China Meets New AIDS Challenges

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Since acknowledging the HIV/AIDS epidemic,[1,2] significant efforts to understand the epidemic in China have been undertaken resulting in a comprehensive policy response based on those understandings.[3,4] From 2003 onwards, China has implemented ambitious treatment, prevention, and control programs, and significant resources to combat HIV/AIDS have been allocated, resulting in increased government infrastructure and capacity.[3,4] Many successes have occurred since 2003; however, new challenges are emerging, and many previously identified challenges remain and continue to evolve. Although the research effort into properly understanding HIV/AIDS in China continues to expand, it is necessary to translate scientific findings into public health programs, which can be implemented nationwide. China does not yet have the luxury of complacency in its response to HIV/AIDS. This special edition of the *AIDS Journal of Acquired Immune Deficiency Syndromes* presents research into these new and continuing AIDS challenges.

New HIV/AIDS challenges emerging in China include transition from previously blood-driven HIV epidemic to now sex-driven HIV epidemic,[3,5] the expanding epidemic among men who have sex with men (MSM),[6,7] increasing drug resistance to antiretroviral therapy among new infections,[8] the fast changing risk behaviors of high-risk populations,[9,10] preventing mother-to-child transmission,[11] and the potential for the HIV and tuberculosis (TB) epidemics to merge.[12]

Among the new HIV/AIDS challenges emerging in China, the expanding epidemic among MSM is undoubtedly the gravest of these new challenges regarding transmission of HIV.[6,7,13] The number of MSM in China is considerable, and a large proportion of them also have unprotected sex with women; therefore, significant subgroups of MSM are a bridging group to heterosexual women who are presumed to be low risk. Several articles documenting HIV prevalence, risk behaviors, stigma, and a pilot program to increase condom use and HIV testing are presented here.[13–15] Chengdu City, the capital city of Sichuan province, with a large population of MSM, seems to be an important city in the emerging MSM epidemic due to it attracting large numbers of domestic migrants and being a major stop on the heroin trafficking route through China. Two articles presented here investigating HIV/sexually transmitted disease prevalence and sexual risk behaviors and stigma in Chengdu found a HIV, herpes simplex virus-2, and syphilis prevalence rate of 9.1%, 24.7%, and 28.1%, respectively, and low condom use rates varying by partner type: 17.8% for steady female partners and 38.6% for casual male partners.[7,15] Stigma and discrimination against HIV/sexually transmitted disease infection and homosexual behaviors were found to be significant barriers to HIV testing and treatment.[15] In a study of nearly 5000 MSM in low prevalence regions of China, HIV prevalence was 2.9% and syphilis was 9.8%.[13]

Encouragingly a trial peer-driven behavioral intervention to increase condom use and HIV testing among MSM in Anhui province significantly increased HIV testing from 10% at baseline to 52.4% postintervention, although the increase in condom use was not as great (55.3% vs. 65.2%), and it was unsuccessful at reducing the number of sexual partners reported.[14] The internet has revolutionized MSM interaction in China, and the full import of this is only beginning to be understood by public health professionals. An investigation into HIV prevalence, sexual risk behaviors, and internet use by MSM in Beijing and Urumqi is

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Preparation of the article was partly supported by the Multidisciplinary HIV and tuberculosis Implementation Sciences Training in China with the National Institutes of Health Research Grant number of 2U2RTW006918-06 funded by the Fogarty International Center, National Institute on Drug Abuse and the National Institute of Mental Health.

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an important contribution to understanding the significance of the internet as a sex partner seeking venue.[6] Results indicate that for MSM who use the internet, the internet was by far the most popular venue to find a sexual partner with 82% of participants using it to find sex partners, the next most popular venue, cafes and bars, were only used by 15% of participants.[6] The implications of this are that outreach activities using traditional venues will not reach MSM who use the internet. The sexual and other risk behaviors of MSM in China have still not been comprehensively described, and it is anticipated that they will play a crucial role in the further transition of China's epidemic from being driven by injection drug use to sexual intercourse; however, the research presented here help shed light on this vulnerable, and important, risk group.

Regarding the treatment of HIV, the most concerning emerging challenge is expected to be increased future transmission of drug-resistant strains of HIV. In a sample of nearly 700 newly reported HIV infections from a variety of transmission modes in 2004—2005, the prevalence of HIV drug-resistant strains was low (3.8%); however, an increase in the transmission of high-level drug resistance was found.[8]

With the increase in sexual transmission of HIV and the majority of HIV-positive people living in China's countryside, preventing mother-to-child transmission will become more important over time. A trial intervention in rural Yunnan to prevent mother-to-child transmission, the province worst affected by HIV, had only a 1% seroconversion rate 18 months postdelivery and had a 96.3% survival 1 year after birth.[11] Scale-up of the program nationwide should be feasible.

China has a high burden of TB, and there is concern that TB and HIV epidemics could merge. Research in Guangxi, a high TB and HIV prevalence province, found HIV prevalence was higher among TB patients than among the general population,[12] therefore, in selected areas of China, programs to address TB/HIV coinfection are needed.

Continuing challenges include rural blood supply safety,[16] providing appropriate support for children affected by HIV/AIDS,[17] preventing further spread among female sex workers, the role migrant workers play in the epidemic,[18] accessing difficult to reach high-risk populations, and having China-appropriate research tools.[19–21]

All HIV infections are tragic, and an especially tragic episode of the HIV epidemic in China was the infection of large numbers of rural commercial plasma donors in the early to mid-1990s through unsafe plasma collection practices.[9] Because commercial plasma donation was outlawed in 1996, significant efforts have been made to increase the safety of the blood supply process, especially in rural China. In a study of the effectiveness of tests to ensure the safety of blood supply in 3 rural blood collection organizations, the sensitivity of the tests for hepatitis B surface antigen, hepatitis C virus, and syphilis were found to be inadequate, indicating much work on improving the quality of laboratory work remains.[16]

As the HIV/AIDS epidemic progresses, more children are affected by the disease through the loss of one or both parents. Research in Yunnan found children from HIV-affected families which experienced parental illness or death suffered from decreased school attendance and performance.[17] In addition, children from HIV-affected families had lower levels of quality of life compared with child from non–HIV-affected families.[17,21] China now needs to expand on the free schooling offered through the 4 Free's and 1 Care program to provide adequate support to the gradually increasing numbers of children affected by the epidemic.[1–3]

The sex industry in China is massive and varied. Although much work has been done to improve condom use rates among female sex workers (FSWs), as research presented here shows, consistent condom use with clients remains inadequate (58% in the past week), and FSWs are also at risk from regular and nonregular noncommercial sexual partners where condom use rates are usually much lower.[22] Undoubtedly, efforts targeting FSWs to increase condom use must continue, but as research from migrant miners in Yunnan shows, where 72% of miners who had ever patronized a FSW had never used a condom with them, efforts must now be made to educate male clients of FSWs on the importance of condom use.[18] In addition, efforts to develop a microbicide, the use of which is completely controlled by the female, must continue.[23] Encouragingly, hypothetical acceptability of microbicides among FSWs and their male clients in a high HIV prevalence region of China seems to be high, however, caution must be taken if microbicides are brought to market to ensure they are not used as a substitute to condom use.[23]

Research instruments are critical to ensuring the quality of data collected. Information on the validity of the Mandarin versions of the fifth English version of the Addiction Severity Index and the PedsQL (pediatric quality of life) are presented.[19]

Finally, this special edition also includes 2 important articles documenting, in English, for the first time using government data, a comprehensive history of the epidemic in Yunnan,[10] the epicenter of China's HIV/AIDS epidemic; and a thorough description of HIV prevalence among affected groups in Henan,[9] the province most affected by unsafe commercial blood collection. The epidemic in Yunnan has undergone significant transformation since first being identified among injection drug users in 1989. By 2007, a total of 57,325 cases of HIV had been reported, and transmission has slowly evolved from injecting drug use long being predominant to sexual transmission in 2007 becoming the most common transmission route. The sociodemographic characteristics of people infected have changed with the share of rural infections decreasing dramatically, and the age range of infected people continues to increase as does the proportion of females. The early stages of the epidemic overwhelmingly affected ethnic minorities, but in 2005, the Han ethnic majority accounted for 63% of all infections. The epidemic in Yunnan is now classified as concentrated, and prevention efforts must change to target the sexual partners of higher risk groups. Given the complexity of ethnic groups, cultures and risk behaviors, containing HIV in Yunnan will remain challenging.

Data from 3 sources in Henan: the case reporting system, the sentinel surveillance system, and special surveys among former plasma donors (FPDs) were used to describe HIV prevalence in that province.[9] By the end of 2006, a total of 35,232 HIV cases had been reported. Overall, HIV prevalence among identified FPDs was 8.6%. HIV prevalence among

FPDs varied widely by county, with 0.09% the lowest recorded and 13% the highest. Sexual transmission among non-FPD risk groups is increasing, and HIV testing and increased condom use is suggested to reduce further transmission.

We hope this special edition will provide additional insights into the challenges facing China as the HIV/AIDS epidemic evolves. We also believe that China will able to adjust and tailor its responses and keep HIV/AIDS epidemic remaining in low rate.

ACKNOWLEDGMENTS

Authors would like to thank Naomi Juniper for her valuable comments and suggestions.

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The Prevalence of Transmitted Antiretroviral Drug Resistance in Treatment-Naive HIV-Infected Individuals in China

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Background: Transmission of HIV drug resistance (TDR) gives rise to reduced efficacy of initial antiretroviral treatment and has become a public health concern.

Methods: A nationwide survey on TDR was conducted in antiretroviral therapy-naive HIV-1–infected individuals from September 2004 to October 2005 in China. Drug resistance genotyping was performed on subjects' plasma samples. Drug resistance mutations were determined and scored by Stanford HIV Drug Resistance algorithm.

Results: Sequences were obtained from 676 individuals, of whom 61.2% were former plasma and blood donors, 17.3% were infected sexually, and 17.2% were intravenous drug users. Subtype B' HIV-1 strains were found in 73.5%, CRF01_AE in 13.9%, CRF07_BC in 6.2%, CRF08_BC in 2.7%, subtype C in 1.04%, subtype B in 0.9%, CRF02_AG in 0.4%, and B'/C intersubtype recombinant strains in 1.3% of the subjects. Twenty-six (3.8%) were found to harbor drug resistance strains. The rates of resistance to protease inhibitors, nucleoside reverse transcriptase inhibitors, and nonnucleoside reverse transcriptase inhibitors were 0.4%, 1.6%, and 2.1%, respectively. Though there was no significant difference in TDR rates between 2004 and 2005 (2.9% vs. 4.4%), an increased trend was observed in the rate of high-level drug resistance (0.8% in 2004 vs. 3.0% in 2005, $P = 0.0634$).

Conclusions: The rate of TDR was relatively low in China, as compared with those in developed countries. Surveys among recently HIV-infected subjects should be performed continually to ensure the success of the scale-up antiretroviral treatment.

Key Words: prevalence, treatment naive, transmitted HIV-1 drug resistance

(*J Acquir Immune Defic Syndr* 2010;53:S10–S14)

INTRODUCTION

Since the first HIV case was identified in 1985 in China, the HIV/AIDS epidemic kept rising during the subsequent 20 years. By the end of 2005, it was estimated that 650,000 individuals living with HIV/AIDS in China, of whom 75,000 were AIDS patients.[1] Intravenous drug use (44.3%), sexual contact (43.6%), and unsafe blood and plasma collection (10.7%) were main transmission routes which contributed to most of the 141,000 HIV cases reported. Furthermore, the distribution of HIV/AIDS cases was not geographically even in China: 5 of 31 provinces and autonomous regions had reported over 10,000 cases, whereas 3 other provinces had less than 100 reported cases.

To improve the life of HIV/AIDS patients and reduce the HIV/AIDS-related morbidity and mortality, the Chinese government put forward a "four free one care" policy in 2003.[2] About 5000 patients received a national free antiretroviral therapy (ART) program in its first year of inception. Since then, the number of patients enrolled in the program has increased rapidly. At the end of 2005, more than 22,000 patients were ever involved in the free ART program, of which about 19,200 were still on ART.[3] Most of them were HIV-infected former blood and plasma donors (FPDs) living in rural areas of central China. Resources for antiretroviral drugs are limited in China. There is a concern that the prevalence of antiretroviral drug resistance would compromise the effect of current regimens and give rise to treatment failure.

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Supported by the Mega-projects of Science Research for the 11th 5-year plan (2008ZX10001-004), the National Basic Research Program (2005CB523103), and the International Cooperation Program (20070FC30230), granted by the Ministry of Science and Technology of China; funds from the China Global Fund AIDS Program Round 3 & 4, the Global Fund to Fight AIDS, Tuberculosis, and Malaria; and the China ICOHRTA with Grant #U2R TW 006918, funded by the US National Institutes of Health, the Fogarty International Center, the National Institute of Drug Abuse and the National Institute of Mental Health.

Presented in part at the 4th IAS Conference on HIV Pathogenesis, Treatment, and Prevention, July 22–25, 2007, Sydney, Australia. Abstract TUPEB051.

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With the scale-up of a free ART program, a nationwide survey was conducted to study the genetic characteristic and antiretroviral drug resistance of HIV type 1 (HIV-1) strains in treatment-naive HIV-infected individuals from 2004 to 2005.

METHODS

Study Population

Treatment-naive HIV-1–infected individuals were randomly enrolled in provinces and autonomous regions where free antiretroviral drugs were available at the time the survey was conducted. The duration of sample collection was from September 2004 to October 2005. In 2004, treatment-naive HIV-infected individuals in 14 provinces were included. With the rapid scale-up of the national free ART program, the geographic range of the study was expanded to 28 provinces and autonomous regions in the subsequent year. Subjects who were below 18 years old were excluded from the study. All the subjects gave written informed consent for participation in this study. The survey was reviewed and approved by the institutional review boards and scientific ethical committees at the Chinese Ministry of Health.

Laboratory Tests

Subjects' whole blood samples were collected and processed in the provincial Centers for Disease Control and Prevention's laboratries. CD4 cell count was measured within 24 hours after sampling. Meanwhile, plasma was separated by centrifugation and instantly stored at −80°C. The plasma samples were then sent in dry ice to the 4 core laboratories of the Chinese HIV Drug Resistance Surveillance Network. Plasma HIV RNA was quantified with real-time nucleic acid sequence based amplification (NASBA) (bioMerieux, Lyon, France), or COBAS (Roche Applied Science, Penzberg, Germany) according to the manufacturer recommendations. For samples with viral loads equal to or greater than 1000 copies per milliliter, HIV drug resistance (HIVDR) genotyping was carried out by an in-house polymerase chain reaction protocol as previously described.[4] HIV-1 *pol* gene (protease 1–99 amino acids and part of reverse transcriptase 1–250 amino acids) was amplified, purified, and bidirectly sequenced in an ABI3100 sequencer (Applied Biosystems, Foster City, CA). For analysis of HIV-1 drug resistance mutation, each sample sequence was compared with the subtype B consensus sequence in the Stanford HIV Drug Resistance Database (http://hivdb.stanford.edu) and was interpreted by HIVdb program. For HIV-1 subtyping, the edited sequences were aligned against reference sequences available at the Los Alamos database (http://hivweb.lanl.gov). Phylogenetic trees were constructed by the neighbor-joining method with 1000 bootstrap replicates using Mega 4.0. Bootscaning analyses were performed on samples possibly having unidentified intersubtype recombinant strains by using Simplot 3.5.1.

