Varicella Seroprevalence and Molecular Epidemiology of Varicella-Zoster Virus in Argentina, 2002

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There is limited data on immunity against varicella-zoster virus (VZV) in adults in different parts of Argentina, and it is not known which VZV strains are circulating in Argentina. The objectives of this study were as follows: (i) to evaluate seroprevalence of varicella among adults, assessing the accuracy of clinical history and determining the sociodemographic factors associated with seropositivity; and (ii) to determine the VZV strains circulating in Argentina. A cross-sectional serological survey enrolling 2,807 women aged 15 to 49 years attending public health-care settings in four cities in Argentina (i.e., Buenos Aires, Salta, Mendoza, and Rosario) and one rural area was conducted from August to November 2002. Specimens for identification of VZV strains were obtained from vesicular lesions from 13 pediatric patients with varicella from different areas of the country. PCR amplification was used for genotyping. The overall seroprevalence of varicella antibodies was 98.5% (95% confidence interval, 98.0 to 98.9), ranging from 97.2% in central Buenos Aires to 99.3% in southern Buenos Aires and Salta. Varicella seroprevalence increased with age. Crowding and length of residence in the same place were associated with seropositivity. The positive predictive value of varicella history for immunity to varicella was 99.4%; however, the negative predictive value was 2.5%. The European genotype was identified in all viral specimens. In Argentina, seroprevalence in women more than 15 years old was high regardless of the area of residence. Negative or uncertain varicella history was not a good predictor of immunity. VZV genotype was stable in all areas of the country.

Varicella is a highly contagious, exanthematous disease caused by the alphaherpesvirus varicella-zoster virus (VZV), which is typically associated with epidemics among children (40). Although varicella is self-limiting, it may result in complications and death in healthy children. Higher morbidity and mortality occurs among adults (15, 33). The risk of complications may be increased in pregnant women (8) and neonates (7).

The epidemiology of varicella varies in tropical and temperate climates. In temperate climates, varicella occurrence is largely limited to childhood. For example, in the United States, more than 90% of varicella cases occur in persons less than 15 years old (39). However, in tropical and subtropical climates, a higher proportion of primary cases are seen in adolescents and young adults (22, 35). In Argentina, a country with a variety of climates, including a subtropical climate in the northern region, there is limited data on immunity against VZV in adults in different parts of the country (12). Additionally, VZV strains

circulating in Argentina are unknown. From August to November 2002, a seroprevalence study was conducted to assess rubella and measles seroprevalence among women of child-bearing age (WCBA) (i.e., aged 15 to 49 years). This study provided an opportunity to describe VZV epidemiology in this age group. In addition, clinical specimens were collected from pediatric varicella patients for VZV genotyping.

The objectives of this study were as follows: (i) to evaluate seroprevalence of varicella in different areas of Argentina, assessing socioeconomic and demographic factors associated with seropositivity and the accuracy of clinical history of the disease; and (ii) to determine the VZV strains circulating in Argentina.

MATERIALS AND METHODS

Population. The seroprevalence survey was a cross-sectional study and consisted of 2,807 women aged 15 to 49 years attending public health-care settings in four cities (Buenos Aires, Salta, Mendoza, and Rosario) and one rural area (Valle de Uco area in Mendoza province) in Argentina. These sites are located in different areas of the country (i.e., eastern [Buenos Aires], central [Rosario], western [Mendoza], and northwestern [Salta]) (Fig. 1). From the health-care perspective, Buenos Aires is traditionally divided into three main zones, because of its size and differences in demographic characteristics; therefore, each zone was considered a separate research site. A convenient sample of public health-

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FIG. 1. Map of the study sites of the varicella seroprevalence and molecular epidemiology study (★) in Argentina in 2002. Serum samples were collected from urban (★) and rural (▲) sites for the varicella seroprevalence study.

care institutions were selected in each site. Participating institutions in Buenos Aires, Rosario, and Mendoza included the main hospital with delivery facilities or maternity hospitals in the public sector. In Salta, the survey was conducted in seven health-care centers in the public sector where pregnant women are seen for prenatal screening. In the rural area of Valle de Uco, the survey was conducted in the three rural hospitals and four health-care centers. The sample size for each site was calculated on the basis of a 90% seroprevalence level, with an error of 3% and a confidence interval of 95%.

