

Estimation of Probability of Unprotected Heterosexual Vaginal Transmission of HIV-1 from Clients to Female Sex Workers in Kaiyuan, Yunnan Province, China*

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Objective To estimate the probability of unprotected heterosexual vaginal transmission of HIV-1 from clients to Female Sex Workers (FSWs) in Kaiyuan County, Yunnan province, China, and analyze factors which impact the transmission probability. **Methods** An open cohort research of FSWs in Kaiyuan was created from surveys conducted in April 2008, October 2008, and April 2009. Two cross-sectional surveys of local clients were also carried out in May 2008 and November 2008. A model was developed to estimate the probability of unprotected heterosexual vaginal transmission of HIV-1 from clients to FSWs. **Results** The transmission probability from clients to FSWs was estimated as 0.0023 [95% CI 0.0014-0.0032] per unprotected heterosexual act. **Conclusion** The transmission probability among this group engaging in commercial sex in Yunnan province differs from that found in studies from other countries, and future studies should estimate the influence factors of HIV-1 transmission probability, such as stage of HIV infection, co-morbid sexually transmitted infections (STIs).

Key words: Transmission Probability; HIV/AIDS; Model; FSW; Clients

INTRODUCTION

Sexual HIV transmission is on the rise in China^[1-3]. Sentinel surveillance data indicate that 30% of HIV cases in China were transmitted through unprotected heterosexual sex. It is estimated that there are 1.8-3.8 million female sex workers (FSWs) and 17.7-37.1 million male clients who purchase sex from FSWs in mainland China^[4]. A high transmission probability per act of unprotected heterosexual intercourse from females to males could lead to strengthening of the epidemic among FSWs and clients^[5].

Little is known about the probability of HIV transmission from unprotected heterosexual intercourse in China. Transmission probability per unprotected intercourse from clients to FSWs in China may differ from that reported in other countries. The probability of unprotected heterosexual transmission may vary with population and be

influenced by many factors, such as the type of sex^[5-7], bleeding during intercourse^[8], semen viral load^[9-12], stage of HIV infection^[5,13-14], and co-morbid sexually transmitted infections (STIs)^[8]. There are no studies on the probability of HIV transmission from clients to FSWs from unprotected heterosexual sex in China.

Kaiyuan County is located in Honghe Prefecture, Yunnan province. Yunnan Province has one of the highest HIV prevalence in China and Honghe Prefecture has the second highest HIV prevalence in Yunnan province. According to a report from the Kaiyuan Center for Disease Control and Prevention (CDC), there were nearly 3 000 surviving HIV/AIDS cases at the end of 2009, with a prevalence of 1% in the entire population. There have been approximately 400 new cases of HIV/AIDS every year since 2006. The Kaiyuan CDC estimates that there are about 1 000 FSWs and 50 000 male clients. The current study estimates the probability of HIV transmission

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from unprotected heterosexual sex from clients to FSWs and the results of this research can better inform HIV intervention programs in this population engaging in commercial sex in Yunnan province.

MATERIALS AND METHODS

Epidemiology Survey

This study was conducted by the Chinese Center for Disease Control and Prevention (China CDC) in Beijing with provincial and Kaiyuan CDC staff in Yunnan. An open cohort of FSWs was created from surveys conducted in April 2008, October 2008, and April 2009. Participants of the study were recruited by local outreach workers and health professionals, who directly approached FSWs in commercial sex establishments and on the street. Women were considered eligible for study participation if they were at least 16 years of age, self-reported to have provided sexual services in exchange for money in the past 3 months, had no regular partners who were HIV positive, and agreed to be tested for HIV, other STIs, and for the use of illegal drugs. After being provided with the informed consent, participants were asked questions about their demographics, basic medical history, and behavioral risk factors. FSWs who were either self-reported using illegal drugs or positive in the urine test for opiates were excluded from this study.

Two cross-sectional surveys of local clients were conducted in May 2008 and November 2008 following the first and the second FSWs surveys respectively. Clients were recruited through convenience sampling by local outreach workers and health professionals. Clients were considered eligible for study participation if they were at least 16 years of age, self-reported to have purchased sex from local FSWs in the past 3 months, and agreed to be tested for HIV, other STIs, and the use of illegal drugs. After being provided with the informed consent, participants were asked questions about their demographics, basic medical history and behavioral risk factors through face-to-face interviews conducted by study staff.

