Sexually Transmitted Diseases, September 2005, Vol. 32, No. 9, p.534-541
DOI: 10.1097/01.olq.0000175413.89733.ae

The Epidemiology of Herpes Simplex Virus Type 2 Infection in Low-Income Urban Populations in Coastal Peru

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Objective: **The objective of this study was to determine the epidemiology of herpes simplex virus type 2 (HSV-2) in general and socially marginalized populations of low-income, urban, coastal Peru.**

Study: **Two low-income populations were administered an epidemiologic survey and serologic tests, determining risk behavior, HSV-2, and HIV prevalence.**

Results: **In the socially marginalized population, HSV-2 prevalence was 72.3% in men who have sex only with men (MSOM), 42.5% in women, and 20.7% in men. In the general population, HSV-2 prevalence was 20.5% in women and 7.1% in men. In all groups except the male general population, HSV-2 prevalence increased with age or number of sexually active years (both $P < 0.001$). HSV-2 infection was associated with HIV infection in MSOM ($P < 0.023$) and other socially marginalized men ($P < 0.01$).**

Conclusion: **HSV-2 was common in both low-income populations, and control programs are needed in Peru given high prevalence and association with HIV infection. Prevention of HSV-2 infection should target individuals before they become sexually active.**

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HERPES SIMPLEX VIRUS TYPE 2 (HSV-2) is a highly prevalent sexually transmitted infection (STI).[1] The prevalence of HSV-2 infection is increasing in many populations and geographic areas.[2] In Latin America, prevalence ranges from 20% to 40% in the female general population and up to 80% in high-risk populations such as sex workers.[3,4] Programs to control HSV-2 infection are uncommon. Current recommendations to prevent HSV-2 acquisition and transmission in individuals include symptom recognition, consistent condom use, abstinence during symptomatic periods, and recently, the use of suppressive antiviral therapy.[5–8]

HSV-2 infection is the most common cause of genital ulcers[9,10]; however, genital herpes infections are often asymptomatic and therefore remain undetected.[11] The genital lesions facilitate the entrance of infectious agents such as human immunodeficiency virus (HIV).[12] The increased risk of HIV acquisition, however, is not isolated to ulcerative outbreaks but also to episodes of subclinical HSV-2 reactivation.[13] Consequently, determining populations with high HSV-2 prevalence and implementing interventions to reduce the transmission of HSV-2 infection might be an effective population-based strategy to reduce HIV transmission.[14]

Most studies on the prevalence of HSV-2 infection have focused on groups engaged in high-risk sexual behavior, but there is limited data regarding the prevalence in the general population. In Latin America, the rates of HSV-2 infection in high-risk groups, including men who have sex with men, are not well described. In this study, we describe the epidemiology of HSV-2 infection in large two population-based samples of low-income, urban, coastal Peruvians as part of a larger international trial supported by the U.S. National Institute of Mental Health on the prevention of HIV and STIs in Peru.

Methods

Study Design

This was a cross-sectional, population-based study using population-based samples from two distinct populations, one from the

The authors thank the counselors and field staff in Peru, without whom this project would not have been possible, as well as the laboratory staff (Rina Meza, Nilda Gadea, Rosa Castillo, Monica Nieto, Juan Carlos Lara, and Federico Fernandez) at the Naval Medical Research Center Detachment in Lima, and Corey Long.

This study was funded by NIH/NIMH grant U10 MH61536, which is a five-country Cooperative Agreement being conducted in China, India, Peru, Russia, and Zimbabwe. Each site has selected a different venue and population with which to implement the prevention program entitled Community Public Opinion Leader (C-POL) Intervention. This article is based on a prebaseline study conducted in all the sites to prepare for initiation of the intervention. The Steering Committee for this trial is Carlos Caceres, MD, MPH (Peru); David Celentano, ScD (U.S./India); Thomas Coates, PhD (U.S./Peru); Tyler Hartwell, PhD (U.S./RTI); Danuta Kaspck, PhD (U.S./Zimbabwe); Willo Pequegnat (NIMH); Mary Jane Rotheram, PhD (U.S./China); Suniti Solomon, MD (India); Godfrey Woelk, PhD (Zimbabwe); and Zunyou Wu, MD (China).

