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RESEARCH ARTICLE

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Prevalence of IgG antibodies induced by the SARS-COV-2 virus in asymptomatic adults in Nuevo Leon, Mexico

Edgar P. Rodríguez-Vidales[1] | Denise Garza-Carrillo[1] | José J. Pérez-Trujillo[2] | Olivia A. Robles-Rodríguez[1] | Ana María Salinas-Martínez[3,4] | Roberto Montes de Oca-Luna[1] | Consuelo Treviño-Garza[1] | Manuel E. De la O-Cavazos[1]

[1]Health Services of the State of Nuevo Leon, Ministry of Health, Monterrey, Nuevo León, Mexico

[2]Department of Histology, School of Medicine, Autonomous University of Nuevo Leon, Monterrey, Nuevo León, Mexico

[3]Epidemiologic and Health Services Research Unit, Mexican Institute of Social Security, Monterrey, Nuevo León, Mexico

[4]School of Public Health and Nutrition, Autonomous University of Nuevo Leon Monterrey, Monterrey, Nuevo León, Mexico

Correspondence

Consuelo Treviño-Garza and Manuel E. De la O-Cavazos, Administrative Tower, 8th floor. Washington Street No. 2000, Col. Obrera, Monterrey, Nuevo Leon, Mexico, ZP 64000.
Email: consuelo.trevino@saludnl.gob.mx and publicacion.investssnl@gmail.com

Abstract

Population-based immunoglobulin G (IgG) seroprevalence studies in asymptomatic individuals in Latin America are scarce. The objective of the study was to estimate the prevalence and geographic distribution of IgG antibodies induced by natural SARS-CoV-2 infection in asymptomatic adults, 5–8 months after the first case was reported in a northeastern state of Mexico. This was a population-based cross-sectional study carried out in Nuevo Leon during August–November 2020. Individuals ≥18 years with no previous diagnosis or symptoms suggestive of COVID-19 were consecutively screened in one of the busiest subway stations. Also, a search for eligible individuals was done from house-to-house, after selecting densely populated geographic sectors of each of the municipalities of the metropolitan area ($n = 4495$). The IgG antibodies to SARS-CoV-2 nucleocapsid protein were analyzed. The IgG antibody positivity rate was 27.1% (95% confidence interval [CI]: 25.8, 28.4); there were no differences by sex or age ($p > 0.05$). Analysis by month showed a gradual increase from 11.9% (August) to 31.9% (November); Week 39 had the highest positivity rate (42.2%, 95% CI: 34.2, 50.7). Most people did not have evidence of previous SARS-CoV-2 infection. Preventive measures and promotion of the COVID-19 vaccine should be strengthened.

KEYWORDS

coronavirus, COVID-19, IgG, SARS-CoV2, seroprevalence

1 | INTRODUCTION

The SARS-CoV-2 (Coronavirus-2 associated with Severe Acute Respiratory Syndrome) is responsible for the COVID-19 disease. Both the virus and the disease were unknown before the outbreak in China in December 2019.[1] Worldwide, there were more than 121 million confirmed cases and 2.7 million deaths (15.8 per 1000 habitants and 2% fatality rate, respectively) as of March 2121. In Mexico, there were 2.2 million confirmed cases (17.2 per 1000 habitants), and it is ranked number 13 internationally. It registered 196 606 deaths (9% fatality rate) and positioned itself as one of the countries with the highest mortality rate.[2] The first COVID-19 confirmed case in the northeastern state of Nuevo Leon was in March 2020, 1 year later, the statistics showed 118 107 cases and 8864 deaths (20.4 per 10 000 habitants and 8% fatality rate, respectively) ranking number four after Mexico City, Mexico State, and Guanajuato.[3]Cultural diversity in the use of COVID-19 prevention measures and disparity in access to health services contribute to higher national and local figures than the world figures. Additionally, differences in the registry contribute to higher local than national rates. Nuevo Leon statistics, unlike the country, include data from all certified and accredited clinical laboratories, not only those endorsed by the INDRE, an institution under the Mexican Ministry of Health. The SARS-CoV-2 symptomatology appears 3–14 days after infection (fever, dry cough, severe fatigue, anosmia, and shortness of breath among others), but the disease may not manifest any symptom.[4] The symptomatic individual transmits the virus, but also the one who does not present symptoms. Serological tests represent a powerful tool for detecting SARS-CoV-2. Seroconversion to SARS-CoV-2 is characterized by the production of immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies 3–5 days and 14–30 days after infection, respectively; both are specific to major SARS-CoV-2 structural antigens such as the spike and nucleocapsid proteins. IgG antibodies indicate previous SARS-CoV-2 infection while IgM antibodies indicate current or recent infection. IgG antibodies have higher specificity and a higher half-life (up to 4 months) than IgM,[5,6] so they can be used to monitor immune response to the infection apart from allowing adjustment to COVID-19 statistics.[7,8]