To facilitate comparison of different age groups, the study recruited the same number of participants in the following age groups: 15 to 19, 20 to 24, 25 to 29, 30 to 34, and 35 to 49 years. After informed consent was obtained, patients residing in the area and attending the selected health-care institutions were enrolled consecutively in the study. Trained interviewers completed a questionnaire detailing personal, demographic, and socioeconomic data: date of birth, length of residency in the area, household income, number of bedrooms, total number of persons living in the household, having health insurance, number of pregnancies, and history of varicella.

Identification of VZV was performed on a convenient sample of 13 specimens collected from vesicular lesions of ambulatory and hospitalized pediatric patients with varicella after their parents or legal guardians provided consent. One swab of vesicular fluid was collected from a single lesion of each selected patient. Specimens were collected during September and October 2002 from varicella cases seen in public health-care facilities in five cities in Argentina: Buenos Aires, Mendoza, Salta, Corrientes, and Comodoro Rivadavia (Fig. 1).

Laboratory methods. The serum specimens for the seroprevalence study were obtained from residual sera collected for routine testing during pregnancy (e.g., syphilis) and were transported on dry ice to the Centers for Disease Control and Prevention (CDC), Atlanta, Ga., to be tested for the presence of VZV-specific immunoglobulin G (IgG) antibodies. Initial testing to detect VZV-specific IgG antibody was performed using a direct whole-virus VZV enzyme-linked immu-

nosorbent assay (ELISA) developed at the CDC. The cutoff values for the test results were established empirically and were as follows: an adjusted optical density (OD) of <0.050 was negative, an OD of 0.050 to 0.165 was equivocal, and an OD of >0.165 was positive. Measured against the "gold standard" fluorescent antibody to membrane antigen (FAMA) assay, the whole-cell ELISA had a sensitivity of 88% and a specificity of 96%. Specimens with negative or equivocal test results (results for which some specific reactivity suggested the presence of small amounts of VZV antibody but which fell outside the statistical limits [cumulative variation of assay results plus 3 standard deviations]) were retested using the more sensitive glycoprotein ELISA (gpELISA) method developed at the CDC using purified VZV glycoproteins (supplied courtesy of Merck & Co, West Point, Pa.). The cutoff values for the gpELISA were as follows: an OD of <0.50 was negative, an OD of 0.50 to 2.0 was equivocal, and an OD of >2.0 was positive. The sensitivity and specificity of this test were 99 and 98%, respectively, compared to the FAMA assay.

For genotyping purposes, a sterile swab was used to swab the base of unroofed vesicular lesions. Specimens were placed in sterile tubes and shipped to the CDC. Total DNA was isolated from each specimen by using NucleoSpin tissue kits (Clontech Laboratories, Inc., Palo Alto, Calif.) and recovered in a final volume of $200\ \mu\text{l}$ in a solution of Tris-HCl (pH 8.0) ($10\ \text{mmol/liter}$). To identify VZV-positive specimens, fluorescence resonance energy transfer (FRET)-based real-time PCR targeting VZV open reading frame ORF62 was performed on specimens using LightCycler (Roche) as previously described (26). Evaluation of PstI and BglI sites in ORF38 and ORF54 was done with fluorescent probes (20).

