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Seroprevalence of herpes simplex 1-2 antibodies in Brazil

ABSTRACT

OBJECTIVE: To estimate the seroprevalence of HSV-1 and HSV-2 antibodies in Brazil and to analyze factors associated.

METHODS: Cross-sectional study including subjects aged 1-40 years from the general population in four different geographical areas in Brazil between 1996 and 1997. All subjects were stratified by age and gender and 1,090 of them were included in the final analysis. Blood samples were tested for HSV-1 and HSV-2 antibodies by type-specific (gG1 and gG2) ELISA. Frequencies and proportions were described and compared among groups using two-sided Fisher's exact test. A logistic regression analysis was performed to assess the influence of the variables age, gender, geographical area, socioeconomic condition, past history of STD, seropositivity for anti-HSV-1 or anti-HSV-2 and interactions of any of these factors on the seroprevalence of HSV-1 and/or HSV-2.

RESULTS: The age-adjusted seroprevalences of HSV-1 and HSV-2 antibodies were 67.2% and 11.3%, respectively, without sex differences and being higher in the North region. Seroprevalences increased with age and, for HSV-2 infection, the higher increase was observed among adolescents and young adults. Subjects who tested positive for HSV-1 were more likely to also test positive for HSV-2 (15.7%) compared to HSV-1 negative subjects (4.7%). In the multivariate analysis past history of STD significantly (OR=3.2) increased the likelihood of HSV-2 infection whereas socioeconomic condition did not affect the results.

CONCLUSIONS: HSV-1 and HSV-2 seroprevalences vary with age and among Brazilian regions. Past history of STD is a major risk factor for HSV-2 infection.

DESCRIPTORS: Herpesviridae Infections, epidemiology. Herpes Simplex, epidemiology. Antibodies, Viral, diagnostic use. Seroepidemiologic Studies.

INTRODUCTION

Herpes simplex virus (HSV) infections are caused by two types of viruses, type 1 (HSV-1) and type 2 (HSV-2), and both are endemic worldwide.[15,17] HSV infection is one of the most prevalent infections worldwide. Each year 640,000 new cases of genital herpes are diagnosed in Brazil,[16] and HSV-1 and HSV-2 infections are highly relevant for public health. The assessment of the seroprevalence of HSV-1 and HSV-2 antibodies allows describing the dynamics of this epidemic.

HSV-1 infection typically occurs during childhood and adolescence through direct oral exposure and, if symptomatic, it is characterized by orolabial or facial lesions. However, recent studies have showed that HSV-1 has become a major causative agent of genital herpes in some developed countries.[14,21]

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The disease caused by HSV-2 is usually genital affecting sexually active adolescents and adults.[17,25] Virus excretion and transmission occur not only from symptomatic infected persons but also from asymptomatic individuals.[9,11,20] Neonatal HSV infection is one of the most serious consequences of maternal genital infection caused by HSV-2, although HSV-1 can be sometimes identified.[6]

Epidemiological studies have showed an important interaction between HSV, HIV-1 and HPV.[3,18,24] HSV-2 infection increases the risk of infection, excretion and transmission of HIV-1 and may accelerate disease progression by HIV-1. It has been also associated with 2.2 to 3.4 times increased risk of invasive cervical carcinoma in women who tested positive for HPV DNA.[18]

The management of genital herpes infections should be a public health priority and be based on updated information on the epidemiology of this infection in the general population and risk groups.

The objective of the present study was to estimate the seroprevalence of herpes simplex virus (HSV-1 and HSV-2) antibodies in different geographic areas in Brazil and to analyze factors associated.

METHODS

This HSV seroepidemiological study conducted in Brazil was part of a large prospective, multinational, cross-sectional study on the prevalence of hepatitis (A, B, and E) and varicella in six Latin American countries during 1996 and 1997. The multinational study included a total of 12,085 individuals, of which 3,879 were from Brazil.[4,22] Brazil was the only country where the prevalence of HSV was analyzed as part of the study.

Healthy individuals, both males and females, of any ethnicity and aged one to 40 years were included in the study sample after signing an informed consent form. Individuals who were HIV-1 positive or vaccinated against hepatitis A, B or varicella were excluded as per the original study, which investigated the seroprevalence of markers of these infections. To avoid a clustering effect and to eliminate therefore a major bias in data analysis, only one subject per household was allowed to participate in the study.

