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Herpes Simplex Virus Type 2 Infection among Commercial Sex Workers in Kunming, Yunnan Province, China

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Summary

A cross-sectional prevalence survey was conducted to determine the sociodemographic correlates of HSV-2 infection among commercial sex workers (CSWs) in Kunming, Yunnan Province of China. HSV-2 prevalence was 33.0%, HIV infection was 2.4%, and HCV infections was 6.8%. Subjects who were positive for HSV-2 had a significantly higher prevalence of HIV infection (5.5% vs. 0.9%, $p=0.002$; OR: 6.4, $p=0.006$) and HCV infection (18.7% vs. 2.4%, $p<0.001$; OR: 7.6, $p<0.001$) compared to HSV-2 negative individuals. Risk factors that increased the odds of HSV-2 infection were HIV infection, HCV infection, being female, and having a steady sex partner within the last six months ($p=0.01$). In a multivariate analysis, female sex workers (OR: 6.6, $p<0.001$), HCV infection (OR: 5.9, $p<0.001$), and having a sex partner within the last 6 months (OR: 2.2, $p<0.05$) had greater odds of being infected with HSV-2. A strong relationship was found between HSV-2, HIV, and HCV infections.

Keywords

commercial sex workers (CSWs); herpes simplex virus type 2 (HSV-2); human immunodeficiency virus (HIV); hepatitis C virus (HCV); China

Introduction

In China, sexual transmitted diseases (STDs) have consistently ranked as the third most common infectious disease resulting in increased health care utilization and high disability adjusted life years lost (DALYs) (1). Herpes simplex virus type 2 (HSV-2) is the most common cause of genital ulcer disease (GUD) worldwide, which leads to lifelong risk of

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viral transmission to sexual partners (2). Recent cross-sectional prevalence surveys revealed HSV-2 seroprevalence ranged from 21.6% to 65.1% among hospitality girls and sex workers in China (1, 3). Nevertheless, STD epidemiological data are not well defined in this region, especially among groups at potential high risk of HIV (1).

There is a strong association between HSV-2 and human immunodeficiency virus (HIV) serostatus (4). Data on HSV-2 antibody status can be useful for the identification of individuals at greater risk of acquiring and transmitting HIV infection, which may be valuable for HIV prevention efforts (5). Nguyen et al. demonstrated that FSWs with positive HSV-2 antibodies had a significantly higher HIV prevalence compared to those who were HSV-antibodies negative (OR: 1.5; $p < 0.05$) (6). Wald and colleagues also suggested that testing persons with HSV type-specific serologic assays and encouraging disclosure may result in a decreased risk of HSV-2 transmission to sex partners (7). HSV-2 antibody status can also provide an objective measure of sexual behaviors such as early age of sexual debut and acquisition rates of genital herpes (8).

In order to effectively monitor the spread of HSV-2 infection from commercial sex workers (CSWs) to their clients, comprehensive and periodic baseline prevalence studies should be conducted. This study detailed the sociodemographic correlates of HSV-2 infection among CSWs in Kunming, Yunnan Province of China.

Materials and Methods

Design, Setting, and Participants

A cross-sectional prevalence survey of HSV-2 was conducted among 500 CSWs who did not use illegal drugs in Kunming, City of Yunnan Province, China in 2004. Because commercial sex work is illegal in China, the majority of our study participants were recruited from local re-education centers, where they were arrested for commercial sex activities. A small portion of sex workers were also recruited from STD clinics where sex workers received a medical check-up. Demographic, behavioral, and clinical information were obtained by interviewer-administered questionnaires. Through this process, respondents who reported involvement in commercial sex work and no illegal drug use were included in the study. Blood samples were also obtained. The Committees on Human Research at the Johns Hopkins University, Baltimore, Maryland, the National Institutes of Health, Bethesda, Maryland, and at the Yunnan University, Yunnan, China approved the study protocol, and all study participants provided informed consent. CSWs in this study are defined as those who are selling sex on the street or those who are linked to commercial sex establishments.

