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Original Article

Evaluation of dengue virus seroprevalence in four boroughs of Mexico City among persons aged 5-35 years in 2022

Eleazar Coba-Alcalá[1 #], Lilia Chihu-Amparán[2 #], Irma Yvonne Amaya-Larios[3], Susana Román-Pérez[4], Rene Santos-Luna[4], Lorena Suárez-Idueta[5], Sonia López-Álvarez[5], Cristal Morales-Trevizo[5], Jesús Felipe González-Roldán[1,5], Ruth Aralí Martínez-Vega[6], José Ramos-Castañeda[2,7]

[1] Master's and doctoral program in medical sciences, Universidad Anáhuac, Mexico City, Mexico
[2] Centro de Investigación sobre Enfermedades Infecciosas, Instituto Nacional de Salud Pública, Cuernavaca, Mexico
[3] Centro Educativo de Humanidades, Cuernavaca, Mexico
[4] Centro de Investigación en Evaluación y Encuestas, Instituto Nacional de Salud Pública, Cuernavaca, Mexico
[5] Sociedad Mexicana de Salud Pública, Mexico City, Mexico
[6] Universidad de Santander, Bucaramanga, Colombia
[7] Centro de Investigación en Ciencias Médicas, Universidad Anáhuac, Mexico City, Mexico

# Authors contributed equally to this work.

Abstract

Introduction: Dengue is currently the most widespread vector-borne disease, and its transmission has been intensively studied in endemic/hyperendemic localities. However, to obtain a complete picture of dengue transmission, it is necessary to study nonendemic localities. Imported dengue cases have been reported in Mexico City, and the presence of eggs of the vector *Aedes aegypti* has been detected.

Methodology: In the present study, we determined the prevalence of IgG antibodies against Dengue virus in four city boroughs via random cluster sampling in individuals aged 5-35 years.

Results: The weighted seroprevalence rate was 1.90% (95% CI 0.75-4.75) at Xochimilco, 1.81% (95% CI 0.64-5.00) at Venustiano Carranza, 1.81% (95% CI 0.54-5.83) at Tlahuac, and 5.48% (95% CI 1.96-14.43) at Gustavo A Madero; seropositivity was concentrated in the adult group, many of whom lived in dengue-endemic localities. The distribution of seroprevalence in the four boroughs is very homogeneous and unrelated to the number of vector eggs in the borough.

Conclusions: These data suggest that there is still no autochthonous transmission of dengue in Mexico City. However, it is important to note that the structural conditions of the dwellings in these boroughs, which offer minimal barriers to vector infestation, could facilitate the establishment of local transmission under favorable conditions.

Key words: *Aedes aegypti*; dengue virus; seroprevalence; transmission.

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Introduction

Dengue is a viral disease caused by any of the four Dengue virus serotypes (DENV-1 to DENV-4) and is transmitted to humans mainly by *Aedes aegypti* mosquitoes [1]. The global incidence has increased, affecting half of the world's population; The WHO reported a 10-fold increase in global case reporting between 2000 and 2019 and by 2023 more than 5 million cases and 5,000 related deaths [2].

Dengue transmission has been intensively studied in endemic localities, distinguished by high seroprevalence levels in the under-18 age group and recurrent intense outbreaks coinciding with a change in the predominance of the circulating serotype [3,4]. Since the spread of *Aedes aegypti* has increased due to climate change, extensive urbanization, and improved communication routes that allow the vector to spread to regions outside the tropics, which, for example, have generated autochthonous outbreaks in Spain and Italy [5], there is an information gap in the components of dengue transmission that enable the establishment of endemic transmission [6]. One of these components is thought to be the number of people susceptible to DENV in the population [7]. This information is highly relevant for estimating possible dengue development scenarios; thus far, only vector dispersal has been considered a determinant of the transition to endemic status [8].

Mexico is an endemic country, with the first cases recorded by the health ministry's surveillance system in 1978 when re-emergence started, and since then, epidemic peaks of approximately 60,000 cases have been reported. The severity of cases has steadily increased since 2014, and 873 confirmed dengue deaths were recorded from 2006 to 2022 [9].