The study population in the Brazilian Northeast (Fortaleza, state of Ceará, urban area), Southeast (Rio de Janeiro, urban and rural areas) and South regions (Porto Alegre, state of Rio Grande do Sul, urban area) was recruited from communities, universities, schools, general and pediatric outpatient clinics, medical offices and up to 5% among blood donors. In the Northern region (Manaus, state of Amazonas, urban areas and riverside communities), subjects were recruited from general and pediatric outpatient clinics.

The estimated sample size of 1,320 individuals was based on a 29% seroprevalence of HSV-2[13] from a study carried out in Rio de Janeiro in blood donors and considering a potential attrition of 20% due to the exclusion of individuals for protocol violation. These 1,320 subjects were randomly selected from a sample of 3,879 subjects in the original study, after stratification by age and gender. Age was stratified into five-year groups and, among adolescents, two year age groups to better capture the dynamics of HSV-2 infection. The sample size per age and sex stratum was 90 evaluable subjects each, which allowed to detect with 80% power a 10% difference in prevalence per ten years of age (based on NHANES III).[20] In each of the four regions studied, a minimum of 100 individuals was selected. In the Southeast region, a larger number of subjects were randomized to assess relevant epidemiological differences if data from all sites could not be pooled for analysis. Moreover, stratification for statistical analysis was performed according to socioeconomic condition and prior history of STDs.

Data on demographics, geographic area, prior history and health status including STDs, socioeconomic factors and number of family members was collected. Socioeconomic class was defined as high (family income over 11 monthly minimum wages [MMWs]), middle (three to 11 MMWs) and low (less than three MMWs).[a]

A 5mL blood sample was drawn from each subject and serum samples were tested in the study laboratory for the presence of IgG antibodies against HSV-1 and HSV-2 using a type-specific ELISA kit (Gull Laboratories, Salt Lake City, US). This assay was used for its high sensitivity for HSV-1 (95%) and HSV-2 (98%), and 97% specificity for both HSV-2 and HSV-1.[1]

The prevalence of HSV-1 and HSV-2 antibodies was described by frequency, proportions and 95% confidence interval. A two-sided Fisher's exact test was used for comparative statistical analysis. Estimates of risk ratios and 95% confidence intervals were also adjusted for age and gender using binomial regression (p-values according to Cochran Mantel-Haenszel test statistics). Statistical analysis was performed using SPSS and Epi Info 6:04.

A logistic regression analysis was conducted to assess the influence of independent factors such as age, gender, region, socioeconomic condition, prior history of STDs, seropositivity for anti-HSV-1 or HSV-2 and interactions

[a] Associação Nacional de Empresa de Pesquisa. Critério de classificação econômica Brasil. São Paulo. 1998[cited 2010 Apr 04]. Available from: www.abep.org/novo

of any of these factors with the seroprevalence of HSV-1 and/or HSV-2. A procedure for progressive selection of variables was used by adding independent factors, if significant, to the model (chi-square test: 0.05) until none of the remaining effects reached the significance level.

The study followed the current Good Clinical Practice guidelines for clinical studies. It was approved by the Ethical Review Committees of Hospital das Clínicas de Porto Alegre, Hospital Universitário Antônio Pedro, Rio de Janeiro, Instituto de Medicina Tropical de Manaus and Hospital Infantil Albert Sabin, Fortaleza.

RESULTS

Table 1 shows the total study population, attrition and demographic characteristics of the final sample analyzed for the seroepidemiology of HSV. Of a total of 3,879 subjects in the original study, 1,320 were randomized for HSV analysis. Of them, 184 subjects were excluded due to insufficient volume of serum samples for further testing of HSV, and 46 were excluded due to missing core demographic data, making a total of 1,090 analyzable subjects. This loss was expected in the protocol. Thus the analysis included 796 subjects from Rio de Janeiro, 106 from Manaus, 85 from Porto Alegre and 103 from Fortaleza.

Of all 1,090 subjects included in the analysis, 560 were females and 530 males (1.05:1.0). This gender distribution was about similar in all age groups and in three out of four regions studied, with the exception of the city of Manaus.