The asymptomatic population contributes to the spread of the disease because individuals are not aware of carrying and propagating the virus.[4] Studies focused on seroprevalence allow public health authorities to reinforce measures to control the SARS-CoV-2 transmission. Furthermore, the serological results in asymptomatic inhabitants, together with those of active cases contribute to knowing the dispersion curve over time with greater precision. Therefore, better planning can be obtained to fight infection and avoid oversaturation of health services use. Population-based seroprevalence studies using different methods of sampling (serology testing on additional blood samples that were originally used for other purposes or home testing at the community level) show a large variation in the prevalence of IgG antibodies to SARS-CoV-2 in asymptomatic individuals. It ranges from less than 1% in China (Duan),[9] to 2.0%–10.8% in European countries,[10–12] and 57.9% in South India.[13] United States went from 1% in July to 23% in September 2020.[14] In Latin America, statistics varied from 1% to 52.5%.[15–19] Population-based serological studies are urgently needed for providing information on the production of antibodies against SARS-CoV-2 in healthy individuals. Also, because they assess the true extent of virus spread and the presence of possible antibody-mediated protection against SARS-CoV-2 at the community level.

Population-based IgG seroprevalence studies in asymptomatic individuals in Latin America are scarce,[18,19] and little is known about the prevalence of antibodies induced by the SARS-COV-2 virus in asymptomatic adults in Nuevo Leon. This state stands out for its high urban density and industrial development. Its metropolitan area includes 13 municipalities, the second most populated in Mexico and the second with the largest territorial extension. Here, lockdown rules were implemented statewide in March 2020, 1 week after the first COVID-19 case was diagnosed. The objective of the present study was to estimate the prevalence and geographic distribution of IgG antibodies induced by natural SARS-CoV-2 infection in asymptomatic adults, 5–8 months after the first case was reported in Nuevo Leon.

2 | MATERIALS AND METHODS

This was a population-based cross-sectional study carried out from August to November in 2020 in Nuevo Leon, Mexico. Individuals ≥18 years with no previous diagnosis or symptoms suggestive of COVID-19 were consecutively screened in one of the busiest subway stations with the interconnection of lines that move passengers between north, east, and west of the city. Eligible subway users were invited to participate before getting on or after getting off the train. Also, a search for eligible individuals was done from house-to-house, after selecting densely populated geographic sectors of each of the municipalities of the metropolitan area. Field workers visited the *colonias* on weekdays or weekends, in no particular order. If there were several eligible individuals in the house, up to two people were selected at random ($n = 4495$). The sample size allowed a margin of error of less than 2% with a confidence level of 95% given the overall observed frequency of asymptomatic patients of 27% in the study. The protocol was approved by the Research Ethics Committee of the Nuevo Leon Ministry of Health (DEISC-190120062) and informed consent was provided by all the participants.

2.1 | Serologic test for SARS-CoV-2 IgG detection

Participant venous blood samples were collected following international and national health protocols (Mexican Official Norm NOM-253-SSA1-2012). The IgG antibodies to SARS-CoV-2 nucleocapsid protein were analyzed using the SARS-CoV-2 IgG kit (ARCHITECT i; Abbott Laboratories; reference 06R86-22) and the SARS-CoV-2 calibration kit (ARCHITECT; Abbott Laboratories; reference 06R86-02) on an Architect i2000 SR analyzer (Abbott Diagnostics). The amount of IgG antibodies to SARS-CoV-2 in each sample was determined by comparing its chemiluminescent relative light unit (RLU) to the calibrator RLU. An RLU value ≥1.4 was considered positive.

2.1.1 | Statistical analyses

Frequencies for categorical variables and mean and standard deviations for continuous variables were obtained. The point positivity rate and 95% confidence intervals (CI) were estimated. The municipalities of the metropolitan area that resulted with a sample size of less than 30 were regrouped in the category of "others." Also, the municipalities outside the metropolitan area were grouped into one category. The χ^2 test was used to analyze differences according to sex, age group, and municipality. The

QGIS v3.16.1 Hannover, a freeware professional geographical information system application was used for visualizing the geographic distribution of positive asymptomatic cases.