However, dengue transmission in Mexico is heterogeneous, and although much of the country has endemic transmission, the distribution of seroprevalence varies regionally; for example, most populations in the southeastern region have overall seroprevalences higher than 70%, whereas those in the center of the country and the Pacific/North region have seroprevalences lower than 30% [10]. This fact allows for studying the determinants of dengue transmission in endemic–hyperendemic populations and nonendemic regions in a relatively homogeneous genetic context.

Mexico City (CDMX), which is the capital of the country, is located at 19°26′N 99°8′W and 2,240 MASL on average. Approximately 9,209,944 people inhabit it with a population density of 6,200 persons/km^2; the vast majority (87%) of the CDMX area has a temperate subhumid climate with an average annual rainfall of approximately 717 mm [11]. In CDMX, 76 dengue cases were reported from 1986 to 2022 [9], and no autochthonous dengue cases were reported. However, a baseline seropositivity from a TAK003 vaccine immunogenicity study conducted among children aged 12-17 years between December 2017 and January 2019 reported a baseline prevaccination seropositivity of 9% [12]. In addition, the number of *Aedes aegypti* eggs has been recorded in CDMX since 2013, and since then, the presence of vector eggs has been maintained at an average of 25 eggs per ovitrap [13,14].

In this study, we determined the prevalence of IgG against DENV in people aged 5-35 years living in CDMX to identify the characteristics of dengue transmission in nonendemic populations, contributing to the knowledge of the transition from nonendemic to endemic status.

Methodology

Study population

The population of CDMX resides in the boroughs of Tlahuac (TL), Xochimilco (XO), Venustiano Carranza (VC), and Gustavo A. Madero (GAM). Participants were included if they were aged 5 to 35 years and signed the informed consent form (adults) or had the assent form signed by their parents (children and adolescents aged 7 to 17).

Sample size

The sample size was calculated by considering a seroprevalence of 9% reported for CDMX from 2017 to 2019 [12], a design effect of 1.5, and an expected error of 6%; the finite population formula of OpenEpi software, version 3, was used [15]. This number was 132 people per borough.

Sampling strategy

Two-stage cluster sampling was conducted. First, blocks in each borough were randomly selected (primary sampling unit) and members of a household were systematically invited to participate, starting with the first house in the northeast corner of the randomly selected block; if the inhabitants of this house did not agree to participate, we continued to the right until at least one person from a household that met the inclusion criteria agreed to participate. Sampling was conducted between May 2022 and February 2023. Trained staff took 5 mL of venous blood from each participant using a vacuum blood collection tube with polymer gel; the samples were transported in plastic coolers with ice packs to the clinical laboratory. They were centrifuged for serum collection and stored at 4 °C until the sample size was complete, after which all the samples were transported in plastic coolers with ice packs to the laboratory of the National Institute of Public Health, where they were cataloged and aliquoted. One aliquot was used to perform the indirect ELISA test, and the remaining samples were stored at -20 °C.

Determination of IgG against DENV

Seropositivity was determined with the ELISA test for IgG-Indirect according to the manufacturer's instructions for Panbio™ Dengue IgG Indirect ELISA kit (Abbott, Ingbert, Germany), which has a specificity of 98% and a sensitivity of 100%. The samples were classified as positive, negative, or indeterminate according to the cutoff point established in each ELISA kit.

Data collection and analysis

Information, including age, sex, level of education, and length of residence in the borough, was captured on a paper survey form for each participant. In addition, the weight and height of each participant were measured. Additionally, for each dwelling, a survey was conducted on characteristics, including geolocation and mosquito nets on access doors and windows. The information was entered into an electronic database by trained data entry clerks.

To determine if the serological survey presents spatial randomization, the nearest neighbor average distance index was calculated for each delegation. To determine the expected average distance, a random distribution in an area of 14 Km^2 was used. The results revealed that the patterns of XO, TL, GAM and VC were dispersed, with z scores of 992.77, 725.84, 1312.94 and 521.39, respectively. A nearest neighbor average distance index less than 1 was considered to indicate a clustering pattern, while an index greater than 1 was considered to indicate a dispersion trend.