The views expressed in this article are those of the author and do not necessarily reflect the official policy or position or the Department of the Navy, Department of Defense, or the U.S. Government.

Previously published as an abstract: Klausner JD, Jones FR, Meza R, et al. A NIMH STD/HIV Collaborative Prevention Trial. The epidemiology of genital herpes in low and high-risk populations for HIV infection, Peru, 2001–2002 [Abstract ThPpC2098]. In: Abstracts of the XV International AIDS Conference, Bangkok, Thailand. MedGenMed 2004; 6:ThPpC2098.

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Received for publication October 24, 2004, and accepted February 4, 2005.

general population and a second one from socially marginalized individuals identified using ethnographic methods. All study subjects were recruited between 2000 and 2002 from low-income neighborhoods in three coastal Peruvian cities: Lima, located in central Peru, Chiclayo, and Trujillo located in the north. We collected epidemiologic and serologic data from eligible members in the two study populations.

For the study of the general population, we conducted a census of household residents within 34 neighborhoods representative of low-income neighborhoods in urban, coastal Peru based on their unmet basic needs index, an indicator used internationally to classify economic resources. Households within these neighborhoods were then enumerated, and a probability sample of 75 houses was randomly chosen per neighborhood. To be eligible, participants had to expect to stay in the area for the next 2 years and to be 18 to 30 years of age.

In the second study, we used ethnographic methods to identify socially marginalized individuals engaging in potentially high-risk sexual behavior. The ethnographic methods used included spatial and social mapping, informal interviews, participant observation, in-depth interviews, and focus groups. The first group of socially marginalized men was un- or underemployed young men often engaged in drug use and or petty theft. They often stood on street corners, and in Peruvian street vernacular they are called "*vagos*" (bums) or "*esquineros*" (corner men). Although they identify as heterosexual, some have sex with men for clothes, food, or money. For the analysis, they are referred to as socially marginalized men. The second group of men is self- and community-identified as "homosexual"; these men have sex only with men (MSOM). Many of the MSOM are transvestites or feminized. The socially marginalized women are generally unemployed young women who go against the societal norms for women by hanging out in the street with the socially marginalized men. In Peruvian street vernacular, they are called "*vagitas*" (bums) or "*movidas*" (loose women). For the analysis, they are referred to as socially marginalized women.

Identification and recruitment of individuals took place in specific locations or venues in the neighborhoods, including football fields, volleyball courts, parks, hair salons, and street corners aiming to enumerate at least 150 individuals per neighborhood. Sufficient numbers of socially marginalized individuals were identified only in 20 of the original 34 neighborhoods and six new neighborhoods were added. All new neighborhoods had comparable levels of unmet basic needs as the communities used in the general population study. To be eligible, participants had to expect to stay in the area for the next 2 years, be 18 to 40 years of age, frequent the targeted venue at least three times per week, and report having had sex in the past 6 months. Eligible individuals were enumerated and approximately 50 were randomly selected to participate from each neighborhood.

Human Subjects

The study was approved by the Committee of Human Research of the University of California, San Francisco; University of California, Los Angeles; and Cayetano Heredia University, Peru. Additionally, the study protocol was approved by the Naval Medical Research Center Institutional Review Board in compliance with all Federal regulations governing the protection of human subjects. Data were collected from all eligible participants who gave their written informed consent to participate in the study.

Data Collection

In both studies, participants were invited to a temporary project office in their neighborhood and privately administered a structured 30-minute questionnaire in Spanish. Audio computer-assisted self-interviewing (ACASI) was used in the general population. Computer-assisted personal interview (CAPI) was used in the socially marginalized population. With ACASI, participants listened to the questions and entered their responses into the computer with staff present to answer questions. In CAPI, trained project staff read the questions to the participants and also entered their answers into the computer. A different questionnaire was used for each study. The questionnaire was changed between studies to improve participant recall by focusing on more recent sexual risk behavior. Both questionnaires collected information regarding sociodemographics, sexual history, and sexual risk behavior, although some variables were collected only in the first or second survey. No definition of sex was given in the survey; therefore, "sex" was participant defined.