Statistical Analysis

The significant differences in categorical variables were analyzed using χ^2 test or Fisher exact tests. Statistical significance was defined as a P value <0.05. All the statistical analyses were performed with SAS 9.1 software (SAS Institute, Cary, NC).

RESULTS

Subjects Included

One thousand one hundred ninety-four ART-naive HIV-1–infected subjects were enrolled (442 in 2004 and 752 in 2005). Two hundred twenty-seven individuals who had a plasma viral load less than 1000 copies per milliliter were excluded from the study, as the possibility of such subjects to be sources of HIV infection would be less than those with a higher viral load. In addition, the genotypic results from samples with a viral load lower than 1000 copies per milliliter were not reliable using routine methods. Of the remaining 967 samples, 676 (69.9%) were successfully sequenced. Among these subjects, 460 (68.1%) were male. Median age was 38 years (range: 18–72). Four hundred fourteen (61.2%) were FPDs, 117 (17.3%) acquired HIV infection through sexual contact, 116 (17.2%) were intravenous drug users, 27 (4.0%) were infected through blood transfusion, and the transmission routes of the remaining 2 subjects were unknown. More than half of the subjects (351 of 676, 51.9%) had a primary school education or less. Four hundred fifty-one (66.7%) were farmers living in rural areas. Median CD4 cells count and viral load at sampling were 280 cells per cubic millimeter (range: 23–723) and 4.59 log copies per milliliter (range: 3.01–6.80), respectively.

HIV-1 Subtypes, Circulating Recombinant Forms, or Intersubtype Recombinant Strains

Phylogenetic trees base on the whole protease (1-99aa) and part of reverse transcriptase (1-250aa) gene revealed that a majority of the HIV-1 isolates (497, 73.5%) studied belonged to subtype Thai-B (B'), the second most prevalent strain was CRF01_AE (94, 13.9%), followed by CRF07_BC (42, 6.2%), CRF08_BC (18, 2.7%), subtype C (7, 1.04%), subtype B (6, 0.9%), and CRF02_AG (3, 0.4%). Bootscaning analyses were performed on sequences from nine samples, which did not cluster with any present known reference sequences. The results revealed the presence of B'/C intersubtype recombinant strains with different mosaic structures from those of CRF07_BC and CRF08_BC (Fig. 1). The distribution of HIV-1 strains was uneven among different risk groups ($P < 0.0001$). Subtype B' HIV-1 strains were more frequently found in FPDs (398, 80.1%) than in other HIV-1–infected populations; CRF07_BC strains were more likely to be found among intravenous drug users (IDUs) (27, 64.3%), whereas most CRF01_AE strains were detected in 2 groups: IDUs (46, 39.7%) and sexually infected individuals (41, 35.0%).

Antiretroviral Drug Resistance-Associated Mutations

Twenty-six of 676 isolates (3.8%) were identified to be resistant to 1 or more antiretroviral drugs (Table 1). Primary drug resistance mutations to protease inhibitors were found in 3 samples (0.4%), which had 1 single mutation each. M46I and N88D, which confer intermediate resistance to nelfinavir, were respectively detected in 1 subject (CNSHD0050) from Shanghai and 1 person (CNHND0066) from Hunan province.

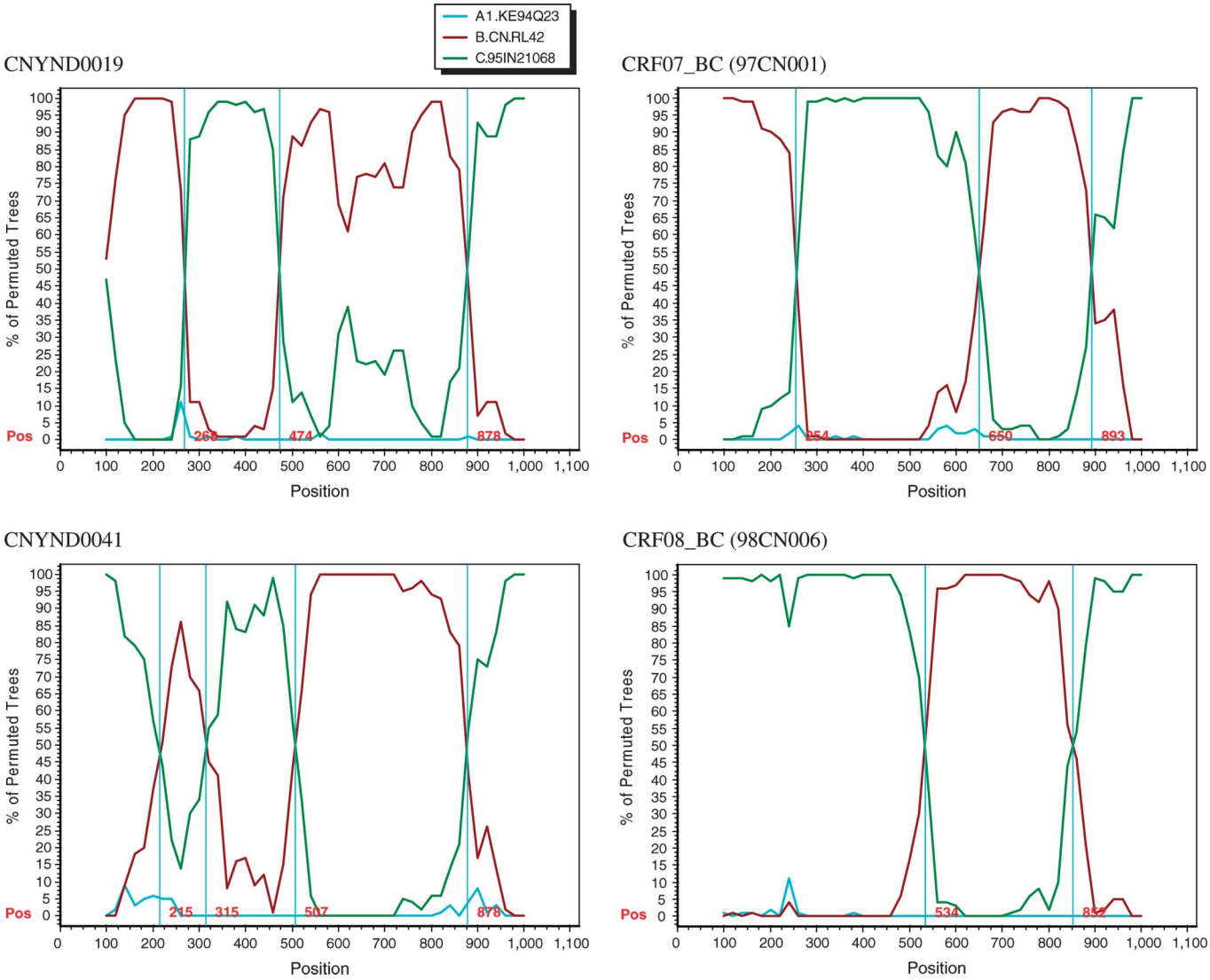

FIGURE 1. Bootscanning analyses to identify new intersubtype recombinant strains. A bootscaning plot was constructed by using Simplot 3.5.1 software based on 100 replicates with a 200-bp sliding window moving in steps of 20 bases. Subtype references were B′ (RL42), India C (95IN21068) and subtype A (KEQ23). The breakpoints in CNYND0019 and CNYND0041 were different from those of the reference strains of CRF07_BC (97CN001) and CRF08_BC (98CN006).

A V82A mutation conferring resistance to atazanavir, indinavir, lopinavir (LPV), and nelfinavir was found in 1 subject (CNGXD0011) from Guangxi province.

Mutations associated with resistance to reverse transcriptase inhibitors were found in 23 subjects. Twenty-one of them were resistant to either nucleoside reverse transcriptase inhibitors (NRTIs) (n = 9) or nonnucleoside reverse transcriptase inhibitors (NNRTIs) (n = 12); 2 were resistant to both NRTIs and NNRTIs. The most frequent NRTI-related mutation was M184V/I, conferring high resistance to lamivudine and emtricitabine and was found in 4 (4 of 23, 17.4%) samples. At least 1 thymidine analogue mutation, which was associated with intermediate or low-level resistance to zidovudine or other NRTIs, was found in 5 samples. The most frequent NNRTI-related mutation was K103N, which was found in 9 (9 of 23, 39.1%) samples.

Comparison of the HIVDR rate in 3 major risk groups revealed that there was no significant difference among FPDs (13 of 414, 3.1%), sexually infected individuals (5 of 117, 4.3%), and IDUs (4 of 116, 3.5%). No significance difference on transmission of HIV drug resistance (TDR) rate was found between female (7 of 216, 3.2%) and male (19 of 460, 4.1%) subjects, those with primary education or below (3.7%), and those with a higher education (4.0%), or between nonfarmers (5.3%) and farmers (3.1%). The rate of TDR in 2004 and 2005 was 2.9% (7 of 244) and 4.4% (19 of 432), respectively, with no significant difference between the 2 years ($P = 0.3207$). The rate of high-level resistance to 1 or more antiretroviral drugs was also

TABLE 1. Genotypic Resistance Mutations Detected and Phenotypic Resistance Predicted (Stanford HIVDB Algorithm)

Gender	Age	Likely Risk Group	Subtype	Resistance Mutations			Predicted Phenotypic Resistance		
				PI	NRTI	NNRTI	PI	NRTI	NNRTI
M	42	Sexual contact	01_AE	M46I	—	—	NFV (I)	—	—
M	38	Sexual contact	01_AE	N88D	—	—	NFV (I)	—	—
M	58	Blood recipient	B'	V82A	—	—	ATV(L), IDV(I), LPV(L), NFV(I)	—	—
F	60	FPD	B'	—	M41L	—	—	AZT(L), d4T(L)	—
M	56	Blood recipient	02_AG	—	D67G	—	—	AZT(L)	—
M	34	IDU	01_AE	—	K70R	—	—	AZT(L)	—
M	48	FPD	B'	—	M41L, D67G	A98G	—	ABC(L), AZT(I), d4T(L), ddI(L)	—
F	42	FPD	B'	—	M184I	—	—	3TC(H), FTC(H)	—
M	31	Blood recipient	B'	—	M184V	—	—	3TC(H), FTC(H)	—
M	38	Sexual contact	B'	—	M184V	—	—	3TC(H), FTC(H)	—
M	38	FPD	B'	—	T215S	—	—	AZT(L), d4T(L)	—
M	30	IDU	01_AE	—	T215S	—	—	AZT(L), d4T(L)	—
F	40	FPD	B'	—	K70R, K219E	K103N	—	AZT(I), d4T(L)	DLV(H), EFV(H), NVP(H)
M	22	IDU	01_AE	—	D67N, M184V, T215Y, K219Q	K101E, G190A	—	ABC(I), AZT(I), d4T(I), ddI(I), 3TC(H), FTC(H), TDF(L)	DLV(I), EFV(I), NVP(H)
F	36	Sexual contact	B'	—	—	K103N	—	—	DLV(H), EFV(H), NVP(H)
M	40	FPD	B'	—	—	K103N	—	—	DLV(H), EFV(H), NVP(H)
M	36	FPD	B'	—	—	K103N	—	—	DLV(H), EFV(H), NVP(H)
F	40	FPD	B'	—	—	K103N	—	—	DLV(H), EFV(H), NVP(H)
M	18	FPD	B'	—	—	K103N	—	—	DLV(H), EFV(H), NVP(H)
M	37	IDU	07_BC	—	—	V179D	—	—	DLV(L), EFV(L), NVP(L)
M	18	Sexual contact	B'	—	—	G190E	—	—	DLV(I), EFV(H), NVP(H)
F	18	FPD	B'	—	—	A98G, K103N	—	—	DLV(H), EFV(H), NVP(H)
M	22	Blood recipient	B'	—	—	K101E, V106I	—	—	DLV(I), EFV(L), NVP(I)
M	18	FPD	B'	—	—	K101E, G190A	—	—	DLV(I), EFV(I), NVP(H)
M	51	FPD	B'	—	—	K103N, G190A	—	—	DLV(H), EFV(H), NVP(H)
F	27	FPD	B'	—	—	K103N, Y181C	—	—	DLV(H), EFV(H), NVP(H)

AZT, zidovudine; ABC, abacavir; d4T, stavudine; ddI, didanosine; FTC, emtricitabine; 3TC, lamivudine; TDF, Tenofovir; EFV, efavirenz; ATV, atazanavir; IDV, indinavir; LPV, lopinavir; NFV, nelfinavir; NVP, nevirapine; L, low-level resistance; I, intermediate resistance; H, high-level resistance; PI, protease inhibitor.

not significant ($P = 0.0634$), although there was an increase in 2005 (3.0%, 13 of 432), compared with 2004 (0.8%, 2 of 244).

DISCUSSION

Our study was the first nationwide survey on TDR in ART-naive individuals and revealed the existence of transmitted HIV drug resistance in China. Evidence of TDR was found in 3.8% of the subjects studied. This result was similar to results from a previous survey, which found 4.4% of HIV drug resistance of 91 ART-naive HIV/AIDS patients in Liaoning, a province in northeastern China.[5] This prevalence was comparable to that of international studies which showed 2.0% TDR during 2003 and 2006 in Thailand,[6] 4.3% from 1999 to 2005 in South Korea,[7] and 4.3% in 2002 in the Democratic Republic of Congo.[8] However, the prevalence of TDR in our study was lower than those in North America and Western Europe where various TDR rates were reported to be from 9.1%[9] to 24.1%.[10] The result was not surprising, as China, like other countries in Asia and Africa, has had a shorter period of access to ART than in developed countries.

In this study, the largest proportion of the HIV-1 strains was subtype B' strains, followed by CRF01_AE, CRF07_BC, CRF08_BC, and other subtypes, circulation recombinant forms or intersubtype recombinant forms. Though the total proportion of 4 predominant HIV-1 strains (subtype B', CRF01_AE, CRF07_BC, and CRF08_BC) and that of CRF01_AE strains alone were similar to what we previously reported on the second nationwide molecular epidemiology survey in 2001 and 2002,[11] the proportion of specific HIV-1 strains was different: CRF_BC strains, including CFR07_BC and CRF08_BC, accounted for more than half of the HIV-1 infections, subtype B' only contributed to about one third of the infections in that molecular epidemiology survey. This discrepancy may be due to a sampling bias in favor of regions where access to ART had been already established before the study began. Additionally, the shift of risk groups of HIV infection that had occurred in recent years may produce an influence in the distribution of HIV-1 strains to some extent.[12] For this study, subtype B' strains also contributed to a substantial proportion of HIV-1 infections through sexual route and intravenous drug use.

Half of the HIV drug resistance (13 of 26) was found in individuals who were infected by unsafe commercial blood and plasma donation. It was believed that most FPDs acquired HIV infection in the mid-1990s, although a large number of HIV infections were confirmed during the intensive screening of FPDs in 2004. Antiretroviral drugs were not introduced in China during the 1990s. It was therefore impossible that these patients were infected with drug resistance viruses at that time. To avoid including subjects who had a history of ART, the ART status of all subjects with detected drug resistance were reinvestigated by phone or interviewing. About 30 persons with drug resistance were excluded from the study because of having taken antiretroviral drugs. The existence of HIV drug resistance in FPDs in this study include subjects who, infected through intravenous drug use or sexual contact, were reluctant to confess to their mode of transmission due to social stigma.[13,14] A portion of FPDs with drug resistance had actually taken antiretroviral drugs at least once, but they were not fully able to understand the questions about their treatment status, or they did not think they had been treated because they only took antiretroviral drugs once or twice. The latter situation would lead to overestimate the prevalence of TDR.