After this preliminary analysis, qualitative variables were described via descriptive analyses of absolute frequency and percentage. Quantitative variables were represented with central tendency and dispersion measures, and their distributions were evaluated with the Shapiro–Wilk test. Seroprevalence was calculated for each borough with a 95% confidence interval, considering the sampling probability of the block, of the dwelling and of the individual, the acceptance frequency of the block and of the individual, and with poststratification by age (5 to 14 years, 15 to 24 years and 25 to 34 years) and sex according to the population projection of each borough of the Instituto Nacional de Estadística Geografia e Informatica, INEGI, on the basis of the 2020 population census [16]. BMI was calculated by dividing weight in kilograms by height in meters squared. Adults were then classified according to the WHO as underweight (BMI < 18.5), normal weight (BMI 18.5–24.9), overweight I (BMI 25.0–

Table 1. Characteristics of individuals by borough.

Characteristics	XO	VC	TL	GAM
	n = 132	n = 132	n = 132	n = 132
Age Median (IQR)	25.2 (20.9-29.7)	25.1 (19.1-31.1)	25.5 (21.2-31.2)	26.9 (22.6-30.5)
Categorical age n (%)				
Under 18s	19 (14.4)	26 (19.7)	18 (13.6)	2 (1.5)
Over and equal to 18	113 (85.6)	106 (80.3)	114 (86.4)	130 (98.5)
Sex Female	90 (68.2)	86 (65.2)	81 (61.4)	84 (63.6)
Level of education				
Basic	20 (15.15)	18 (13.6)	15 (11.4)	6 (4.5)
Secondary	22 (16.67)	31 (23.5)	37 (28.0)	22 (16.7)
High School	46 (34.85)	43 (32.6)	51 (38.6)	44 (33.3)
Technician	14 (10.61)	3 (2.3)	2 (1.5)	5 (3.8)
Bachelor's degree	29 (21.97)	35 (26.5)	27 (20.5)	53 (40.2)
Postgraduate	1 (0.76)	0	0	2 (1.5)
No information	0	2 (1.5)	0	0
Occupation				
Worker	59 (44.7)	57 (43.2)	49 (37.1)	56 (42.4)
Housewives	23 (17.4)	24 (18.2)	38 (28.8)	31 (23.5)
Students	31 (23.5)	36 (27.3)	35 (26.5)	34 (25.8)
Student and worker	17 (12.9)	8 (6.1)	6 (4.5)	5 (3.8)
Unemployed/others	2 (1.5)	7 (5.3)	4 (3.0)	6 (4.5)
Currently studying	49 (37.1)	45 (34.1)	43 (32.6)	39 (29.5)
Health insurance				
Social security	71 (53.8)	61 (46.2)	50 (37.8)	62 (46.9)
Private	0	0	8 (6.1)	3 (2.3)
None	59 (44.7)	69 (52.3)	73 (55.3)	62 (47.0)
Not assessed	2 (1.5)	2 (1.5)	1 (0.8)	5 (3.8)
Lived all life in the town	106 (80.3)	99 (75.0)	98 (74.2)	105 (79.5)
Residence in the town (Years) Median (IQR)*	5.3 (2.1-18.3)	3.7 (1.7-6.1)	6.4 (2.8-10.8)	4.1 (2.0-10.1)
Any reported diseases n (%)	19 (14.4)	10 (7.6)	8 (6.1)	20 (15.2)
Gastritis/gastric ulcer	11 (8.3)	3 (2.3)	2 (1.5)	6 (4.5)
Asthma	1 (0.8)	2 (1.5)	3 (2.3)	3 (2.3)
Hypertriglyceridaemia	2 (1.5)	1 (0.8)	1 (0.8)	3 (2.3)
Hypercholesterolemia	3 (2.3)	2 (1.5)	0 (0)	0 (0)
Hypertension	0 (0)	1 (0.8)	2 (1.5)	3 (2.3)
Diabetes	2 (1.5)	2 (1.5)	0 (0)	2 (1.5)
Another disease	5 (3.8)	1 (0.8)	1 (0.8)	7 (5.3)
History of dengue fever	0 (0)	0 (0)	0 (0)	2 (1.5)
History of chikungunya	0 (0)	0 (0)	0 (0)	2 (1.5)
History of Zika	0 (0)	0 (0)	0 (0)	1 (0.8)
Yellow fever vaccine	3 (2.3)	1 (0.8)	0 (0)	1 (0.8)
Dengue fever vaccine	3 (2.3)	0 (0)	0 (0)	2 (1.5)
Weight status n (%)				
Underweight	4 (3.0)	6 (4.5)	9 (6.8)	4 (3.0)
Normal weight	61 (46.2)	62 (47.0)	48 (36.4)	59 (44.7)
Overweight	42 (31.8)	27 (20.5)	39 (29.5)	41 (31.1)
Obesity	25 (18.9)	36 (27.3)	36 (27.3)	27 (20.5)
No information	0	1 (0.8)	0	1 (0.8)