The sample size estimated in the protocol (N = 90) was reached for almost all age/gender groups, except in Manaus. The mean age was 18.6 years (SD = 9.8), and thus three years older than in the original seroepidemiological study. The main explanation for the higher mean age in Manaus was the attrition among younger individuals due to insufficient volume of serum samples for HSV testing after other antigens were tested. The mean age was similar in all regions, except in Manaus, where the mean was 23.2 years (SD= 10.9). A total of 476 subjects were in the low and 590 in the middle socioeconomic class. Since few subjects (23) were in the high socioeconomic stratum, they were grouped together with those of the middle socioeconomic class for analysis purposes. As forethnicity, 51.5% were caucasians, 37.9% were mixed 10.2% were black and 0.4% were Asian.

Overall, 51 individuals reported prior history of STDs, mostly gonorrhea (N = 35). Eight subjects reported prior clinical diagnosis of genital herpes infection.

Table 2 shows the prevalence of HSV-1 antibodies which was 67.2% (95% CI: 64.3, 70.2) after adjusting for age and gender. There was no difference in the prevalence among males (66.2%; 95% CI: 62.0; 70.4) and females (68.2%; 95% CI: 64.1; 72.3, p = 0.19) overall nor within any age group. Approximately 25% of the subjects in the study were diagnosed positive for HSV-1 at the age of four, 50% at the age of seven, and 75% at the age of 24.

The overall adjusted prevalence of HSV-2 was 11.3% (95% CI: 9.5; 13.0), 11.2% (95% CI: 8.7; 13.8) in males and 11.3% (95% CI: 8.9; 13.6) in females (p =

Table 1. Population of the original study: seroprevalence of hepatitis A/B and varicella in Brazil and in the subset of HSV. Brazil, 1996–1997.

	N	Age (SD) (years)	Gender: F/M ratio	High/middle and low Socioeconomic condition
Seroprevalence of hepatitis A and B in Brazil[4]				
Total sample	3879			
Missing data	177			
Non-analyzable serum sample	49	15.4 (10.0)	1.06	54/46
Analyzed sample	3653			
HSV seroprevalence in Brazil				
Total randomized sample	1320	15.9 (9.7)	1.05	54/46
Missing data	46			
Non-analyzable serum sample	184			
Analyzed sample	1090[a]	18.6 (9.8)	1.05	56/44
Rio de Janeiro	796	17.9 (9.5)	1.06	59/41
Manaus	106	23.2 (10.9)	0.90	56/44
Fortaleza	103	19.5 (9.4)	1.10	49/51
Porto Alegre	85	17.8 (9.6)	1.10	46/54

[a] One subject was tested only for HSV-2 antibodies

Table 2. Seroprevalence of HSV-1 antibodies in the sample studied by gender and age. Brazil, 1996–1997. (N = 1089)

Age (years)	Gender				Total HSV-1 positive	
	Males HSV-1 positive		Females HSV-1 positive			
	% (95% CI)	Total (n/N)	% (95% CI)	Total (n/N)	% (95% CI)	Total (n/N)
1-5	44.2 (30.5;58.7)	23/52	38.3 (24.5;53.6)	18/47	41.4 (31.6;51.8)	41/99
6-10	55.1 (40.2;69.3)	27/49	58.0 (43.2;71.8)	29/50	56.6 (46.2;66.5)	56/99
11-15	65.6 (56.6;73.9)	82/125	74.6 (66.1;81.9)	94/126	70.1 (64.0;75.7)	176/251
16-20	69.8 (60.6;77.8)	83/119	75.8 (67.4;82.9)	97/128	72.9 (66.9;78.3)	180/247
21-30	76.6 (67.5;84.3)	82/107	81.0 (73.0;87.4)	102/126	79.0 (73.2;84.0)	184/233
31-40	85.9 (76.2;92.7)	67/78	81.7 (71.6;89.4)	67/82	83.8 (77.1;89.1)	134/160
Total	68.7 (64.5;72.6)	364/530	72.8 (68.9;76.4)	407/559	70.8 (68.0;73.5)	771/1,089
Age-corrected total	66.2 (62.0;70.4)		68.2 (64.1;72.3)		67.2 (64.3;70.2)	P=0.19[a]

N = total number of subjects
n = total number of seropositive subjects
[a] Cochran Mantel Haenszel test – association between gender and age adjusted for HSV1-positive subjects

0.82) (Table 3). Although the seroprevalence of HSV-2 antibodies seemed higher in the very young subjects, the sample size in these age groups was small and the differences were not significant, and therefore it is likely to be a random finding. A significant increase of HSV-2 seroprevalence was seen during adolescence with a plateau reached between 20 and 30 years of age when about 25% of the study sample was HSV-2 positive. At the age of 20, twice as many women were HSV-2-positive compared to men (21.2% vs. 10.6%). The decline in the seroprevalence of HSV-2 seen in older age groups was not significant and was probably a cohort effect in a cross-sectional study.

