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## Herpes Simplex Virus Type 2 Risks in Female Sex Workers in the China-vietnam Border County of Hekou

WANG Jun Jie<sup>1</sup>, ZHU Zhi Bin<sup>2</sup>, YANG Xi<sup>2</sup>, WU Jing<sup>1</sup>, WANG Hai Bo<sup>1</sup>, FENG Lin<sup>3</sup>, DING Guo Wei<sup>1</sup>, Jessie L. NORRIS<sup>1</sup>, and WANG Ning<sup>1,#</sup>

<sup>1</sup>National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing 102206, China

<sup>2</sup>Hekou Center for Disease Control and Prevention, Hekou 661300, Yunnan, China

<sup>3</sup>Yunnan Center for Disease Control and Prevention, Kunming 650022, China

### Abstract

**Objective**—To survey the prevalence and risk factors of HSV-2 among Chinese and Vietnamese female sex workers (FSW) in the border county of Hekou, Yunnan Province, China.

**Methods**—A cross-sectional survey was conducted on demographics, sexual behavior, medical history, and drug use among FSWs. Laboratory samples were obtained to test for HSV-2 and other STIs such as HIV, Syphilis, *Trichomonas vaginalis*, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, Bacterial vaginosis, and Yeast infections. Cervicitis and genital warts were also diagnosed.

**Results**—Of the 345 FSWs who participated in this study, 112 (32.5%) were ethnic Chinese and 233 (67.5%) were Vietnamese. Among FSWs in Hekou, the prevalence rates were 58.3% for HSV-2, 5.5% for HIV, and 4.1% for bacterial vaginosis (BV). Age <21 (OR: 0.5; 95% CI: 0.3, 0.8), duration of commercial sex work  $\geq$  3 months (OR: 0.5; 95% CI: 0.3, 0.8), oral and vaginal sex with the last client (as opposed to only vaginal sex) (OR: 1.6; 95% CI: 1.0, 2.7), HIV (OR: 11.4; 95% CI: 1.5, 87.2), and bacterial vaginosis (BV) (OR: 5.6; 95% CI: 1.2, 26.9) were significantly correlated with HSV-2 infection.

**Conclusion**—Multivariate analysis showed that several factors were significantly correlated with the high prevalence of HSV-2 in FSWs in the border area between China and Vietnam. Further studies and interventions are needed for HSV-2 epidemiology in the border area.

### Keywords

China; Vietnam; Female sex workers; HSV-2

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<sup>#</sup>Correspondence should be addressed to: WANG Ning, wangnbj@163.com, Tel: 86-10-58900605 Biographical note of the first author: WANG Jun Jie, male, born in 1974, Ph. D, majoring in AIDS epidemiology. Biographical note of the first author: WANG Jun Jie, male, born in 1974, Ph. D, majoring in AIDS epidemiology.

## INTRODUCTION

In some cross-border areas around the world, sex workers have been found to be at high risks for STIs and HIV infection<sup>[1–3]</sup>. Sexual transmission now plays an increasingly greater role in the transmission of HIV in China, especially in Yunnan Province<sup>[4]</sup>. Previous studies have demonstrated that the Herpes simplex virus type 2 (HSV-2) infection is one of the more common sexually transmitted infections (STIs) among female sex workers in Yunnan Province, with the highest provincial HIV prevalence rate in China<sup>[5–7]</sup>.

Some studies have indicated that people infected by HSV-2 have a higher risk of acquiring HIV-1<sup>[7–8]</sup>. A study in four African cities showed a strong and consistent association between HIV and HSV-2 infection<sup>[9]</sup>. Esther E Freeman, et al.<sup>[10]</sup> concluded through a systematic review and the meta-analysis of 19 longitudinal studies that prevalent HSV-2 infection was associated with a three-fold increase in the general population's risk of acquiring HIV. Timothy Schacker et al.<sup>[11]</sup> found that HIV-1 virions could be detected consistently in genital ulcers caused by HSV-2, which suggests that genital herpes infection may increase the efficiency of the sexual transmission of HIV-1.

However, little information is available about the prevalence of HSV-2 among female sex workers (FSWs) in some areas on the China-Vietnam border, which had the highest HIV caseload at the beginning of the Chinese epidemic<sup>[12]</sup>. Hekou County, in Yunnan Province, is a flourishing hub for trade and tourism on the Chinese-Vietnamese border, and it is estimated that there are over 1000 FSWs<sup>[13]</sup>. This study aims to survey the prevalence of HSV-2 among FSWs in Hekou and analyze the relationship between HSV-2 infection and its risk factors in this border area of China.

