	6843	1331	5250	5633	4869	3330
Family member with	0	1	9	18	44	1	22	32	20	26
COVID 19, n (%)	(0.0)	(2.4)	(9.9)	(26.1)	(25.7)	(2.2)	(25.0)	(18.5)	(6.0)	(31.3)
Only one household	11	27	50	21	67	24	33	80	34	43
per house, n (%)	(37.9)	(65.9)	(51.5)	(30.4)	(39.2)	(53.3)	(37.5)	(46.2)	(44.2)	(51.8)

n: absolute frequency; %: relative frequency; IQR: interquartile range

Fig. 4.– Sex and age-strata specific prevalence of positive SARS-CoV2 IgG with confidence interval 95%

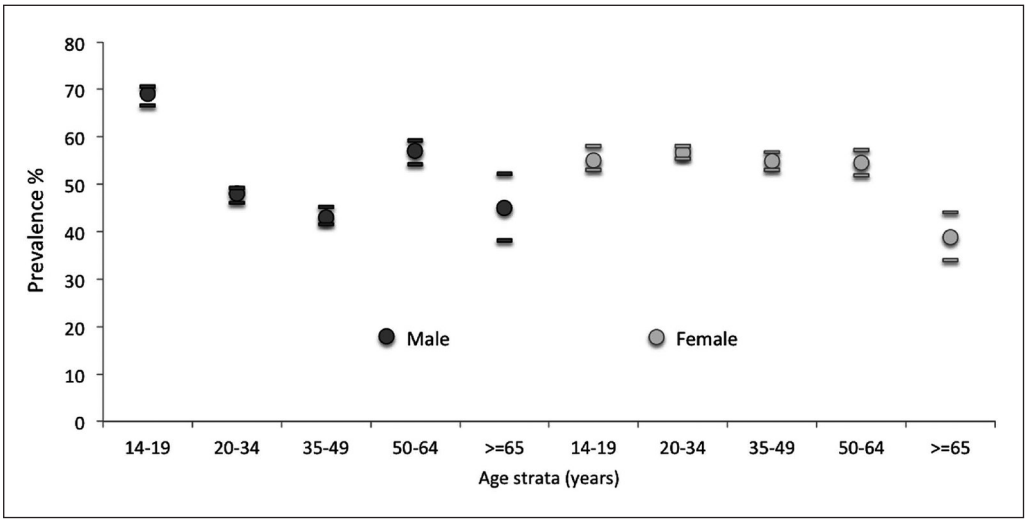


Fig. 5.– Barrio Mugica. COVID-19 SARS-CoV2 IgG seroprevalence by sector

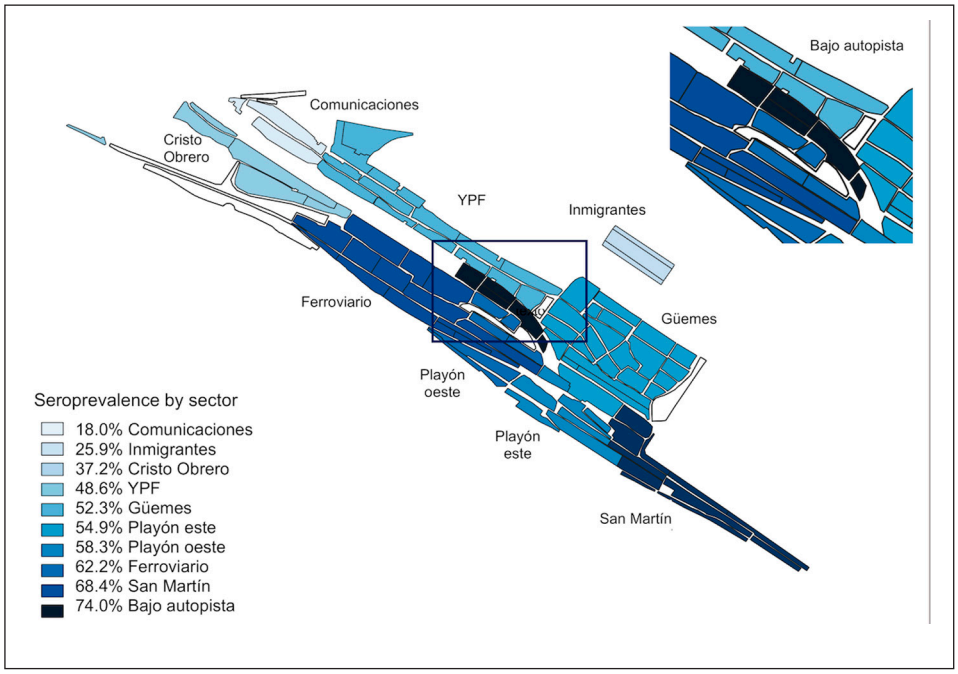


TABLE 2.– *Multivariable model (random effect logistic regression) to determine whether* SARS-CoV 2 IgG is associated with individual, household or sector variables