* For people who have not lived in the city all their lives.

29.9), or obese (BMI > 30). For children, the CDC BMI percentile calculator was used, and they were classified as underweight (below the 5th percentile), normal weight (5th percentile to below the 85th percentile), overweight (85th percentile to below the 95th percentile), or obese (equal to or greater than the 95th percentile) [17]. The analysis was performed with Stata 16.1 software®.

In addition, data from 4,462 ovitraps from the period from 2013 to 2022 of the CDMX entomological surveillance were used, and the data were obtained from the Integral System of Vector Monitors [14]. In Mexico, entomological surveillance with ovitraps is conducted according to the Methodological Guide for Entomological Surveillance with Ovitraps. In brief, egg counting is done with the naked eye, but if the number of eggs is greater than 100, a 10x magnifying glass or stereo microscope is used. In addition, a fraction of the samples collected in ovitraps are sent to the reference center to evaluate resistance to larvicides and adulticides used in the vector control program. [18] The entire entomological surveillance period was chosen to mitigate variation due to mosquito oviposition behavior and thus determine the areas where at least one egg was detected in the time series. The inverse distance weighting (IDW) interpolation spatial analysis method was used to construct an average surface area for *Aedes aegypti* mosquito eggs. This method determines cell values through a linearly weighted combination of a set of sample points. This method assumes that the variable being mapped decreases in influence with greater distance from its sample location [19].

Ethical considerations

The present study is a minimal-risk research in which only subjects who agreed to participate voluntarily and signed the informed consent form were considered. The research protocol was approved by the Ethics Committee of the Faculty of Health Sciences, Universidad Anahuac (folio 202143).

Table 2. Characteristics of the dwellings by borough

Characteristic	XO (n=105)	VC (n=93)	TL (n=100)	GAM (n=102)
Total cohabitants Median (IQR)	5 (4-6)	5 (4-7)	5 (4-7)	5 (4-6)
Home ownership n (%)				
Own	86 (81.9)	66 (71.0)	75 (75.0)	81 (79.4)
Rented	17 (16.2)	25 (26.9)	18 (18.0)	18 (17.7)
Another	2 (1.9)	2 (2.2)	7 (7.0)	3 (2.9)
Drainage connected to n (%)				
Public network	82 (78.1)	93 (100)	89 (89.0)	102 (100)
Septic tank	18 (17.1)	0	11 (11.0)	0
No drainage(3) / Not specified(2)	5 (4.8)	0	0	0
Toilet n (%)				
Direct flush toilet	56 (53.3)	73 (78.5)	54 (54.0)	82 (80.4)
Manual flush toilet	48 (45.7)	20 (21.5)	46 (46.0)	20 (19.6)
Toilet without water intake	1 (1.0)	0	0	0
Availability of piped water n (%)				
Public mains inside the dwelling	72 (68.6)	78 (83.9)	62 (62.0)	96 (94.1)
Public mains outside the dwelling	10 (9.5)	15 (16.1)	29 (29.0)	1 (1.0)
Public tap or hydrant	18 (17.1)	0	4 (4.0)	0
Other*	5 (4.8)	0	5 (5.0)	5 (4.9)
Flooring material n (%)				
Cement or firm	71 (67.2)	30 (32.3)	55 (55.0)	85 (83.3)
Wood, mosaic or other material	32 (30.5)	63 (67.7)	45 (45.0)	10 (9.8)
Earth	1 (1.0)	0	0	7 (6.9)
Not specified	1 (1.0)	0	0	0
Number of rooms Medium (IQR)	4 (3-5)	4 (3-5)	4 (3-6)	4 (4-6)
Availability of television n (%)	102 (97.1)	93 (100)	98 (98.0)	96 (94.1)
Refrigerator availability n (%)	101 (96.2)	91 (97.9)	97 (97.0)	98 (96.1)
Availability of washing machine n (%)	88 (83.8)	86 (92.5)	93 (93.0)	94 (92.2)
Computer availability n (%)	68 (64.8)	65 (69.9)	48 (48.0)	72 (70.6)
Availability of air conditioning n (%)	1 (1.0)	3 (3.2)	2 (2.0)	9 (8.8)
Availability of window screens n (%)				
In all	6 (5.7)	0	6 (6.0)	2 (2.0)
In some	13 (12.4)	15 (16.1)	19 (19.0)	8 (7.8)
No	84 (80.0)	77 (82.8)	75 (75.0)	92 (90.2)
Not assessed	2 (1.9)	1 (1.1)	0	0
Insect screens on access doors n (%)				
In all	0	1 (1.1)	1 (1.0)	4 (3.9)
In some	2 (1.9)	3 (3.2)	5 (5.0)	5 (4.9)
No	102 (97.1)	88 (94.6)	93 (93.0)	93 (91.2)
Not assessed	1 (1.0)	1 (1.1)	1 (1.0)	0