## METHODS

### Participants and Procedures

A cross-sectional study of all recruited FSWs was conducted in Hekou, Yunnan Province, from May to June 2009. The study included both ethnic Chinese and Vietnamese FSWs. The eligibility criteria for study participation were: female participants at least 16 years of age, having sold sex for money in the previous six months, and being willing to answer questions about HSV-2, HIV, other STIs, and illegal drug use. Local trained interviewers collected data on demographics, behavioral risk factors, and medical history in face-to-face interviews, using a standardized questionnaire.

### Laboratory Tests

Local trained physicians collected laboratory specimens. Plasma specimens were tested for the HSV-2 antibody (HerpeSelect-2 ELISA IgG, Focus, Technologies, Cypress, CA), syphilis [rapid plasma reagin (RPR) test, Xinjiang Xindi, China] and HIV-1 antibody [enzyme-linked immunosorbent assay (ELISA), Organon Teknika, Boxtel, Co., Ltd., the Netherlands]. HIV-1 positive tests were confirmed by HIV-1/2 Western blot assay (HIV Blot 2.2 WBH; Genelabs Diagnostics, Singapore). Specimens positive for syphilis were confirmed by using *T. pallidum* particle assay (Serodia; Fujirebio, Inc., Fuji, Japan). Vaginal swabs were collected and a wet-mount was prepared to detect *Trichomonas vaginalis*.

Endocervical swabs were collected and tested for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* by polymerase chain reaction (PCR, AMPLICOR, Roche, USA). Bacterial vaginosis (BV) was diagnosed by using Amsel's criteria<sup>[14]</sup>. Yeast infections were diagnosed through microscopy with a potassium hydroxide (KOH, 10% of concentration) solution to determine the presence of pseudohyphae and budding yeast cells. Cervicitis and genital warts were diagnosed by visual inspection. Urine was collected for opiate screening (MOP One Step Opiate Test Device, ACON Laboratories, Inc., USA).

### Data Analysis

EpiData 3.1 (Odense, Denmark) was used to enter the data from questionnaires and laboratory tests. SAS 9.1 (Cary, NC) was used to perform statistical tests. Chi-squared and Fisher's exact tests (FET) were used to examine associations between risk factors and HSV-2 seropositivity in univariate analyses. Variables significant ( $P < 0.1$ ) in univariate analyses were considered for inclusion in the multivariate regression model. Variables were entered and eliminated from the model in a stepwise manner with entry and exit criteria of  $\alpha < 0.1$ .

Study participants were recruited through convenience sampling by local outreach workers and health staff. Before being interviewed or having specimens taken, participants provided written voluntary informed consent. All study staff were trained for standardized methods of data collection and laboratory testing. The standard questionnaire was completed through face-to-face interviews by the study staff fluent in both Chinese and Vietnamese. All participants were asked to return for a follow-up visit and post-test counseling in four to six weeks as of the date of the study visit. This study was approved by the China CDC and Yunnan CDC institutional review boards.

## RESULTS

Of the 351 FSWs who agreed to participate in this study, six were excluded because they were younger than 16 years old. A final total of 345 FSWs fit the inclusion criteria and were enrolled in the study, including 112 (32.5%) Chinese and 233 (67.5%) Vietnamese. Table 1 describes the demographics of the study population in Hekou. Table 2 illustrates the behavioral characteristics of the FSWs in Hekou.

Table 3 describes the prevalence of HSV-2, HIV-1, and other sexually transmitted infections in the sample population. The FSWs population in Hekou had prevalence rates of 58.3% for HSV-2, 5.5% for HIV, 15.4% for cervicitis, 13.9% for yeast infections, 4.1% for bacterial vaginosis (BV), 2.6% for genital warts, 2.0% for trichomoniasis vaginitis (TV), and 0.6% for syphilis.