The results of this study was not generalizable to overall HIV infections for the following reasons. First, a large proportion of the subjects were not infected recently. As drug resistance strains become minor quasispecies in the plasma after a period of infection, the regular population-based sequencing method will fail to detect them.[15] Second, the selection of the studied population could skew the estimate of the TDR rate in HIV-1 infections. Third, a relative low amplification rate of samples with viral loads equal to or greater than 1000 copies per milliliter may impose an impact on the evaluation of TDR rate. Analysis of the distribution among risk groups revealed that the proportion of the unamplified samples from IDUs and subjects who were infected sexually was higher than those from FPDs (P = 0.0008). However, our data have shown that there was no significant difference on the TDR rate in these 3 populations.

In this survey, we demonstrated the presence of TDR among treatment-naive individuals. More than half of the sample with HIV drug resistance showed resistance to NNRTI drugs. Though the TDR rate was relatively low comparing to those in developed countries, comprehensive measures are needed to prevent the spread of HIV drug resistance. More studies should be performed to investigate the rate of TDR among recent infections and provide implications to first-line therapy.

ACKNOWLEDGMENTS

We appreciate the contribution of all subjects included in this study. We are greatly grateful to the staff from provincial and county Center for Disease Control and Preventions for participating in sample collection and investigation. We thank Dr. Adrian Liau for his academic editing of the article.

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The Associations of hA3G and hA3B mRNA Levels With HIV Disease Progression Among HIV-Infected Individuals of China

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Objective: To explore correlations between mRNA (hA3G, hA3F, and hA3B) levels and $CD4^+$ T-cell counts and HIV-1 viral loads to evaluate their respective roles in disease progression.

Methods: Real-time polymerase chain reaction was used to quantify the mRNA levels of hA3G, hA3B, and hA3F in peripheral blood mononuclear cells from slow progress patients (SP), asymptomatic HIV-infected patients (AS), AIDS patients, and HIV-negative controls.

Results: The levels of hA3G and hA3B mRNA correlated positively with $CD4^+$ T-cell counts ($r = 0.436$, $P = 0.002$, $r = 0.334$, $P = 0.025$), and negatively with HIV-1 viral loads ($r = -0.306$, $P = 0.038$, $r = -0.301$ $P = 0.044$). The levels of hA3G and hA3B mRNA in HIV-infected subjects were lower than in HIV-negative controls ($P < 0.05$), and hA3G and hA3B mRNA levels were significantly higher in SP than in AIDS patients ($P < 0.05$). There was no correlation between the hA3F mRNA level and $CD4^+$ T-cell counts or between the hA3F mRNA level and HIV-1 viral loads.

Conclusions: Higher expression levels of hA3G and hA3B mRNA in the peripheral blood mononuclear cells of Chinese HIV-infected individuals were found to be associated with slower HIV disease progression, suggesting their potential roles in antiviral innate immunity.

Key Words: hA3G, hA3B, hA3F, HIV-1, slow progress patients

(*J Acquir Immune Defic Syndr* 2010;53:S4–S9)

INTRODUCTION

The human apolipoprotein B mRNA-editing enzyme-catalytic polypeptide-like 3G (hA3G) belongs to a family of apolipoprotein B–editing catalytic polypeptide (APOBEC) proteins whose cytidine deaminase activity are cellular factors found to play a role in innate immunity.[1,2] Other known members of this family include APOBEC1, 2, APOBEC3A-3H, and AID.[3] hA3G has been found to induce dC-to-dU mutations in minus-strand DNA formed during reverse transcription, resulting in hypermutation of plus strand DNA. This enzymatic editing of HIV reverse transcripts leads to degradation of deaminated minus-strand DNA, thus restricting HIV type 1 (HIV-1) replication.[2]

HIV-1 and other lentiviruses encode the virion infectivity factor (Vif), an accessory protein that is critical for in vivo replication of HIV-1.[4,5] Vif counteracts the antiviral activity of hA3G by preventing the virion incorporation of endogenous APOBEC3G, thereby effectively depleting the intracellular levels of this enzyme in HIV-1–infected T cells. The translation of APOBEC3G mRNA becomes impaired and its degradation by a ubiquitine-proteasome pathway is induced.[6–8] However, Vif expression reduces hA3G levels in a dose-dependent manner: at lower Vif to hA3G ratios, it has no detectable effect on hA3G levels, whereas higher expression levels of hA3G can overcome the Vif-induced degradation.[8]

hA3G, hA3F, and hA3B are expressed in human cells, tissues, and peripheral blood mononuclear cells (PBMCs).[9] As with hA3G, hA3F also induces G-to-A hypermutation, though both the dinucleotide target for deaminase and degree of mutagenesis are different between these 2 proteins in vitro observations.[10] Another APOBEC protein, hA3B, also inhibits HIV-1 in cultured cells assayed. Other than hA3G, hA3B has, at most, a modest effect on HIV-1 infectivity. Furthermore, hA3B also differs from hA3F and hA3G in that it is unable to bind to HIV-1 Vif in coexpressing cells and is therefore efficiently packaged into HIV-1 virions regardless of Vif expression.[11] It is therefore resistant to HIV Vif and is able to suppress the infectivity of both Vif-deficient and wild-type HIV-1 virus with equal efficiency. These studies on hA3G, hA3F, and hA3B underscore the need for further investigation of the significance in vivo infection, especially among individual differences in HIV disease progression.

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Supported by the mega projects of national science research for the 11th five-year plan (2008ZX10001-001); 973 programs about the development of national significant elementary research (2006CB504206); and Liaoning province department of higher education program for excellence in research (2006R55).

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The natural history of HIV-1 infection and progression to AIDS shows high variability. Slow progressors (SP) make up about 20% of HIV-infected individuals and are defined as those who remain free from AIDS-related diseases and maintain normal $CD4^+$ T-cell counts for more than 10 years after infection without any antiretroviral therapy.[12–14] Mechanisms for this slow progression are not well understood, however, the effects of hA3G, hA3F, and hA3B which block retroviral infection in vitro, may play a role. Recent studies investigating the relationship between mRNA level of hA3G and viral load and $CD4^+$ T-cell counts have not delivered consistent results.[15,16] The contribution of these cellular defense factors to HIV disease progression deserves more in vivo investigation, particularly in the case of hA3B which has not been examined to date.

This study uses real-time polymerase chain reaction (PCR) assay to quantify hA3G, hA3F, and hA3B mRNA levels in PBMCs of Chinese HIV-1–infected individuals and healthy HIV-negative controls. We hypothesize that due to the similarity of viral factors, the individual variation of hA3G, hA3F, and hA3B mRNA expression levels in different disease progression stages would represent, to some extent, the contribution of each cytidine deaminase to the disease progression. To test this, we determined the mRNA expression levels of hA3G, hA3F, and hA3B and measured the correlations between these mRNA levels, $CD4^+$ T-cell counts, and HIV-1 viral loads to evaluate their respective roles in individual variations of disease progression rates.

METHODS

Study Subjects

PBMC samples of 46 HIV-infected and treatment-naive subjects and 17 HIV-uninfected healthy controls were recruited from Henan province after obtaining written informed consent. All subjects had been infected with B' subtype of HIV-1 via blood donation and were diagnosed as HIV-1 positive by confirmatory Western blot test. HIV-infected subjects were classified into 3 groups: slow progressors (SP), asymptomatic HIV-infected (AS), and AIDS patients (AIDS). Those who were infected with HIV-1 for more than 10 years with $CD4^+$ T cells $\geq$500 cells per microliter and showed no HIV symptoms were classified as SP; those infected for more than 5 years with $CD4^+$ T cells between 200 cells per microliter and 500 cells per microliter and without defined symptoms were classified as AS; and those with $CD4^+$ T-cell counts $<$200 cells per microliter were classified as the AIDS group. All 17 healthy controls were HIV-antibody negative. HIV-1 B′ subtype was determined and confirmed by phylogenetic analysis based on segments of *env*, *pol*, and *gag* gene regions.

Determination of $CD4^+$ T-Cell Counts

$CD4^+$ T-cell count was measured using TriTEST CD4FITC/CD8PE/CD3PerCP reagent with 20 μL anticoagulated whole blood. After incubation for 15 minutes in the dark at room temperature, Fluorescence-activated cell sorting lysis solution was added, and the sample was then incubated for another 15 minutes in the dark at room temperature. $CD4^+$ T-cell count and corresponding ratios were obtained by flow cytometer analysis with Fluorescence-activated cell sorting MULTISET software.

HIV Viral Load Assay

HIV RNA was extracted from plasma samples stored at −70°C and amplified by a standardized reverse transcription–PCR assay according to the manufacturer's instructions (COBAS Amplicor; HIV-1 Monitor Test Version 1.5; Roche Diagnostics, Branchburg, NJ). All viral load values were transformed to $\log_{10}$ values for statistical analysis.

Quantitative Real-time PCR

Whole blood was collected by venipuncture in vacutainer tubes containing EDTA (Becton Dickinson, Plymouth, UK), and PBMCs were separated with lymphocyte separation medium. RNA was isolated from 5×10^6 cells and treated with DNase (Qiagen, Hilden, Germany). cDNA products were synthesized with Random Primers and ImProm-II Reverse Transcriptase (Promega, Madison, WI). hA3G (NM_021822), hA3F (NM_145298), and hA3B (NM_004900) mRNA expression levels were quantified using TaqMan chemistry with a primer/probe combination to distinguish among highly homologous sequences of cytidine deaminases.

Gene	Lot Number (ABI)	Probe sequence
hA3G	Hs00222415_m1	FAM-GCAACCAGGCTCCAC ATAAACACGG-NFQ
hA3F	Hs00736570_m1	FAM-AAGGAGATTCTCAGA AACCCGATGG-NFQ
hA3B	Hs00358981_m1	FAM- GCTAAAGGAGATTCT CAGATACCTG-NFQ

First-strand cDNA products were used in a 25 μL reaction mixture containing 2 × TaqMan Universal PCR Master Mix 12.5 μL and 20 × TaqMan Gene Expression Assay 1.25 μL. A commercially available primer/probe combination was used to quantify glyceraldehyde-3-phosphate dehydrogenase (GAPDH) as a normalizing control sequence for the number of cell equivalents in total RNA starting material.

All reactions were run in an ABI 7500 analyzer, with 1 cycle at 50°C (2 minutes) followed by 95°C (10 minutes), and 40 cycles of 95°C (15 seconds) proceeded by 60°C (1 minute). Data were collected and analyzed using Sequence Detection software (Applied Biosystems, Foster City, CA). Absolute mRNA copy numbers were calculated by generating standard curves using serial dilutions of plasmids containing the desired gene (hA3G, hA3F, hA3B, or GAPDH). Each sample was run in duplicate. hA3G, hA3F, hA3B mRNA expression levels were calculated as number of copies per 100,000 copies of GAPDH.

Statistical Analyses

Statistical analyses were performed using SPSS 13.0. Differences between the groups were assessed using either a 2-sample *t* test for 2 groups or a 1-way Analysis of Variance and subsequent Student-Newman–Keuls test for more than 2

groups. The viral loads data were transformed into $\log_{10}$ before analysis, and the mRNA copies of hA3G, A3B, and A3F were calculated as copies per 100,000 copies of GAPDH mRNA and then log transformed (base e) for statistical analysis. The means and standard deviations were used for comparison. Correlation between 2 quantitative variances was determined using the Pearson correlation coefficient. A P value of <0.05 was considered statistically significant.

RESULTS

Forty-six HIV-infected patients consisting of 18 SP, 19 AS; 9 AIDS; and 17 HIV-uninfected healthy controls were investigated in our study (Table 1). Analysis of hA3G, hA3B, and hA3F levels revealed significant differences between HIV(+) and HIV(−) subjects in terms of hA3G ($t = -4.887$, $P < 0.001$) and hA3B ($t = -2.168$, $P = 0.045$) levels but not for hA3F ($t = -1.666$, $P = 0.109$). The results showed that expression levels of hA3G were higher in SP than in AS or AIDS ($P < 0.05$), that hA3B levels were higher in SP than in AIDS ($P < 0.05$), and that hA3B levels in AS were also higher than in AIDS ($P < 0.05$). Regarding different mRNA levels among the APOBEC proteins in HIV-infected subjects, hA3B expression levels were found to be significantly lower than those of hA3F and hA3G ($P < 0.001$), whereas there was no statistically significant difference between the levels of expression of hA3F and hA3G (Table 2).

A comparison of coexpression of these proteins in HIV-infected patients and healthy controls revealed a strong positive correlation among these 3 gene mRNA expressions (Fig. 1).

CD4$^+$ Cell Counts and Expression Levels of hA3G, hA3B, and hA3F mRNA

Pearson correlation tests revealed that hA3G and hA3B expression levels were both positively correlated with CD4$^+$ T-cell counts ($r = 0.436$, $P = 0.002$ and $r = 0.334$, $P = 0.025$, respectively) and that there was no correlation between hA3F mRNA level and CD4$^+$ cell counts ($r = 0.104$, $P = 0.490$) (Fig. 2).

Viral Load and Expression Levels of hA3G, hA3B, and hA3F mRNA

The results showed that hA3G and hA3B mRNA expression levels were negatively correlated with viral loads ($r = -0.306$, $P = 0.038$, $r = -0.301$, $P = 0.044$) respectively. There was no statistical correlation between hA3F mRNA levels with viral loads ($r = -0.265$, $P = 0.075$) (Fig. 3).

DISCUSSION

We examined potential role of hA3G, hA3F, and hA3B in HIV disease progression by measuring the mRNA levels of these proteins and their correlation with CD4$^+$ T-cell counts and HIV-1 viral loads. Our results suggest a link between APOBEC protein expression and disease progression: hA3G and hA3B levels were consistently lower in HIV-positive patients as compared with HIV-negative healthy controls, and hA3G and hA3B levels were significantly higher in SP compared with AIDS patients; hA3G and hA3B levels were positively correlated with CD4$^+$ T-cell counts but negatively correlated with viral loads in HIV/AIDS patients. However, Ulenga et al[17] found that the expression of hA3G and hA3F increase after infection. This possibly due to the increase of interferon-α upon HIV-1 infection which has been found to elevate levels of hA3G expression in the early stages of disease progression.[18,19] On the other hand, the infection period in subjects of both ours and Cho et al's are longer, particularly in our study, which are all more than 7 years. This may explain the difference between the results of ours and Ulenga's. As the disease progresses, however, there is greater variance in hA3G levels among HIV-1-infected individuals which is shown in our study. However, the differences in hA3G mRNA expression between HIV-infected and HIV-negative healthy controls remain to be explained by further studies.

Jin et al[16] found a significant inverse correlation between hA3G mRNA levels with HIV viral loads and a highly significant positive correlation with CD4$^+$ T-cell count in highly active antiretroviral therapy (HAART)–naive subjects. Adversely, Cho et al[15] did not find correlation between hA3F or hA3G mRNA levels and viral loads or CD4$^+$ T-cell counts in HIV-positive subjects. The opposite conclusion might come from sample treatment or subjects with or without HAART therapy. In study of Jin et al, CD4$^+$ T cells were costimulated with anti-CD3 and anti-CD28 antibodies before RNA extraction.[16] In study of Cho,[15] HIV-infected individuals had not taken HAART therapy for at least 3 months. HAART therapy may improve the cell immunity status of patients, such as increasing the production of cytokines. Studies have shown that the expression of hA3G mRNA could be induced by cytokines.[20] Considering possible effects of HAART and antibody stimulation on the expression of cytidine deaminases, we

TABLE 1. Clinical Parameters for HIV(+) Patients and HIV(−) Healthy Controls in the Study

Groups		n	Sex (M/F)	Age (Mean ± SD)	CD4 Count /μL (Mean ± SD)	Viral Load (Log Copies/mL) (Mean ± SD)
HIV(+)	SP	18	11/7	45.11 ± 7.28	609 ± 79	3.8 ± 1.1
	AS	19	9/9	37.95 ± 8.62	376 ± 102	4.0 ± 1.1
	AIDS	9	6/3	47.33 ± 8.03	105 ± 46	5.2 ± 0.7
HIV(−)	—	17	9/8	37.47 ± 8.77	759 ± 155	—

M, male; F, female.

