

Seroprevalences of varicella-zoster virus, herpes simplex virus and cytomegalovirus in a cross-sectional study in Mexico



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ABSTRACT

We estimated the seroprevalences of varicella-zoster virus (VZV), herpes simplex virus (HSV) and cytomegalovirus (CMV) in this cross-sectional database study. Serum samples collected during the National Health and Nutrition survey (ENSANUT 2006) were obtained from subjects aged 1–70 years between January and October 2010. Serological assays for the determination of antibodies against VZV, HSV and CMV were performed. The overall seroprevalences of VZV, HSV-1, HSV-2 and CMV were 85.8%, 80.9%, 9.9% and 89.2%, respectively. Seroprevalences of VZV, HSV-1 and CMV were comparable between males and females. For HSV-2, although the seroprevalence rate was higher in females when compared to males, this difference in seroprevalence was not statistically significant. Seroprevalence rates for VZV, HSV-1, HSV-2 and CMV increased with age (p -value < .0001). Differences in seroprevalence rate for VZV by socioeconomic status (SES) were significant (p -value < .0001). Results of the serological analyses reported high VZV seroprevalence, indicating high transmission in the Mexican population with children and adolescents at risk of acquiring VZV. Global HSV-1 seroprevalence was high, especially in adults. HSV-1 and HSV-2 seroprevalences were consistently higher in women than men, particularly for HSV-2. CMV seroprevalence was higher in Mexico when compared to developed countries. Seroepidemiological data on VZV supports the fact that varicella vaccination may serve as an alternative effective solution to reduce transmission in the Mexican population. For CMV and HSV, since no vaccines are available, activities to reduce transmission are important to reduce the risk of complications and therefore need to be considered.

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1. Introduction

Varicella-zostervirus, herpes simplex virus and cytomegalovirus are the commonest viral infections worldwide

[1–6] and are associated with significant morbidity and mortality in developing countries [7–9].

1.1. Varicella-zoster virus (VZV)

VZV causes chickenpox on primary exposure and can reactivate later in life to cause herpes zoster in adults [10]. Varicella infection is generally self-limiting, but it may lead to complications which result in outpatient visits and hospitalization, specifically in adults, pregnant women, neonates and immunosuppressed individuals [11–15]. Following the recommendation from the World Health Organization (WHO) to consider varicella vaccination in countries where varicella is a significant public health problem [16], several countries have implemented universal childhood varicella vaccination [17–20]. Vaccination against varicella can be achieved through the use of monovalent varicella vaccines – *Varivax*[®] (Sanofi Pasteur Merck Sharp and Dohme [MSD], Lyon, France) and *Varilrix*[™] (GlaxoSmithKline Vaccines) or the new combination measles, mumps,

Abbreviations: CI, confidence interval; ELISA, enzyme-linked immunosorbent assay; ENSANUT, National Health and Nutrition Survey; CMV, cytomegalovirus; HSV, herpes simplex virus; SAS, statistical analysis software; SES, socioeconomic status; VZV, varicella-zoster virus.

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rubella, varicella (MMR-V) vaccines – *ProQuad*[®] (Merck and Co., Inc., Whitehouse Station, New Jersey) and *Priorix-Tetra*[™] (Glaxo-SmithKline Vaccines).

1.2. Herpes simplex virus (HSV)

Symptomatic HSV-1 infection manifests as oro-labial and facial lesions [21] and has emerged as an important worldwide cause of genital herpes [21–24]. Symptomatic HSV-2 infection results in genital herpes, genital ulcer disease and central nervous complications such as herpetic encephalitis and neonatal herpes [20–26]. Transmission of HSV-2 from an infected mother to the child results in neonatal herpes, which is associated with significant economic implications [25,26]. Both HSV types are transmitted sexually; however HSV-1 is also transmitted horizontally in childhood [23,24]. The clinical management of HSV infections include preventive measures such as the use of barrier techniques to prevent viral transmission and shedding; and antiviral therapy. Education of the public regarding HSV infections and its complications are important in the management of HSV infections worldwide [27].

1.3. Cytomegalovirus (CMV)

CMV causes a spectrum of diseases in both children and adults. Congenital CMV infection remains a public health concern as it is one of the most important causes of childhood deafness, neurological disabilities and visual impairment [28]. CMV also causes viral hepatitis and severe complications in immunocompromised individuals and transplant-recipients. Management of CMV infection relies on antivirals and behavioral interventions that are designed to reduce transmission in high-risk groups [4], which can be realized through awareness of the public.

1.4. Rationale and objective

Decision about implementing universal varicella vaccination in Mexico is not yet made; this may be due in part to limited seroepidemiological data and the perception that varicella is generally not a serious disease. Currently no vaccines against HSV and CMV are available; however, with several HSV and CMV vaccines in clinical development, a clear understanding of the seroepidemiology of CMV, HSV-1 and HSV-2 in Mexico are important to design the most effective infection prevention and control strategies [4,27,29]. This population-based study provides seroprevalence data on VZV, CMV and HSV which may guide decision-making regarding prevention and control of these infections in Mexico.