* Including water from neighbor dwelling, pipe, well, river, stream, lake, other or not specified.

Results

Characteristics of the participants

For each borough, the necessary number of participants was recruited, with a total of 528 participants spread across the area of each borough (average nearest neighbor z scores of 992.77 XO, 725.84 TL, 1312.94 GAM, and 521.39 VC). The participants had a median age between 25.1 and 26.9 years, with the majority being over 18 years old. In the GAM borough, there were no participants under the age of 15 years. The proportion of females was similar between the boroughs (61.4% - 68.2%). In terms of educational level, all participants had some formal education, and more than half obtained a high school degree or higher. The most common occupation was workers, followed by students, and approximately 50% did not have health insurance. In addition, most participants reported having lived all their lives in their borough of residence (74.2% to 80.3%), whereas 50% of those who reported not having lived in CDMX all their life had been living in their borough for more than three years (Table 1).

The prevalence of self-reported chronic diseases, including gastritis/ulcer, asthma, diabetes, and hypertension, was low overall. A small percentage of participants reported having had dengue, chikungunya, or Zika and reported infrequent vaccination against vector-borne diseases. In addition, according to body mass index (BMI), less than half of the population was of an appropriate weight (Table 1).

Characteristics of the dwellings

In total, participants from 400 households were included. The median number of cohabitants was five per household. More than 70% of the dwellings in the four boroughs were owned by the inhabitants. With respect to the availability of sewerage and water in the dwelling and toilets, connection to public sewerage was high in the four boroughs, whereas the type of toilet and the source of piped water varied among the boroughs. Flooring materials also differed between boroughs. The dwellings in the four boroughs had a median of 4 rooms (Table 2).

In terms of amenities and technologies, most households had a television, refrigerator, and washing machine, while computer ownership varied across boroughs; It is complicated to analyze the availability of water in dwellings with water-using household appliances available in the house, because in some households water is supplied by different means that were not assessed, e.g. the proportion of households with washing machines is higher than the number of households with piped water. In addition, few households experienced air conditioning. Notably, the availability of window and door screens was low in the four boroughs, at less than 20% and 5%, respectively (Table 2).

Seroprevalence against DENV

Among the 528 participants, 18 were seropositive (5 in XO, 4 in VC, 3 in TL, and 6 in GAM). The median age of the participants was 27.9 years (Min: 17.4 and Max: 35.6 vs. seronegative median 25.5, Mann–Whitney test $p = 0.1774$), and 72.2% were women (women 13/18 vs. 328/510, Fisher's exact test $p = 0.620$). In addition, 50% reported having lived outside these boroughs, and seven participants had lived in a dengue-endemic city. Only 5.6% (n = 1) reported

Table 3. Characteristics of seropositive individuals.