PCR amplification of the ORF22 target region was performed by using $100\ \text{ng}$ of total DNA or $5\ \mu\text{l}$ of DNA extracted from skin lesions of chicken pox patients. The PCR forward primer p22R1f ($5'$ -GGG TTT TGT ATG AGC GTT GG-3', positions 37837 to 37856) and the reverse primer p22R1r ($5'$ -CCC CCG AGG TTC GTA ATA TC-3', positions 38383 to 38356) were designed to amplify a 447-bp fragment (positions 37837 to 38264) of VZV ORF22. DNA amplification reactions were performed with a GeneAmp PCR System 9700 (Applied Biosystems) in $50\text{-}\mu\text{l}$ reaction volumes, using AmpliTaq Gold PCR Master Mix ($0.025\ \text{U}$ of GoldTaq DNA polymerase enzyme, $1\times$ PCR buffer II, $2.5\ \text{mM}$ MgCl_2 , a $200\ \mu\text{M}$ concentration of each deoxynucleotide triphosphate, a $0.2\ \mu\text{M}$ concentration of each primer, and 1 to $5\ \mu\text{l}$ of VZV DNA extract). Sequence variation observed at four polymorphic loci in the amplicon of European strain Dumas (GenBank accession number 9625875) and Japanese OKA parental strain (14) (GenBank accession number 26665422) was used to assign genotype (25). Full homology to the OKA strain characterizes the VZV Japanese genotype, and strains with complete identity in the designated region to the Dumas strain characterize the European genotype. The third genotype, called mosaic, carries both Japanese and European genotype mutations.

Statistical analysis. Data were entered and analyzed using EPI Info 2000 (10). For statistical analysis, negative and equivocal results were grouped together and classified as negative. VZV seropositivity in the different sites was reported as percentages with 95% confidence intervals. The chi-square test (or the Fisher exact test if an expected value in any cell was less than five) was used to assess the association between VZV seroprevalence and sociodemographic variables among the study sites. The Cochran-Armitage trend test was used to assess seroprevalence trends among age groups. In addition, logistic regression analysis was performed to identify independent predictors of varicella seropositivity. Statistical significance was set at a P value of <0.05 .

Using the presence of varicella IgG antibodies as the gold standard for immunity, the sensitivity, specificity, positive predictive value, and negative predictive value of self-reported history of varicella were calculated. For this analysis, those with negative or uncertain history of varicella were considered history negative. The proportion of seropositive individuals who reported a positive history of disease was defined as the sensitivity of self-reported history, and the proportion of seronegative participants who did not report prior disease (i.e., history negative) was defined as the specificity. The positive predictive value of history was defined as the proportion of history-positive women who were seropositive, and the negative predictive value was defined as the proportion of history-negative women who were seronegative.

RESULTS

Seroprevalence study. Differences in demographic characteristics of the study population ($n = 2,807$) were observed for the different areas of Argentina sampled (Table 1). A lower percentage of people living more than 5 years in the same place was observed in Buenos Aires and the rural area. House-