2. Materials and methods

2.1. National Health and Nutrition Survey, 2006 (ENSANUT)

During 2005–2006, the Mexican National Institute of Public Health implemented a nationally representative Health and Nutrition Survey (ENSANUT 2006) that obtained information on the prevalence of infectious diseases and associated risk factors; and the use of health services in Mexico using a previously standardized questionnaire. Military, religious and health institutions were excluded. ENSANUT has been widely used in similar observational studies in Mexico [30,31] and its methodology has been described [32]. ENSANUT is a cross-sectional study conducted across all Mexican states and is designed to be representative of individuals living in Metropolitan (state capitals or cities with a population above 100,000 inhabitants), urban (2500–99,999 inhabitants) and rural settings (less than 2500 inhabitants).

A multistage, stratified and probabilistic sampling procedure was used. A random sample of Basic Geographical Statistical Units was obtained in each state. Neighborhood blocks were randomly selected. In each household, one randomly selected adult (age: ≥ 20 years), adolescent (age: 10–19 years) and child (age: < 10 years) were invited to participate. The total number of households was 47,152 (4731 individuals and 1476 households was estimated for each state). The sample size was considered capable of detecting risk factors at the state level with at least a prevalence of 8.1% (relative error of estimation: 0.25, design effect: 1.7 and a non-response rate of 20%). This sample size allowed the assessment of conditions with a prevalence greater than 0.4%. Blood samples were collected from 30% of selected individuals in ENSANUT. A socioeconomic index was developed based on household conditions such as building materials, number of rooms, domestic property, electricity, electronic goods, etc. [23]. This survey was approved by the Ethics Committee from the Mexican National Institute of Public Health.

2.2. Study design

This retrospective surveillance was based on data and serum samples from subjects in ENSANUT 2006. Data for this analysis was extracted between January and October 2010 (NCT01160081). Information from questionnaires used in ENSANUT regarding subjects' gender, age, geographical region and SES were compiled into a subset database. A total of 4000 subjects (age: 1–70 years) previously enrolled in ENSANUT who had already provided their consent were selected by random simple sampling, stratified by age in the serum bank. This sample size was expected to provide 80% statistical power assuming an overall seroprevalence ranging from 25% in children to 95% in adults. Subjects were excluded if informed consent had not been previously obtained, or information required was incomplete, or due to insufficient quantity of serum sample, or wrongly identified serum sample. This study was conducted in accordance with the Declaration of Helsinki, 1996, Good Clinical Practice guidelines and the local regulations of Mexico. The study protocol and informed consent forms were approved by the independent institutional review board (Comité de Ética e investigaciones Instituto Nacional de Salud Pública de México).

2.3. Laboratory methods

Serum samples stored in 2.5 ml aliquots in liquid nitrogen chambers at -150°C were used for the serological detection of antibodies against VZV, CMV and HSV. Detection and quantitative determination of antibodies was done at the Instituto Nacional de Salud Pública de México as follows: anti-VZV-enzyme immunoassay *Enzygnost*[®] Anti-VZV/IgG (Dade Behring, Marburg, Germany), anti-HSV-*Euroimmun*[®] (Medizinische Labordiagnostika, Germany) enzyme-linked immunosorbent assay (ELISA) type-specific HSV-1 and HSV-2 IgG antibody differentiation assays, anti-CMV-*ARCHITECT*[®] (Abbot Laboratories, USA) CMV IgG assay.

2.4. Data analysis

Seropositivity was defined as follows: VZV: anti-VZV antibody titer values ≥ 0.2 , HSV: a semi-quantitative detection of anti-HSV antibodies, ratio 1:1 and CMV: anti-CMV antibody titer values ≥ 6 . Seronegativity/non-reactivity was defined as follows: VZV: anti-VZV antibody titer values < 0.1 , HSV: ratio < 1.1 of anti-HSV antibodies and CMV: anti-CMV antibody titers values < 6 [33–35].

Overall seroprevalences of VZV, CMV and HSV were estimated where a post-stratification weight for each individual was obtained by considering demographic parameters. Seroprevalences by gender, age group (children [age: 1–9 years], adolescents [age: 10–19

years], adults [age: ≥ 20 years], region (Central, Mexico City, Southern, Northern Mexico) and SES (low, medium, high) were tabulated with 95% confidence interval (CI). Comparison of differences in seroprevalence by gender, age groups, region and SES was performed using the Chi-squared test (χ^2). Odds ratios (OR) were calculated for the univariate association of demographic risk correlates with anti-VZV, anti-HSV-1, anti-HSV-2 and anti-CMV. Chi-squared test (χ^2) was used to assess the statistical significance of these associations. A multiple logistic regression model was used to describe the relationship of dependent variables. All statistical analyses were performed using Statistical Analysis Software (SAS) v9.1.