TABLE 2. Comparison of HA3G, HA3B, and HA3F MRNA Expression Levels in PBMCs Among HIV(−) and HIV(+) Subjects at Different Disease Progressions (SP, AS, AIDS)

	mRNA (Mean±SD)		
Group	**hA3G**	**hA3B**	**hA3F**
HIV(−)	8.39 ± 0.79*	4.19 ± 1.32†	7.18 ± 0.98‡
SP	7.54 ± 0.95§‖	3.63 ± 0.44‖	6.86 ± 0.77
AS	6.91 ± 0.83	3.54 ± 0.69¶	6.77 ± 0.74
AIDS	6.26 ± 1.16	2.68 ± 0.83	6.27 ± 0.82
F	5.839	6.883	2.046
P	0.006	0.003	0.141

*hA3G between HIV(−) group and HIV(+) group (7.03 ± 1.04), $t = -4.887$, $P < 0.001$.

†hA3B between HIV(−) group and HIV(+) group (3.42 ± 0.71), $t = -2.168$, $P = 0.045$.

‡hA3F between HIV(−) group and HIV(+) group (6.75 ± 0.75), $t = -1.666$, $P = 0.109$.

§The mRNA level of SP was compared with the AS, $P < 0.05$.

‖SP was compared with the AIDS group, $P < 0.05$.

¶AS was compared with the AIDS , $P < 0.05$.

selected HAART-naive individuals and extracted RNA without any treatment on PBMCs. The APOBEC proteins mRNA expression levels investigated represent the natural physiologic steady state in vivo and their true significance for disease progression.

Based on the expression differences of hA3G among SP, AS, and AIDS groups and the correlation of it with $CD4^+$ T-cell counts, and HIV viral loads, the results have provided evidence that the expression levels of hA3G mRNA are negatively associated with HIV disease progression, and higher levels of hA3G mRNA may play an important role in controlling HIV infection in vivo. When hA3G is expressed in high levels, it could overcome the degradation of HIV-1 Vif and inhibit HIV-1 replication in vivo. Thus, with fewer viruses released, less $CD4^+$ cells are damaged, which may in turn delay the progression rate, as observed in the SP group. However, more in vitro and in vivo studies on the intrinsic mechanisms need to be performed.

hA3B has similar aminoacid sequences with hA3G proteins. A report found that hA3B mRNA was not detectable in primary tissues that coexpress hA3G and hA3F, and hA3B mRNA was also not detected in a range of primary human tissue samples including PBMCs when using semiquantitative reverse transcription–PCR assay. However, when we used real-time quantitative PCR to quantitative hA3B mRNA, we found that it was expressed in PBMCs but at lower levels compared with hA3G and hA3F. This result is encouraging because although hA3B has, at most, a modest effect on HIV-1 infectivity, it inhibits both Vif-deficient and wild-type HIV-1 virus in vitro. Furthermore, this inhibition is not influenced by Vif expression.[11] The results in our study showed that the hA3B mRNA levels of SP are significantly higher than that of AIDS subjects. The hA3B mRNA levels in HIV/AIDS patients are positively correlated with $CD4^+$ T-cell counts and negatively with viral loads. Our results suggest that hA3B is also associated with HIV disease progression and could be another protective factor.

There was no statistical difference in hA3F mRNA levels among these groups, and there was no correlation between hA3F mRNA levels with $CD4^+$ T-cell count or viral load. These results suggest that hA3F is most likely not associated with HIV disease progression. Studies have shown that hA3F is a strong inhibitor of Vif-deficient HIV-1, though not as potent as A3G. A3F is also efficiently inhibited by HIV-1 Vif via proteasomal degradation. However, the domains interacted with HIV-1 Vif, and the dinucleotide target for deaminase, and degree of mutagenesis are different between

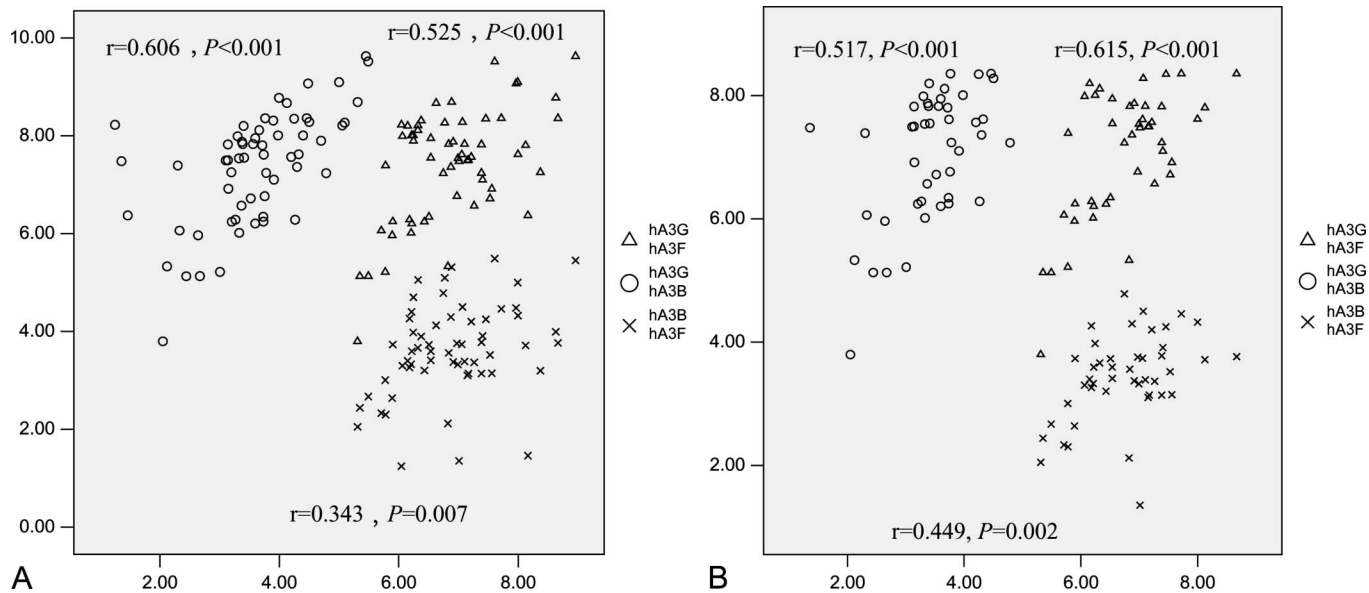
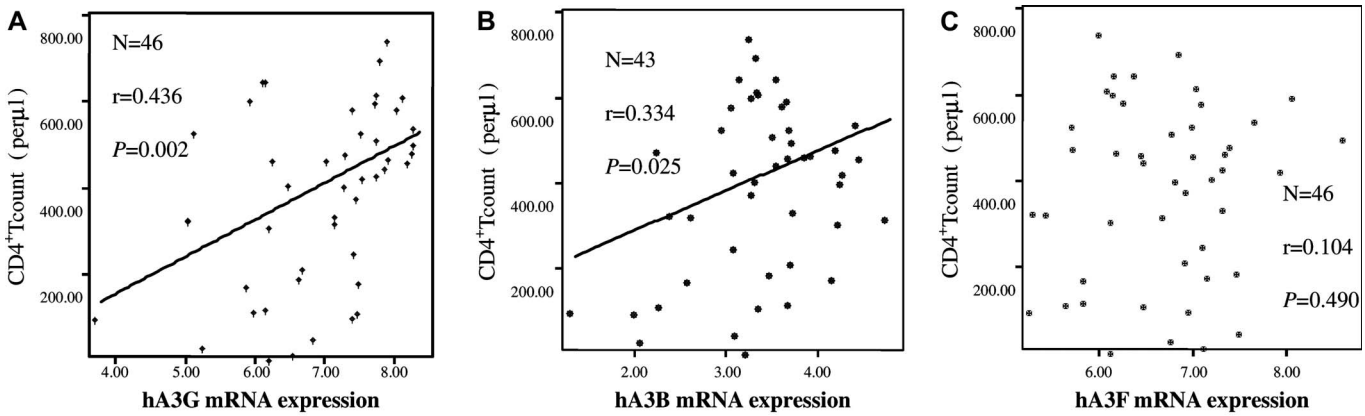
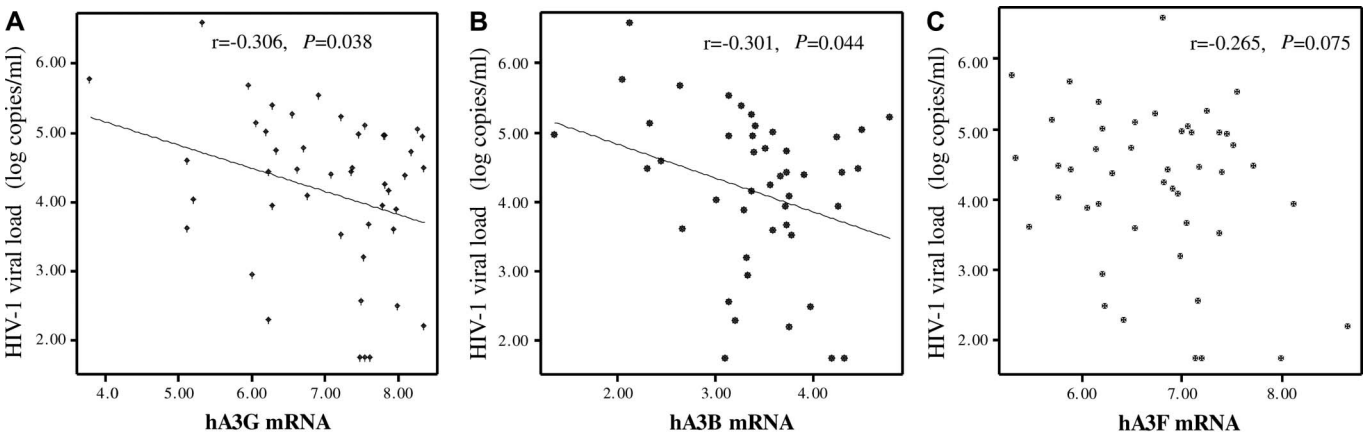


FIGURE 1. The correlation between hA3G, hA3F, and hA3B mRNA expression levels. A, All 46 HIV-infected patients and 17 healthy controls were analyzed. B, Forty-six HIV-infected patients were analyzed.



N: number of subjects; r: Pearson's correlation coefficient; *P*: p-value

FIGURE 2. Results of correlation test between hA3G, hA3B, hA3F mRNA expression levels and $CD4^+$ T-cell count of HIV-infected individuals.



r: Pearson's correlation coefficient; *P*: p-value

FIGURE 3. Results of correlation test between hA3G, hA3B, hA3F mRNA expression levels with viral load in all HIV-infected individuals.

hA3G and hA3F.[21–22] Consequently, their significance in vivo are not the same as our results have provided.

To investigate if these 3 genes are coexpressed in vivo, the correlation between their expression levels were analyzed. We found that there were significantly positive correlations with one another. However, as mentioned, the expression levels of hA3B mRNA is lower than that of hA3G and hA3F.

There has been an increasing focus on hA3G and its family members due to their innate antiretroviral functions. Our results illustrate that when the hA3G and hA3B mRNA expression levels of HIV/AIDS patients are higher, their $CD4^+$ T-cell counts are higher and their viral loads are lower. As such, modulating the mRNA expression of hA3G and hA3B and increasing the syntheses of their respective active proteins may be an effective way to control viremia and the replication of HIV in $CD4^+$ T cells in vivo. Because our results focused on the mRNA level, the protein levels of hA3G and hA3B in $CD4^+$ T cells of HIV-infected individuals and their enzyme activities are yet unknown, and this area deserves further study.

ACKNOWLEDGMENTS

The authors thank Kumi Smith and Naomi Juniper for their editing assistance.

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The Prevalence of Transmitted Antiretroviral Drug Resistance in Treatment-Naive HIV-Infected Individuals in China

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Background: Transmission of HIV drug resistance (TDR) gives rise to reduced efficacy of initial antiretroviral treatment and has become a public health concern.

Methods: A nationwide survey on TDR was conducted in antiretroviral therapy-naive HIV-1–infected individuals from September 2004 to October 2005 in China. Drug resistance genotyping was performed on subjects' plasma samples. Drug resistance mutations were determined and scored by Stanford HIV Drug Resistance algorithm.

Results: Sequences were obtained from 676 individuals, of whom 61.2% were former plasma and blood donors, 17.3% were infected sexually, and 17.2% were intravenous drug users. Subtype B' HIV-1 strains were found in 73.5%, CRF01_AE in 13.9%, CRF07_BC in 6.2%, CRF08_BC in 2.7%, subtype C in 1.04%, subtype B in 0.9%, CRF02_AG in 0.4%, and B'/C intersubtype recombinant strains in 1.3% of the subjects. Twenty-six (3.8%) were found to harbor drug resistance strains. The rates of resistance to protease inhibitors, nucleoside reverse transcriptase inhibitors, and nonnucleoside reverse transcriptase inhibitors were 0.4%, 1.6%, and 2.1%, respectively. Though there was no significant difference in TDR rates between 2004 and 2005 (2.9% vs. 4.4%), an increased trend was observed in the rate of high-level drug resistance (0.8% in 2004 vs. 3.0% in 2005, $P = 0.0634$).

Conclusions: The rate of TDR was relatively low in China, as compared with those in developed countries. Surveys among recently HIV-infected subjects should be performed continually to ensure the success of the scale-up antiretroviral treatment.

Key Words: prevalence, treatment naive, transmitted HIV-1 drug resistance

(*J Acquir Immune Defic Syndr* 2010;53:S10–S14)

INTRODUCTION

Since the first HIV case was identified in 1985 in China, the HIV/AIDS epidemic kept rising during the subsequent 20 years. By the end of 2005, it was estimated that 650,000 individuals living with HIV/AIDS in China, of whom 75,000 were AIDS patients.[1] Intravenous drug use (44.3%), sexual contact (43.6%), and unsafe blood and plasma collection (10.7%) were main transmission routes which contributed to most of the 141,000 HIV cases reported. Furthermore, the distribution of HIV/AIDS cases was not geographically even in China: 5 of 31 provinces and autonomous regions had reported over 10,000 cases, whereas 3 other provinces had less than 100 reported cases.

To improve the life of HIV/AIDS patients and reduce the HIV/AIDS-related morbidity and mortality, the Chinese government put forward a "four free one care" policy in 2003.[2] About 5000 patients received a national free antiretroviral therapy (ART) program in its first year of inception. Since then, the number of patients enrolled in the program has increased rapidly. At the end of 2005, more than 22,000 patients were ever involved in the free ART program, of which about 19,200 were still on ART.[3] Most of them were HIV-infected former blood and plasma donors (FPDs) living in rural areas of central China. Resources for antiretroviral drugs are limited in China. There is a concern that the prevalence of antiretroviral drug resistance would compromise the effect of current regimens and give rise to treatment failure.