A total of 11.1% (95% CI: 9.3, 13.1) of the subjects studied were positive for both HSV-1 and HSV-2, with no statistical gender difference (p = 0.78). Yet 15.7% of HSV-1 positive subjects also had HSV-2 antibodies. In contrast, only 4.7% of HSV-1 negative subjects were HSV-2 positive.

Of 51 subjects with prior history of STDs, 43 (84.3%, 95% CI: 71.4, 93.0) were positive for anti-HSV-1 and 21 for anti-HSV-2 (41.2%, 95% CI: 27.6; 55.8). These seroprevalence rates are significantly higher than those of 70.1% (95% CI: 67.2; 72.9) for anti-HSV-1 (p = 0.03) and 11.1% (95% CI: 9.2; 13.1) for anti-HSV-2 (p<0.001) found in 1,037 subjects with no prior history of STDs.

Table 3. Seroprevalence of HSV-2 antibodies in the sample studied by gender and age. Brazil, 1996–1997. (N = 1090)

Age (years)	Gender				Total HSV-2 positive	
	Males HSV-2 positive		Females HSV-2 positive			
	% (95% CI)	Total (n/N)	% (95% CI)	Total (n/N)	% (95% CI)	Total (n/N)
1-5	3.9 (0.5;13.2)	2/52	0 (0;7.5)	0/47	2.0 (0.2;7.1)	2/99
6-10	2.0 (0.1;10.8)	1/49	0 (0;7.1)	0/50	1.0 (0;5.5)	1/99
11-12	5.8 (1.2;15.9)	3/52	0 (0;7.0)	0/51	2.9 (0.6;8.3)	3/103
13-14	0 (0;7.2)	0/49	2.0 (0.1;10.6)	1/50	1.0 (0;5.5)	1/99
15-16	3.8 (0.5;13.0)	2/53	9.1 (3.0;20.0)	5/55	6.5 (2.6;12.9)	7/108
17-18	4.7 (0.6;15.8)	2/43	10.6 (3.5;23.1)	5/47	7.8 (3.2;15.4)	7/90
19-20	10.6 (3.6;23.1)	5/47	21.2 (11.1;34.7)	11/52	16.2 (9.5;24.9)	16/99
21-22	27.3 (10.7;50.2)	6/22	25.8 (11.9;44.6)	8/31	26.4 (15.3;40.3)	14/53
23-24	31.0 (15.3;50.8)	9/29	18.2 (7.0;35.5)	6/33	24.2 (14.2;36.7)	15/62
25-29	26.7 (14.6;42.0)	12/45	21.6 (11.3;35.3)	11/51	24.0 (15.8;33.7)	23/96
30-34	30.2 (17.2;46.1)	13/43	33.3 (20.8;47.9)	17/51	31.9 (22.7;42.3)	30/94
35-40	17.4 (7.8;31.4)	8/46	21.4 (10.3;36.8)	9/42	19.3 (11.7;29.1)	17/88
Total	11.9 (9.3;15.0)	63/530	13.0 (10.4;16.1)	73/560	12.5 (10.6;14.6)	136/1,090
Age-corrected total	11.2 (8.7;13.8)		11.3 (8.9;13.6)		11.3 (9.5;13.0)	p=0.82[a]

N = total number of subjects
n = total number of seropositive subjects
[a] Cochran Mantel Haenszel test – association between gender and age adjusted for HSV2-positive subjects

Of the eight subjects who had prior clinical history of genital herpes, three were positive for anti-HSV-1 and anti-HSV-2, four were positive for anti-HSV-1 only and one was negative for HSV-1 and HSV-2.