3. Results

3.1. Study population

A total of 3658 subjects from ENSANUT were included considering availability of sufficient serum sample volume (1030 children, 1719 adolescents, 905 adults). Median age of subjects was 29.0 years (range: 1–95 years); 51.1% of subjects were male.

3.2. Seroprevalence of VZV

Of 3658 subjects, 3595 subjects were tested for VZV (age: 29.0 years [range: 1.0–95.0 years]; males: 50.8%). VZV seroprevalence was 85.8% (95%CI: 83.6–87.9). VZV seroprevalences between females (86.8% [95%CI: 84.4–89.3]) and males (84.6% [95%CI: 81.3–87.9]) were comparable (Fig. 1a). VZV seroprevalence increased with age (p -value $< .0001$) (Table 1). In children aged 1–4 years VZV seroprevalence was 42.8% (95%CI: 31.3–54.3), whereas in children aged 5–9 years and adolescents aged 10–14 and 15–19 years, the seroprevalences were 69.3 (95%CI: 65.0–73.6) and 81.2% (95%CI: 78.0–84.3) and 87.8% (95%CI: 84.0–91.5), respectively. VZV seroprevalence was higher in Mexico City when compared to other regions (Fig. 1b). Difference in VZV seroprevalence by SES was statistically significant (p -value $< .0001$) (Table 1). Urban population reported higher VZV seroprevalence when compared to the rural population ($p < .0001$). Among the risk factors, associations of seroprevalence and age, geographic origin and SES were statistically significant (Table 2). The multiple logistic regression analysis indicates that seroprevalence by area was statistically significant (Table 3).

3.3. Seroprevalence of HSV

A total of 3646 and 3616 were tested for HSV-1 and HSV-2 (median age: 29.0 years [range: 1.0–95.0 years], males: 51.1% [HSV-1] and 51.2% [HSV-2]). HSV-1 and HSV-2 seroprevalences were 80.9% (95%CI: 78.3–83.4) and 9.9% (95%CI: 7.9–12.0), respectively (Table 1). HSV-1 seroprevalences by gender were similar (females: 82.8% [95%CI: 79.7–85.8], males: 78.8% [95%CI: 74.7–82.9]) whereas for HSV-2 the seroprevalence was higher in females than males (13.2% [95%CI: 10.0–16.3] vs. 6.6% [95%CI: 4.2–18.9]) (p -value: 0.0011) (Fig. 2a). HSV-1 and HSV-2 seroprevalences increased with increasing age (p -value $< .0001$). HSV-2 seroprevalence was higher in Mexico City compared to other regions (Fig. 2b). HSV-1 seroprevalence was higher in the high SES group compared to the low SES group (Table 1; p -value: 0.3362). HSV-2 seroprevalence was higher in the low SES group compared to the high SES group (Table 1; p -value 0.1398) (Table 1). For both, HSV-1 and HSV-2, associations of seroprevalence and age were statistically significant, whereas for HSV-2, gender and geographic location were important for acquiring infection (Table 2). In a multiple logistic regression model, seroprevalence by age in both cases; and

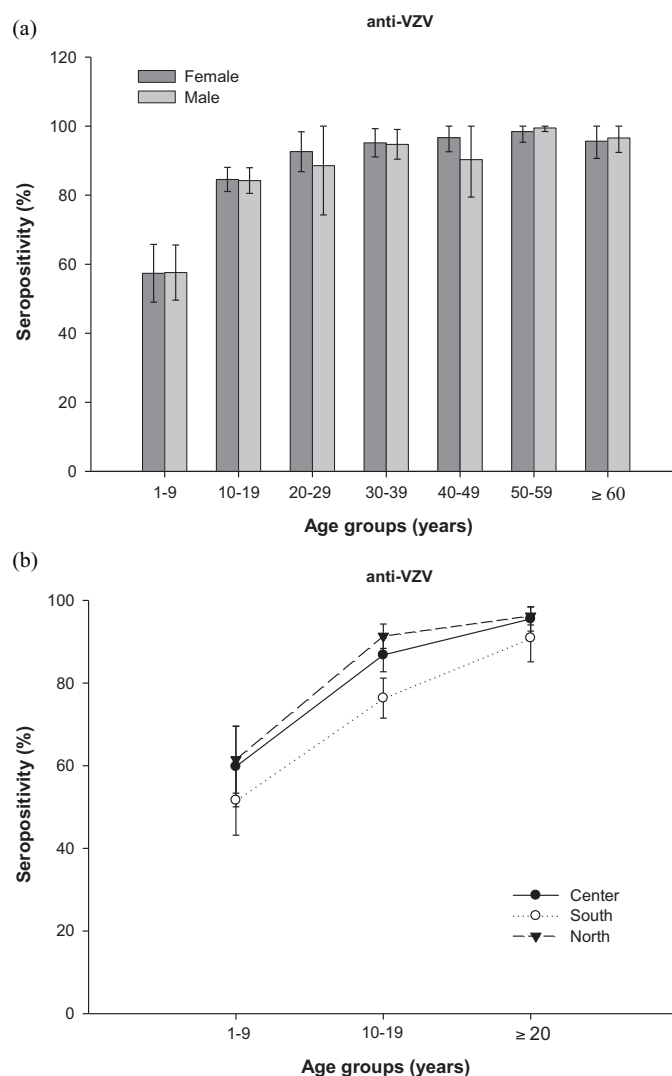


Fig. 1. Seroprevalence of varicella zoster virus (a) age-groups and gender, (b) age-groups and region.