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Supported by the Mega-projects of Science Research for the 11th 5-year plan (2008ZX10001-004), the National Basic Research Program (2005CB523103), and the International Cooperation Program (20070FC30230), granted by the Ministry of Science and Technology of China; funds from the China Global Fund AIDS Program Round 3 & 4, the Global Fund to Fight AIDS, Tuberculosis, and Malaria; and the China ICOHRTA with Grant #U2R TW 006918, funded by the US National Institutes of Health, the Fogarty International Center, the National Institute of Drug Abuse and the National Institute of Mental Health.

Presented in part at the 4th IAS Conference on HIV Pathogenesis, Treatment, and Prevention, July 22–25, 2007, Sydney, Australia. Abstract TUPEB051.

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With the scale-up of a free ART program, a nationwide survey was conducted to study the genetic characteristic and antiretroviral drug resistance of HIV type 1 (HIV-1) strains in treatment-naive HIV-infected individuals from 2004 to 2005.

METHODS

Study Population

Treatment-naive HIV-1–infected individuals were randomly enrolled in provinces and autonomous regions where free antiretroviral drugs were available at the time the survey was conducted. The duration of sample collection was from September 2004 to October 2005. In 2004, treatment-naive HIV-infected individuals in 14 provinces were included. With the rapid scale-up of the national free ART program, the geographic range of the study was expanded to 28 provinces and autonomous regions in the subsequent year. Subjects who were below 18 years old were excluded from the study. All the subjects gave written informed consent for participation in this study. The survey was reviewed and approved by the institutional review boards and scientific ethical committees at the Chinese Ministry of Health.

Laboratory Tests

Subjects' whole blood samples were collected and processed in the provincial Centers for Disease Control and Prevention's laboratries. CD4 cell count was measured within 24 hours after sampling. Meanwhile, plasma was separated by centrifugation and instantly stored at −80°C. The plasma samples were then sent in dry ice to the 4 core laboratories of the Chinese HIV Drug Resistance Surveillance Network. Plasma HIV RNA was quantified with real-time nucleic acid sequence based amplification (NASBA) (bioMerieux, Lyon, France), or COBAS (Roche Applied Science, Penzberg, Germany) according to the manufacturer recommendations. For samples with viral loads equal to or greater than 1000 copies per milliliter, HIV drug resistance (HIVDR) genotyping was carried out by an in-house polymerase chain reaction protocol as previously described.[4] HIV-1 *pol* gene (protease 1–99 amino acids and part of reverse transcriptase 1–250 amino acids) was amplified, purified, and bidirectly sequenced in an ABI3100 sequencer (Applied Biosystems, Foster City, CA). For analysis of HIV-1 drug resistance mutation, each sample sequence was compared with the subtype B consensus sequence in the Stanford HIV Drug Resistance Database (http://hivdb.stanford.edu) and was interpreted by HIVdb program. For HIV-1 subtyping, the edited sequences were aligned against reference sequences available at the Los Alamos database (http://hivweb.lanl.gov). Phylogenetic trees were constructed by the neighbor-joining method with 1000 bootstrap replicates using Mega 4.0. Bootscaning analyses were performed on samples possibly having unidentified intersubtype recombinant strains by using Simplot 3.5.1.

Statistical Analysis

The significant differences in categorical variables were analyzed using χ^2 test or Fisher exact tests. Statistical significance was defined as a P value <0.05. All the statistical analyses were performed with SAS 9.1 software (SAS Institute, Cary, NC).

RESULTS

Subjects Included

One thousand one hundred ninety-four ART-naive HIV-1–infected subjects were enrolled (442 in 2004 and 752 in 2005). Two hundred twenty-seven individuals who had a plasma viral load less than 1000 copies per milliliter were excluded from the study, as the possibility of such subjects to be sources of HIV infection would be less than those with a higher viral load. In addition, the genotypic results from samples with a viral load lower than 1000 copies per milliliter were not reliable using routine methods. Of the remaining 967 samples, 676 (69.9%) were successfully sequenced. Among these subjects, 460 (68.1%) were male. Median age was 38 years (range: 18–72). Four hundred fourteen (61.2%) were FPDs, 117 (17.3%) acquired HIV infection through sexual contact, 116 (17.2%) were intravenous drug users, 27 (4.0%) were infected through blood transfusion, and the transmission routes of the remaining 2 subjects were unknown. More than half of the subjects (351 of 676, 51.9%) had a primary school education or less. Four hundred fifty-one (66.7%) were farmers living in rural areas. Median CD4 cells count and viral load at sampling were 280 cells per cubic millimeter (range: 23–723) and 4.59 log copies per milliliter (range: 3.01–6.80), respectively.

HIV-1 Subtypes, Circulating Recombinant Forms, or Intersubtype Recombinant Strains

Phylogenetic trees base on the whole protease (1-99aa) and part of reverse transcriptase (1-250aa) gene revealed that a majority of the HIV-1 isolates (497, 73.5%) studied belonged to subtype Thai-B (B'), the second most prevalent strain was CRF01_AE (94, 13.9%), followed by CRF07_BC (42, 6.2%), CRF08_BC (18, 2.7%), subtype C (7, 1.04%), subtype B (6, 0.9%), and CRF02_AG (3, 0.4%). Bootscaning analyses were performed on sequences from nine samples, which did not cluster with any present known reference sequences. The results revealed the presence of B'/C intersubtype recombinant strains with different mosaic structures from those of CRF07_BC and CRF08_BC (Fig. 1). The distribution of HIV-1 strains was uneven among different risk groups ($P < 0.0001$). Subtype B' HIV-1 strains were more frequently found in FPDs (398, 80.1%) than in other HIV-1–infected populations; CRF07_BC strains were more likely to be found among intravenous drug users (IDUs) (27, 64.3%), whereas most CRF01_AE strains were detected in 2 groups: IDUs (46, 39.7%) and sexually infected individuals (41, 35.0%).

Antiretroviral Drug Resistance-Associated Mutations

Twenty-six of 676 isolates (3.8%) were identified to be resistant to 1 or more antiretroviral drugs (Table 1). Primary drug resistance mutations to protease inhibitors were found in 3 samples (0.4%), which had 1 single mutation each. M46I and N88D, which confer intermediate resistance to nelfinavir, were respectively detected in 1 subject (CNSHD0050) from Shanghai and 1 person (CNHND0066) from Hunan province.

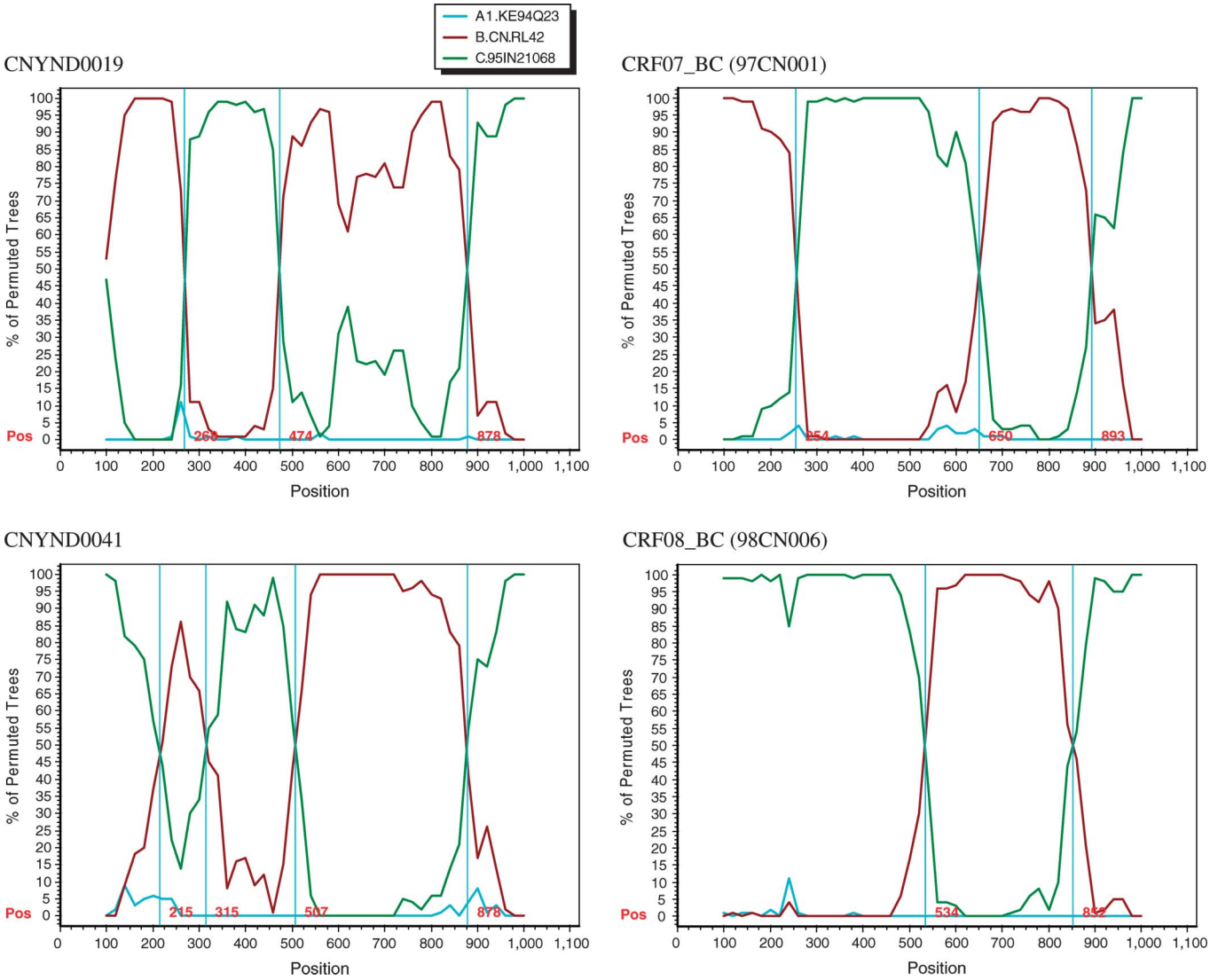

FIGURE 1. Bootscanning analyses to identify new intersubtype recombinant strains. A bootscaning plot was constructed by using Simplot 3.5.1 software based on 100 replicates with a 200-bp sliding window moving in steps of 20 bases. Subtype references were B′ (RL42), India C (95IN21068) and subtype A (KEQ23). The breakpoints in CNYND0019 and CNYND0041 were different from those of the reference strains of CRF07_BC (97CN001) and CRF08_BC (98CN006).

A V82A mutation conferring resistance to atazanavir, indinavir, lopinavir (LPV), and nelfinavir was found in 1 subject (CNGXD0011) from Guangxi province.

Mutations associated with resistance to reverse transcriptase inhibitors were found in 23 subjects. Twenty-one of them were resistant to either nucleoside reverse transcriptase inhibitors (NRTIs) (n = 9) or nonnucleoside reverse transcriptase inhibitors (NNRTIs) (n = 12); 2 were resistant to both NRTIs and NNRTIs. The most frequent NRTI-related mutation was M184V/I, conferring high resistance to lamivudine and emtricitabine and was found in 4 (4 of 23, 17.4%) samples. At least 1 thymidine analogue mutation, which was associated with intermediate or low-level resistance to zidovudine or other NRTIs, was found in 5 samples. The most frequent NNRTI-related mutation was K103N, which was found in 9 (9 of 23, 39.1%) samples.

Comparison of the HIVDR rate in 3 major risk groups revealed that there was no significant difference among FPDs (13 of 414, 3.1%), sexually infected individuals (5 of 117, 4.3%), and IDUs (4 of 116, 3.5%). No significance difference on transmission of HIV drug resistance (TDR) rate was found between female (7 of 216, 3.2%) and male (19 of 460, 4.1%) subjects, those with primary education or below (3.7%), and those with a higher education (4.0%), or between nonfarmers (5.3%) and farmers (3.1%). The rate of TDR in 2004 and 2005 was 2.9% (7 of 244) and 4.4% (19 of 432), respectively, with no significant difference between the 2 years ($P = 0.3207$). The rate of high-level resistance to 1 or more antiretroviral drugs was also

TABLE 1. Genotypic Resistance Mutations Detected and Phenotypic Resistance Predicted (Stanford HIVDB Algorithm)

Gender	Age	Likely Risk Group	Subtype	Resistance Mutations			Predicted Phenotypic Resistance		
				PI	NRTI	NNRTI	PI	NRTI	NNRTI
M	42	Sexual contact	01_AE	M46I	—	—	NFV (I)	—	—
M	38	Sexual contact	01_AE	N88D	—	—	NFV (I)	—	—
M	58	Blood recipient	B'	V82A	—	—	ATV(L), IDV(I), LPV(L), NFV(I)	—	—
F	60	FPD	B'	—	M41L	—	—	AZT(L), d4T(L)	—
M	56	Blood recipient	02_AG	—	D67G	—	—	AZT(L)	—
M	34	IDU	01_AE	—	K70R	—	—	AZT(L)	—
M	48	FPD	B'	—	M41L, D67G	A98G	—	ABC(L), AZT(I), d4T(L), ddI(L)	—
F	42	FPD	B'	—	M184I	—	—	3TC(H), FTC(H)	—
M	31	Blood recipient	B'	—	M184V	—	—	3TC(H), FTC(H)	—
M	38	Sexual contact	B'	—	M184V	—	—	3TC(H), FTC(H)	—
M	38	FPD	B'	—	T215S	—	—	AZT(L), d4T(L)	—
M	30	IDU	01_AE	—	T215S	—	—	AZT(L), d4T(L)	—
F	40	FPD	B'	—	K70R, K219E	K103N	—	AZT(I), d4T(L)	DLV(H), EFV(H), NVP(H)
M	22	IDU	01_AE	—	D67N, M184V, T215Y, K219Q	K101E, G190A	—	ABC(I), AZT(I), d4T(I), ddI(I), 3TC(H), FTC(H), TDF(L)	DLV(I), EFV(I), NVP(H)
F	36	Sexual contact	B'	—	—	K103N	—	—	DLV(H), EFV(H), NVP(H)
M	40	FPD	B'	—	—	K103N	—	—	DLV(H), EFV(H), NVP(H)
M	36	FPD	B'	—	—	K103N	—	—	DLV(H), EFV(H), NVP(H)
F	40	FPD	B'	—	—	K103N	—	—	DLV(H), EFV(H), NVP(H)
M	18	FPD	B'	—	—	K103N	—	—	DLV(H), EFV(H), NVP(H)
M	37	IDU	07_BC	—	—	V179D	—	—	DLV(L), EFV(L), NVP(L)
M	18	Sexual contact	B'	—	—	G190E	—	—	DLV(I), EFV(H), NVP(H)
F	18	FPD	B'	—	—	A98G, K103N	—	—	DLV(H), EFV(H), NVP(H)
M	22	Blood recipient	B'	—	—	K101E, V106I	—	—	DLV(I), EFV(L), NVP(I)
M	18	FPD	B'	—	—	K101E, G190A	—	—	DLV(I), EFV(I), NVP(H)
M	51	FPD	B'	—	—	K103N, G190A	—	—	DLV(H), EFV(H), NVP(H)
F	27	FPD	B'	—	—	K103N, Y181C	—	—	DLV(H), EFV(H), NVP(H)

AZT, zidovudine; ABC, abacavir; d4T, stavudine; ddI, didanosine; FTC, emtricitabine; 3TC, lamivudine; TDF, Tenofovir; EFV, efavirenz; ATV, atazanavir; IDV, indinavir; LPV, lopinavir; NFV, nelfinavir; NVP, nevirapine; L, low-level resistance; I, intermediate resistance; H, high-level resistance; PI, protease inhibitor.

not significant ($P = 0.0634$), although there was an increase in 2005 (3.0%, 13 of 432), compared with 2004 (0.8%, 2 of 244).