TABLE 1. Characteristics of the 2,807 women studied in Argentina in 2002

Characteristic	% Women						
	Bueno Aires			Rosario (n = 405)	Mendoza (n = 402)	Salta (n = 411)	Rural (n = 400)
	Northern (n = 392)	Central (n = 390)	Southern (n = 407)				
Age group (yr)							
15–19	18.6	17.9	19.7	20.2	20.6	19.7	18.3
20–24	22.2	24.4	19.7	20.2	20.1	20.9	22.7
25–29	20.4	28.2	20.8	19.8	20.4	20.7	20.7
30–34	16.1	16.7	19.9	20.5	19.7	20.0	18.3
35–49	22.7	12.8	19.9	19.3	19.2	18.7	20.0
Residence							
<5 yr living in the same place	36.2	37.9	35.6	6.4	24.9	8	28.8
≥5 yr living in the same place	61.5	59.7	64.4	89.9	75.1	72.5	71.0
Unknown	2.3	2.3	0.0	3.7	0.0	19.5	0.2
Crowding							
≤2 persons per bedroom	67.1	60.8	70.5	53.8	46.5	41.8	52.0
>2 persons per bedroom	32.1	39.0	29.0	45.4	53.5	58.2	48.0
Unknown	0.8	0.3	0.5	0.7	0.0	0.0	0.0
Household monthly income							
<75 US \$	16.1	18.2	36.9	41	35.3	51.8	38.0
≥75 US \$	81.4	80.3	63.1	58.5	64.5	45.0	61.8
Unknown	2.5	1.5	0.0	0.5	0.2	3.2	0.2
Health insurance							
Yes	18.9	11.0	2.0	10.4	21.9	12.9	19.5
No	81.1	89.0	98.0	89.6	78.1	86.9	80.5
Unknown	0.0	0.0	0.0	0.0	0.0	0.2	0.0
No. of pregnancies							
<4	86.2	85.1	88.5	79.3	74.9	74	77.3
≥4	13.8	14.9	11.5	20.7	25.1	26	22.8
Unknown	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Education							
Primary incomplete	6.4	10.0	3.2	16.8	14.7	4.9	21.3
Primary complete	45.4	54.1	54.8	56.5	54.0	57.7	53.2
Secondary complete	33.4	25.6	36.9	19.3	18.9	30.1	19.0
Tertiary or university complete	14.3	10.3	5.1	7.4	12.2	7.3	6.5
Unknown	0.5	0.0	0.0	0.0	0.2	0.0	0.0
Varicella history							
Positive	57.4	55.1	65.8	52.6	61.4	40.9	45.3
Negative or does not know	42.6	44.9	34.2	47.2	38.6	59.1	54.8
Unknown	0.0	0.0	0.0	0.2	0.0	0.0	0.0

holds with more than two persons per bedroom were more frequent in Salta and Mendoza. Households with a monthly income of <\$75 (United States dollars) were also more frequent in Salta.

Of the total 2,807 participants in Argentina, specimens were available for 2,803 (99.9%). The overall seroprevalence of varicella antibodies was 98.5% (95% confidence interval, 98.0 to 98.9), ranging from 97.2% in central Buenos Aires to 99.3% in Bueno Aires and Salta (Table 2). No negative or equivocal specimens retested using the more-sensitive gpELISA were found to be positive. No significant differences were found between rural and urban areas or areas with subtropical climates, such as Salta, and other areas with temperate climates (Table 2).

Seroprevalence was more than 97% in all age groups, reaching 100% for women 35 years and older (Table 3). Although

most women were seropositive, a tendency for higher seropositivity in the higher age groups was observed ($P = 0.005$ by the Cochran-Armitage trend test). Women living for more than 5 years in the same place were more likely to be immune to varicella than women who had lived less than 5 years in the same place (Table 3). Living in a household with more than two people per bedroom and having more than four previous pregnancies were also factors associated with higher seroprevalence against varicella (Table 3). In the multivariate analysis, age, living in the same place for more than 5 years, and crowding remained significant factors (Table 4). Living in southern Buenos Aires was marginally associated with seropositivity.

A self-reported varicella history was available for 2,202 participants; reports of positive history varied from 40.9 to 65.8% in the study sites (Table 1). The sensitivity and specificity of

TABLE 2. Varicella laboratory results by geographical location in Argentina in 2002

Site	No. of samples	% Samples (95% CI) ^a		
		Positive	Negative	Equivocal
Buenos Aires				
Northern	388	97.4 (95.2–98.7)	2.3 (1.1–4.5)	0.3 (0–1.7)
Central	390	97.2 (94.9–98.5)	2.3 (1.1–4.5)	0.5 (0.1–2)
Southern	407	99.3 (97.7–99.8)	0.5 (0.1–2)	0.2 (0–1.6)
Rosario	405	99.0 (97.3–99.7)	0.5 (0.1–2)	0.5 (0.1–2)
Mendoza	402	99.0 (97.3–99.7)	0.5 (0.1–2)	0.5 (0.1–2)
Salta	411	99.3 (97.7–99.8)	0.7 (0.2–2.3)	0
Rural	400	98.5 (96.6–99.4)	1.3 (0.5–3.1)	0.2 (0–1.6)
Total	2,803	98.5 (98.0–98.9)	1.1 (0.8–1.6)	0.3 (0.2–0.6)