Note: Seropositivity is defined as anti-VZV antibody titer values ≥ 0.2 ; error bars represent 95% confidence intervals.

area for HSV-1 and gender for HSV-2 were statistically significant (Table 3).

3.4. Seroprevalence of CMV

All the subjects included in the analysis were tested for CMV infection ($n=3658$). CMV seroprevalence was 89.2% (95%CI: 87.4–91.1) (Table 1). CMV seroprevalences were comparable in females (89.6% [95%CI: 87.1–92.1]) and males (88.8% [95%CI: 86.1–91.6]) (Fig. 3a). CMV seroprevalence increased with increasing age (p -value $< .0001$). CMV seroprevalence in children aged 1–4 years (62.5% [95%CI: 51.0–73.9]) was lower than in children aged 5–9 years (76.2% [95%CI: 71.5–80.9]). CMV seroprevalences were higher in the South when compared to Center, Mexico City and North regions (p -value: 0.0357) (Fig. 3b). No statistically significant difference was observed in CMV seroprevalence with respect to SES (Table 1). Risk factors for CMV infection are provided in Table 2. The multiple logistic regression analysis indicates that seroprevalence by area was statistically significant (Table 3).

Table 1
Seroprevalences of varicella zoster virus, herpes simplex virus and cytomegalovirus.

Seropositivity		VZV ^a		HSV-1 ^b		HSV-2 ^c		CMV ^d	
		% (95% CI)	P-value	% (95% CI)	P-value	% (95% CI)	P-value	% (95% CI)	P-value
Overall		85.8 (83.6–87.9)	–	80.9 (78.3–83.4)	–	9.9 (7.9–12.0)	–	89.2 (87.4–91.1)	–
Age	Children (1–9 years)	57.5 (51.9–63.1)	<.0001	48.8 (43.2–54.4)	<.0001	2.6 (1.3–4.0)	<.0001	70.1 (64.0–76.1)	<.0001
	Adolescent (10–19 years)	84.4 (81.8–87.0)		71.1 (67.8–74.3)		2.9 (1.8–4.0)		82.4 (79.4–85.3)	
	Adult (≥20 years)	94.4 (92.1–96.6)		93.3 (90.2–96.4)		14.4 (11.0–17.7)		97.0 (95.5–98.6)	
Region	Center	85.1 (81.2–89.1)	0.0009	81.3 (76.9–85.7)	0.8984	6.6 (4.1–9.1)	0.0178	90.8 (88.3–93.4)	0.0357
	Mexico city	91.1 (86.1–96.0)		82.4 (74.8–90.1)		16.4 (7.7–25.1)		88.2 (81.3–95.0)	
	North	89.5 (86.8–92.2)		79.3 (73.3–85.4)		10.2 (6.4–14.0)		84.6 (80.8–88.5)	
	South	80.1 (76.0–84.2)		80.6 (77.6–83.7)		8.8 (6.4–11.1)		91.9 (90.0–93.8)	
SES ^e	Low	83.0 (79.9–86.0)	<.0001	81.8 (78.9–84.7)	0.3362	8.5 (6.2–10.8)	0.1398	89.3 (86.5–92.1)	0.9209
	Medium	90.0 (87.0–93.0)		80.8 (75.8–85.9)		13.1 (8.9–17.3)		90.3 (87.7–92.8)	
	High	97.1 (94.6–99.5)		88.7 (80.6–96.8)		7.2 (0.0–15.0)		90.0 (81.3–98.6)	

Note: seropositivity was defined as follows – (1) VZV: anti-VZV antibody titer values ≥ 0.2 (2) HSV: a simple detection of anti-HSV antibodies and (3) CMV: anti-CMV antibody titer values ≥ 6 .

^a Varicella zoster virus.

^b Herpes Simplex virus type 1.

^c Herpes Simplex virus type 2.

^d Cytomegalovirus.

^e Socioeconomic status.

4. Discussion

This study is one of the few recent studies that provides nationally representative seroprevalences of VZV, HSV and CMV in Mexico by using a population-based approach rather than focusing on high-risk groups such as parents of children in day care, pregnant women or clinic attendees, specifically for sexually transmitted diseases, e.g.: for HSV-2. Whilst there are few published reports on the seroepidemiology of VZV and HSV infections, there is limited epidemiological information on CMV infection in Mexico.