Laboratory Tests

The performance of commercial HSV-2 serological assays were evaluated using sera samples from 500 CSWs tested by HerpeSelect HSV-2 ELISA (Focus Technologies; Cypress, CA, USA), Kalon HSV-2 ELISA (Kalon Biological, Ltd.; Surrey, UK), and Biokit rapid assay (Sure-Vue; Lexington, MA, USA) performed according to the manufacturers' protocol. All seropositive results ($N=275$) by Biokit, Focus and Kalon were further tested by

WB for HSV-1 and HSV-2 performed by University of Washington (Seattle, Washington, USA) as previously described (11). This final HSV-2 prevalence was based on a positive screening test confirmed by WB.

The 500 sera were also tested for HIV-1 by Vironostika Microelisa System (bioMérieux, Inc.; Durham, NC, USA) then confirmed by HIV-1 WB (Calypte Biomedical Corporation; Rockville, MD, USA). Hepatitis C virus (HCV) was detected by the Ortho HCV Version 3.0 ELISA Testsystem (Ortho-Clinical Diagnostics, Inc.; Raritan, NJ, USA).

Statistical Analysis

Statistical analyses were performed using Intercooled Stata 9.2 (STATA Statistical Software for Professionals: Release 9, StatCorp LP, College Station, TX, 2006). Prevalence rates of STDs and their 95% confidence intervals (CI) were reported. The Pearson chi-square test was used to compare distributions of risk factors among HSV-2 infected and non-infected groups and between Male Sex Workers (MSWs) and FSWs. Where appropriate, the Student's *t*-test was also used for comparisons. Univariate and logistic regression models were applied to estimate the odds ratios (unadjusted & adjusted OR) of HSV-2 infection and risk factors. Stepwise logistic regression was used to determine the best fit model for the prediction of HSV-2 infection.

Results

Study Population's Characteristics

Among the 500 CSWs, the median age was 26 years old ($SD \pm 7.7$) with 17.3% ($n=85$) under the age of 20. The majority of the study participants were FSWs (62.0%, $n=310$), and the rest (38%, $n=190$) were MSWs. Only 34% ($n=170$) of the subjects were in a marital relationship while 66% reported being single. Approximately 47.2% of the CSWs had another occupation in addition to commercial sex work as indicated in Table 1.

HSV-2, HIV, HCV Prevalence

After confirmation by WB of all seropositive samples by the three screening antibody assays, HSV-2 prevalence was 33.0% (95% CI: 28.9, 37.1); 84.8% ($n=140$) of HSV-2 infected individuals were females. The prevalence of HIV infection was 2.4% (95% CI: 1.1, 3.7), and all HIV-positive cases were females. HCV infection was present in 6.8% (95% CI: 4.6, 9.0) of the study population, and 82.3% (28/34) were FSWs. Co-infections of HSV-2/HIV/HCV accounted for 1.6% ($n=8$) of the study population; all were females. The same eight individuals were infected with HIV and HCV. HSV-2/HIV coinfection was 1.8% (all were females), and HSV-2/HCV coinfection was 5.2% (96.2% were females).

Subjects who were positive for HSV-2 had a significantly higher prevalence of HIV infection than those who were negative (5.5% vs. 0.9%, $p=0.002$; OR= 6.4, $p=0.006$). The prevalence of HCV was higher among those who tested positive for HSV-2 compared to those who tested negative (18.7% vs. 2.4%, $p<0.001$; OR=7.6, $p<0.001$).