After completing the survey, participants went through pretest counseling for STIs, including HIV infection with a trained counselor, and then a trained phlebotomist took a blood sample. Interview data and the serologic samples were linked only to the participants' 10-digit code assigned by the project; no personal identifiers were attached. When participants returned for their results, they went through a posttest counseling session to make certain that they understood the meaning of both positive and negative test results. If any test result was positive, the participant obtained appropriate referral(s) for care and were encouraged to share results with recent sex partners. Additionally, the date of birth and initials of those individuals identified as HIV-positive were reported to the Peruvian Ministry of Health. Participants received compensation for their time and transportation; 15 Peruvian Soles (approximately $4) was given at the first visit and 10 Peruvian Soles (approximately $3) when they came back for their test results.

Laboratory Methods

Blood specimens were transported to the U.S. Naval Medical Research Center Detachment (NMRCD) in Lima for testing. HSV-2 antibody status was determined by type-specific enzyme immunoassay (EIA) (HerpeSelect; Focus Technologies, Cypress, CA) using the manufacturer's suggested cutoff index ratio of 1.10. HIV antibody status was determined using two enzyme immunoassays (Biomerieux and Biorad) and confirmed with Western Blot (Biorad).

Data Analysis

The primary outcome was HSV-2 infection, analyzed as a binomial variable. The study populations were categorized into five study groups: general population males, general population females, socially marginalized males, socially marginalized females, and MSOM. Except when noted, comparisons were made within each study group. Six covariates collected both in the first and second survey were analyzed: age, marital status, education, number of sex partners in the past 3 months, any unprotected sex with primary sex partners, and unprotected sex with nonprimary sex partners. Additionally, from the first survey, we analyzed the variables number of lifetime partners and same-sex behavior in men, and from the second survey, the number of sexually active years. Primary partners include both spouses and live-in partners. Individuals with missing data were excluded only from the affected analysis. Continuous variables were categorized in quartiles with the upper 5% separated for descriptive purposes. In the multivariate analysis, categories were aggregated post hoc if they did not explain a significant amount of the variation. The bivariate analysis used contingency tables and chi-squared tests to deter-

mine the association between the prevalence of HSV-2 infection and covariates.

Multivariate analysis of HSV-2 prevalence was conducted with a logarithmic binary regression implemented using binomial-family generalized linear models with a logarithmic link function.[15] Logarithmic binary regression directly calculates a ratio of prevalences (log [prev1/prev2]) instead of calculating a ratio of odds (log [odds1/odds2]). Odds ratios can overestimate risk when the prevalence is high; and we opted to use prevalence ratios and not the traditional odds ratios to avoid magnification of the associations in HSV-2 prevalence. Prevalence ratios are not interpretable as risk ratios without certain assumptions, which we cannot fulfill in a cross-sectional study; however, they describe more accurately the differences in disease frequency within a cross-sectional study. Likelihood ratio tests were used to determine the statistical significance of each variable. Age and number of sexually active years were found to be collinear and were not used simultaneously in the same regression model. We used Stata 8.0 (Stata Corp., College Station, TX) for the statistical analysis. All confidence intervals were calculated at the 95% level.

Results

We identified 2,271 eligible individuals from the general population and 1,645 (72%) participated, of whom 1,635 (99.4%) provided a blood sample. From the socially marginalized population, 1,347 individuals were identified and 1,205 (89%) participated, of whom 1,193 (99.1%) provided a blood sample.

Participant Characteristics

The five groups differed significantly for all variables shown in Table 1 ($P < 0.001$). The mean age (± standard deviation) was 26.7 ± 5.2 for MSOM, 22.5 ± 4.2 for the socially marginalized men, and 25.4 ± 5.7 for the socially marginalized women. In the general population, the mean age of the women was 23.6 ± 3.7 and 22.3 ± 3.5 in the men.

Table 1 shows the risk behavior differences by study group. All five study groups differed significantly ($P < 0.001$) in pairwise comparisons for unprotected sex with a nonprimary partner in the past 3 months and number of sexual partners in the past 3 months. For unprotected sex in the past 3 months, all groups differed significantly (all P values < 0.001) except socially marginalized men and MSOM in which the difference was only borderline significant ($P = 0.076$). The number of lifetime sexual partners was assessed only in the general population and was higher in males than in females ($P < 0.001$). The number of sexually active years was assessed only in the socially marginalized population and differed significantly between all three socially marginalized groups (all P values < 0.001).