We estimated an overall seroprevalence of VZV of 85.8%; with seroprevalences increasing with age ($p < 0.01$). Similar seroepidemiological profile has been observed in Europe [36], and from surveillance reports in Mexico [37]. We report higher seroprevalence of VZV in adults and adolescents than children. However, a relatively lower seroprevalence in children aged 1–4 years when compared to children aged 10–14 years was estimated. Given that

varicella is a prevalent childhood disease [2], we hypothesize that high attack rates in childhood may have resulted in high seropositivity rates in the older children. Similar findings were reported in Europe [36], where a rapid acquisition of antibodies to VZV led to a seropositive status in most adolescents, thereby characterizing varicella as a childhood disease. Evidence from literature suggests that varicella seroprevalence is dependent on socioeconomic conditions [38,39]. In Brazil, seroprevalence in children were lower in the high/middle SES group [38]. However, we report higher seroprevalences of VZV in the higher SES group than the low/middle SES group. This disparity in findings might be attributed to migration of rural communities to larger cities which may have led to an increase in VZV seroprevalence in urban areas that is related to crowding [40]. This difference can also be attributed to the definition of SES index used in ENSANUT [23]. ENSANUT confirmed access to government programs which aimed at improving conditions for people of low and middle SES. These programs contribute in

Table 2
Simple logistic regression analysis of risk factors for varicella zoster virus, herpes simplex virus and cytomegalovirus.

Category		VZV ^a		HSV-1 ^b		HSV-2 ^c		CMV ^d	
Characteristics	Parameters	OR (95% CI)	p-Value	OR (95% CI)	p-Value	OR (95% CI)	p-Value	OR (95% CI)	p-Value
Age	Children vs. adult	0.1 (0.0, 0.1)	<.0001	0.2 (0.1, 0.3)	<.0001	0.2 (0.1, 0.3)	.0009	0.1 (0.0, 0.1)	<.0001
	Adolescent vs. adult	0.3 (0.2, 0.5)	.3751	0.1 (0.0, 0.1)	.0136	0.2 (0.1, 0.3)	.0015	0.1 (0.1, 0.2)	.0005
Gender	Female vs. male	1.2 (0.9, 1.6)	.2639	1.3 (0.9, 1.8)	.1162	2.2 (1.3, 3.4)	.0014	1.1 (0.7, 1.6)	.6889
Area	Urban vs. rural	2.1 (1.5, 3.0)	<.0001	0.8 (0.6, 1.1)	.2605	1.8 (1.8, 2.7)	.0067	0.8 (0.6, 1.2)	.299
Region	Center	1.0	–	1.0	–	1.0	–	1.0	–
	Mexico city	1.8 (0.9, 3.5)	.0812	1.1 (0.6, 2.0)	.6348	2.8 (1.3, 5.9)	.0274	0.8 (0.4, 1.6)	.7021
	North	1.5 (1.0, 2.3)	.0947	0.9 (0.6, 1.4)	.527	1.6 (0.9, 2.9)	.9008	0.6 (0.4, 0.8)	.0067
	South	0.7 (0.5, 1.1)	.0002	1.0 (0.7, 1.4)	.8604	1.4 (0.8, 2.2)	.3676	1.1 (0.8, 1.7)	.0212
SES ^e	Low vs. high	0.1 (0.1, 0.4)	<.0001	0.6 (0.2, 1.3)	.3189	1.2 (0.4, 3.9)	.6653	0.9 (0.3, 2.5)	.7723
	Medium vs. high	0.3 (0.1, 0.7)	.1989	0.5 (0.2, 1.2)	.1839	1.9 (0.6, 6.3)	.0993	1.0 (0.4, 2.9)	.8271
Smoking status	Yes vs. no	2.3 (0.4, 13.9)	.3505	1.6 (0.4, 7.0)	.5033	1.0 (0.4, 2.7)	.9493	1.6 (0.2, 12.9)	.6600
Drinking status	Yes vs. no	1.1 (0.4, 3.1)	.8741	3.0 (0.9, 9.8)	.0757	1.1 (0.5, 2.3)	.7579	3.0 (0.7, 12.9)	.1341

Note: children: age 1–9 years; adolescent age 10–19 years; adult: age ≥ 20 years.

^a Varicella zoster virus.

^b Herpes simplex virus type 1.

^c Herpes simplex virus type 2.

^d Cytomegalovirus.

^e Socioeconomic status.

Table 3
Multiple logistic regression analysis of risk factors for varicella zoster virus, herpes simplex virus and cytomegalovirus.