Risk factors of HSV-2 infection among 500 CSWs

HSV-2 prevalence varied among different age groups ($p<0.001$). The lowest prevalence was among subjects ≥ 35 years of age (20.4%), and the highest was among subjects within age range of 20 to 24 (47.4%). A high frequency of risky behaviors was noted among this population. The median age of first sexual debut was 19 years old ($SD\pm 3.1$). Approximately 86.4% (431/499) of the CSWs reported having sex without a condom. HSV-2 infection was significantly higher among CSWs who did not have another occupation and individuals with age of first sexual debut <20 ($p<0.01$). Subjects without history of sex abuse had higher HSV-2 prevalence relative to individuals who were sexually abused (38.0% vs. 15.5%, $p<0.001$). Not using a condom during sexual intercourse was not associated with HSV-2 infection ($p=0.49$). There was no association between HSV-2 infection and marital status ($p=0.36$). (Table 1)

Risk factors between FSWs and MSWs

There was a significantly higher proportion of FSWs who were infected with HSV-2 compared to MSWs (45.2% vs. 13.1%, $p<0.001$). The prevalence of HIV infection was 3.9% among FSWs while no MSW was infected. HCV infection was also higher among FSWs compared to MSWs (7.7% vs. 3.1%, $p=0.006$). The median age at first sex was lower among FSWs than MSWs (18.5 vs. 21.9, $p<0.001$). A higher proportion of MSWs had their first sexual debut ≥ 20 years of age compared to FSWs (66.3% vs. 27.1%, $p<0.001$). There was no statistically significant difference between the number of FSWs and MSWs reported no condom use during sexual intercourse (82.6% vs. 88.4%, $p=0.056$). Greater number of FSWs than MSWs reported being single (76.1% vs. 47.9%, $p<0.001$), having a sex partner within the last six months (72.9% vs. 48.9%, $p<0.001$), and having a steady sex partner (81.6% vs. 22.1%, $p<0.001$). Conversely, a higher proportion of MSWs compared to FSWs had another occupation in addition to commercial sex work (72.1% vs. 31.9%, $p<0.001$) and had history of sex abuse (44.7% vs. 8.1%, $p<0.001$). (Table 2)

Univariate & Multivariate Analysis

Within the univariate analysis, risk factors that increased the odds of HSV-2 infection were HIV infection, HCV infection, being female, having a steady sex partner or a sex partner within the last six months ($p=0.01$). Risk factors that decreased the odds of HSV-2 infection were having another occupation, older age at first sexual debut, had history of sex abuse ($p<0.01$). In a multivariate analysis, FSWs (OR: 6.6, 95% CI: 2.7, 13.8; $p<0.001$), HCV infection (OR: 5.9, 95% CI: 2.1, 15.9; $p=0.001$), and having a sex partner within the last six months (OR: 2.2, 95% CI: 1.1, 4.3; $p<0.05$) had greater odds of being infected with HSV-2. (Table 3)

In the stepwise analysis, FSWs were 7.7 (95% CI: 4.0, 15.4; $p<0.001$) times more likely to be infected with HSV-2 compared to MSWs when adjusted for all other factors. HCV positive individuals had 6.6 (95% CI: 2.6, 16.7; $p<0.001$) greater odds of HSV-2 infection compared to HCV negative persons. Study subjects with a sex partner within the last six months had significantly higher odds of HSV-2 infection than those without (OR: 2.0, 95% CI: 1.0, 3.8; $p<0.05$).

Discussion

A high prevalence of HSV-2 infection was observed among CSWs, particularly FSWs, in Yunnan Province of China. Higher HSV-2 infections were seen among younger age groups. Comparable rates were noted among CSWs in Mexico, Kenya, and the Republic of Congo (9). Only 13.2% of the study population reported using a condom during sexual activities indicated that no effective prevention strategies have been implemented among this high risk population. Behavioral surveys from 2000 and 2005 also found that unprotected sex is still a common practice among CSWs within this region with reported condom use of only 10% (10, 11, 12).

HSV-2 infection was higher among younger CSWs. Subjects who reported first sexual encounter <20 years of age showed higher odds of HSV-2 infections similar to other studies from both developing and developed countries (8). In this study, the age of first sexual debut was as young as 14 years old. These findings implied that knowledge and awareness of STIs are low among this young population. The sex industry in China is comprised of mostly young girls from the rural regions; these women have a low literacy rate and little knowledge of STIs and condom use (13).