^a Percentage of samples with positive, negative, or equivocal varicella laboratory result. 95% CI, 95% confidence interval.

disease history were 54.5 and 78%, respectively. Of the 1,515 women who reported having had varicella, 1,506 tested positive for VZV IgG. The positive predictive value of varicella history was 99.4%. Of 1,287 who did not know ($n = 618$) or stated a negative history of varicella ($n = 669$), 32 were seronegative, resulting in a negative predictive value of 2.5%. The negative

TABLE 3. Factors associated with varicella seropositivity in women aged 15 to 49 years in Argentina in 2002

Characteristic	Total no. of women	Varicella-positive women		<i>P</i> value
		No.	%	
Age group (yr)				
15–19	540	527	97.6	0.005
20–24	602	595	98.8	
25–29	604	590	97.7	
30–34	526	519	98.7	
35–49	531	531	100.0	
Residence				
<5 yr living in the same place	707	687	97.2	0.001
≥5 yr living in the same place	1,982	1,962	99.0	
Crowding				
≤2 persons per bedroom	1,570	1,538	98.0	0.007
>2 persons per bedroom	1,224	1,215	99.3	
Household monthly income				
<75 US \$	955	945	99.0	0.23
≥75 US \$	1,815	1,784	98.3	
Health insurance				
Yes	385	378	98.2	0.69
No	2,417	2,383	98.6	
No. of pregnancies				
≥4	2,262	2,222	98.2	0.01
<4	541	540	99.8	
Education				
Primary incomplete	308	303	98.4	0.31
Primary complete	1,507	1,488	98.7	
Secondary complete	733	723	98.6	
Tertiary or university complete	252	245	97.2	

TABLE 4. Multivariate analysis of possible risk factors for varicella seropositivity in women in Argentina in 2002

Possible risk factor	Odds ratio (95% confidence interval)	<i>P</i> value
Age ^a	1.06 (1.00–1.11)	0.04
Residence		
<5 yr living in the same place	1.00 (referent)	0.008
≥5 yr living in the same place	2.46 (1.27–4.77)	
Crowding		
≤2 persons per bedroom	1.00 (referent)	0.015
>2 persons per bedroom	2.70 (1.22–5.99)	
No. of pregnancies		
<4	1.00 (referent)	0.2
≥4	3.81 (0.48–30)	
Site		
Bueno Aires		0.9
Northern	0.96 (0.39–2.36)	
Central	1.00 (Referent)	
Southern	3.74 (1.01–13.78)	0.05
Rosario	1.58 (0.47–5.31)	0.46
Mendoza	1.95 (0.6–6.36)	0.27
Salta	1.80 (0.48–6.8)	0.38
Rural	1.39 (0.49–3.9)	0.54

^aAge range, 14 to 49 years.

predictive value ranged from 2.2% in women with incomplete primary education to 4.5% among women with complete tertiary or university level education ($P < 0.001$).

Molecular epidemiology. Of the 13 children aged 3 to 13 years, from whom specimens were obtained, 7 were ambulatory patients, and the rest were hospitalized for varicella complications (Table 5). All 13 samples carried VZV DNA and were Pst⁺ Bgl[−] according to the classification of LaRussa et al. (20) and Sma[−]. The 447-bp ORF22 sequences of all samples tested were identical to that of the European reference strain.

DISCUSSION

We found that more than 97% of women attending prenatal clinics in Argentina were immune to VZV by 15 to 19 years of age. We did not find significant differences in seroprevalence by geographical region or rural versus urban areas. Varicella seroprevalence increased with age. However, after adjusting for age, sociodemographic variables, such as crowding and length of residence in the same place, were associated with the presence of anti-VZV serum antibodies, although these effects were small, given the overall seroprevalence.