Seropositive individuals	Borough	Sex	Age (Years)	BMI	Lived all life in the borough	History of dengue fever	History of Zika	Yellow fever vaccine	Dengue fever vaccine	Yellow fever vaccine
1	GAM	Masculine	20.7	20.7	No	No	No	No	No	No
2	GAM	Masculine	20.8	34.0	No	Yes	No	No	No	No
3	GAM	Masculine	26.1	31.6	Yes	No	No	No	No	No
4	GAM	Female	30.1	30.9	Yes	No	No	No	No	No
5	GAM	Female	31.0	30.9	Yes	No	No	No	No	No
6	GAM	Masculine	31.0	41.2	Yes	No	No	No	No	No
7	TL	Female	23.6	33.7	Yes	No	No	No	No	No
8	TL	Masculine	23.7	26.3	No	No	No	No	No	No
9	TL	Female	32.4	28.8	No	No	No	No	No	No
10	VC	Female	23.1	18.4	No	No	No	No	No	No
11	VC	Female	26.1	37.7	No	No	No	No	No	No
12	VC	Female	29.0	22.5	No	No	No	No	No	No
13	VC	Female	34.2	25.8	No	NR	NR	NR	NR	NR
14	XO	Female	17.4	20.8	Yes	No	No	No	No	No
15	XO	Female	26.7	22.0	Yes	No	No	No	No	No
16	XO	Female	30.4	23.3	Yes	No	No	No	No	No
17	XO	Female	33.7	30.1	Yes	No	No	No	No	No
18	XO	Female	35.6	30.8	No	No	No	No	No	No

NR: Not reported.

having had dengue, none had been vaccinated against DENV or yellow fever, and none of the seropositive people reported having become ill with the Zika virus (Table 3). The seroprevalence in GAM was the highest (5.48%), whereas in XO, it was 1.90%, and in the other two boroughs, it was 1.81% (Figure 1). We georeferenced the households of 524 participants, including all seropositive participants; overall, the dispersion of participants was appropriate for the sampling design (Figure 2).

Abundance of Aedes aegypti eggs

Given the low seroprevalence determined in this study, we asked if the vector was present in the boroughs via historical data from 2013-2022 from the entomological surveillance system of the Ministry of Health. *Aedes aegypti* eggs had been identified in 36% of the 4,462 monitoring sites in CDMX, according to data from 2013 to 2022 from the Comprehensive Vector Monitoring System based on ovitraps. A map showing the presence of *Aedes aegypti* eggs in the area where the participants lived is presented in Figure 2. The highest vector egg counts occurred in four boroughs, two of which were included in the study (GAM and VC), whereas the remaining two (XO and TL) generally presented low vector egg counts (Figure 2). With respect to the distribution of the sample and, in particular, the seropositive survey participants, as is clear, all were found in areas associated with the presence of *Aedes aegypti* eggs except XO; this is interesting because the seroprevalence against DENV in the four boroughs studied was very similar, an observation consistent with exposure to DENV in a location outside the boroughs studied. Additionally, this observation shows that the positive cases could initiate successful chains of transmission if these mosquitoes have an efficient infectious capacity; this is because when adapting to localities with different ecological characteristics, mosquitoes are modified in some features, such as vectorial capacity [20,21].

Figure 1. Prevalence of IgG antibodies to DENV by borough.