Table 4 displays the risk factors from univariate and multivariate logistic regression models for HSV-2 infection of FSW in Hekou. Age  $< 21$ , history of illicit drug use, duration of sex work  $\geq 3$  months, ever having a fixed partner, last client's payment  $< 150$  RMB (\$22 USD), oral and vaginal sex with the last client (*vs.* only vaginal sex), condom use with the last client, having at least one repeat customer, positive for HIV, and positive for BV were considered significant for HSV-2 infection at the univariate level. The multivariate model

found that age <21, duration of work as an FSW > 3 months, oral and vaginal sex with the last client (vs. only vaginal sex), positive for HIV, and positive for BV were significant for HSV-2 infection.

## DISCUSSION

The study population had an HSV-2 prevalence of 58.3%. Other studies of FSWs in Yunnan Province have found similar HSV-2 prevalence rates between 45% and 68%, and these studies also found the same significant associations between HIV and HSV-2 infections detected in this study<sup>[5-7]</sup>. Researchers have hypothesized that HSV-2 infection may facilitate the acquisition of HIV<sup>[10,15]</sup>. Herpes simplex virus (HSV) is one of the most common infectious etiologies of genital ulcers, which may contribute to the acquisition of HIV<sup>[16-17]</sup>. Some studies explained the molecular biological mechanism by which HSV-2 amplified susceptibility to HIV<sup>[18-19]</sup>. In addition, those who are HIV positive may also be more likely to have infectious outbreaks of HSV-2 due to a weakened immune response, which could also increase transmission of HSV-2 to others<sup>[11]</sup>. The prevalence of HSV-2 in our study population was high and this may pose greater risks for HIV acquisition.

Risk factors for HSV-2 infection included older age, duration of sex work >3 months, oral sex and vaginal sex with the last client (as opposed to only vaginal sex), HIV infection, and BV. Those who are older with a longer duration of sex work have more time for exposure to STIs and are therefore, more likely to have incurable STIs like HSV-2. Similar to our findings, a study in the United States also found that oral sex was a risk factor for HSV-2 infection in women<sup>[20]</sup>. While some studies have found HSV-1 is playing an increasingly prominent role in genital infections<sup>[21-22]</sup>, HSV-2 is not commonly associated with oral infections<sup>[23-25]</sup>. Oral sex with the most recent partner may be a proxy measure of other high-risk sexual behaviors that were not captured in this study. Findings from another study also indicated an association between HSV-2 and BV<sup>[26]</sup>. Although this relationship is not fully understood, it has been hypothesized that the association between HSV-2 and BV is related to disruption to the vaginal flora or to hormonal fluctuations<sup>[26]</sup>.

This study has several limitations. The survey covered questions about sensitive topics, which may have resulted in information bias. Furthermore, as some questions were related to the past behaviors of FSWs, this may have led to recall bias. In addition, selection bias may have been an issue due to convenience sampling, which may indicate that the findings may not be applicable to all FSWs in this border area.

This is the first study to survey the HSV-2 prevalence and risk factors among Vietnamese and Chinese FSWs in the border area of Hekou County in Yunnan Province, China. It is important to paint a clear picture of HSV-2 transmission in trans-border areas in order to better understand its potential impact on the international HIV epidemic.

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**Table 1**Demographic Characteristics of FSWs in Hekou ( $n=345$ )

Variable	Status	No.(%)
Nationality	Chinese	112 (32.5)
	Vietnamese	233 (67.5)
Age	<21years	156 (45.2)
	≥21years	189 (54.8)
Ethnicity	Ethnic majority*	228 (66.1)
	Other	117 (33.9)
Education	≤6 years	99 (28.7)
	>6 years	246 (71.3)
Marital status	Married or cohabitating	47 (13.6)
	Other	298 (86.4)
Residence	Commercial sex market	247 (71.6)
	Other	98 (28.4)
Alcohol use	Yes	131 (38.0)
	No	214 (62.0)
History of illicit drug	Yes	4 (1.2)
	No	341 (98.8)

*Note.*

\* Han Chinese or Kinh Vietnamese.