All study staff were trained in standardized methods of data collection. Participants were scheduled for a follow-up visit in four to six weeks as of the date of the study visit for post-test counseling. Data from the questionnaires and laboratory tests were entered into EpiData 3.1 (Odense, Denmark) and analyzed by using SAS 9.1 (Cary, NC, USA). The probability model was developed by using MATLAB 7.0 (Natick, MA, USA). The study received approval from institutional review boards of both China CDC and Yunnan Province CDC.

Laboratory Methods

All laboratory specimens were collected by

trained physicians. Blood samples were obtained to test for HIV infection and other STIs. Plasma specimens were screened for HIV antibodies by enzyme-linked immunosorbent assays (ELISA: Organon Teknika, Boxtel, Co., Ltd., the Netherlands), and positive tests were confirmed by HIV-1/2 Western blot assays (HIV Blot 2.2 WBH; Genelabs Diagnostics, Singapore). Plasma specimens were also tested for antibodies to herpes simplex virus (HSV-2) by ELISA (Herpe Select-2 ELISA IgG; Focus Technologies, Cypress, CA). Syphilis was tested by using rapid plasma reagin (RPR; RPR Diagnostics kit; Xinjiang Xindi, China) for *Treponema pallidum* and positive specimens were confirmed by using *T. pallidum* particle assays (Serodia; Fujirebio, Inc., Fuji, Japan). Bacterial vaginosis (BV) was diagnosed with Amsel's criteria^[15], and urine was collected for opiate screening (MOP One Step Opiate Test Device, ACON Laboratories, Inc., USA).

Transmission Probability Model

The transmission probability per unprotected heterosexual act from clients to FSWs, β , is related to 7 parameters:

- *The number of FSWs, N ;
- *The working days per FSW per year, d ;
- *The number of clients of per FSW per day, m ;
- *HIV-1 incidence of FSW cohort per year, I_{inc} ;
- *The proportion of infected male clients, P_c ;
- *The proportion of condom use for vaginal intercourse, c ;
- *The condom efficacy in heterosexual sex, η .

Transmission probability per unprotected heterosexual act between clients and FSWs is the probability that an FSW will acquire HIV from one episode of vaginal intercourse with an HIV positive client without using a condom. Transmission probability was estimated with the following model, which is a modification of two models^[16-17]. For the incident cases:

$$I_{inc} \times N = N \times m \times d \times \beta \times (1 - \eta c) \times P_c,$$

$$\text{So } \beta = \frac{N \times I_{inc}}{N \times m \times d \times (1 - \eta c) \times P_c}.$$

It is assumed that FSW-client contacts follow a Poisson distribution^[5,19], that one client has sex with one FSW at a time and only has one episode of vaginal intercourse at this time, and that the FSWs in the cohort do not have regular partners who are HIV positive.

RESULTS

Sociodemographic Characteristics

There were 217 HIV-1 negative, non-drug using FSWs that participated in at least two surveys. Table 1

describes the sociodemographic characteristics of FSWs in the open cohort. Of the 217 open cohort participants aged from 16 to 51 with an average age of 29.22 ± 8.98 , the average duration of education for those who were formally educated was 7.77 ± 3.53 years. Sociodemographic characteristics were compared between FSWs who were included in the study ($n=217$) and those who were lost in follow-up ($n=245$). No difference was found except for the work venues ($P < 0.001$, data not shown).

Table 2 illustrates the sociodemographic characteristics of male clients. The 558 clients were aged from 16 to 75, with an average age of 33.94 ± 12.56 .

Determination of Parameter Values (Table 3)

The number of FSWs in the cohort, N : There were 217 FSWs who took part in at least two surveys.

Working days per FSW per year, d : It is assumed that FSWs do not work for 25 days for the Chinese Spring Festival, 5 days each month due to menstruation, and an additional 5 days for personal affairs each month. It is therefore assumed that FSWs work 220 days per year.

The number of clients of per FSW per day, m : According to self-reported data, the average number of male clients whom FSWs had intercourse with in the last day was 1.52, which was regarded as the number of clients per FSW per working day in one year.

HIV-1 incidence of FSW cohort per year, I_{inc} : All 217 FSWs were HIV negative at baseline. It is assumed that those who were tested HIV positive in the second or third survey were regarded as recently infected cases. In this cohort, there were 3 new cases of HIV, one was serum positive at the second survey, and two additional FSWs were seroconverted at the third survey. The total follow-up time was 184 person-years. So HIV incidence is 1.63/100 person-years.