Herpes Simplex Virus Type 2 Infection Prevalence

The prevalence of HSV-2 infection varied significantly ($P < 0.001$) among all five groups, except between women in the general population and socially marginalized men ($P = 0.845$). Males in the general population had the lowest HSV-2 prevalence at 7.1% (95% confidence interval [CI], 5.3–9.3%) followed by 20.5% (CI, 17.9–23.2%) for females in the general population and 20.7% in socially marginalized males (CI, 18.1–23.4%). Women in the socially marginalized group had the next highest prevalence 42.5% (CI, 33.5–52.9%) and the highest HSV-2 prevalence was found in the MSOM 72.3% (CI, 64.8–78.9%). Compared with the male general population, the prevalence ratio (PR) of HSV-2 infection in the female general population was 2.88 (CI, 2.13–3.89); 2.90 in the socially marginalized men (CI, 2.15–3.94); 5.99 in the socially marginalized women (CI, 4.21–8.52); and 10.17 in the MSOM (CI, 7.62–13.63).

HIV Infection Prevalence

The HIV prevalence in the MSOM was 9.7% (95% CI, 5.6–15.2%), a rate significantly higher compared with each of the remaining four groups (all P values < 0.001). The prevalence in the other four groups was comparable ($P = 0.238$ – $P = 0.961$, pairwise comparison). HIV prevalence in the female general population was 0.2% (95% CI, 0.0–0.7%) and 0.0% in the male general population (95% CI, 0.0–0.1%). HIV prevalence in socially marginalized women was 0.0% (95% CI, 0.0–3.8%) and 0.2% in socially marginalized men (95% CI, 0.0–0.7%).

Bivariate Analysis

The prevalence of HSV-2 infection by select demographic and behavioral characteristics as well as a bivariate analysis of HSV-2 infection per group are shown in Table 2. HSV-2 infection was associated with unprotected sex in the past 3 months in all groups except females in the socially marginalized population and MSOM. HSV-2 infection was associated with HIV infection in both MSOM (PR = 1.34; CI, 1.13–1.57) and in socially marginalized men (PR = 5.11; CI, 4.50–5.80).

Multivariate Analysis

Table 3 presents the results of separate multivariate analysis for each of the five study groups. Only variables that were independently significant in the multivariate model are presented in the table. In all five groups, HSV-2 prevalence was associated with age or a lifetime measure of sexual risk behavior such as lifetime partners, number of sexually active years, or lifetime same-sex sexual behavior. Variables describing recent sexual behavior were not associated to HSV-2 infection in all groups except for males in the general population.

Age and Herpes Simplex Virus Type 2 Infection

The prevalence of HSV-2 infection increased with age in each subgroup except the male general population. Figure 1 shows the change in HSV-2 prevalence by age for each study population. In the 18- to 20-year-old age range, the prevalence of HSV-2 infection ranged from 4.8% in the general population males to 16.1% to 53.8% in all other groups. The average age of sexual debut in the socially marginalized men was 15.4 ± 2.1 years, 16.3 ± 2.5 years in the socially marginalized women, and 13.7 ± 2.9 years in the MSOM; this data were only collected in the socially marginalized population.

Discussion

This study demonstrates high prevalence of HSV-2 infection across all study subgroups in low-income populations of urban, coastal Peru, except the general population males. High prevalence of HSV-2 infection was not limited to the three socially marginalized groups but was also present in the general population females. Among all high-prevalence groups, HSV-2 prevalence was 16% or greater in 18 to 20 year olds and risk increased with additional years of sexual activity or age. These findings indicate the need for prevention and control programs to address both the burden of HSV-2 disease and the increased chance of HIV acquisition among HSV-2-infected individuals.[16] Such programs should start before the onset of sexual activity and continue throughout one's sexually active life.[17]

TABLE 1. Characteristics of Survey Participants From Low-Income Neighborhoods in Three Coastal Peruvian Cities, 2000–2002