The high percentage of immunity among adults found in this survey suggests that in Argentina, varicella occurs during childhood. The high seroprevalence rates found are comparable and even higher than those observed in the United States (19). Similar seroprevalence rates have been reported in other temperate climates, such as Switzerland, where 96.5% of adolescents aged 13 to 15 years were immune (17), or Belgium with a reported seroprevalence of 97.2% among individuals aged 15 to 19 years (38). Similar results were described in Germany

TABLE 5. Molecular genotyping of VZV in vesicular lesions of children in Argentina in 2002

Site	Region	Age (yr)	Sex ^a	Date (mo/day/yr) of onset	Date (mo/day/yr) of specimen	Patient type	VZV strain
Buenos Aires	Eastern	5	M	10/19/02	10/21/02	Ambulatory	European
Buenos Aires	Eastern	3	M	10/19/02	10/21/02	Ambulatory	European
Buenos Aires	Eastern	4	M	10/21/02	10/23/02	Hospitalized	European
Buenos Aires	Eastern	3	M	10/17/02	10/18/02	Hospitalized	European
Corrientes	Northeastern	10	F	10/29/02	4/11/02	Ambulatory	European
Corrientes	Northeastern	3	M	10/31/02	11/4/02	Hospitalized	European
Corrientes	Northeastern	4	M	3/11/02	4/11/02	Hospitalized	European
Salta	Northwestern	13	F	5/11/02	7/11/02	Hospitalized	European
Salta	Northwestern	12	F	5/11/02	7/11/02	Hospitalized	European
Mendoza	Western	6	M	1/11/02	3/11/02	Ambulatory	European
Mendoza	Western	4	M	2/11/02	3/11/02	Ambulatory	European
Comodoro Rivadavia	Southern	5	M	11/14/02	11/15/02	Ambulatory	European
Comodoro Rivadavia	Southern	6	F	11/21/02	11/22/02	Ambulatory	European

^a M, male; F, female.

(41) and Spain (34). High seroprevalence levels were also observed in other countries of Latin America, such as Brazil, where 95.5% of individuals aged 16 to 20 years were seropositive (9), or Mexico, where 91.6% of people 20 to 24 years old were seropositive (3).

These findings contrast with the much lower immunity found in some tropical areas of the world (22, 35). For example, a survey conducted in Singapore in 1990 revealed that less than 50% of individuals 15 to 24 years old were immune to VZV (31). Another seroprevalence study showed that 46.7% of persons 16 to 20 years old had positive IgG VZV antibodies in Pakistan (1). Low seroprevalence rates in adolescents were found in other tropical and subtropical countries, such as India (24), Thailand (28), or St. Lucia in the Caribbean (11). However, most tropical studies have been conducted in relatively homogenous populations, and few studies have been reported from countries with different climatic zones (30). Our data indicate that climate is unlikely to be a major influence on varicella transmission in Argentina, since we did not find lower seroprevalence VZV levels in subtropical areas of the country (i.e., Salta). These findings are in agreement with a much smaller study of 298 adult women in Australia, a country with different climatic zones (30), and another study conducted in different regions of Brazil (9).

Except for a marginally significant difference in the southern part of Buenos Aires, Argentina, which is probably incidental, we did not find significant differences in seroprevalence in the areas we studied, and there was no variation between rural and urban areas. One study conducted in India reported marked differences in susceptibility in adults living in urban and rural areas (27). However, similar to our study, no seroprevalence differences for rural versus urban areas were found in other studies conducted in Bolivia (5) and Switzerland (17). Although this may reflect the frequent migration between rural and urban areas due to better labor conditions in the cities, differences in population density and definitions of rural and urban areas may have influenced the results.

Although in some studies, socioeconomic variables (e.g., social class, educational level) do not seem to help predict varicella antibody status (1, 24, 28, 34), varicella seroprevalence has been associated with socioeconomic factors in children in Brazil and England (9, 32). The lower immunity ob-

served in women living in households with less than two persons per bedroom in Argentina is consistent with the results of a study conducted in Lebanon, where coming from homes with a smaller number of rooms and smaller families were predictors of a lack of immunity to varicella (29). Although the level of education was not related to immunity in our study, low education was a risk factor for susceptibility to varicella in Mexico (3).