The proportion of infected clients, P_c : In May 2008 and November 2008, 558 male clients participated in the cross-sectional studies. For those clients who participated twice in the study, only the more recent study visit was taken into consideration. The proportion of infected clients was 4.66% (26/558).

The proportion of condom use for vaginal intercourse, c : In this study, reported condom use differed between FSWs and male clients. Almost all (96.31%) FSWs self-reported condom use in the last week, while only 69.5% of clients self-reported condom use in the last month. The Joint Assessment of HIV/AIDS Prevention, Treatment and Care in China (2006) reported that the proportion of FSWs

who always used condoms in the last three months was 41.4%^[1]. In this study, the more conservative estimate of the male clients proportion of condom use for heterosexual sex was used: $c=69.50\%$.

The condom efficacy in heterosexual sex, η : According to clients' self-reports, 22.50% condoms were broken during vaginal intercourse with FSWs in the last month (and no anal sex was self-reported). The condom efficacy for vaginal intercourse is therefore assumed to be, $\eta=1-22.50\%=77.50\%$.

Estimation of Probability of Unprotected Heterosexual Transmission of HIV-1 from Male to Female

$$\begin{aligned} \beta &= \frac{N \times I_{inc}}{N \times m \times d \times (1 - \eta \times c) \times P_c} \\ &= \frac{I_{inc}}{m \times d \times (1 - \eta \times c) \times P_c} \\ &= \frac{1.63 / 100}{1.52 \times 220 \times (1 - 69.5\% \times 77.5\%) \times 4.66\%} \\ &= 0.0023 \quad (95\% \text{ CI: } 0.0014 - 0.0032) \end{aligned}$$

DISCUSSION

In this study, the transmission probability from male clients to FSWs was estimated as 0.0023 [95% CI: 0.0014-0.0032] infections per unprotected heterosexual act. This result is within the range from the findings of a meta-analysis of transmission probabilities in low-income countries (male-to-female 0.30 per act [95% CI: 0.14-0.63]), but higher than that found in discordant couples in high-income countries (male-to-female 0.08 per act [95% CI: 0.06-0.11])^[18]. Our probability is lower than a reported of FSWs from Thailand^[5]. The transmission probability from males to females has been found to be higher than from females to males^[8,18]. A higher transmission probability than that was found in discordant couples in the United States, Europe^[19], and Uganda^[20]. These studies, however, did not differentiate the direction of the transmission. The scenario in Thailand, however, cannot be generalized to China since the epidemic is also dependent on the HIV incidence and the proportion of the population that engages in high risk behaviors. Other factors which may impact the incidence of HIV include percentage of condom use, the number of clients and episodes of vaginal intercourse per day, and the HIV prevalence among clients. The HIV epidemic can be controlled through interventions^[21], so the epidemic situation should be assessed and forecasted through incidence which is reflected by transmission probability, and the effect of ongoing interventions should also be considered.

TABLE 1

Sociodemographic Characteristics of FSWs ($n=217$)

Demographic Characteristics	Number (%)	Demographic Characteristics	Number (%)
No Education	22(10.14)	Divorced*	65(29.95)
Formally Educated	195(89.86)	Cohabiting	45(20.74)
Han Ethnicity	162(74.65)	Percentage of Syphilis	8(3.69)
Others Ethnicities	55(25.34)	Percentage of HSV-2	153(70.51)
Local	70(32.26)	Percentage of Gonorrhea	15(6.91)
Other Counties	62(28.57)	Reside in Nightclubs	51 (23.50)
Other Prefectures	47(21.66)	Reside in Karaoke Bars	72 (33.18)
Other Provinces	38(17.51)	Reside in Beauty Salons	41 (18.89)
Single	62(28.57)	Reside in Street	41 (18.89)
Married	45(20.74)	Reside in Other Location	12 (5.53)

Note. *Including separated & widowed.