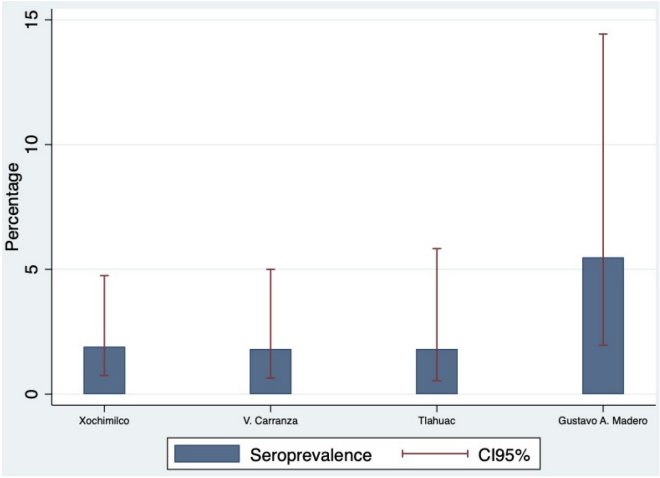
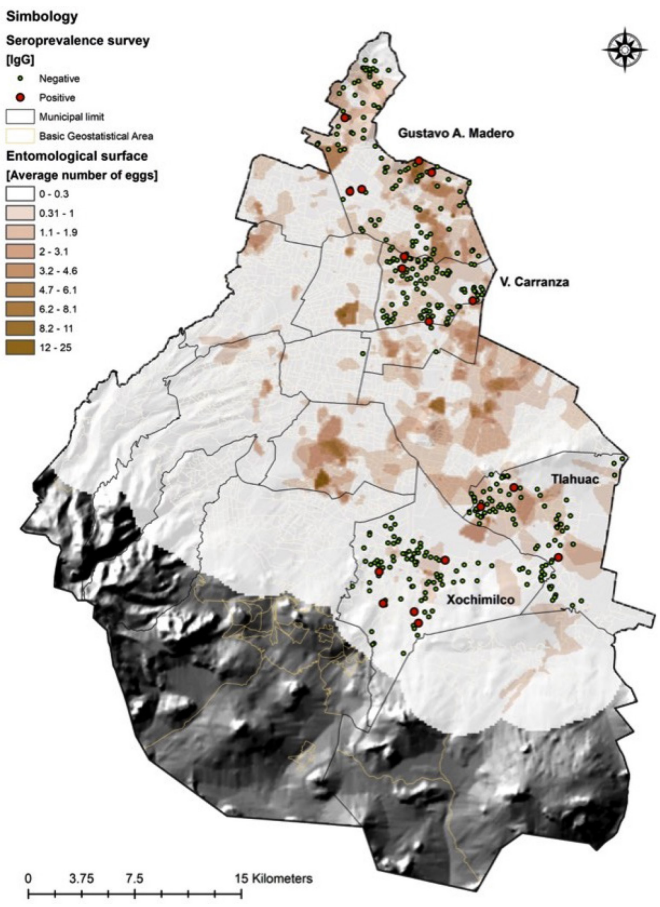


Figure 2. Seropositivity of DENV antibodies and average number of *Aedes aegypti* eggs in the study area.



Each red circle represents a DENV IgG-positive person except in GAM, where one of the five circles represents two seropositive persons living in the same household.

Discussion

In this report, we determined that the seroprevalence of IgG against DENV in four boroughs of the CDMX is between 1.81% and 5.48% in the population aged 5-35 years from May 2022 to February 2023 (Figure 1). This result contrasts with the data reported by Biswal *et al*., who reported that for the cohort of participants aged 12-17 years in the phase 3 immunogenicity clinical trial of the TAK003 dengue vaccine, the baseline seroprevalence was 9% [12]; this difference may be because Biswal's study design was not randomized and the age group was more restricted.

The characteristics of seropositive people suggest that people were infected in places other than where they lived because 38.8% (7/18) of seropositive

participants lived at some point in their lives in dengue-endemic localities; additionally, 94.4% (17/18) of seropositive people were adults, and 41.1% (7/17) were working, which decreases the likelihood of becoming infected at the place of residence. Finally, in Mexico, there is no public vaccination program against yellow fever. Although Mexico was the first country to grant sanitary registration for the Dengvaxia vaccine, there is also no public vaccination program with this biologic; in line with the above, no seropositive participants reported having been vaccinated with these vaccines. Taken together, these data suggest that exposure to DENV took place outside CDMX.