DISCUSSION

Our study was the first nationwide survey on TDR in ART-naive individuals and revealed the existence of transmitted HIV drug resistance in China. Evidence of TDR was found in 3.8% of the subjects studied. This result was similar to results from a previous survey, which found 4.4% of HIV drug resistance of 91 ART-naive HIV/AIDS patients in Liaoning, a province in northeastern China.[5] This prevalence was comparable to that of international studies which showed 2.0% TDR during 2003 and 2006 in Thailand,[6] 4.3% from 1999 to 2005 in South Korea,[7] and 4.3% in 2002 in the Democratic Republic of Congo.[8] However, the prevalence of TDR in our study was lower than those in North America and Western Europe where various TDR rates were reported to be from 9.1%[9] to 24.1%.[10] The result was not surprising, as China, like other countries in Asia and Africa, has had a shorter period of access to ART than in developed countries.

In this study, the largest proportion of the HIV-1 strains was subtype B' strains, followed by CRF01_AE, CRF07_BC, CRF08_BC, and other subtypes, circulation recombinant forms or intersubtype recombinant forms. Though the total proportion of 4 predominant HIV-1 strains (subtype B', CRF01_AE, CRF07_BC, and CRF08_BC) and that of CRF01_AE strains alone were similar to what we previously reported on the second nationwide molecular epidemiology survey in 2001 and 2002,[11] the proportion of specific HIV-1 strains was different: CRF_BC strains, including CFR07_BC and CRF08_BC, accounted for more than half of the HIV-1 infections, subtype B' only contributed to about one third of the infections in that molecular epidemiology survey. This discrepancy may be due to a sampling bias in favor of regions where access to ART had been already established before the study began. Additionally, the shift of risk groups of HIV infection that had occurred in recent years may produce an influence in the distribution of HIV-1 strains to some extent.[12] For this study, subtype B' strains also contributed to a substantial proportion of HIV-1 infections through sexual route and intravenous drug use.

Half of the HIV drug resistance (13 of 26) was found in individuals who were infected by unsafe commercial blood and plasma donation. It was believed that most FPDs acquired HIV infection in the mid-1990s, although a large number of HIV infections were confirmed during the intensive screening of FPDs in 2004. Antiretroviral drugs were not introduced in China during the 1990s. It was therefore impossible that these patients were infected with drug resistance viruses at that time. To avoid including subjects who had a history of ART, the ART status of all subjects with detected drug resistance were reinvestigated by phone or interviewing. About 30 persons with drug resistance were excluded from the study because of having taken antiretroviral drugs. The existence of HIV drug resistance in FPDs in this study include subjects who, infected through intravenous drug use or sexual contact, were reluctant to confess to their mode of transmission due to social stigma.[13,14] A portion of FPDs with drug resistance had actually taken antiretroviral drugs at least once, but they were not fully able to understand the questions about their treatment status, or they did not think they had been treated because they only took antiretroviral drugs once or twice. The latter situation would lead to overestimate the prevalence of TDR.

The results of this study was not generalizable to overall HIV infections for the following reasons. First, a large proportion of the subjects were not infected recently. As drug resistance strains become minor quasispecies in the plasma after a period of infection, the regular population-based sequencing method will fail to detect them.[15] Second, the selection of the studied population could skew the estimate of the TDR rate in HIV-1 infections. Third, a relative low amplification rate of samples with viral loads equal to or greater than 1000 copies per milliliter may impose an impact on the evaluation of TDR rate. Analysis of the distribution among risk groups revealed that the proportion of the unamplified samples from IDUs and subjects who were infected sexually was higher than those from FPDs (P = 0.0008). However, our data have shown that there was no significant difference on the TDR rate in these 3 populations.

In this survey, we demonstrated the presence of TDR among treatment-naive individuals. More than half of the sample with HIV drug resistance showed resistance to NNRTI drugs. Though the TDR rate was relatively low comparing to those in developed countries, comprehensive measures are needed to prevent the spread of HIV drug resistance. More studies should be performed to investigate the rate of TDR among recent infections and provide implications to first-line therapy.

ACKNOWLEDGMENTS

We appreciate the contribution of all subjects included in this study. We are greatly grateful to the staff from provincial and county Center for Disease Control and Preventions for participating in sample collection and investigation. We thank Dr. Adrian Liau for his academic editing of the article.

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Prevention of Mother-to-Child Transmission of HIV-1 Using Highly Active Antiretroviral Therapy in Rural Yunnan, China

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Objective: To demonstrate that the use of highly active antiretroviral therapy (HAART) to interrupt transmission of HIV-1 from mother to baby is effective, safe, and feasible in a remote rural region of China.

Methods: Between November 2005 and May 2009, we enrolled 279 HIV-1–infected pregnant women to receive HAART to interrupt transmission of HIV-1 to their newborns across 16 counties in Yunnan. All women were started on triple combination therapy and submitted to regular blood draws to monitor CD4 T cells and viral load in their blood plasma. Infants received a single dose of nevirapine at birth and 1 or 4 weeks of zidovudine depending on the length of the mother's regimen. Exclusive formula feeding was recommended, and families were provided with 12-month supply of formula. Mothers and infant pairs were followed for 12–18 months postdelivery.

Results: Of 279 enrolled HIV-infected women, 222 (79.6%) were identified and started treatment by 28 weeks of pregnancy. Viral load was undetectable at time of delivery for 62.4% (136 of 218) at delivery, with a mean 1.76 log viral load reduction between enrollment and delivery. Two of 193 babies (1.0%) who have already been tested became infected with HIV-1. Seven of 223 babies have died. By Kaplan–Meier analysis, cumulative one-year survival was 96.3%.

Conclusions: The project demonstrated that HAART for all infected pregnant women is effective with a vertical transmission rate of ~1%. Thus, this project provides a model for China to scale up its efforts to prevent mother-to-child transmission of HIV-1.

Key Words: HAART, HIV/AIDS, PMTCT, Yunnan

(*J Acquir Immune Defic Syndr* 2010;53:S15–S22)

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The projects on which this research is based were supported by the Gracious Glory Buddhism Foundation, the Elizabeth Glaser Pediatric AIDS Foundation, the Tai Foundation, and other contributions from Oscar Tang, Kevin Tang, Walter and Shirley Wang, and Miranda Wong Tang.

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INTRODUCTION

The prevention of mother-to-child transmission (PMTCT) is a critical focal point for global HIV-1 prevention efforts. Without intervention, 15%–35% of HIV-1–exposed infants will become infected with HIV-1 during pregnancy, delivery, or breastfeeding.[1] Prevention of vertical transmission with highly active antiretroviral therapy (HAART) for the mother, prophylactic antiretroviral (ARV) dose for the baby, and avoidance of breastfeeding, however, can reduce infection rates to ~1%.[2]

Although in the United States and Europe vertical transmission has been virtually eliminated with HAART-based PMTCT regimens,[3,4] in resource-limited settings, millions of infants continue to become infected. Globally, World Health Organization estimates that in low-income and middle-income countries in 2007, only 33% of HIV-1–infected women accessed any PMTCT services, and only 8% of the those women who received any PMTCT intervention received HAART.[5] Furthermore, regimens with suboptimal efficacy continue to be widely endorsed by international and national HIV-1 programs. A single dose of nevirapine (sdNVP) for mothers at onset of labor and for neonates combined with replacement feeding yields a transmission rate of 10.8%.[6] The administration of zidovudine (AZT) starting in the third trimester of pregnancy and sdNVP for the mother during labor and for neonates combined with replacement feeding yields a transmission rate as low as 1.9% [confidence interval (CI): 0.9 to 3.0%], according to one study.[7] However, it is well established that monotherapy and dual therapy will breed mutations in the virus that could lead to drug resistance, limiting future treatment options for mothers and potentially for infants who become infected. Weeks to months of AZT alone would be considered malpractice in the developed world because monotherapy will, without fail, lead to the development of drug-resistant viruses. The lack of widespread implementation of HAART-based PMTCT, therefore, represents one of the major failures of the global effort to combat HIV/AIDS.

Yunnan is home to the highest number of HIV-1–positive people in China, comprising 24% of cumulatively reported cases nationally and 25% of new cases reported in 2008.[8] The total number of people living with HIV-1 and AIDS in Yunnan is estimated at 85–100,000.[9] The epidemic is attributable to injection drug use and sex; among newly reported cases in 2008, 56.5% were attributed to sexual

transmission (including heterosexual and homosexual transmission), 33.1% to injecting drug use, 1.6% to vertical transmission, and 8.8% to unknown transmission route.[8] The epidemic is shifting toward women: in 2008, there were 1.7 men for every 1 woman reported,[8] compared with a ratio of 2.5:1 for the cumulative cases between 1989 through 2007.[10] This trend of more women infected increases the likelihood that more babies will be at risk of infection by their mothers if screening and PMTCT interventions are not effectively implemented and scaled up. Nationally, an estimated 9000 infants were infected in 2005.[11] The Yunnan government estimates that 1000 HIV-1–infected women are pregnant each year, of which, about 65% will choose to deliver.

Bordering Vietnam, Laos, and Myanmar in southwestern China, Yunnan is a mountainous province with an ethnically diverse, poor, and relatively uneducated population. More than 84% of the land is classified as mountainous,[9] leaving many villages without easy access to roads and health services, especially in the rainy season. Ethnic minorities comprise 34% of the population.[9] Average per capita income varies widely between rural and urban areas; in 2006, it was $286 in rural and $1260 in urban areas.[9] Average number of years of education achieved was 6.8 years across the total population,[9] however, for rural women, this must be lower still. In terms of access to health care facilities, there are 1.7 beds per 1000 people in rural areas as compared with 2.5 beds per 1000 in urban areas. These statistics point to the difficulties of implementing a PMTCT program in a poor, remote, underresourced setting.

The national and provincial governments have invested heavily to combat the spread of the AIDS epidemic in Yunnan. In 2003, the national PMTCT program was piloted in 2 Yunnan counties. By 2006, all 129 counties in Yunnan were covered in the national PMTCT program that recommended and provided AZT starting at 28 weeks of pregnancy plus sdNVP during labor and delivery for the mother and neonate. In practice, because many women are identified as HIV-1 infected only when they present in labor, the use of sdNVP is still highly prevalent. Infants are diagnosed by antibody test after 18 months of age when maternal antibodies are no longer present in the child's blood. Twelve months of formula are provided as well.

In this context, in 2005, the Aaron Diamond AIDS Research Center and the Yunnan Province Bureau of Health launched a demonstration project to test whether optimal intervention, that is, HAART for HIV-1–infected pregnant women to interrupt HIV-1 transmission to their infants was safe, effective, and feasible in 16 counties in Yunnan (Fig. 1). Here we present findings from a project to evaluate the feasibility, tolerability, and effectiveness of HAART-based PMTCT in these counties in Yunnan.

The 2 primary objectives were to limit the infection rate among HIV-1–exposed infants to less than 2% and to improve maternal health. Four secondary objectives included (1) increasing the proportion of HIV-1–identified pregnant women enrolled in the project; (2) earlier identification of HIV-1–infected women during pregnancy, defined as before 28 weeks gestation; (3) close follow-up of women during pregnancy and

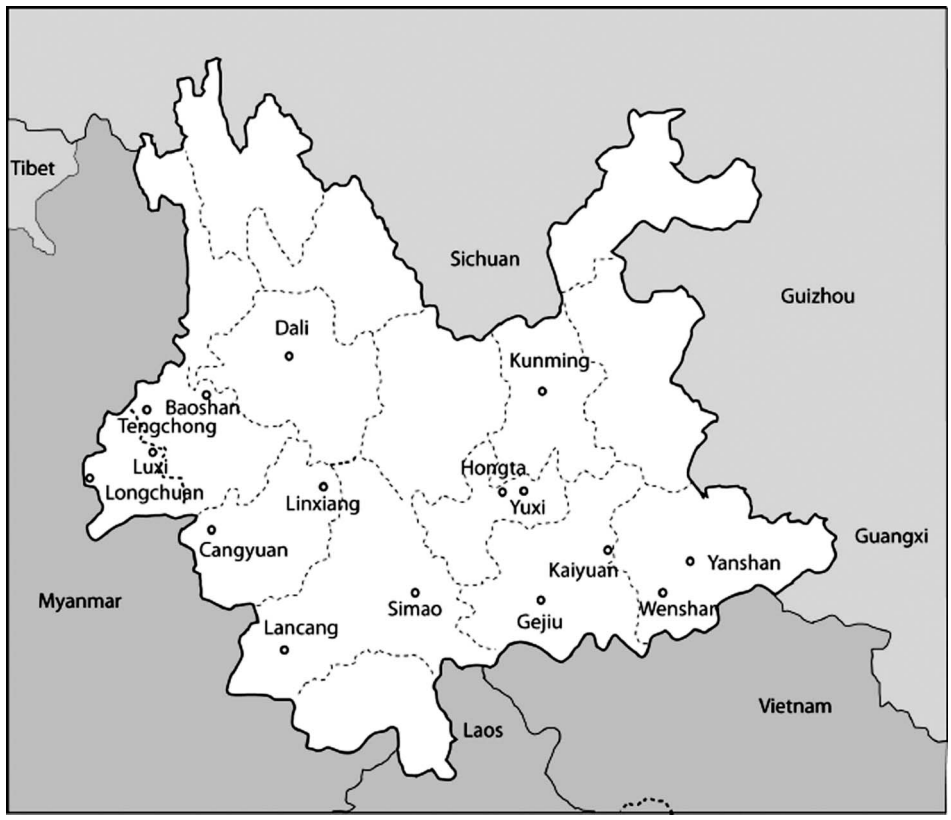

FIGURE 1. Distribution of enrolled women across project sites including Baoshan 0.4%, Cangyuan 4.7%, Dali 1.4%, Gejiu 12.2%, Hongta 7.5%, Kaiyuan 4.3%, Kunming 4.3%, Lancang 3.2%, Linxiang 14.0%, Longchuan 12.2%, Luxi 21.5%, Simao 0.4%, Tengchong 7.2%, Yanshan 2.9%, Yuxi 1.4%, and Wenshan 2.5%.

beyond, and (4) use of dry blood spot (DBS) to perform DNA polymerase chain reaction (PCR) to diagnose infection status in infants by 12 weeks of age.

METHODS

Site Selection

Considerations for site selection included high HIV-1 prevalence among antenatal care clients, existing HAART services at the county hospital, and some experience in PMTCT interventions. Sixteen sites were selected, including 11 county-level maternal child health (MCH) clinics, 4 prefectural level MCH clinics, and 1 municipal MCH clinic in the provincial capital of Kunming (Fig. 1). Five sites began enrolling in 2005, 9 more in 2006, and 2 in 2008. Half of the counties are designated poverty counties, and 7 counties report average per capita income of less than $1 a day.[12–18]

Patient Enrollment

From November 2005 through May 2009, more than 1100 HIV-1–infected pregnant women were identified in 16 counties in Yunnan. Between 35% and 40% of women decided to terminate their pregnancies. Of the remaining 800 or so pregnant women, 279 (35.0%) were enrolled into the program based on the following criteria: they planned to deliver their babies; they were able to give written informed consent; and they did not intend to move outside the county during the pregnancy period. The remainder met one or more of the following exclusion criteria: serious opportunistic infection or AIDS-related tumor; abnormal liver or renal function; coinfected with hepatitis B or C virus; severe anemia, thrombocytopenia, and leukopenia; serious risk of other pregnancy complication; acute or chronic pancreatitis; alcohol or drug addiction; and serious psychiatric illness.

