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HERPES SIMPLEX VIRUS TYPE 2 SEROPOSITIVITY AMONG EVER MARRIED WOMEN IN SOUTH AND NORTH VIETNAM: A POPULATION-BASED STUDY

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Abstract

Objective—To investigate herpes simplex virus type–2 (HSV-2) seropositivity and associated risk factors in Vietnamese women.

Methods—Cross-sectional study with personal interviews and gynecological examinations among population-based samples of ever married women, aged 15–69 years, living in Ho Chi Minh City (HCMC) and Hanoi in 1997. Type-specific IgG antibodies against HSV-2 were detected using HerpeSelect ELISA (Focus Diagnostics). Adjusted prevalence ratios were estimated with log-binomial regression.

Results—HSV-2 seroprevalence was higher in 1,106 women from HCMC (30.8%, 95% CI: 28.1–33.4, age-standardized to 2000 world standard population) than in 1,170 women from Hanoi (8.8%, 95% CI: 7.1–10.5). In HCMC, HSV-2 seroprevalence was higher for women who were not married, HPV DNA positive, current hormonal contraceptive users, or had a history of multiple sexual partners or spontaneous abortion. HCMC seroprevalence was inversely associated with educational attainment, age at first intercourse, and age at first pregnancy. In the multivariable model for HCMC, a trend of increasing HSV-2 seroprevalence with age was observed, and prevalence ratios were nearly identical to age-adjusted prevalence ratios for marital status, age at first pregnancy, and HPV DNA positivity.

Conclusion—HSV-2 was notably less prevalent in Hanoi than HCMC, where it was associated with traditional HSV-2 risk factors. These results are likely explained by socio-cultural, historical, economic, and demographic factors related to urban-rural and regional differences. Future population-based studies should include men and never-married women as a next step toward obtaining a more nearly complete picture of HSV-2 epidemiology in Vietnam.

Keywords

herpes simplex virus 2; risk factor; Vietnam; epidemiology; human papillomavirus

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INTRODUCTION

Herpes simplex virus type–2 (HSV-2) infection, one of the most common sexually transmitted infections (STIs) worldwide[1], is the main cause of genital ulcers and may increase susceptibility to human immunodeficiency virus (HIV)[2,3,4]. Since most HSV-2 infections are asymptomatic, seroprevalence data provide a better measure of the burden of genital herpetic disease than clinical data[5,6]. We analyzed data collected by the International Agency for Research on Cancer (IARC), the National Cancer Institute in Hanoi, and the Hung Vuong Obstetric and Gynecology Hospital in Ho Chi Minh City (HCMC), Vietnam, as part of a multicentric population-based study of sexually transmitted infection prevalence[7].

MATERIAL AND METHODS

Study population and enrollment

This cross-sectional study recruited married women registered with family planning clinics in an urban area in HCMC (April–October 1997) and a peri-urban district in Hanoi (April-May 1997)[8,9]. The HCMC sample was drawn from three communes randomly chosen out of the 15 that constitute HCMC District 10. The Hanoi sample was drawn from four randomly selected communes of the 26 communes in Soc Son. In each location (HCMC, Hanoi), 120 women ages 15 years and older were randomly selected within each of eleven age groups. Health workers visited each woman at her home to check exclusion criteria (pregnancy, history of hysterectomy or conization, mental impairment), explain study aims, and obtain written informed consent. Overall, 1,122 in HCMC (87.7% of 1,279 contacted) and 1,246 women in Hanoi (94.4% of 1,320 contacted) came to the commune health centre for a structured interview and gynecological examination, including a 10-ml blood sample and Pap smear. All protocols were approved by the Ministry of Health Board of Vietnam and the Ethical Committee of the IARC, Lyon, France.

Specimen processing and laboratory techniques

Specimens were shipped daily to central laboratories in each study site for processing and storage. Blood samples were centrifuged at 1,500 g. The plasma was placed in Nunc tubes and frozen at –20° for shipment to Lyon for storage. IgG antibodies against HSV-2 were detected from plasma samples using Focus Diagnostics/MRL type specific HSV-2 ELISA assays in a central laboratory in Seattle, Washington. A formal validation study for HSV-2 was conducted in each site by retesting 100 samples with the Western blot, the gold standard test for type-specific HSV serology[8,10]. Index values of <0.9 were classified as negative, those >1.1 as positive, and others as equivocal, according to manufacturer's instructions. HPV DNA testing was performed on cervical exfoliated cells with a general primer-mediated GP5+/6+-PCR, and PCR positivity was assessed by using two HPV oligoprobe cocktails to detect 36 individual HPV types[8,11].