3 | RESULTS

The mean age was 44.4% ± 15.5% and 97% of the study population resided in the metropolitan area. The female sex and the 25–44 age group predominated in the surveyed population. The overall IgG antibody positivity rate for SARS-CoV-2 was 27.1% (95% CI: 25.8, 28.4); there were no differences by sex or age group ($p = 0.10$ and $p = 0.09$, respectively). The IgG antibody positivity rate for the metropolitan area was 27.1% (95% CI: 25.8, 28.4). The municipality with the highest positivity rate was Guadalupe and the lowest Santa Catarina ($p < 0.0001$) (Table 1).

The epidemiological Week 39 had the highest positivity rate (42.2%, 95% CI: 34.2, 50.7), followed by week 45 (40.30%, 95% CI: 32.0, 49.3), that is, 6 and 8 months after the first COVID-19 case was reported in the state (Figure 1). The adjusted incidence rate for the study period (Weeks 32–48) was 17.6 per 1000 habitants (symptomatic plus asymptomatic cases).

Most of the municipalities within the metropolitan area showed a positivity rate between 25% and 29%; two had less than 25% (Santa Catarina y San Nicolás) and two, 30% or higher (Escobedo y Guadalupe) (Figure 2). Weeks 39 and 45 were the weeks with the

TABLE 1 Sociodemographic and IgG antibody positivity rate for SARS-CoV-2 in asymptomatic individuals

	Number of tested subjects	%	Number of positive cases	IgG antibody positivity rate for SARS-CoV-2	
				%	95% CI (%)
Municipality					
Inside metropolitan area					
Apodaca	364	8.1	96	26.4	22.1, 31.1
Escobedo	246	5.5	83	33.7	28.1, 39.9
Guadalupe	919	20.4	335	36.5	33.4, 39.6
García	76	1.7	17	22.4	14.5, 32.9
Juárez	372	8.3	107	28.8	24.4, 33.6
Monterrey	1198	26.7	335	28.0	25.5, 30.6
San Nicolás de los Garza	729	16.2	137	18.8	16.1, 21.8
San Pedro Garza García	42	1.0	10	23.8	13.5, 38.5
Santa Catarina	403	9	56	13.9	10.9, 17.6
Others	29	0.6	10	34.5	18.8, 32.8
Outside the metropolitan area	117	2.6	30	25.6	18.6, 34.2
Sex					
Male	1632	36.3	465	28.5	26.4, 30.7
Female	2861	63.6	751	26.2	24.7, 27.9
Group age (years)					
18–24	507	11.3	136	26.8	23.2, 30.8
25–44	1809	40.2	459	27.5	25.5, 29.6
45–60	1465	32.6	418	28.5	26.3, 30.9
61–64	264	5.9	75	25.0	20.2, 30.6
≥65	450	10	90	22.0	18.4, 26.1

Note: August–November 2020, 5–8 months after the first case was reported in Nuevo Leon, Mexico ($n = 4495$).

Abbreviations: CI, confidence interval; IgG, immunoglobulin G.