	General Population				Socially Marginalized Population					
	Males (N = 670)		Females (N = 965)		Males (n = 919)		Females (N = 108)		MSOM (N = 167)	
Variables*	No.	%	No.	%	No.	%	No.	%	No.	%
Demographics										
Age (y)										
18–20	253	37.8	250	25.9	367	39.9	27	25.0	26	15.6
21–23	183	27.3	232	24.0	263	28.6	23	21.3	17	10.2
24–26	130	19.4	226	23.4	138	15.0	16	14.8	41	24.6
27–30	104	15.5	257	26.7	96	10.4	19	17.6	45	26.9
31+	—	—	—	—	55	6.0	24	21.3	37	22.7
Relationship status										
Single	516	77.0	459	47.5	636	69.2	31	28.7	149	89.8
Previously married	22	3.3	53	5.5	56	6.1	15	13.9	5	3.0
Primary partner	132	19.7	452	48.9	227	19.7	62	57.4	12	7.2
High school education										
No	135	20.2	242	25.1	491	53.4	66	61.1	60	35.9
Yes	534	79.8	721	74.9	428	46.6	42	38.9	107	64.1
Drug use‡										
No	608	91.8	957	97.0	822	89.5	109	100.0	161	99.4
Yes	54	8.2	6	0.6	97	10.6	0	0.0	5	3.0
Employment status										
Stable work	—	—	—	—	183	19.9	16	14.7	70	42.2
Occasional work	—	—	—	—	550	59.9	46	42.2	54	32.5
Support of family/friends	—	—	—	—	186	20.2	47	43.1	42	25.3
Sexual risk behaviors†										
No. of partners in the last 3 mo										
0	329	51.1	407	43.3	85	9.3	6	5.7	7	4.2
1	226	35.1	493	52.5	464	50.5	80	75.5	46	27.5
2–3	78	12.1	32	3.4	280	30.5	15	14.2	54	32.3
4+	11	1.7	7	0.8	89	9.7	5	4.6	60	35.9
Had unprotected sex in the last 3 mo										
No	468	71.9	536	56.9	215	23.5	11	10.3	50	29.9
Yes	183	28.1	413	43.1	699	76.5	96	89.7	117	70.1
Had unprotected sex with nonprimary partner(s) in the last 3 mo										
No	619	95.8	938	98.7	620	67.8	90	84.1	86	51.5
Yes	27	4.2	12	1.3	294	32.2	17	15.9	81	48.5
Same-sex behavior during lifetime										
No	560	88.5	—	—	—	—	—	—	—	—
Yes	73	11.5	—	—	—	—	—	—	—	—
No. of sex partners during lifetime										
0	95	15.1	148	15.9	—	—	—	—	—	—
1	114	18.2	411	44.1	—	—	—	—	—	—
2	103	16.4	194	20.8	—	—	—	—	—	—
3–9	254	40.5	161	17.2	—	—	—	—	—	—
10+	62	9.8	19	2.0	—	—	—	—	—	—
Sexually active years										
≤4	—	—	—	—	309	33.7	35	32.4	7	4.2
5–7	—	—	—	—	254	27.6	13	12.0	25	15.0
8–11	—	—	—	—	192	20.9	24	22.2	39	23.4
12–18	—	—	—	—	140	15.2	30	27.8	66	39.5
19+	—	—	—	—	24	2.6	6	5.6	30	17.9
HIV										
Negative	670	100.0	963	99.8	917	99.8	108	100.0	151	90.4
Positive	0	0.0	2	0.2	2	0.2	0	0.0	16	9.6

*Some variables have different counts as a result of missing data.
†Sex was participant-defined.
‡For the general population during the last 3 months. For the socially marginalized population, the last month.
MSOM indicates men who have sex only with men.