TABLE 2

Sociodemographic Characteristics of Male Clients ($n=558$)

Demographic Characteristics	Number (%)	Demographic Characteristics	Number (%)
No Education	47(8.42)	Other Counties	83 (14.87)
Primary School	155 (27.78)	Other Prefectures	105 (18.82)
Middle School	285 (51.08)	Other Provinces	55 (9.86)
High School	62(11.11)	<1500 Yuan (\$221 USD)**	365 (65.41)
College and Above	9(1.61)	1500-3000Yuan (\$221-\$441USD)**	156 (27.96)
Single	278 (49.82)	>3000 Yuan (\$441 USD)**	37 (6.63)
Married	161 (28.85)	Live in Urban	439 (78.67)
Divorced*	119 (21.33)	Live in Rural	119 (21.33)
Han Ethnicity	368 (65.95)	Percentage of IDUs	35(6.27)
Yi Ethnicity	117 (20.97)	Percentage of Syphilis	13(2.33)
Others Ethnicities	73 (13.08)	Percentage of HSV-2	141(25.27)
Local	315 (56.45)	Percentage of HARRT	2/26(7.69)

Note. *Including Separated & Widowed. **Month Income.

TABLE 3

Value Estimation of Parameters for Transmission Probability

Parameters	Implication	Value Estimation
N	Number of FSWs	217
d	Working Days per FSW per Year	220
m	Number of Clients per FSW per Day	1.52
I_{inc}	HIV Incidence of FSW Cohort per Year (/100 person-years)	1.63
P_c	HIV Prevalence of Male Clients	4.66%
c	Proportion of Condom Use for Vaginal Intercourse	69.50%
η	Condom Efficacy in Vaginal Intercourse	77.50%

The efficiency of heterosexual HIV transmission varies between countries and is influenced by several factors. The stage of infection^[19] and viral load^[20] have an important impact on transmission probability, because viral load fluctuates with the stage of infection^[13]. Since HIV viral load was not measured and no data on the stage of HIV infection was

collected, it is difficult to estimate how these variables impact the transmission probability in this study. A study from Uganda reported a transmission probability of 0.0043 per unprotected heterosexual act, although the studied group was treated HIV-infected patients (HIV RNA<10 copies per mL)^[22]. Highly active antiretroviral therapy (HAART) has

been demonstrated to be able to lower HIV viral load^[23], which could lead to lower transmission probability^[24]. In our study, only 2/26 (7.7%) of HIV positive male clients were on HAART.

Co-infection with genital ulcers may also increase transmission probability by increasing the susceptibility to HIV infection, but the probability of transmission varies with the type of STI^[20,25]. In our study, the STI prevalence is lower than that reported in Thailand^[26]. Transmission efficiency may also vary in different populations with HIV subtypes^[2] but no difference in transmission probability based on HIV subtypes has been reported^[20]. In Kaiyuan, the main HIV-1 subtypes of FSWs are CRF_BC and C^[27], which differ from those found in Thailand (subtype E and B)^[2]. Therefore, subtypes of HIV-1 infection may also influence transmission probability. Male circumcision may decrease the probability of HIV transmission^[25,28-32], however, there is a lower prevalence of circumcision in China compared with other countries^[33-35]. There are different findings concerning the effect of circumcision on HIV transmission^[36]. The different probabilities between non-transactional sexual partners and commercial sex workers also indicate that the sexual mode and STIs status were also influence factors. In Yunnan province, clients often visit FSWs for a “fast snack” (vaginal intercourse in a short period of time), during which lubricant is not always used and the FSWs are more likely to bleed from the friction. FSWs may therefore, be at greater risks for acquiring HIV infection^[35].

This study was subject to several limitations. FSWs who participated in more than one survey were more likely to work at night clubs, which were considered to be a lower risk venue compared to those who worked in beauty salons or brothels^[27]. Therefore, HIV incidence in this cohort may be somewhat underestimated. The percentage of condom use and the number of clients seen by FSWs were based on self-report and may be subject to social desirability and recall biases. In order to reduce these bias, participants were ensured that all of their responses would be de-identified and confidential. Clients and FSWs were recruited by convenience sampling, so participants in this study may not reflect all those engaging in commercial sex in Kaiyuan county, and these clients may not represent all local clients. This study also assumes that male clients and FSWs included in this study were in a closed system of commercial sex, but it is likely that male clients and FSWs were engaged in commercial sex with those not included in this study. Due to limited data, only the transmission probability from clients to FSWs was estimated. Studies indicate that male-to-female HIV transmission is more efficient

than female-to-male^[8,37-38]. Future studies should also investigate the female-to-male transmission probability among commercial sex partnerships.

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