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**Table 2**Sexual Risk Behaviors of FSWs in Hekou ( $n=345$ )

Variable	Status	No.(%)
Age of sexual debut	16 years old	74 (21.4)
	>16 years old	271 (78.6)
Duration of sex work	3months	148 (42.9)
	>3months	197 (57.1)
Main contraception method	Condom	329 (95.4)
	Other	16 (4.6)
Condom use with the last client	Yes	322 (93.3)
	No	23 (6.7)
Convenient access to condoms at work	Yes	293 (84.9)
	No	52 (15.1)
Ever had a steady sexual partner	Yes	259 (75.1)
	No	86 (24.9)
Currently has a steady sexual partner	Yes	160 (46.4)
	No	185 (53.6)
History of pregnancy	Yes	160 (46.4)
	No	185 (53.6)
Had at least 5 clients in the last day	Yes	186 (53.9)
	No	159 (46.1)
Last client's payment	150 RMB (\$22 USD)	136 (39.4)
	>150 RMB (\$22 USD)	209 (60.6)
Sexual acts with the last client	Oral and vaginal sex	110 (31.9)
	Only vaginal sex	235 (68.1)
Repeat customer	1	154 (44.6)
	0	191 (55.4)
Douches more than once a day	Yes	225 (65.2)
	No	120 (34.8)



**Table 3**HIV/STDs in FSWs of Hekou ( $n=345$ )

Variable	Positive	No.(%)
HIV	Yes	19 (5.5)
HSV-2	Yes	201 (58.3)
Syphilis	Yes	2 (0.6)
Trichomonas vaginalis	Yes	7 (2.0)
Genital warts	Yes	9 (2.6)
Cervicitis	Yes	53 (15.4)
Bacterial vaginosis	Yes	14 (4.1)
Yeast infection	Yes	48 (13.9)

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**Table 4**Risk Factors for HSV-2 Infection among FSWs in Hekou ( $n=345$ )

Variable	OR (95% CI)	AOR (95% CI)
Country of origin (Vietnam vs. China)	0.7 (0.5, 1.1)	
Age (<21 years vs. ≥21 years)	0.5 (0.3, 0.8) <sup>§</sup>	0.5 (0.3, 0.8) <sup>§</sup>
Ethnicity (majority <sup>◇</sup> vs. minority)	1.1 (0.7, 1.8)	
Education (<6 years vs. ≥6 years)	1.3 (0.8, 2.1)	
Married or cohabitating (yes vs. no)	1.1 (0.6, 2.0)	
Resides at commercial sex market (yes vs. no)	1.1 (0.7, 1.7)	
Alcohol use (yes vs. no)	1.1 (0.7, 1.8)	
History of illicit drug use (yes vs. no)	6.5 (0.4, 123.3) <sup>* †</sup>	
Condom used as a main contraception method (yes vs. no)	0.8 (0.3, 2.3)	
Duration of sex work (>3 months vs. ≤3 months)	2.0 (1.4, 3.3) <sup>§</sup>	2.0 (1.3, 3.3) <sup>§</sup>
Age of sexual debut (<16 years old vs. ≥16 years old)	1.3 (0.8, 2.2)	
Has ever had a steady sexual partner (yes vs. no)	1.7 (1.0, 2.7) <sup>‡</sup>	
Currently has a steady partner (yes vs. no)	1.2 (0.8, 1.8)	
Douches more than once a day (yes vs. no)	1.4 (0.9, 2.1)	
At least 5 clients in the last day (yes vs. no)	0.7 (0.5, 1.1)	
Last client's payment less than 150 RMB (\$22 USD) (yes vs. no)	1.5 (0.9, 2.3) <sup>‡</sup>	
Sexual acts with the last client (oral and vaginal vs. only vaginal)	1.6 (1.0, 2.6) <sup>‡</sup>	1.6 (1.0, 2.7) <sup>‡</sup>
Condom use with the last client (yes vs. no)	0.4 (0.1, 1.0) <sup>‡</sup>	
Convenient access to condoms at work (yes vs. no)	1.4 (0.7, 2.4)	
Has at least one repeat customer (yes vs. no)	1.5 (1.0, 2.3) <sup>‡</sup>	
HIV (yes vs. no)	14.1 (1.9, 106.6) <sup>§</sup>	11.4 (1.5, 87.2) <sup>‡</sup>
Syphilis (yes vs. no)	3.6 (0.2, 76.0) <sup>*</sup>	
Trichomonas vaginitis (yes vs. no)	0.3 (0.05, 1.5)	
Bacterial vaginosis (yes vs. no)	4.5 (1.0, 20.5) <sup>‡</sup>	5.6 (1.2, 26.9) <sup>‡</sup>

**Note.**

\* 0.5 used to calculate OR in cells with a count of 0.

<sup>†</sup> P-value <0.1.<sup>‡</sup> P-value <0.05.<sup>§</sup> P-value <0.01.

◇ Han Chinese or Kinh Vietnamese.