The seroprevalence of HSV-1 in the four geographic regions was, after adjusting for age and gender, 73.3% (95% CI: 62.6; 84.9) in Manaus, 68.6% (95% CI: 65.3; 71.8) in Rio de Janeiro, 62.1% (95% CI: 50.8; 73.5) in Porto Alegre and 47.0% (95% CI: 38.9; 55.0) in Fortaleza (p = 0.0001). Regarding HSV-2 the seroprevalence was 16.8% (95% CI: 10.9; 25.3) in Manaus, 14.6% in Rio de Janeiro (95% CI: 12.6; 17, 2), 5.9% in Porto Alegre (95% CI: 1.4; 12.7) and 3.3% (95% CI: 0.7; 9.4) in Fortaleza (p = 0.004).

There were no significant differences between the two socioeconomic groups regarding the seroprevalence of anti-HSV-1 (p=0.26) or anti-HSV-2 (p=0.27). Among those with low socioeconomic condition, 72.6% (95% CI: 68.4; 76.6) were HSV-1 positive and 11.2% (95% CI: 8.5; 14.3) were HSV-2 positive; among those in the middle/high class, 69.3% (95% CI: 65.5; 73) and 13.5% (95% CI: 10.9; 16.4) were HSV-1 and HSV-2 positive, respectively. However, subjects of the low socioeconomic stratum tended to have HSV-1 antibodies at a younger age. At the age of five, 50% of children in the lower socioeconomic class were already HSV-1 positive, while the same infection rate was only seen at the age of 11 among those in the middle/high class. As for HSV-2 there was no effect of socioeconomic class on the prevalence of HSV infection (data not shown).

The logistic regression analysis showed that HSV-1 seroprevalence was significantly associated with age and geographic region, but not with gender, socioeconomic condition, prior history of STDs or HSV-2 antibodies. Subjects with prior history of STDs had a higher prevalence of HSV-2 compared to those without prior history of STDs (OR = 3.2). The risk of HSV-1 infection was highest in Rio de Janeiro, followed by Fortaleza and Manaus, and lowest in Porto Alegre.

Regarding HSV-2, the logistic regression revealed that age, geographic region, prior history of STDs and seropositivity for HSV-1 were significant and independent factors for HSV-2 infection (Figure).

DISCUSSION

The present study identified a prevalence of HSV-1 antibodies of 67.2% with no gender difference but increasing with age. The seroprevalence of HSV-1 is not consistent across Brazil, ranging from 47.0% in Fortaleza to 73.3% in Manaus (North region). There are three other seroepidemiological studies of HSV-1 published in Brazil using a type-specific test. In the 1998 study, Lupi[12] reported an overall prevalence of HSV-1 of 87% in the city of Rio de Janeiro, which is higher than that found in the state of Rio de Janeiro (68.6%) in our study. The only age- and type-specific data available in Brazil are from a study by Cowan [5] who compared the seroprevalence of HSV antibodies with those in India, Morocco, Sri Lanka and Estonia. The ages at which 25% and 50% of Brazilian subjects were anti-HSV-1 positive were similar to those in the present study, but an anti-HSV-1 prevalence of 75% was seen at the age of 15 years in Cowan study and at 24 years in our study. The risk of HSV-1 infection by age group in Brazil was consistent to that described in Estonia and Sri Lanka, but significantly lower compared to that in India and Morocco.

A decrease in the prevalence of HSV-1 antibodies was seen in adolescents in many developing countries. Another recent observation was the relative increase in the rate of primary genital herpes caused by HSV-1.[8]

The overall rate of HSV-2 infection in the present study was 11.3%. Age was the most significant correlation factor for HSV-2 seropositivity in the logistic regression analysis. In those age groups who are sexually active, the seroprevalence of HSV-2 was 30% in adults.

No differences in the seroprevalence of HSV-2 antibodies were seen between men and women (11.2% vs. 11.3%), which is unusual since women typically have higher seroprevalence rates.[11,25] However, female adolescents were more likely to get HSV-2 infection at younger ages compared to males where more than twice as much were HSV-2 positive (10.7% vs. 4.6 % at the age of 18). This difference can be due to partner selection because adolescent girls are likely to have older male partners who are more likely to be infected by HSV-2. The high rate of HSV-2 infection in childbearing women also increases the risk of neonatal herpes.