Category		VZV ^a		HSV-1 ^b		HSV-2 ^c		CMV ^d	
Characteristics	Parameters	OR (95% CI)	p-Value	OR (95% CI)	p-Value	OR (95% CI)	p-Value	OR (95% CI)	p-Value
Age	Children vs. adult	0.1 (0.0, 0.1)	<.0001	0.1 (0.0, 0.1)	<.0001	0.2 (0.1, 0.3)	.0050	0.1 (0.0, 0.1)	<.0001
	Adolescent vs. adult	0.3 (0.2, 0.5)	.2890	0.2 (0.1, 0.3)	.0098	0.2 (0.1, 0.3)	.0029	0.1 (0.1, 0.2)	.0007
Gender	Female vs. male	1.2 (0.8, 1.8)	.2967	1.3 (0.9, 1.9)	.1413	2.3 (1.3, 3.8)	.0025	1.0 (0.7, 1.5)	.9053
Area	Urban vs. rural	1.6 (1.1, 2.3)	.0170	0.6 (0.4, 0.9)	.0111	1.5 (1.0, 2.3)	.0799	0.8 (0.5, 1.2)	.2417
Region	Center	1.0	–	1.0	–	1.0	–	1.0	–
	Mexico city	1.3 (0.5, 3.3)	.4970	1.0 (0.5, 1.9)	.7680	2.9 (1.3, 6.8)	.0511	0.6 (0.3, 1.3)	.4046
	North	1.2 (0.8, 1.9)	.1933	0.8 (0.4, 1.4)	.4529	1.7 (0.9, 3.3)	.8625	0.5 (0.3, 0.8)	.0021
	South	0.7 (0.4, 1.0)	.0111	0.9 (0.6, 1.3)	.9524	1.6 (0.8, 2.8)	.6784	1.2 (0.8, 1.8)	.0054
SES ^e	Low vs. high	0.5 (0.2, 1.5)	.1309	1.1 (0.4, 2.7)	.7323	3.7 (1.0, 13.5)	.1762	1.5 (0.5, 4.6)	.6972
	Medium vs. high	0.7 (0.3, 1.9)	.9164	0.9 (0.4, 2.4)	.7288	4.7 (1.3, 17.4)	.0167	1.7 (0.6, 5.3)	.2871

Note: children: age 1–9 years; adolescent: age 10–19 years; adult: age ≥ 20 years.

^a Varicella zoster virus.

^b Herpes simplex virus type 1.

^c Herpes simplex virus type 2.

^d Cytomegalovirus.

^e Socioeconomic status.