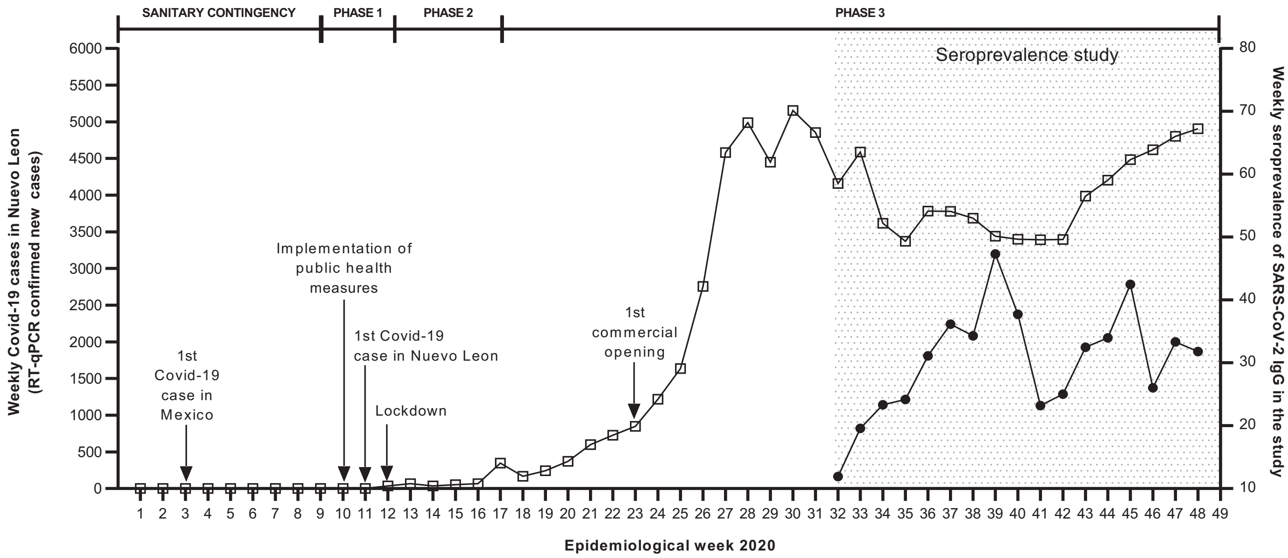


FIGURE 1 Weekly IgG antibody positivity rate for SARS-CoV-2 in asymptomatic individuals and new COVID-19 confirmed cases in Nuevo Leon, Mexico, 2020. IgG, immunoglobulin G

highest positivity rates in Apodaca, Juárez, Guadalupe, and Monterrey (Figure 3).

4 | DISCUSSION

Statistics on asymptomatic populations show how much of the population is still susceptible to SARS-CoV-2 and allow assessment of contingency measures' effectiveness. This study showed one-third (27.1%) of asymptomatic adults positive for IgG antibodies for SARS-CoV-2 and the positivity rate ranged from 13.9% to 36.5% during the period August-November 2020, 5–8 months after the first case was reported in Nuevo Leon. A nationwide population-based study from Spain reported rates between 21.9% and 35.8% in asymptomatic seropositive participants from April 27 to May 11, 2020.[12] An estimation across the USA showed statistics that ranged from fewer than 1%–23% between July and September 2020.[14] A population-based study in a large slum in South India conducted 3 months after the index case determined an overall seroprevalence of IgG antibody for COVID-19 of 57.9%.[13] In contrast, a study in China in healthy individuals without COVID-19 clinical symptoms returning to work for a medical examination from March 6 to May 3, 2020, in 30 provinces in Mainland China revealed a 0.68% positivity rate (first reported case was in December of 2019 in Wuhan City).[9] These statistics reveal important differences of magnitude and distribution of immunity induced by natural infection. The differences could reflect the timing of the humoral immune response after infection and seroprevalence studies are important for understanding the role of antibodies in protective immunity and in informing vaccine development.[20]

There were no differences by sex and age group similar to other studies.[10,13,21] In the United States, there were no consistent differences between men and women,[14] but in China and South India, the positivity rate was higher in females.[9,13] Results by age have been contradictory, a study showed a higher rate in individuals more than 50 years,[9] but other authors revealed lower rates at that age.[14,21] Analysis by month showed a gradual increase in the positivity rate from 11.9% (August) to 31.9% (November). This increase of 20 points could be due to greater dispersion over time, as occurred worldwide. Also, to failures in contingency measures. In April 2020, the mandatory use of face masks and social distancing was implemented,[22] but their effectiveness largely depends on compliance by the population. In the United States, changes in seroprevalence over 2 months were generally modest and differed across jurisdictions, some showed an increase of 6.2% and others, 4.5%.[14] In Manaus, Brazil the rate went from 4.8% in April to 52.5% in June 2020.[17]

The analysis by municipality showed mostly a 25%–29% positivity rate, only two municipalities registered ≥30% or ≤25%. Differences in the average income could hardly explain the difference between Guadalupe (highest seropositivity rate) and Santa Catarina (lowest seropositivity rate). According to the National Institute of Statistics and Geography, these municipalities do not have the lowest and highest economy as indicated by the percentage of white-collar and commerce-related workers. These positions are held by Juárez and San Pedro Garza García (61.6% and 81% of the working population, respectively).[23] The variation could be due to the greater need of some inhabitants to use public transportation to travel to jobs that were considered essential during the lockdown. A case study by Luo et al.[24] found closed windows with running ventilation on the buses could have created an ideal environment for aerosol transmission. Also, due to differences in the history of comorbidity, attendance to closed spaces with poor ventilation, and adherence to contingency measures that could control the spread of the virus. The same with