	OR (95% CI)	P value
Residence at Comunicaciones, Inmigrantes and Cristo Obrero*	Reference	
Residence at Güemes, Playón Este and Playón Oeste	5.53 (2.62-11.66)	< 0.001
Residence at YPF	3.49 (1.26-9.67)	0.016
Residence at Ferroviario	12.07 (3.78-38.51)	< 0.001
Residence at San Martín	12.64 (4.23-37.80)	< 0.001
Residence at Bajo Autopista	30.39 (5.50-168.01)	< 0.001
Male sex	0.73 (0.47-1.08)	0.108
Age	0.99 (0.98-1.01)	0.326
Only one home per dwelling	0.89 (0.56-1.41)	0.625
Family member with COVID 19	2.15 (1.18-3.90)	0.012
Symptoms	1.01 (0.54-1.87)	0.983

**Sectors Comunicaciones, Inmigrantes; Cristo Obrero reference category; OR: odds ratio 95%; CI: confidence interval 95%*

Discussion

We found an unexpectedly high seroprevalence (53%) and strong evidence of a within household clustering effect in an extremely deprived population in Buenos Aires, Argentina.

Although a small geographical area was covered in this community-level seroprevalence survey, selecting participants in a probabilistic way, allows extrapolation of results to similar low-income urban communities.

Our study is the first detailed seroprevalence evaluation in a highly vulnerable population in a large slum in Buenos Aires. Most COVID-19 seroprevalence studies to date were carried out on the general population, showing usually low rates of antibodies, ranging from 0.9% to 21%[2–5].

The high seroprevalence found is consistent with the recent evidence that COVID-19 has disproportionately affected marginalized populations; the UK and US are reporting higher in-hospital mortality rates for black people and minority ethnic groups[15, 16].

The COVID-19 incidence rate at *Barrio Mugica*, according to RT-qPCR of suspected cases, was 5.9%. Strikingly, we found that in these communities, for each patient diagnosed by RT-qPCR there were nine IgG-positive individuals, suggesting a strikingly high rate of asymptomatic infection. This relationship has also shown in other studies, it was 1 to 11 in Geneve[3] and 1 to 10 in New York[17].

Reporting bias could be present in the IgG rate for symptomatic cases, minimal symptoms might not have been noticed since the survey asked for symptoms during the two previous months when only people having fever were considered to be COVID-19 cases. Even though case definition has changed as new evidence, such as lack of taste and smell, was discovered about the course of the infection around the world, the high degree of cases under ascertainment suggests that clinical criteria and epidemiological nexus should be considered.

The precise percentage of the population required to be immune against SARS-CoV-2 for herd immunity to occur is currently undefined; however, assuming projections, if the SARS-CoV-2 basic reproductive number (R0) shifted from 2 to 3.5, the threshold would shift from 40% to 75%[18,19]. In our series, the R0 reached that threshold and the prevalence found was in agreement with such assumptions.

A caveat must be kept in mind: sex was not associated with higher prevalence, but male subjects between 14 and 19 years showed the highest prevalence of IgG compared with the other groups. This could be attributed to lower risk perception and lower compliance with the quarantine measures among young people.

Due to the high virus transmission found in our study, we would have expected a higher lethality rate among this population. However, in *Barrio Mugica* 1.5% of people are older than 65 years vs. 17% in the rest of Buenos Aires City, with a higher working-age population (37% vs. 30%). As a working-class neighborhood, it has a high immigration rate that tends to avoid elders, who stay living in their places of origin[9]. In our study, we also found a low proportion of elderly people (4.5%), this finding makes a difference with the rest of Buenos Aires City and also with many cities in developed countries, and could contribute to explain why, in spite of high virus transmission, the lethality rate was not as high as reported in other countries.

Social distancing recommendations intended to reduce SARS-CoV-2 transmission have a low impact in these settings. Our study showed a high cluster correlation, the variance within the households was smaller compared with that between households, showing a household-specific effect: an individual in one household is more likely to be SARS-CoV2 positive than an individual in another household (between correlation)[20]. In this regard, those who had a family member diagnosed with RT-qPCR had two-fold chance of becoming infected by the virus. Recently evidence shows that household contacts, tested for SARS-CoV-2 by RT-PCR in a clinical follow-up, were at higher risk of infection (odds ratio 6.27 (95% CI 1.49–26.33) than other close contacts, and those having a household member who had received a diagnosis of COVID-19 were 15 times more likely to have had positive IgG test results for SARS CoV-2 than were those who did not[21,22].

We also found sector differences: those living in worse conditions (*Bajo Autopista*) had a higher rate of infection. This could be associated with a severe shortage of water supply in April 2020, which put the whole community in distressing alert.

IgG antibody response against different SARS-CoV-2 antigens becomes detectable in immunocompetent patients after at least eight days with over 90% of individuals seropositive after day 14 of infection. In theory, seropositive individuals are expected to be at lower risk for re-infection compared to seronegative persons. However, neither the level nor the duration of protective immunity against COVID-19 is currently known[22], therefore we will consider this study as a baseline cohort for a serial seroprevalence study that could provide a better understanding of transmission patterns and may help to determine if it's possible to reach the herd immunity state.

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Conflicts of interest: None to declare

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