The Yunnan AIDS Care Center Institutional Review Board approved the project. All women provided written informed consent for themselves and on behalf of their infants. Women who did not meet enrollment criteria were referred to the government PMTCT program through which they received a prophylactic regimen of AZT and NVP or sdNVP.

Intervention

All women received HAART, beginning as early as the fourteenth week of pregnancy. Women were started on a regimen of AZT, lamivudine, and either NVP for those with CD4 T-cell counts of less than 250 cells per milliliter of blood or efavirenz for those with CD4 counts greater than 250 cells per milliliter (cut off was later changed to 350 cells per milliliter). Women were required to have standard blood work and physical exam at enrollment and at regular intervals throughout their pregnancy. In addition, blood was drawn to measure CD4 counts and viral loads at enrollment, at labor and delivery, and at 1, 3, 6, and 12 after initiation of HAART.

Women were counseled to come to the county MCH clinic for all antenatal care visits. They were given the option of a vaginal birth if they had been on treatment for more than 3 months, and their viral load was under 1000 copies per milliliter or a planned c-section if they had been on treatment for less than 3 months, and their viral load remained greater than 1000 copies per milliliter.

Neonates were given sdNVP within 24 hours of birth and 1 week of AZT if the mother had been on treatment for more than 4 weeks, or 4 weeks of AZT if the mother had been on treatment for less than 4 weeks at time of labor. Parents were counseled to formula-feed their baby exclusively and to bring their infants to the MCH for regular follow-up visits at 1 week, 1 month, and once a month thereafter and immediately in the event of any health problems. A small amount of blood was drawn from each baby between 6 and 12 weeks to be used to conduct PCR to diagnose the baby's HIV-1 status. All babies received an antibody test to confirm the diagnosis between 12 and 18 months.

Women with CD4 counts greater than 350 cells per milliliter at enrollment discontinued treatment after delivery, unless their CD4 counts at time of delivery had fallen below 350 cells per milliliter. These women were referred to the county Center for Disease Control (CDC) for regular follow-up. Women with CD4 counts less than 350 cells per milliliter at enrollment were referred to the government treatment program managed by the infectious disease ward at the county hospital 6 weeks postdelivery to continue treatment.

Finally, women's partners were counseled to consent to an HIV-1 test provided for free through the project.

Implementation

The project was managed by a provincial project office and implemented by health workers, clinicians, and obstetricians in government health facilities who were provided with reinforcement trainings and continual technical support from the provincial project office. A project office in each county MCH clinic managed the day-to-day operations of the project, working closely with doctors at the infectious disease ward of the county comprehensive hospital for support on treatment issues, and the staff at the county CDC for laboratory support. Blood samples for CD4 T-cell counts and viral load tests were transported to the Yunnan AIDS Care Center laboratory.

DBS from HIV-1–exposed infants were collected in each project county and shipped through the postal service at room temperature to the Yunnan AIDS Care Center laboratory, which has been certified to perform DNA PCR. Genomic DNA was isolated from DBS by extraction with a polyvalent cationic resin, chelex 100 (Biorad, Marnes-la-Coquette, Paris, France). HIV-1 DNA (gag, pol, and env gp41 regions) was amplified and detected by PCR. Primers and amplification conditions were as described by Yang et al.[19]

Statistical Analysis

Clinical and demographic characteristics of mothers in the program were evaluated with descriptive statistics. Changes in CD4 values and HIV-1 RNA level during therapy and differences in clinical characteristics over calendar time were examined with linear regression. All CIs are at the 95% level of significance, and P values of $\sim$0.05 were considered statistically significant. Kaplan–Meier method was used to estimate survival of infants. All data were analyzed using STATA10.0 (College Station, TX).

RESULTS

Descriptives

The age range for women enrolled in this project was from 17 to 41 years, with a mean and median of 26 years (Table 1). Close to 37% of the cohort were ethnic minorities, including members of 18 different ethnicities and several women from Myanmar. One third of enrolled women (33.3%) reported primary school education or less, 56.6% middle school education, and 10.0% high school education or more. All were married. Among the 248 husbands tested (88.6%), 51.2% were HIV-1 positive, whereas 48.8% of the couples were serodiscordant.

All women received HAART, ranging in duration from 1 day to 202 days with a mean of 95 days (median 94 days). Among those who had delivered by May 31, 2009, and had CD4 count reported, 131 women (62.4%) had CD4 counts higher than 350 cells per milliliter at enrollment and discontinued treatment postdelivery. Seventy-nine women (37.6%) with CD4 counts less than 350 cells per milliliter at enrollment continued on treatment. Ninety-one percent were enrolled at county MCH clinics, 4.6% at prefectural MCH clinics, and 4.3% at a municipal district MCH in the provincial capital.

Two hundred eighteen women have delivered 223 babies to date, including 5 sets of twins. All received the infant dose of NVP plus 1 or 4 weeks of AZT. All babies were formula fed. By May 31, 2009, 61 mothers have not yet delivered their babies.

TABLE 1. Characteristics of Mothers, Deliveries, and Infants

Characteristics	Analysis
Mothers	
No. women receiving HAART	279
Age at enrollment (yr)	26
Median	26
Interquartile range	23–29
Length of gestation at start of HAART (wk)	
Median	24
Interquartile range	17–31
CD4 count at baseline (cells/mL)	
Median	335
Interquartile range	216–485
Viral load at baseline (copies/mL)	
Median	7743
Interquartile range	1729–23,843
Cumulative survival (%)	100
Deliveries	
Total no. deliveries	218
Duration of maternal HAART (d)	
Median	94
Interquartile range	51–140
Cesarean delivery (%)	72
CD4 count at delivery (cells/mL)	
Median	415
Interquartile range	277–557
Viral load at delivery (copies/mL)	
Median	50
Interquartile range	50–99
Live-born infants	
Total no.	223
Lost to follow up	3
HIV-1 tested	193
HIV-1 infected	2
Infection rate (%) (95% CI)	1 (0.04 to 3.9)
Deaths	7
Cumulative 1-year survival (%)	96

Primary Outcomes

Infection Rate and Survival

Of 193 babies who have been tested, 2 have become infected with HIV-1, an infection rate of 1.04% (CI: 0.04 to 3.9) (Table 1). Four babies have not been tested, of which, one died at 3 days of age and 3 have been lost to follow-up. The remaining 26 infants have not reached 12 weeks of age and have not yet been tested by DNA PCR.

Seven of 223 infants (3.1%) have died, a cumulative 1-year survival of 96.3% (CI: 92.4 to 98.2) by Kaplan–Meier analysis. Of those babies who died, 1 was HIV-1 infected, 1 was untested, and 5 were HIV-1 free. Age ranged from 3 to 130 days with a mean of 61 days. Causes of death included diarrhea (2), respiratory illness (2), malnutrition (1), encephalitis (1), and sepsis (1).

Maternal Health and Safety

CD4 T-cell count at enrollment ranged from 2 to 961 cells per milliliter, with a mean of 353 cells per milliliter (median 335 cells/mL). At delivery, CD4 count ranged from 19 to 1359 cells per milliliter, with an increased mean of 436 cells per milliliter (median 414 cells/mL). Between enrollment and delivery, the proportion of women with CD4 counts less than 350 cells per milliliter decreased from 55% to 38% (Fig. 2A). Mean viral load saw a 1.74 log reduction between enrollment and delivery. Viral load was undetectable at time of enrollment for 7 of 279 of women (2.5%) and 136 of 218 (62.4%) at delivery (Fig. 2B). One hundred fifty-seven of 218 deliveries (71.9%) were by c-section; however, this proportion has decreased over time from ~92% in 2005 to ~54% in 2009 (Fig. 3A). Note that the c-section rate in China is around 50%.[20]

Eighty-one mothers (29.0%) suffered side effects from the medication, including nausea and dizziness (48), anemia (17), rash (16), and liver dysfunction (1). Severity of side effects was not systematically quantified. However, only 6 women switched to an alternate regimen, no women discontinued treatment due to side effects, and all mothers in the cohort remain alive.

Secondary Outcomes

Pace of Enrollment and Proportion of HIV-1–Infected Women Enrolled

The pace of enrollment and the proportion of women identified who were enrolled increased as well. Between 2006, the first full year of enrollment, and 2008, the last full year of enrollment, there was an 88.0% increase from 58 to 109

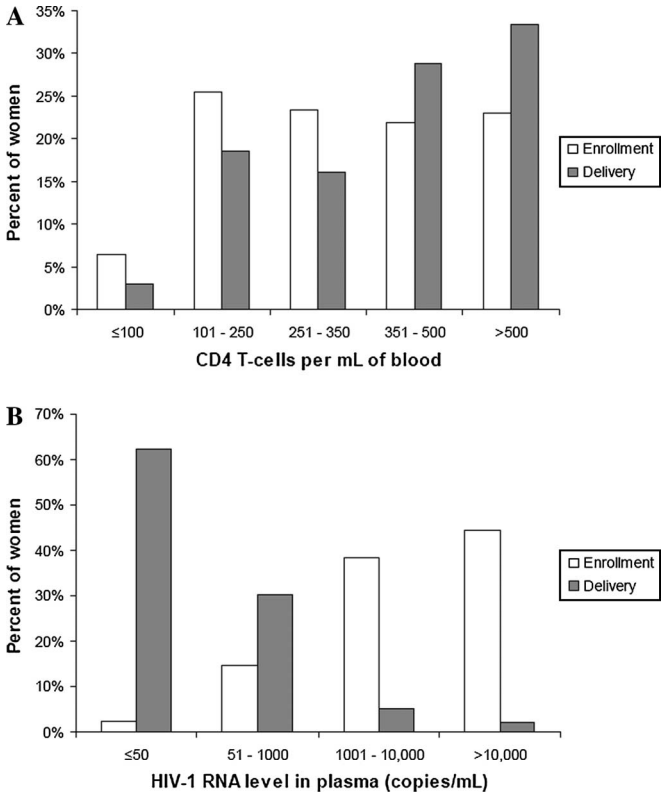

FIGURE 2. Maternal CD4 T-cell counts (A) and plasma viral load (B) at enrollment and delivery.

women enrolled. In the first 6 months of 2009, 76 women were enrolled, and this pace has continued throughout the year.

Based on data collected in 7 of the 16 counties, of the 117 women who were identified as HIV-1 infected in 2006 and chose to deliver their baby, 25.6% (30 of 117) were enrolled into the project. In 2008, this proportion increased to 65.6% (78 of 119) of women across 7 counties, with 1 county enrolling over 90% of HIV-1–infected women.

Early Enrollment

Of 279 women enrolled into the project, 222 (79.6%) were identified before the beginning of the third trimester of gestation or 28 weeks. The program has seen steady improvement since its inception in week of enrollment and duration on treatment before delivery. Since 2005, there has been a statistically significant improvement, with an average 1.1-week earlier enrollment each year and corresponding increase in average days on therapy by 9 days each year. Comparing 2005 with 2009, length of gestation at start of therapy decreased an average of 5.5 weeks (Fig. 3B), and duration of HAART at delivery rose by an average of 35 days.

This early detection translates into more women accessing treatment earlier in their pregnancy, allowing more time for the ARV drugs to control the virus before delivery. On average, women received 95 days of HAART before delivery with a corresponding 1.74 log copies per milliliter reduction in viral load and average 82 cells per milliliter increase in CD4 T cells between enrollment and delivery (Fig. 2A).

Follow-Up

Of 1036 planned visits, among all enrolled women through May 31, 2009, 803 visits (77.5 %) were recorded as actually taking place. Follow-up did not improve over time.

Ninety-nine percent of babies (221 of 223) were delivered at the county MCH or county hospital. The 2 infants born at home received the sdNVP prophylactic dose within 24 hours of birth.

Early Infant Diagnostics

Of 187 babies who have reached 12 weeks of age, 166 (89.8%) have submitted DBS for HIV-1 diagnosis using DNA PCR. For 117 babies for which we have data, infant age when blood was drawn ranged from 23 days to 214 days, with mean of 69 days (median 61 days). Although the mean age is higher than the 6 weeks at which the DNA PCR can be performed, the mean age decreased across time. Among the 22 babies for whom we have test date in 2006 and 2007, mean age of babies at blood draw was 109 days (median 94 days). Among 95 babies tested in 2008 and 2009, mean age of babies was 59 days (median 56 days), a statistically significant reduction in age at diagnosis ($P < 0.0001$). For those infants who had an antibody test at 12 months, there was 100% concordance between the DBS DNA PCR and the enzyme-linked immunosorbent assay.

DISCUSSION

This demonstration project has successfully enrolled close to 300 HIV-1–infected pregnant women into optimal treatment to maximize the reduction of transmission to their infants and minimize the chance for drug resistance. With an infection rate among HIV-1–exposed infants of 1%, the project has demonstrated that using HAART for all HIV-1–infected pregnant women is feasible and effective even in this poor remote region of China.

Although infection rate is low, mortality in this cohort of HIV-1–exposed infants seems to be significantly higher than among unexposed children. Province wide, the 2008 under-one mortality rate was 1.5%.[21] The morality rate among this group of exposed infants was 3.7% (CI: 1.8% to 7.2%). We are reasonably confident that babies in this sample are more than twice as likely to die, by 1 year of age, than babies in the general population. This is in line with studies in Africa that have shown that HIV-1–exposed children die at a higher rate than unexposed children, even when not infected with HIV-1.[22–26] A second explanation for this higher mortality rate may be related to the selection of poor counties with higher underlying mortality rates than in the general population of infants. In project counties, the under-one infant mortality rate ranged from 1.1% to 3.6% in 2007, so it is possible that some of the discrepancy may be due to geographic factors and HIV-1 exposure.[27,28] Further investigation is required to better understand the reasons for higher mortality among HIV-1–exposed children in this setting. Programmatically, in this fifth year of the program, increased resources are being invested in infant follow-up.