Statistical analysis

Crude and age-standardized (2000 world standard population[12]) HSV-2 seroprevalence and 95% confidence intervals (CIs) were calculated separately for each study area. Age-adjusted (aaPR) and multiply-adjusted prevalence ratios for HSV-2 seropositivity and CIs were calculated by log-binomial regression, with and without controlling for variables significant in the age-adjusted analysis in either HCMC or Hanoi.

RESULTS

After we excluded women without HSV-2 serostatus data (16 HCMC, 76 Hanoi), data from 1,106 women from HCMC and 1,170 women from Hanoi were analyzed. HCMC women had more schooling and were older at first pregnancy (Table I). Fewer HCMC women began coitus before age 19 years. Primary methods of contraception were IUDs (ever used by 55.8% of HCMC women and 43.2% of Hanoi women, not shown) and male condoms (46.7% ever used in HCMC, not shown). Most women reported having had only one sexual partner (93.6% HCMC, 94.6% Hanoi). HPV DNA was found in 9.0% of HCMC women and 1.7% of Hanoi women.

HSV-2 seroprevalence

HSV-2 seropositivity was higher in HCMC (34.4%, 95% CI 31.7–37.3; age-standardized: 30.8%, 95% CI: 28.1–33.4) than in Hanoi (9.2%, 95% CI 7.6–10.9; age-standardized: 8.8%, 95% CI: 7.1–10.5) (Table II). In HCMC, HSV-2 seroprevalence increased monotonically with age, from 15.7% to 51.5% (aaPR 3.3: 2.2–4.8). HSV-2 seropositivity was inversely associated with educational attainment. HSV-2 seroprevalence was higher in divorced women and widows. The corresponding associations in Hanoi were weaker and less consistent.

Menstrual and reproductive factors

Among HCMC women, HSV-2 prevalence was inversely associated with age at first intercourse (aaPR 1.4: 1.1–1.7 for age < 19 years) and age at first pregnancy (aaPR 1.3: 1.1–1.6 for age < 21 years). HSV-2 prevalence was not related to IUD use, but was higher for women who reported current oral contraceptive use (aaPR 1.5: 1.1–2.2). HSV-2 seroprevalence was higher for nulliparous women. Higher crude HSV-2 prevalence among women reporting 5+ pregnancies likely resulted from confounding by age, since the aaPR for parity were not elevated. HSV-2 was slightly higher for HCMC women who reported a spontaneous abortion, though not for those reporting an induced abortion. Again, the corresponding associations for Hanoi were inconsistent or absent.

HSV-2 prevalence was higher among HCMC women reporting more than one lifetime sexual partner but not among their counterparts from Hanoi. Moreover, most HSV-2 infections (209/381 in HCMC, 77/108 in Hanoi) occurred in women who reported that both she and her husband had each had only one sex partner ever. In HCMC, HSV-2 prevalence was higher among HPV DNA positive women (aaPR 1.4: 1.2–1.7); in Hanoi, only one HPV DNA positive woman was HSV-2 seropositive.

In multiple regression models, the age-related rise in HSV-2 prevalence was still present in HCMC. Multiply-adjusted prevalence ratios for HCMC were slightly higher than the aaPRs for marital status, age at first pregnancy, and HPV DNA positivity, but weaker for having had more than one sex partner (Table III).

DISCUSSION

Age standardized HSV-2 seroprevalence in ever-married HCMC (30.8%) was nearly 3.5 times that in Hanoi (8.8%) despite similarly low proportions of women reporting multiple lifetime sexual partners and earlier onset of sexual intercourse in HCMC. Underreporting of sexual partner risk factors is likely for both geographical areas, as most HSV-2 seropositive women reported only one lifetime sex partner. The higher HSV-2 seroprevalence in HCMC was likely not due to false positive tests because all specimens were examined in parallel within the same laboratory.

We believe that the marked difference in HSV-2 seroprevalence between the two samples is related to socio-cultural, historical, economic, and demographic factors including urbanicity and migration[13,14,15]. The HCMC sample came from an urban district, and only 44% reported having been born in HCMC. The Hanoi sample was peri-urban, with most women born in Hanoi. The prevalence of HSV-2 and other STIs tends to be higher in urban areas[6,16], and the urban-rural ratio in HIV seroprevalence among Vietnamese women is about 2:1[17]. Regional differences are also likely. The HSV-2 prevalence differential parallels the differential in invasive cervical cancer incidence (26.0/100,000/year in HCMC, 6.3/100,000 in Hanoi[18,19]), for which HSV-2 may be a cofactor with high-risk HPV infection[20]. Also, HSV-2 seroprevalence in female sex workers is higher in southern provinces (Dong Thap 32.3%, An Giang 33.3% and Kien Giang 29.9%) than in a northern border area (Lai Chau 5.0%)[21]. Such regional differences could reflect South Vietnam's greater mid-20th century wartime exposure to social, economic, and political disruption, internal migration, and U.S. military personnel and contractors.