TABLE 2. Prevalence of Herpes Simplex Virus Type 2 (HSV-2) Infection by Select Characteristic in Survey Participants From Low-Income Neighborhoods in Three Coastal Peruvian Cities, 2000–2002

	General Population				Socially Marginalized Population					
	Males (N = 670)		Females (N = 965)		Males (n = 919)		Females (N = 108)		MSOM† (N = 167)	
Variables	no./No.	HSV-2 Prevalence (%)	no./No.	HSV-2 Prevalence (%)	no./No.	HSV-2 Prevalence (%)	no./No.	HSV-2 Prevalence (%)	no./No.	HSV-2 Prevalence (%)
HSV-2 infection	47/670	7.0	196/965	20.0	190/919	20.7	46/108	42.6	121/167	72.5
Demographics										
Age (y)										
18–20	12/253	4.8	42/250	16.8	59/367	16.1	6/27	22.2	14/26	53.8
21–23	21/183	11.5	32/232	13.8	38/263	14.4	8/23	34.8	8/17	47.1
24–26	10/130	7.7	49/226	21.7	37/138	26.8	8/16	50.0	31/41	75.6
27–30	4/104	3.8	73/257	28.4†	30/96	31.3	6/19	31.6	34/45	75.6
31+	—	—	—	—	26/55	47.3†	10/24	79.2†	34/37	89.2†
Relationship status										
Single	36/516	7.0	65/459	14.2	97/636	15.3	10/31	32.3	108/149	72.5
Previously married	0/22	0.0	16/53	30.2	25/56	44.6	10/15	66.7	3/5	60.0
Primary partner	11/132	8.3	115/452	25.4‡	68/227	30.0‡	26/62	42.9	10/12	81.8
High school education										
No	16/135	11.9	75/242	31.0	118/491	24.0	31/66	47.0	42/60	70.0
Yes	31/534	5.8*	121/721	16.8†	72/428	16.8†	15/42	37.2	79/107	73.6
Sexual risk behaviors										
No. of partners in the last 3 mo										
0	13/329	4.0	67/407	16.5	17/85	20.0	1/6	16.7	5/7	71.4
1	18/226	8.0	110/493	22.3	90/464	19.4	31/80	39.5	31/46	66.7
2–3	10/78	12.8	9/32	28.1	63/280	22.5	8/15	53.3	38/54	70.4
4+	2/11	18.2†	3/7	42.9*	20/89	22.5	5/5	100.0*	47/60	78.3
Unprotected sex in the last 3 mo										
No	26/468	5.6	96/536	17.6	34/215	15.8	4/11	36.4	34/50	68.0
Yes	19/183	10.4*	97/413	23.5*	154/699	22.0*	42/96	44.3	87/117	74.1
Unprotected sex with nonprimary partner(s) in the last 3 mo										
No	39/619	6.3	187/938	19.9	130/620	21.0	38/90	42.9	57/86	65.9
Yes	6/27	22.2†	2/12	16.7	58/294	19.7	8/17	47.1	64/81	79.0
Same-sex behavior during lifetime										
No	26/560	4.6	—	—	—	—	—	—	—	—
Yes	15/73	20.5‡	—	—	—	—	—	—	—	—
No. of sex partners during lifetime										
0	1/95	1.1	10/148	6.8	—	—	—	—	—	—
1	4/114	3.5	78/411	19.0	—	—	—	—	—	—
2	5/103	4.9	52/194	26.8	—	—	—	—	—	—
3–9	24/254	9.4	43/161	26.7	—	—	—	—	—	—
10+	10/62	16.1†	4/19	21.1†	—	—	—	—	—	—
No. of sexually active years										
<4	—	—	—	—	44/309	14.2	4/35	11.4	1/7	14.3
5–7	—	—	—	—	36/254	14.2	6/13	46.2	15/25	60.0
8–11	—	—	—	—	42/192	21.9	10/24	41.7	27/39	69.2
12–18	—	—	—	—	55/140	39.3	22/30	74.2	53/66	80.0
19+	—	—	—	—	13/24	54.2†	4/6	66.7†	25/30	83.3†
HIV										
Negative	47/670	7.0	195/963	20.3	188/917	20.5	46/108	42.3	106/151	70.2
Positive	0/0	—	1/2	50.0	2/2	100.0†	0/0	—	15/16	93.8*

*P <0.05, †P <0.01, ‡P <0.001 chi-squared tests/chi-squared test for trends was used for age; no. of partners in the last 3 mo; no. of sex partners during lifetime; and no. of sexually active years.
†MSOM indicates men who have sex only with men.