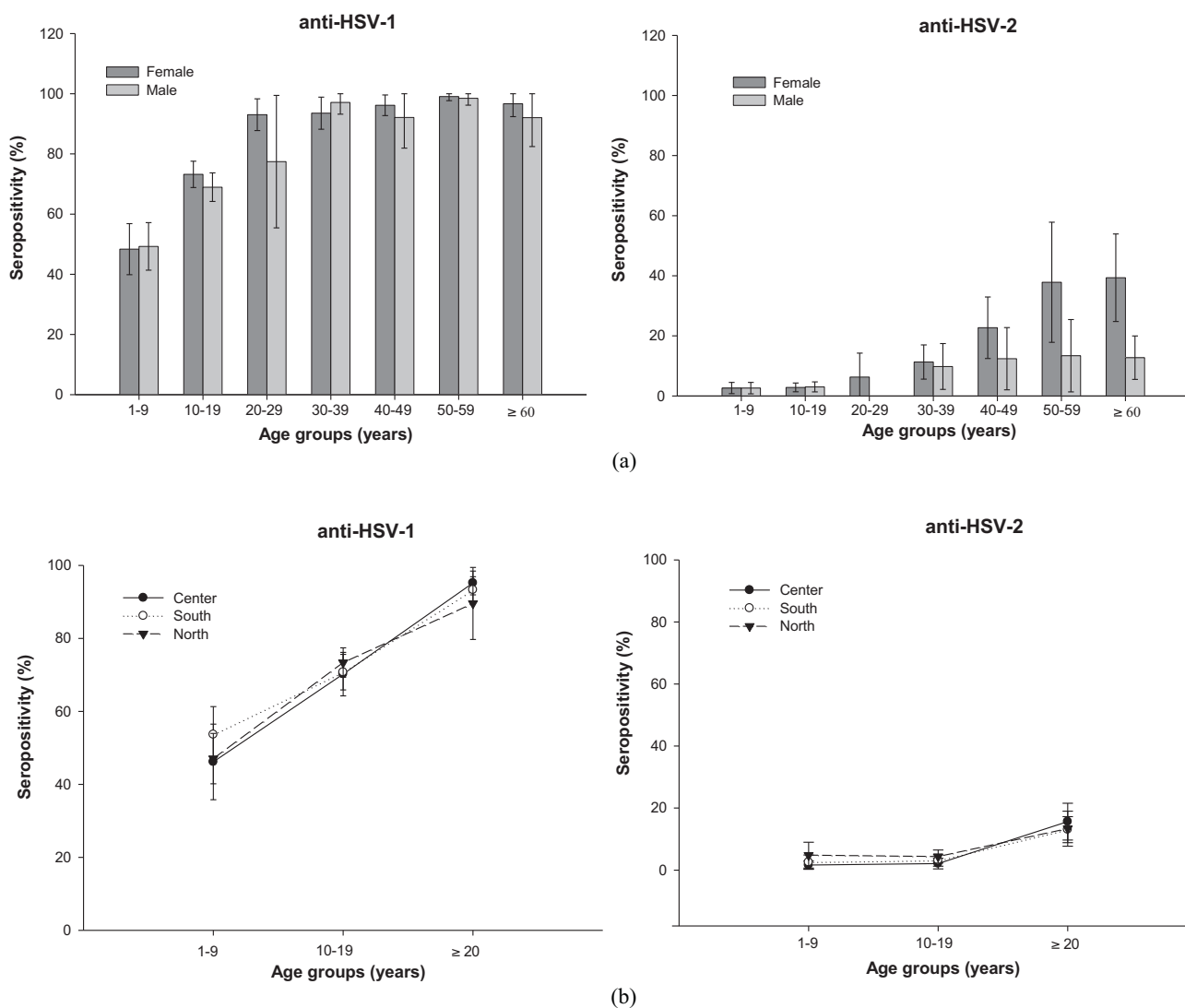


Fig. 2. Seroprevalence of herpes simplex virus (a) age-groups and gender, (b) age-groups and region.

Note: Seropositivity is defined as a simple detection of anti-HSV antibodies; error bars represent 95% confidence intervals region.

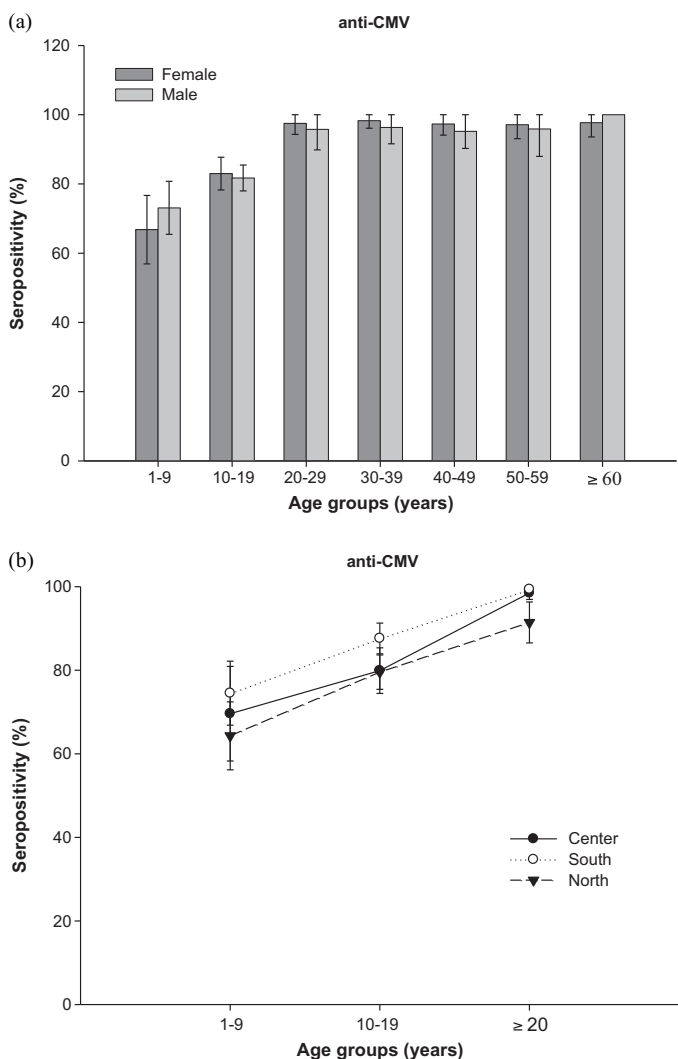


Fig. 3. Seroprevalence of cytomegalovirus (a) age-groups and gender, (b) age-groups and region.
 Note: Seropositivity is defined as anti-CMV antibody titer values ≥ 6 ; error bars represent 95% confidence intervals region.

ways to reduce poverty through the development of basic capabilities thereby facilitating access to better socioeconomic conditions. Consequently, we speculate that the relatively larger numbers of subjects from low and middle SES groups than high income groups enrolled may have contributed to this result.

The WHO recommends that varicella vaccine be offered to adolescents and adults without a history of varicella [16] and where this disease is an important socioeconomic problem. In 2006, the Advisory Committee on Immunization Practices adopted revised recommendations regarding the use of varicella vaccines [8]. Countries that have implemented universal childhood varicella vaccination have demonstrated a significant reduction in the burden of varicella [17–20]. From the region, Uruguay has reported a dramatic decline in the burden of varicella following implementation of universal varicella vaccination [20]. High VZV seroprevalence reported here and evidence on the complications associated with varicella [41] may be useful to help assess the need for a universal varicella vaccination program in Mexico. Varicella vaccination by use of MMR-V vaccines may be an optimal solution (due to reduced costs and improved compliance) to reduce the clinical and economic burden of varicella in Mexico. The high seroprevalence of VZV in adults also suggests a need to devise

strategies for the management of herpes zoster in the elderly in Mexico.