The age standardized HSV-2 prevalence in Hanoi (8.8%) was similar to that reported for several other Asian populations: 9.2% in Manila[16], below 7% in Japanese women[22,23], and 11% among family planning clients in Dhaka[24] and below the 18% in Hong Kong[25] and 18.7% among females in Indonesia[26] reported by others. The 30.8% in HCMC is higher than these but less than the 41% reported for Jordanian female university students and42.2% among women attending antenatal clinics in Turkey[27].

Our cross-sectional findings for HCMC of a positive association between HSV-2 and age, and of greater HSV-2 prevalence for widows and divorced women than for currently married women are consistent with studies in Brazil[16], Columbia[28], Mexico[29], Peru[28], Spain[28] and the Phillipines[16]. Similarly, the association of HSV-2 with earlier age at first intercourse is consistent with most[6,29] but not all[26] reports. The association with history of multiple sexual partners has been regularly observed[6,29,30]. Higher HSV-2 seroprevalence among users of hormonal contraceptives has been reported for the Philippines[16] but not in several other studies[16,28]. Similarly, our finding of an association between HSV-2 seroprevalence and cervical HPV infection is consistent with previous studies[29,31].

Although the data were collected in 1997, to our knowledge the present study remains the largest population-based study of HSV-2 seroprevalence conducted in Vietnam to date. Nevertheless, the samples of ever-married women in HCMC and Hanoi were not designed to be representative of the larger Vietnamese population, nor to test rural-urban or regional differences. Future studies are needed to provide national and regional seroprevalence estimates and to obtain data on men and never-married women.

In conclusion, we observed a moderately high prevalence of HSV-2 and associations with traditional HSV-2 risk factors in an urban general population sample of ever-married women in HCMC. A similarly-obtained sample of ever-married peri-urban women in Hanoi had relatively low HSV-2 seroprevalence, with few risk factor associations observed. Our findings are similar to those seen for HPV DNA prevalence in the same two geographic sites[8].

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TABLE I

CHARACTERISTICS OF STUDY PARTICIPANTS IN HO CHI MINH CITY AND HANOI, VIETNAM (1997)

	HO CHI MINH CITY (N=1,106) (%)*	HANOI (N=1,170) (%)*	p for Difference†
Age (years, median, range)	41 (16–69)	43 (17–82)	>0.05
<25	16.7	13.1	
25–34	18.7	19.2	
35–44	19.9	19.5	
45–54	18.1	18.0	
55–64	17.5	19.2	
≥65	9.1	11.0	
Education			<0.0001
None	9.0	20.6	
Grade 1–5	31.2	34.4	
Grade 6 or higher	59.8	45.0	
Marital status			> 0.05
Currently married	80.9	82.6	
Divorced	6.5	4.3	
Widowed	12.6	13.1	
Age at first intercourse (years)			<0.001
<19	21.1	34.8	
19–20	25.5	34.6	
≥21†	53.4	30.5	
Age at first pregnancy (years)			<0.001
<21	36.6	45.3	
21–24	32.2	40.3	
≥25	31.2	14.4	
Lifetime number of sexual partners > 1	6.4	5.4	>0.05
HPV DNA detected	9.0	1.7	<0.001

*Denominators for percentages exclude observations with missing values;

†Two-sided.

TABLE II

SEROPREVALENCE OF HSV-2 INFECTION AND AGE-ADJUSTED SEROPREVALENCE RATIOS, BY AGE AND SELECTED CHARACTERISTICS OF PARTICIPANTS IN HO CHI MINH CITY AND HANOI, VIETNAM (1997)

	HO CHI MINH CITY			HANOI		
	N‡	% positive	aaPR§ (95% CI)	N‡	% positive	aaPR§ (95% CI)
Overall	1,106	34.4	(31.7–37.3)	1,170	9.2	(7.6–10.9)
Age-standardized*	1,106	30.8	(28.1–33.4)	1,170	8.8	(7.1–10.5)
Age (years)						
<25†	185	15.7	1.	153	6.5	1.
25–34	207	21.7	1.4 (0.9–2.1)	225	9.8	1.5 (0.7–3.1)
35–44	220	34.1	2.2 (1.5–3.2)	228	9.7	1.5 (0.7–3.0)
45–54	200	42.0	2.7 (1.8–3.9)	211	7.6	1.2 (0.5–2.5)
55–64	193	49.7	3.2 (2.2–4.6)	224	11.2	1.7 (0.8–3.5)
≥65	101	51.5	3.3 (2.2–4.8)	129	10.1	1.5 (0.7–3.4)
Education						
None†	99	50.5	1	241	10.0	1
Up to grade 6	345	42.0	1.0 (0.8–1.2)	403	9.9	1.1 (0.6–2.0)
Grade 6 or higher	661	28.0	0.8 (0.6–1.0)	526	8.4	1.0 (0.5–1.8)
Marital status						
Currently married†	895	29.6	1	966	8.7	1
Divorced	72	45.8	1.3 (1.0–1.7)	50	14.0	1.6 (0.8–3.4)
Widowed	139	59.7	1.5 (1.2–1.8)	153	11.1	1.2 (0.7–2.1)
Age at menarche						
≤16†	823	34.0	1	728	8.7	1
≥17	282	35.5	0.9 (0.7–1.0)	442	10.2	1.1 (0.8–1.6)
Age at first intercourse						
<19	233	39.5	1.4 (1.1–1.7)	407	8.1	0.9 (0.6–1.5)
19–20	282	37.9	1.3 (1.1–1.6)	405	10.6	1.2 (0.8–1.8)
≥21†	591	30.8	1	357	9.0	1