TABLE 3. Factors Associated With Herpes Simplex Virus Type 2 Infection by Select Characteristics of Survey Participants From Low-Income Neighborhoods in Three Coastal Peruvian Cities, 2000–2002

	P Value*	*P* Value*	Adjusted PR	95% CI	*P* Value*
Male general population					
Any unprotected sex with nonprimary partner in the last 3 mo		0.009			0.024
No	Ref		Ref	—	
Yes	3.53		3.12	1.45–6.73	
Any same sex behavior during lifetime		0.000			0.000
No	Ref		Ref	—	
Yes	4.43		3.88	2.14–7.04	
Female general population					
Age (y)†	1.08	0.000	1.06	1.02–1.10	0.000
High school education		0.000			0.000
No	Ref		Ref	—	
Yes	0.54		0.57	0.45–0.74	
No. of sex partners during lifetime		0.000			0.000
0	Ref		Ref	—	
1+	3.34		2.67	1.43–5.00	
Socially marginalized males					
Relationship status		0.000			0.000
Single	Ref		Ref	—	
Previously married	2.93		2.25	1.59–3.20	
Has a primary partner	1.96		1.53	1.15–2.05	
No. of sexually active years		0.000			0.000
0–8	Ref		Ref	—	
9–12	1.81		1.61	1.17–2.22	
13–17	2.38		1.87	1.34–2.62	
18+	3.57		2.64	1.78–3.93	
Socially marginalized females					
No. of sexually active years		0.000			0.000
0–8	Ref		Ref	—	
9–12	2.63		3.09	1.53–6.25	
13–17	3.21		3.74	1.90–7.33	
18+	3.53		4.12	2.13–7.97	
MSOM					
Age (y)		0.000			0.000
18–23	Ref		Ref	—	
24–30	1.48		1.42	1.05–1.92	
31+	1.75		1.73	1.29–2.33	
HIV		0.023			0.052
Negative	Ref		Ref	—	
Positive	1.34		1.27	1.15–1.41	

*All *P* values were calculated using likelihood ratio tests.
†Age as a continuous variable.
PR indicates prevalence ratio; CI = confidence interval; MSOM = men who have sex only with men.

Currently, most STI prevention and control programs in the developing world target high-risk groups such as men who have sex with men, sex workers, or intravenous drug users. Our study demonstrates the value of using ethnographic techniques to identify groups with high frequency of sexual risk behaviors outside of traditional high-risk groups.[18] The populations identified in our study are camouflaged within the general population and often are not reached by conventional STI interventions. The identification of new high-risk core groups could open new avenues for both interventions and research,[19] and potentially lead to the further identification of bridging populations.

Measures of recent sexual behavior were associated with HSV-2 prevalence in all groups during the bivariate analysis, but only in one group after multivariate adjustment. Conversely, measures of lifetime sexual behavior were highly associated with HSV-2 prevalence across the all study groups both before and after multivariate regression. HSV-2 is an incurable, chronic infection; therefore, lifetime measures of sexual behavior more accurately represent one's risk of exposure. These results highlight the importance of measuring the duration of sexual risk behaviors and not solely their occurrence.

Our results suggest that HSV-2 infection is strongly associated with male same-sex sexual behavior. A history of lifetime same-sex sexual behavior was associated with a fivefold increase in HSV-2 prevalence in the general population men. The socially marginalized men, a group with frequent same-sex sexual behavior according to our ethnographic assessment, also presented high rates of HSV-2 infection. Finally, MSOM had the highest prevalence of HSV-2 infection. HSV-2 infection is associated with the acquisition of HIV infection, and in Peru, HIV is primarily concentrated in men who have sex with men (MSM).[20,21] Therefore, HSV-2 control efforts aimed to prevent HIV infection should focus on all males with same-sex sexual behavior and not only on MSOM, because all MSM are at potential risk for HIV infection.