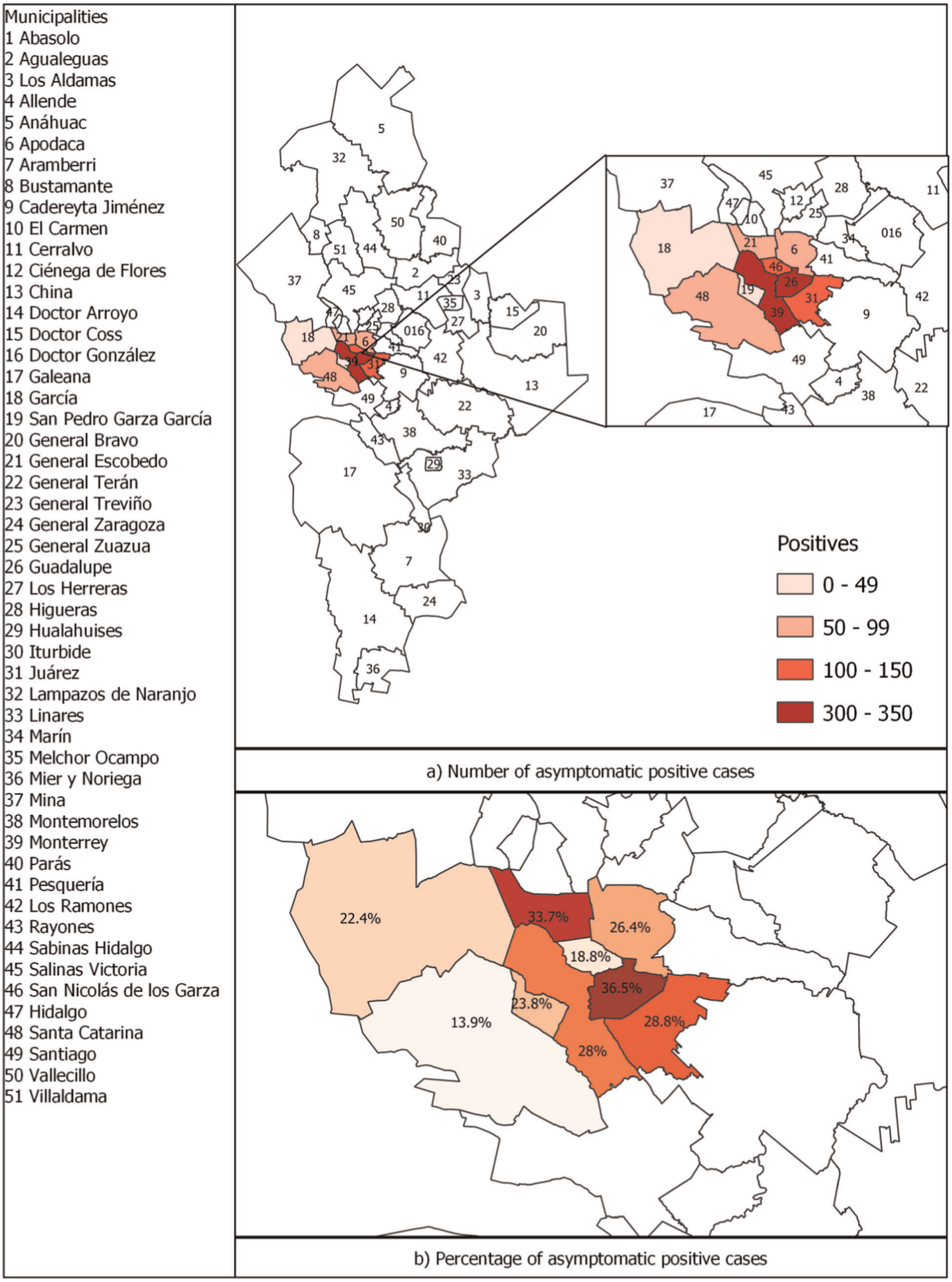
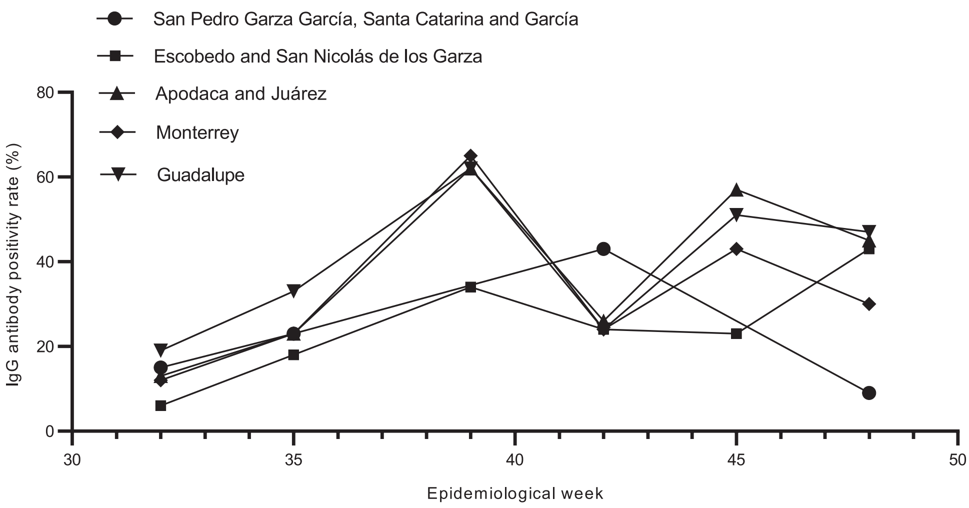