	HO CHI MINH CITY			HANOI		
	N‡	% positive	aaPR§ (95% CI)	N‡	% positive	aaPR§ (95% CI)
Age at first pregnancy						
<21	405	39.5	1.3 (1.1–1.6)	530	10.0	1.3 (0.9–1.9)
21–24	356	32.0	1.1 (0.9–1.4)	472	8.3	0.9 (0.5–1.5)
≥25†	345	31.0	1	168	9.5	1
IUD use						
Never†	628	35.0	1	517	9.1	1
Ever	478	33.7	1.0 (0.8–1.1)	653	9.3	1.1 (0.7–1.7)
Oral contraceptive						
Never†	990	33.7	1	1154	9.3	1
In past only	82	37.8	1.0 (0.8–1.3)	4	0	||
Current use	32	43.8	1.5 (1.1–2.2)	12	8.3	||
Condom use						
Never†	590	30.0	1	1055	9.5	1
Ever	516	39.5	1.1 (0.9–1.3)	115	7.0	0.7 (0.3–1.5)
Parity						
None	33	48.5	1.5 (1.1–2.0)	6	33.3	||
1–2†	518	30.3	1	369	8.9	1
3–4	266	36.1	0.8 (0.6–1.0)	388	9.3	1.0 (0.6–1.6)
≥5	225	44.9	0.8 (0.6–1.0)	377	9.8	1.0 (0.5–1.8)
Spontaneous abortion						
Never†	787	32.4	1	766	9.1	1
Ever	256	44.9	1.1 (1.0–1.4)	373	10.2	1.1 (0.7–1.6)
Induced abortion						
Never†	741	36.6	1	858	10.1	1
≥1	302	32.8	1.0 (0.8–1.2)	282	7.5	0.7(0.4–1.2)
Lifetime number of sexual partners						
1†	1029	33.8	1	1107	9.2	1
>1	70	47.1	1.3 (1.0–1.7)	63	9.5	1.0 (0.5–2.3)
HPV DNA						

	HO CHI MINH CITY			HANOI		
	N‡	% positive	aaPR§ (95% CI)	N‡	% positive	aaPR§ (95% CI)
No†	1006	33.3	1	1089	9.3	1
Yes	99	46.5	1.4 (1.2–1.7)	19	5.3	||

*2000 world standard population;

†Reference category;

‡Number of women with data for HSV-2 and the indicated variable;

§Age-adjusted prevalence ratio from log-binomial regression model;

||Too few cases to estimate reliably.

TABLE III

FACTORS ASSOCIATED WITH HSV-2 PREVALENCE IN HO CHI MINH CITY AND HANOI, VIETNAM (1997)

	HO CHI MINH CITY PR* (95% CI)	HANOI PR* (95% CI)
Age (years)		
<25†	1	1
25–34	1.6 (1.1–2.4)	1.4 (0.7–3.0)
35–44	2.5 (1.7–3.6)	1.5 (0.7–3.2)
45–54	2.8 (2.0, 4.1)	1.0 (0.4–2.3)
55–64	2.9 (2.0–4.1)	1.5 (0.7–3.2)
≥65	2.5 (1.7, 3.7)	1.4 (0.6–3.3)
Marital status		
Currently married†	1	1
Divorced	1.2 (0.9–1.6)	1.6 (0.7–3.5)
Widowed	1.5 (1.2–1.8)	1.1 (0.6–2.0)
Age at first pregnancy		
<21	1.2 (1.0–1.5)	1.3 (0.8–1.9)
21–24	1.2 (0.9–1.4)	0.8 (0.4–1.4)
≥25†	1	1
Lifetime number of sexual partners		
1†	1	1
>1	1.0 (0.8–1.3)	1.0 (0.5–2.2)
HPV DNA		
No†	1	1
Yes	1.4 (1.2–1.7)	0.6 (0.1–3.9)

*Prevalence ratio estimated with log-binomial regression model with all variables listed in the table;

†Reference category.