In the general population, women's increased risk of HSV-2 infection cannot be explained solely by their sexual risk behavior. Almost all of women's unprotected sex occurs with their primary

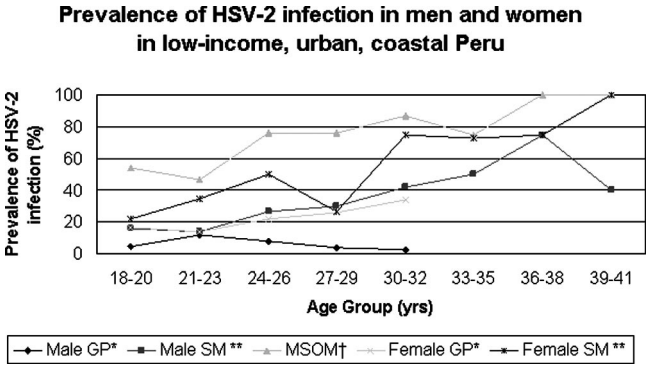

Fig. 1. Herpes simplex virus type 2 antibody status by age in years among persons in low-income neighborhoods in three coastal Peruvian cities, 2000–2002. *GP = general population; **SM = socially marginalized population; †MSOM = men who have sex only with men.

partner and only 3% with nonprimary partners (1.3 of 41.8). However, women reporting only one lifetime partner already have an HSV-2 prevalence of 19%. Although this finding could be affected by underreporting, it is more likely that this increased risk results from the behavior and sexual network of women's primary partners. Men in both the general and socially marginalized populations have higher number of partners as well as more frequent unprotected sex with nonprimary partners in addition to some same-sex sexual behavior. The partners' sexual network and their behavior are probably the main factors influencing women's HSV-2 prevalence and possibly their risk for other STIs.

Our results should be interpreted considering two aspects of the methodology that varied between the surveys of the general and socially marginalized population. First, we used different interviewing techniques, ACASI and CAPI. The literature suggests that participant reporting of sensitive behaviors is higher in ACASI,[22,23] indicating that the risk among the socially marginalized population could be higher than reported. Second, sex in the past 6 months was an inclusion criterion in the socially marginalized population, whereas recent sexual activity was not required for general population participants. This inclusion criterion selected individuals with increased higher sexual activity, although did not explain the increased HSV-2 prevalence of socially marginalized populations. Among those who had sex in the past 3 months from both populations, the rate of HSV-2 infection and sexual risk behavior remained statistically increased in the socially marginalized population compared with the general population (data not shown).

Our results could be affected by false-positive HSV-2 tests. Eleven individuals tested positive despite reporting never having had sex, results consistent with findings reported by Detels et al.[24] All 11 individuals were from the general population, one male and 10 female. Given the HSV-2 prevalence in these two groups and the corresponding positive predictive value of the test, we would have expected a different male to female ratio if the apparent inconsistencies were the result of false-positives. Therefore, it is more likely that some of these apparent false-positives actually have had sexual experience. The sensitive nature of questions regarding sexual activity as well because sex being participant-defined could lead to underreporting of sexual behavior. HSV-2 infection can be transmitted even through oral sex and close skin-to-skin contact (frottage), sexual acts that could be excluded from the participants' definition of sex. These possible sources of misclassification could result in weaker associations between risk measures and disease outcomes. However, these potential biases are not likely to affect our conclusions, because our results show strong associations that remain significant even after multivariate analysis.

In summary, this large, population-based study yielded valid and valuable description of the epidemiology of HSV-2 infection in low-income, urban populations in coastal Peru. There was a high prevalence of HSV-2 infection in socially marginalized groups and the female general population. Currently, there are few HSV-2 prevention and control programs, especially in the developing world. Interventions should involve both increasing awareness of the risks associated with HSV-2 infection as well as effective measures to decrease the likelihood of transmission such as the use of condoms,[25] symptom recognition, and abstinence during symptoms for individuals already infected with HSV-2. Recently, the use of valacyclovir to decrease the infectiousness and thereby the transmission of HSV-2 has been described and approved by the U.S. Food and Drug Administration.[8,26] Vaccine trials are currently underway to test the effectiveness of a vaccine to prevent HSV-2 infection. Such interventions are needed both to prevent HSV-2 infection, preferably before their onset of sexual activity, as well as to prevent further transmission throughout sexually active life. These programs may help reduce the transmission of HSV-2 and consequently decrease susceptibility to other STIs, including HIV.[27,28] The implementation of prevention and control programs for HSV-2 infection is urgently needed.

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