High rates of HSV-2 infection along with co-infections with HIV and/or HCV reflect the rise in commercial sex activities within the province. All 12 (2.4%) cases of HIV infection in our study population were females <35 years of age. A higher HIV prevalence (10.3%) had been reported among FSWs in Yunnan, and similar rates were also seen in Vietnam (1). Two factors that could contribute to the lower HIV prevalence in our study were the high proportion of individuals reported being in a marital relationship and the presence of MSWs. Subjects who reported being in a marital relationship might not be as involved in commercial sex activities as frequent as those who are single. An STI prevalence survey conducted in 1999–2000 among FSWs from Yunnan Province showed that approximately 25% of the women were married (1). This is consistent with our study where 24% of FSWs were married. Therefore, it is not uncommon for sex workers in this region to be in a marital relationship. Meanwhile, other studies have shown that males are at lower risk for HSV-2 infection (14, 15). This factor also contributed to a lower HSV-2 infection prevalence compared to previous studies only among FSWs in this region (1, 6).

The majority (91.2%) of HCV infection were among females <35 years of age which might indicate the participation in injection drug use (IDU) (13). In our study, individuals who were HSV-2/HCV coinfectd were also HIV infected. However, results from our survey revealed no IDU status. Nonetheless, the presence of HCV infection among this population implied the sexual interaction between IDUs and CSWs which may lead to greater transmission rates. Globally, HIV and HCV have often extended from FSWs and IDUs into the general population through sexual transmission or needle sharing. Therefore, prevention strategies should be focused on these core high risk groups to monitor the dissemination of HSV-2 that could potentially fuel the transmission of HIV and HCV.

Commercial sex activities are often reported among FSWs in China; however, 38.0% of our study population was comprised of the MSWs. To our knowledge, there is limited research

on MSWs in Asia, particularly China. A recent study from Hanoi, Vietnam demonstrated that MSWs were involved in high risk behaviors such as having sex without a condom along with having multiple sex partners (male/female), and using drugs (16). Low condom use was seen among MSWs in our study (17.4%). The same study from Vietnam also noted a high percentage of MSWs with history of sexual victimization (16). Within our study, 44.7% of MSWs reported history of sex abuse compared to 8.1% among FSWs. This data demonstrated a need for future research on male sex work for proper interventions specific to MSWs in this region.

It is difficult to understand the social dynamic of CSWs in Yunnan Province because prostitution is illegal in China (13, 17). Therefore, the commercial sex industry in Yunnan Province is disguised as massage parlors, nightclubs, and karaoke bars (13, 17,). The demographic characteristics and social/sexual dynamic within our study population are different than previous behavioral surveys. Approximately 34.2% of our study population was in a marital relationship, and 47.3% reported employment status other than commercial sex work. These factors contributed to a more complex commercial sex dynamic within this region. There was a higher, but not statistically significant, proportion HSV-2 infection among subjects reported being single compared to those who were in a marital relationship. We observed higher HSV-2 infection in CSWs who responded no to other occupation in addition to commercial sex work. This association indicates that the commercial sex industry in region encompassed a broader spectrum of individuals and not just young women.

There are several limitations to this study. Our survey was not able to capture other important risk factors such as education, social economic status, and the number of sex partners. Due to the illegal status of commercial sex activities, these factors were difficult to obtain from our participants. Since many CSWs were recruited from re-education center and STD clinics, they might not fully represent the characteristics of commercial sex work population in Yunnan Province. It is difficult to compare HSV-2 prevalence in CSWs from different areas especially when different sampling and detection procedures were used.

In this high risk population, we found a strong relationship among HSV-2, HIV, and HCV. The complex social dynamic combined with risk factors such as having sex at younger age, unemployment, low condom use may fuel the transmission of HSV-2 and other STIs to the general population. Comprehensive prevention strategies such as health education, condom promotion, and STIs services for CSWs, particularly for younger sex workers, are crucial to control the spread of STIs.