Direct comparisons of HSV epidemiology in our study with other studies should be made with caution due to differences in the populations studied, age composition, and laboratory methodology. As HSV-1 and HSV-2 are antigenically related, the diagnostic test used is critical to the validity of HSV seroprevalence studies. Most previous studies in Brazil and Latin America were conducted in a single geographic area and recruited volunteers from specific, non-representative populations such as blood donors, pregnant women,[2,23] and high-risk groups.[5,13,19,24] This approach entails the possibility of selection bias and thus only generates data representative of the populations studied.

The seroprevalence of HSV-2 in Brazilian adolescents and young adults in our study is higher than that reported in the recent NHANES study conducted in the U.S. from 1999 to 2004.[25] The prevalence of HSV-2 in specific age groups in both the recent NHANES study from 1999 to 2004 and NHANES III[20] from 1988 to 1994 was 1.6% and 5.8% in 14–19; 10.6% and 17.2% in 20–29; and 22.1% and 27.8% in 30–39, respectively.

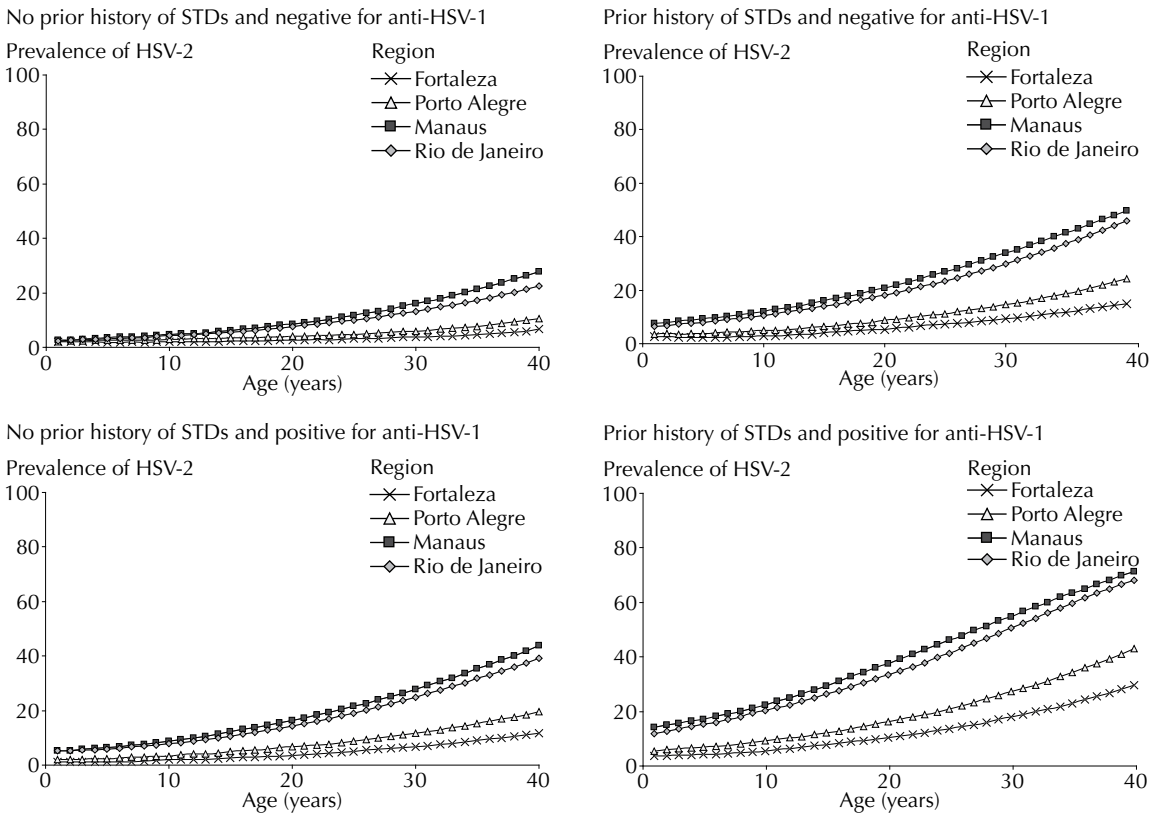

Figure. Seroprevalence of HSV-2 compared to historical data on STDs and HSV-1 serology. Brazil, 1996–1997.