The presence of *Aedes aegypti* in CDMX has been documented since 2013 [13]. Since then, health authorities have monitored the number of *Aedes aegypti* eggs in public places (parks, markets, cemeteries, etc.), finding up to 15–25 *Aedes aegypti* eggs per ovitrap in some places (Figure 2); typically, in endemic localities, the number of eggs exceeds the hundreds. As seen, in CDMX, there are boroughs with high egg counts that are not necessarily associated with water sources; for example, the GAM and VC boroughs have no natural water concentrations and tend to have a dry to semidry climate, whereas the XO and TL boroughs have abundant water concentrations (Xochimilco lake and its canals, for example) and a climate that tends to be temperate subhumid. In addition, the number of people who are IgG positive against DENV is practically the same in boroughs with high egg counts (GAM and VC) as in those with low egg counts (XO and TL); this is an additional argument that reinforces the idea that there is no autochthonous transmission in CDMX.

Moreover, this result highlights the vulnerability of CDMX to dengue transmission because the presence of the vector in overpopulated urban areas and high susceptibility represent a risk for establishing autochthonous dengue transmission and, subsequently, endemic transmission [22,23].

Dengue is a public health problem related to water management; transmission is more intense in localities where water must be stored [24]. In general, participants' dwellings do not seem water tanks to have problems with water management since the vast majority of them have water available from the public network (between 78% in XO and 100% in TL) and are connected to the public sewage system (75.9% XO, 100% VC, 89% TL, and 100% GAM). However, we did not collect specific information on the storage of water in water tanks or pools, which are breeding grounds for the vector [25]. There is much information on vector control measures in endemic communities; one that is associated with protection from infection is the presence of mosquito nets on doors and windows of dwellings [23]. In this study, we found that more than 75% of participants' houses lacked nets on doors and windows, which adds an element of vulnerability to dengue transmission in these boroughs.

This study has several limitations. The proportion of children included in the study should be approximately 40%, according to the 2020 census, but in no case was this proportion reached (14.4% XO, 19.7% VC, 13.6% TL, and 1.5% GAM), which increases the risk of selection bias; however, considering that the seroprevalence found in both the child and adult groups was extremely low and that in endemic communities, seroprevalence increases with age, we believe that even if we had achieved the aforementioned proportion of children, the seroprevalence would not have changed much from what we found (less than 6%, Figure 1). In addition, to reduce the impact of sampling, poststratification by age and sex was performed for prevalence estimation. Another limitation is that in the GAM, no children under 15 years of age were enrolled. Therefore, the estimated seroprevalence is restricted to the 15-35 age group in this borough. Another relevant aspect is that the decision of which boroughs to sample was arbitrary because, at the time, we did not have complete entomological surveillance information; two other boroughs stand out for the number of *Aedes aegypti* eggs that have been determined. In retrospect, this was the best option for the study because, as mentioned above, having two boroughs with high egg counts and two boroughs with low egg counts allowed us to make comparisons within the same city (CDMX). We consider that to complete the scenario of DENV immunity in CDMX, we should have included a neutralizing antibody study in determining the diversity of the immune response.

Finally, this is the first serological study with randomized sampling to be conducted in a nonendemic dengue locality in Mexico and provides information that is useful for evaluating *Aedes aegypti* surveillance and potential risks of virus transmission in the CDMX population.

Authors' contributions

ECB and LCA conducted the experiments and analyses. SRP and RSL conducted the georeferenced analysis and vector egg extrapolation. LSI, SLA, CMT, and JFGR supervised the field work and overall management of the project. IYAL, RAMV, and JRC elaborated the theoretical framework and

justification of the project, carried out the project design, interpreted the results and produced the first draft of the manuscript. All the authors contributed to the final version of the manuscript.

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Ethical approval

The research protocol was approved by the Research Committee of the Faculty of Health Sciences, Universidad Anahuac (202143).

Corresponding author

Dr José Ramos–Castañeda
Instituto Nacional de Salud Publica
Av Universidad 655, Santa Maria Ahuacatitlan, Cuernavaca, 62100, Morelos, Mexico
Tel: +527773293000x2106
Email: jramos@insp.mx

Conflict of interest

ECB currently is a Bayer employee. IYAL and RAMV worked on a project supported by Sanofi-Pasteur. The JRC reports grants and personal fees from Sanofi-Pasteur and honoraria from Takeda; it is also a member of the Scientific Advisory Board on Dengue Vaccine by Sanofi-Pasteur.

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