We estimated an overall HSV-1 seroprevalence of 80.9% suggesting high transmission in the Mexican population. These data are consistent with observations from developing countries (75.5–97.8%) [7,42] and are higher than that observed in Europe [6]. HSV-2 seroprevalence was estimated to be 9.9% which reflects the susceptibility for acquisition of primary HSV infection. HSV-2 seroprevalence reported here is in-line with findings from Europe and the USA [6,43–45]. In Mexico, seroprevalence studies of HSV-1 and HSV-2 in specific groups based on variables related to sexual behavior [46–50] have been conducted; however, very few studies in Mexico report population-based seroprevalences [50]. In adults the estimated seroprevalence of 14.4% (95%CI: 11.0–17.7) was similar to data from a recent population-based study in Mexico in the same group (17.3% [95%CI: 15.8–18.8]) [50]. Increase in seroprevalence with increasing age was observed for both HSV-1 and HSV-2 infection which is similar to the trend reported for developing settings [7], Europe [6,44] and Mexico [47,48]. This trend confirms that the majority of HSV-1 infections occur during childhood, although the age of acquisition varies between countries. By contrast, very few children were seropositive for HSV-2 thereby confirming that the age effect correlates with cumulative sexual exposure.

HSV-2 seroprevalence was reportedly higher in females than males which is also the case with recent published observations from Brazil, Estonia, India, Morocco and Sri Lanka [7], Europe, USA and Mexico [6,43,50]. Our data strengthens the previously observed finding that female sex is a risk factor for HSV-2 infection [51]. Consequently, females of child-bearing potential are at a higher risk of transmission to the neonate that could result in neonatal herpes usually resulting in death [52]. Contrary to this and as evident from our results, a large proportion of females is also seronegative for HSV-2. Given the seronegative status and the anatomical feature of the female genitalia, it has been suggested that the female sex is also at a higher risk of acquiring HSV-2 infection [51]. Therefore, appropriate measures for the control of HSV infection in this group should be considered.

CMV seroprevalence in Mexico was 89.2% and it did differ by SES which is consistent with data from developing countries [53,54]. CMV seroprevalence increased with age which is in-line with published reports [55]. CMV seroprevalence data reported here warrants further investigation to establish the burden of disease associated with congenital CMV infection, particularly deafness [56] and mental retardation [9,57].

Our analysis had some limitations. First, our analysis was based on samples stored from 2006 and therefore the seroprevalence data may have changed since the collection of data. Second, our analysis presents only a snapshot of the immune status of the Mexican population. Therefore it was difficult to ascertain the exact timing of exposure of the subject to the disease or differentiate asymptomatic and symptomatic cases. We were also unable to determine HSV-2 infection in high-risk groups due to the characteristics of the population included in ENSANUT and this may have led to an underestimation of HSV-2 seroprevalence. The relationships of seroprevalence and risk factors are descriptive and do not provide evidence of confirmatory associations between the dependent variables. Risk factors such as household crowding [55] were unavailable for the estimation of seroprevalence rates of CMV. Finally, due to a limited number of adults, we were not able to detect differences by socioeconomic variables, geographic areas and gender in this group.

Our analysis provides important seroepidemiological data on common viral infections. These data may help realize the need for a universal varicella vaccination program in Mexico, through the use of either a monovalent or combination MMR-V vaccines; which may help reduce the transmission of VZV. Global HSV-1 seroprevalence rate was high, especially in adults, whereas

HSV-2 seroprevalence was low. Seroprevalence data based on socio-demographic variables suggest that management of these viral infections in young adults, specifically in females of gestational age is of public health priority. Follow-up active surveillance studies to assess the time trends of seroprevalence rates and cost-effectiveness analyses are necessary to fully corroborate our findings and help guide the introduction of any public health policies to tackle the burden associated with these herpes viruses in Mexico.

Trademark

Enzygnost is a registered trademark of Dade Behring, Marburg, Germany. *Euroimmun* is a registered trademark of Medizinische Labordiagnostika, Germany. *ARCHITECT* is a registered trademark of Abbott Laboratories, USA. *Priorix-Tetra* and *Varilrix* are trademarks of GlaxoSmithKline group of companies. *ProQuadis* a registered trademarks of Merck and Co., Inc. *Varivax* is a registered trademark of Sanofi Pasteur Merck Sharp and Dohme (MSD).

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Conflict of interest

Rodrigo DeAntonio, Luis Romano-Mazzotti, Yolanda Cervantes and Eduardo Ortega-Barría are employed by the GlaxoSmithKline group of companies. Yolanda Cervantes, Rodrigo DeAntonio and Luis Romano-Mazzotti declare GlaxoSmithKline stock options; Eduardo Ortega-Barría declares GlaxoSmithKline stock ownership.

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