In our study, seroprevalence of anti-HSV-2 was 7.6% in 13–20; 24.6% in 20–29; and 25.8% in 30–40, which are similar to the results of NHANES III.[20]

In Brazil, the seroepidemiology of HSV-2 has been assessed with a type-specific test only in few studies in limited populations, mainly in the states of São Paulo and Rio de Janeiro. Several studies with adolescents, pregnant or not pregnant women, and blood donors found a seroprevalence of anti-HSV-2 ranging between 22.6% and 42%.[5,12,13,19,23] In one study, the control group of a cervical cancer study in São Paulo (N=181) and the Philippines (N=371) showed a prevalence of HSV-2 of 42% in Brazilian women and of only 9.2% in the Philippines.[19] In contrast, the seroprevalence of HSV-2 in our study was 23.8% in same-age women. Another study was conducted in the city of Campinas[2] in three different populations (students, pregnant women, individuals with an STD), and the seroprevalence of anti-HSV-2 was higher in patients with STDs (53.1%) and higher in men than women (63.5% vs. 40.9%, $p<0.05$). In our study, 41.2% of those with a prior STD were HSV-2 positive compared to 11.1% of those without prior history of this disease, which confirms that prior history of STDs increases three to four times the risk of HSV-2 infection.[9]

HSV-2 infection is most often asymptomatic. In the Campinas study, only 4.3% of pregnant women and 21.6% of STD patients who were positive for HSV-2 had a prior clinical history of genital herpes.[2] In our study, the sensitivity of prior clinical history of genital herpes to identify HSV-2 positive individuals was 2.2% in the general population and 14.3% in those with prior history of STDs. Therefore, epidemiological studies of HSV that base their conclusions on prior history of genital herpes may largely underestimate the magnitude of this problem.

There are conflicting results from studies on the risk of HSV-1 positive individuals of acquiring HSV-2.[8] Some studies have reported that HSV-1 positive individuals have a lower risk of concurrent HSV-2 genital infection.[1,15] But a recent prospective study[11] showed that HSV-1 positive individuals were almost equally likely to acquire HSV-2 compared to those HSV-1 negative (OR=0.98). In our study, HSV-1 antibodies were not associated with a lower rate of HSV-2 infection but showed an inverse relationship: 15.7% of HSV-1 positive subjects were also concurrently infected with HSV-2, whereas only 4.7% of HSV-1 negative subjects were co-infected with HSV-2. HSV-1 infections usually occur earlier in life, and therefore one can argue that prior HSV-1 infection does not protect against subsequent HSV-2 infection. However, this should be confirmed in a longitudinal study.

There are some limitations and potential biases in our study. One was the upper age limit of 40 years. Some studies[20,25] have described a small increase in the prevalence of HSV-1 and HSV-2 antibodies beyond this age. Since few individuals with high socioeconomic status were recruited to this study, our investigation was not ideally balanced among low, middle and high socioeconomic class. The multivariate logistic regression analysis ruled out socioeconomic class as an independent risk factor for HSV infection. Another potential selection bias was the pattern of recruitment in Manaus, where most subjects were recruited from outpatient clinics, while recruitment in other geographic areas was better distributed across general and pediatric outpatient clinics, schools, colleges and day care centers, among others. To be able to more accurately identify the age at which HSV-2 seroprevalence increases, some age groups were overrepresented in the sample. To adjust for this imbalance, we applied a statistical correction factor to the results of age-specific seroprevalence.

Given the magnitude of the genital herpes epidemic[15,16,17] and the fact that asymptomatic patients are apparently responsible for most HSV transmissions,[9,11,20] a prophylactic vaccine seems to be the most effective disease control action. The HSV vaccine in the most advanced stage of development uses a recombinant glycoprotein D with an adjuvant. Two clinical studies have demonstrated that this vaccine is highly effective for preventing genital herpes disease in HSV-1 and HSV-2 double-negative women (73% e 74%) whilst also showing a trend to protect against HSV infections (39% e 48%).[10] A prophylactic vaccine against HSV for women only may have a major epidemiological impact because it could reduce also the rate of infection among men.[7] More importantly, the rate of neonatal herpes disease could be reduced by reducing genital herpes caused by HSV-2 in childbearing women.

In conclusion, the results of the present study showed that the prevalence of HSV-2 significantly increases with age when sexual activity starts. Health providers should therefore include in their counseling of adolescents information about HSV and behavourial acquisition risks with the goal to prevent genital herpes infections, and thus also complications such as neonatal herpes or in concomitant HIV-1 infections.

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