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TABLE 1

Prevalence of HSV-2 Infection by Demographic and Behavioral Characteristics

		<u>Prevalence of HSV-2 Infection</u>	
Factors	Sample Size	% (n)	* χ^2 <i>p-value</i>
Age in years			
19	58	22.4 (13)	<0.001
20–24	154	47.4 (73)	
25–29	111	30.6 (34)	
30–34	78	32.1 (25)	
35	98	20.4 (20)	
Gender			
Male	190	13.1 (25)	<0.001
Female	310	45.2 (140)	
Marital status			
Single	330	34.2 (113)	0.362
Married	170	30.6 (52)	
Age of first sexual debut			
Yes	210	25.2 (53)	0.002
No	289	38.8 (112)	
Other Occupation			
Yes	236	23.7 (56)	<0.001
No	263	41.4 (109)	
Sex without condom			
Yes	431	33.6 (145)	0.491
No	68	29.4 (20)	
History of sex abuse			
Yes	110	15.5 (17)	<0.001
No	389	38.0 (148)	

* Pearson Chi-square Test, p-value <0.05 was considered statistically significant

TABLE 2

Risk Factor Distributions among MSWs and FSWs

Factors	Gender		<i>p-value</i> *
	MSWs (190) (%, n)	FSWs (310) (%, n)	
Age (median, $\pm$ SD)	32.7 ($\pm$ 7.7)	24.4 ($\pm$ 5.1)	<0.001
Age at first sex (median, $\pm$ SD)	21.9 ($\pm$ 2.2)	18.5 ($\pm$ 2.2)	<0.001
HSV-2 infection (+)	13.1 (25)	45.1 (140)	<0.001
HIV infection (+)	0 (0)	3.9 (12)	0.006
HCV infection (+)	3.1 (6)	7.7 (24)	0.011
Marital status (single)	47.9 (91)	76.1 (236)	<0.001
Age of first sexual debut 20	66.3 (126)	27.1 (84)	<0.001
Having other occupation	72.1 (137)	31.9 (99)	<0.001
Sex without condom	82.6 (157)	88.4 (274)	0.056
History of sex abuse	44.7 (85)	8.1 (25)	<0.001
Having a steady sex partner	22.1 (42)	81.6 (253)	<0.001
Having a sex partner within the last 6 months	48.9 (93)	72.9 (226)	<0.001

MSWs: male sex workers; FSWs: female sex workers

* The Student's t-test was used to compare age and age at first sex between MSWs and FSWs; the Pearson chi-square test was used for all other factors; *p*-value <0.05 was considered statistically significant.

TABLE 3

Univariate & Multivariate Analysis of HSV-2 Infections by Risk Factors

Factors	Univariate (Un-adjusted)		Multivariate (Adjusted)	
	OR	(95% CI)	OR	(95% CI)
HIV infection	6.4 [*]	(1.7,23.8)	1.7	(0.4,7.7)
HCV infection	7.6 ^{**}	(3.4,17.3)	5.9 ^{**}	(2.1,15.9)
Female	5.5 ^{**}	(3.4,8.9)	6.1 ^{**}	(2.7,13.8)
Age at first sex	0.9 ^{**}	(0.9,1.0)	1.0	(0.9,1.2)
Age of first sexual debut 20 years old	1.0	(0.6,1.7)	1.0	(0.5,1.9)
Other occupation	0.4 ^{**}	(0.3,0.7)	0.9	(0.5,1.3)
History of sex abuse	0.3 ^{**}	(0.2,0.5)	0.6	(0.3,1.2)
Steady sex partner	2.3 ^{**}	(1.6,3.5)	0.5	(0.2,1.1)
Sex partner within the last 6 months	1.7 [*]	(1.1,2.5)	2.2 [*]	(1.1,4.3)

*
p-value<0.05;**
p-value 0.01;

OR: odds ratios; 95% CI: 95% Confidence Interval