FIGURE 2 IgG antibody positivity rate for SARS-CoV-2 in asymptomatic individuals from municipalities within the metropolitan area. August–November 2020, 5–8 months after the first case was reported in Nuevo Leon, Mexico (*n* = 4349). IgG, immunoglobulin G



[a] Information from some municipalities was combined due to low incidence of cases in some epidemiological weeks.

FIGURE 3 Weekly IgG antibody positivity rate for SARS-CoV-2 in asymptomatic individuals by municipalities within the metropolitan area. Nuevo Leon, Mexico, 2020. IgG, immunoglobulin G

the different histories of closeness or coexistence with a symptomatic case of COVID-19 in the last 2 weeks. Unfortunately, this information was not available. Further research is required for identifying the origin of the divergences.

4.1 | Limitations of the study

The positivity rate results apply to municipalities from the urban metropolitan area, more studies are needed for determining immunity status in less densely populated areas such as suburban and rural areas. The study by Wong et al.[25] showed population density was an effective predictor of cumulative infection cases. However, the results represent a good approximation of the state-level rate because the metropolitan area concentrates 87% of the population. The sampling carried out in a subway station excluded vehicle users. In addition, the household sampling considered mainly middle- and lower-class urban areas, so care must be taken to generalize the findings to upper-class ones due to differences in underlying health, exposure risk or adherence to masks use and social distancing.

5 | CONCLUSIONS

Most people did not have evidence of previous SARS-CoV-2 infection 5–8 months after the first case was reported in Nuevo Leon, Mexico and future waves of outbreaks can be expected in the absence of vaccines. Positivity rate estimates varied by municipality, but not by sex and age group. Public health authorities need to strengthen contingency measures, security protocols, and the COVID-19 vaccine.

CONFLICT OF INTERESTS

The authors declare there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Conceptualization, methodology, and formal analysis: Edgar P. Rodríguez-Vidales, Roberto Montes de Oca-Luna, and Denise Garza-Carrillo; *writing—original draft preparation, data curation, formal analysis*: José J. Pérez-Trujillo, Olivia A. Robles-Rodríguez, and Ana María Salinas-Martínez; *design, analysis, writing—review and editing*: Manuel E. De la O-Cavazos and Consuelo Treviño-Garza. All authors have read and agreed to the published version of the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in the Nuevo Leon state transparency system at https://transparencia.nl.gob.mx/archivos/PREVALENCE_OF_IgG_ANTIBODIES_INDUCED_BY_THE_SARSCOV2_VIRUS_IN_ASYMPTOMATIC_ADULTS_SS_1622137122.zip

ORCID

Edgar P. Rodríguez-Vidales http://orcid.org/0000-0002-1626-6271
Denise Garza-Carrillo http://orcid.org/0000-0001-6669-8673
José J. Pérez-Trujillo http://orcid.org/0000-0002-6737-6155
Olivia A. Robles-Rodríguez http://orcid.org/0000-0003-4689-9114
Ana María Salinas-Martínez http://orcid.org/0000-0001-9977-4193
Roberto Montes de Oca-Luna http://orcid.org/0000-0001-8253-680X
Consuelo Treviño-Garza http://orcid.org/0000-0002-6544-3780
Manuel E. De la O-Cavazos http://orcid.org/0000-0002-8123-1294

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