The accuracy of a past positive history of varicella was confirmed in our study. As in other studies, we found a very high positive predictive value of varicella history (6, 13, 28, 29, 37). However, we found a strikingly low predictive value of negative history (i.e., 2.5%); therefore, a high percentage of women with negative or uncertain history of varicella were immune. Although some studies conducted among adults reported that 70 to 90% of adults with a negative or uncertain history of varicella were VZV seropositive (2, 12, 13, 18), we found that 97.4% of participants with a negative or uncertain history of varicella tested positive. This high percentage is due to an unusually high percentage (approximately 50%) of women who did not recall having had varicella. In our study, this phenomenon may be explained by the fact that some women, especially those with a low education level, may not have understood the question or recognized the disease; others may have had varicella at such a young age they did not remember it.

Our findings may be used to guide practitioner practices aimed at preventing the occurrence of neonatal and maternal morbidity related to VZV. At this time, there is no varicella vaccination program for children or adults in place in Argentina; however, the vaccine is available in the private sector. On the basis of our findings, physicians may assume that WCBA with a positive history are immune; however, most WCBA with unknown or negative history of varicella will also be immune. Therefore, it would be very difficult to detect truly VZV-susceptible WCBA based on a history of varicella, and women with negative history should be tested to determine if they should be vaccinated.

VZV is a very stable virus in terms of genomic structure, and it has been postulated that VZV isolates are similar in the same geographical area (21, 36). Our analysis of seven variable mutations in four separate open reading frames (ORF22,

ORF38, ORF54, and ORF62) showed no variation of the VZV virus isolated from ambulatory and hospitalized patients from different parts of Argentina. A restriction fragment polymorphism method (20) modified for use with fluorescent probes showed the similarity of tested Argentinean isolates with Pst⁺ Bgl⁻ strains circulating in North America and Eastern Australia by the LaRussa classification (21). According to a newly developed VZV genotyping method (25), samples from all areas in Argentina were genotyped as European VZV strains, which usually circulated in countries with temperate climates in Europe, North America, and eastern Australia. This is not surprising, because about 85% of the population in Argentina is of European origin, and there is much travel between Argentina and Europe. VZV in countries with tropical climates (Guinea Bissau, Zambia, Bangladesh, and southern India) in general have a Bgl⁺ marker in ORF54 (4) and carry mosaic strains (25). Genetic diversity was observed within and between samples in the United Kingdom, Brazil (4), and United States (21), which has been attributed to the history of recent human migration from other parts of the world. The significant increase in the prevalence of certain strains in cases of varicella, in parallel with the increase in the immigrant population found in the United Kingdom, also reflects differences in molecular epidemiology in different countries (16). Therefore, circulation of VZV strains seems to be related not only to geographical location but also to migration from other countries. Our findings in Argentina seem to confirm this theory.

Our study has some limitations. First, the population surveyed was not randomly sampled; however, convenience sampling is unlikely to differentially sample seropositive and seronegative women. Second, our study included only the female population, and its results may not be generalized to the total population. Although some reports suggest that women have slightly higher rates of VZV susceptibility than men do (9, 23), which is attributed to a higher contact of women with children, significant differences by gender have not been found in most seroprevalence studies conducted in different parts of the world (3, 6, 17, 28, 29, 31, 34).

This is the first study to show the serological and molecular epidemiology of varicella in different areas of Argentina. In conclusion, VZV genotype was stable in all areas of the country. The seroprevalence of anti-VZV antibodies was high in women in different areas of Argentina. We found a good correlation between varicella history and seropositivity; however, a high percentage of participants with negative or uncertain varicella history and a low predictive value of negative history were observed. These findings will have to be considered by physicians who want to improve their ability to counsel WCBA to prevent varicella infection during pregnancy and potentially congenital or perinatal rubella infection.

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