Maternal health was improved through the project as well. The 154 women whose CD4 counts were below 350 cells

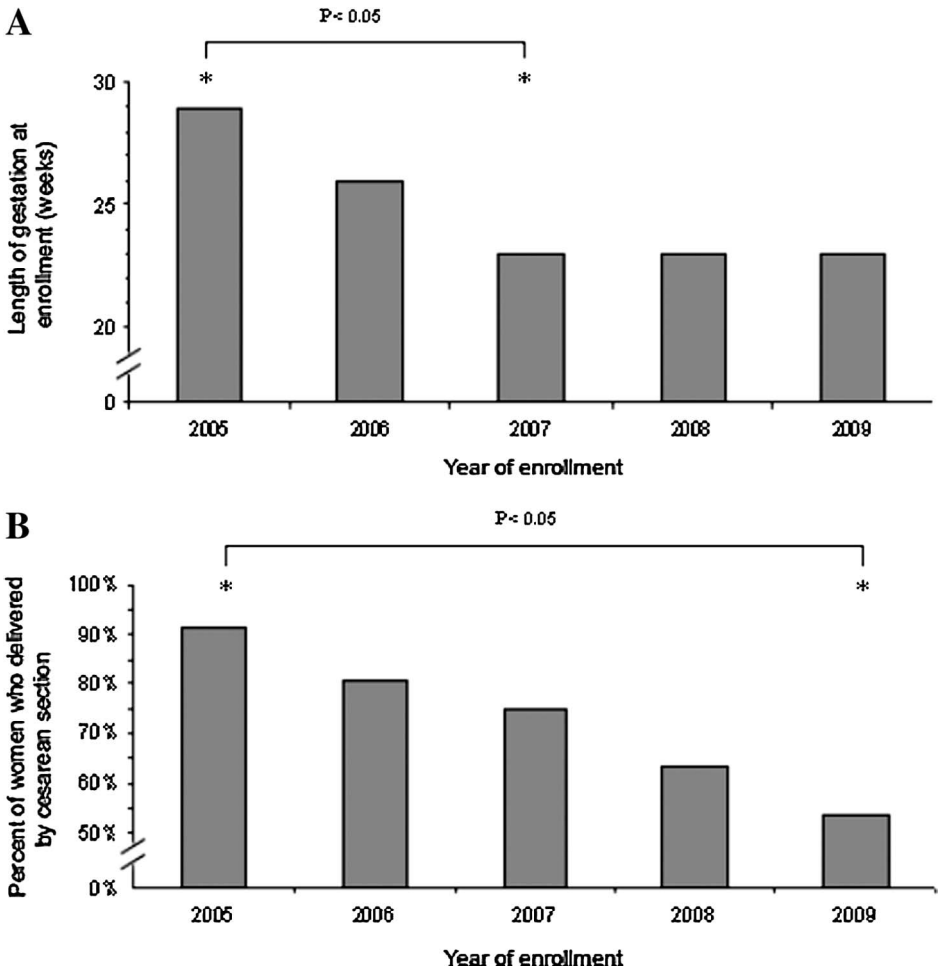

FIGURE 3. A, Decrease in length of gestation at identification of HIV-1 status and enrollment across time. B, Decrease in proportion of women delivering by cesarean section across time.

per milliliter at the time of enrollment and initiated HAART during their pregnancy were referred to the local HIV-1 treatment center and will remain on treatment after delivery. Through this referral system and the close follow-up given to all the women, the project helped strengthen the integration of treatment and PMTCT programming at each of the county sites.

Process indicators collected suggest that over time, implementation of the project has improved. First, the pace of enrollment has significantly increased as a greater proportion of women in each county are enrolled into the program. Selection bias is likely to have occurred in the early years of the program as county doctors picked women whom they assessed to be "reliable" patients, that is, women who lived closer to the county seat and with whom they were able to communicate more easily. However, since 2008, an increasing proportion of HIV-1–infected women in each county have been enrolled into the program. Discussions with project staff and doctors reveal that they attribute this increase in enrollment to earlier identification of HIV-1–infected pregnant women and greater confidence in their own skills. In 2005 and 2006, PMTCT was a relatively new area, health care workers were inexperienced, and sdNVP was the standard intervention. However, through collaboration between the program and the national and provincial health system, health care workers' capacity was built as they gained experience in both treatment and patient management. They are now willing to enroll women into more complicated regimens because they believe in the feasibility and effectiveness of the intervention and in their own ability to manage these cases. Therefore, we believe that selection bias is becoming less of an issue over time and that this model is replicable and scalable across Yunnan.

Second, each year of the project, HIV-1–infected women have been identified earlier in pregnancy. This is a significant trend because it enables women to start on treatment earlier, allowing more time for the ARV regimen to reduce viral load. Longer duration on therapy before delivery has also decreased the proportion of women delivering by c-section to around 54% in 2009, which is in line with national estimates of ~50% for c-section delivery rates in the general population of women.[20]

Earlier identification can be attributed to the scale up and improved quality of universal screening for antenatal care clients. Our project has given significant technical assistance to support the local health system to expand HIV-1 counseling and testing to peripheral health centers in townships and villages through capacity-building trainings in counseling and the introduction of rapid tests.

Third, relatively high levels of follow-up were achieved by the project. No women were lost to follow-up before delivery and 3 mother–infant pairs have been lost. The project required regular laboratory tests, which were used as a proxy measure for follow-up. Although no improvement was seen over time on this measure—across all years proportion of actual to planned visits ranged from 77.3% to 77.7%—close to 80% follow-up should be seen as a success in this context where women live in villages that require anywhere from 1 hour to several days of travel to reach the MCH clinic.

Finally, as early infant diagnosis by DNA PCR becomes standard, HIV-1–infected infants will be identified earlier and they will be provided with the appropriate interventions to minimize morbidity and mortality. After an initial learning period in the first few years of the project, the procedure has become more acceptable to the doctors interfacing with the parents, more familiar to the laboratory technicians, and the laboratory has become certified. Mean age at diagnosis has decreased across time, and most babies born in 2008 and 2009 have been tested between 6 and 12 weeks of age. Starting in the second half of 2008, all HIV-1–exposed babies in county sites, not just those born to women enrolled in the program, will be able to submit a DBS to the Yunnan AIDS Care Center for early diagnosis.

Limitations

Since these findings are based on an ongoing operational research project rather than a clinical research study, some of the data are incomplete. In addition, some indicators were not collected. Severity of side effects to the drugs was not quantified, detailed information on infant feeding practices was not collected, and information on testing of partners had to be gathered retrospectively. However, these indicators are now being collected so that more complete analysis will be possible in the future.

Conclusions

The project demonstrated that HAART for all pregnant women is effective and feasible across a range of settings in Yunnan. Through the program, we were able to promote HIV-1 screening earlier in pregnancy, to monitor women's health closely, and to test babies as early as possible to assess their infection status and provide timely intervention to those who are HIV-1 infected. Although the numbers are still small, it seems at this stage that the infection rate of exposed infants is similar to that of infants born to HIV-1–positive women in urban areas in the United States.[3,4] The key factors that made HAART for all pregnant women in this setting feasible, effective, and safe were the existence of a functioning ARV treatment program in each county with which the PMTCT program could be integrated, investment in reinforcement training to build the capacity of health care workers, close collaboration among the MCH clinic, ARV treatment sites, and the CDC for patient management, and ongoing technical assistance for county project offices from the provincial program office and international partners. We believe that this model is replicable and scalable across other counties in Yunnan (and perhaps across China) and could drastically reduce the number of infants infected with HIV-1 in Yunnan each year.

ACKNOWLEDGMENTS

The authors wish to thank the late Tony Yeung and family for their support to launch this project. We also extend thanks to Drs. Zhiwei Chen and Linqi Zhang for their technical assistance. We are grateful for the dedication of health care workers at participating health care facilities whose hard work is the foundation on which this project has been built. The facilities include: Luxi MCH Hospital, Longchuan MCH Hospital, Linxiang MCH Hospital, Tengchong MCH Hospital, Cangyuan MCH Hospital, Langcang MCH Hospital, Hongta MCH Hospital, Gejiu MCH Hospital, Kaiyuan MCH Hospital, Wenshan MCH Hospital, Yanshan MCH Hospital, Dali County 2nd People hospital, Kunming 3rd People's Hospital, Yuxi MCH Hospital, Baoshan MCH Hospital, and Puer MCH Hospital. Finally, we thank all the mothers and babies for their participation in this project.

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Safety of the Blood Supply in a Rural Area of China

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Objective: To determine the sensitivity and specificity of tests for hepatitis B surface antigen (HbsAg), hepatitis C virus (HCV), and syphilis conducted by laboratories of 3 blood collection organizations in a rural area of China.

Methods: From October to December 2003, 1068 samples were collected from blood donors presenting to the 3 collection centers. All samples were tested twice using 2 different test kits for HBsAg, HCV, and syphilis. An aliquot was sent to the China National Center for Clinical Laboratories to confirm the local test results. Sensitivities and specificities of the 3 local blood centers/banks were calculated using the results of the National Center for Clinical Laboratories as the gold standard.

Results: The sensitivity of the 3 blood collection center/banks ranged from 0% to 63.2% for HBsAg. For HCV, the sensitivity was 0%, and for syphilis, ranged from 0% to 85.7%. There were no HBsAg positives in one of the blood center/banks, and no syphilis positives in the other. Thus, sensitivity could not be measured for these tests in these 2 facilities. Combining all 3 tests, the overall sensitivity was 55.6%. The specificity was 100%.

Conclusions: The sensitivity of the local laboratories was inadequate and could cause possible infection for an unacceptable number of blood recipients. Action needs to be taken to improve the quality of testing to ensure the safety of the rural blood supply.

Key Words: blood safety, hepatitis B, hepatitis C, rural China, syphilis

(*J Acquir Immune Defic Syndr* 2010;53:S23–S26)

INTRODUCTION

Blood transfusions, although potentially life saving, carry significant risk to the recipients, including transmission of infectious diseases such as HIV, hepatitis B virus (HBV), hepatitis C virus (HCV), and syphilis. The epidemics of HIV and sexually transmitted diseases (STDs) have rapidly increased in China,[1–5] HIV contaminated the plasma collection and supply in the 1990s.[6–10] Until recently, very few at-risk persons have been tested for HIV, and routine testing for HIV is often not done in rural areas.[11] The rapid rise in HIV and sexually transmitted diseases (STDs) has not been paralleled by an equivalent rise in HIV testing rates, which remain low.[12–17] Excluding contaminated blood from the blood supply by means of accurate and reliable testing is therefore a critical step in ensuring the safety of blood particularly in rural areas.

In urban areas of China, good laboratory facilities are available, and there is a high enough demand for blood to sustain high quality laboratories. In rural areas, however, the safety of the blood supply is threatened by limited ability to sustain sophisticated laboratories with adequate quality management processes.[13–17] In a rural area of Hebei, China, retesting of 5344 "safe" blood specimens collected by a city blood center showed false negative rates of 0.112% and 0.131% for HBV and HCV, respectively.[12] To assess the situation, we compared test results for 3 infectious diseases from laboratories in the rural blood banks in another rural area of China with those from a reference laboratory.

SUBJECTS AND METHODS

One city-level blood center and 2 county-level blood banks, 1 in proximity to the county site and 1 remote, were selected for study. Blood collection organizations are authorized by the Department of Health. The city blood center serves a population of 4.6 million and collects about 25,000 units of blood annually; county blood bank A serves 950,000 persons and collects about 4000 units annually; and blood bank B serves 430,000 persons and collects approximately 2000 units annually. Donors included individual volunteers, groups of volunteers, and paid donors.

All donors presenting to the 3 collection sites from October through December 2003 were asked to participate in the study. If a donor consented, an additional 10 mL of blood was collected for supplementary testing. The study was approved by the institutional review boards of the University of California, Los Angeles, and the Chinese Academy of Preventive Medicine.

All samples were tested for HCV, HBV, and syphilis, in duplicate using 2 different test kits for each agent according to the routine procedures of the 3 blood collection organizations (Table 1). All tests were done by certified laboratory technicians. All testing procedures including results reading followed the instructions in the user manuals provided by test kit

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Supported by the US National Institute of Health Fogarty International Center training grant D43 TW000013.

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TABLE 1. Test Methods and Test Kits Used by China NCCL and the 3 Blood Center/Banks

Organization	Serologic Indicator	Screening*		Confirmation/Screening†	
		Method	Test Kits (Company)	Method	Test Kits (Company)
NCCL	HBsAg	ELISA	Xinchuang (Xiamen Xinchuang), Wantai (Beijing Wantai), Ortho (Johnson and Johnson)	Neutralization assay	Ortho (Johnson and Johnson)
	Anti-HCV	ELISA	Wantai (Beijing Wantai), Xinchuang (Xiamen Xinchuang), Ortho (Johnson and Johnson)	Recombinant immunobot assay	Ortho (Johnson and Johnson)
	Antisyphilis	ELISA	GBI (Beijing GBI), Xinchuang (Xiamen Xinchuang), Huamei (Luoyang Huamei)	Treponema pallidum particle agglutination test	Fuji (Fuji Co Ltd)
City blood center	HBsAg	ELISA	Huamei (Luoyang Huamei)	ELISA	Pusheng (Tianjin Pusheng), Xinchuang (Xiamen Xinchuang)
	anti-HCV	ELISA	Huamei (Luoyang Huamei)	ELISA	Lili (Henan Lili), Xinchuang (Xiamen Xinchuang), Pusheng (Tianjin Pusheng)
	Antisyphilis	ELISA	Huamei (Luoyang Huamei), Jinhao (Beijing Jinhao)	ELISA	Xinchuang (Xiamen Xinchuang), GBI (Beijing GBI)
County blood bank A	HBsAg	ELISA	Huamei (Luoyang Huamei)	ELISA	Xinchuang (Xiamen Xinchuang)
	Anti-HCV	ELISA	Huamei (Luoyang Huamei)	ELISA	Xinchuang (Xiamen Xinchuang)
	Antisyphilis	RPR	Rongsheng (Shanghai Rongsheng)	Rapid plasma reagin test	Kehua (Shanghai Kehua)
County blood bank B	HBsAg	ELISA	Xinchuang (Xiamen Xinchuang)	ELISA	Huamei (Luoyang Huamei)
	Anti-HCV	ELISA	Xinchuang (Xiamen Xinchuang)	ELISA	Huamei (Luoyang Huamei)
	Antisyphilis	TRUST	Rongsheng (Shanghai Rongsheng)	Toluidine red untreated serum test	Kehua (Shanghai Kehua)

*NCCL used the methods and test kits to do three times of screening, and the blood center/banks used the methods and test kits to do the first screening.
†NCCL used the methods and test kits to do confirmation, and the blood center/banks used the methods and test kits to do the second screening.
ELISA, enzyme-linked immunosorbent assay.

manufacturers. All test kits were licensed and manufactured domestically (in China). A positive sample or suspicious positive on either test was considered to be infected. An aliquot of each sample was transported to the China National Center for Clinical Laboratories (NCCL) for confirmation. NCCL is the only agency appointed by the Chinese Ministry of Health and the "Chinese Blood Bank Regulations" that is authorized to make a final confirmatory laboratory test result. Serology tests for hepatitis B surface antigen (HbsAg), HCV, and syphilis were performed at the NCCL, using 3 different test kits (1 imported, 2 domestic; Table 1) for initial screening. Imported confirmatory tests were used to confirm all positive or suspicious samples in the screening tests (Table 1). All tests by NCCL were performed by senior technicians and in accordance with manufacturer's instructions.

The study was reviewed and approved by the Institutional Review Board at the University of California at Los Angeles and the Institute Review Board at the National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and Prevention.

RESULTS

Samples were collected from 1068 donors. The city blood center collected 650 samples, county blood bank A collected 200 samples, and county blood bank B collected 218 samples. The refusal rates were 5%–10% in the city blood center, 0.5% in county blood bank A, and 1.4% in county blood bank B. Table 2 presents the demographic characteristics of the donors at the 3 centers. Donors at the city blood bank were younger than those at the county blood banks. Table 3 compares test results for the 3 rural blood collection organizations and NCCL, and Table 4 presents the sensitivity and specificity of the tests performed by the 3 local centers, using the NCCL test results as the gold standard.

Hepatitis B Surface Antigen

All 12 HBsAg positives identified by the city blood center reported positive (Table 2). However, 7 of the reported negatives were actually positive according to the NCCL laboratory; the sensitivity was therefore 63.2% (Table 3). In

TABLE 2. Basic Demographic Characteristics of the Blood Donors in the 3 Rural Blood Center/Banks

	City Blood Bank, n (%) (n = 650)	County Blood Bank A, n (%) (n = 200)	County Blood Bank B, n (%) (n = 221*)
Gender			
Male	312 (48.0)	107 (53.5)	111 (50.2)
Female	338 (52.0)	93 (46.5)	110 (49.8)
Average age	28.5†	41.6	37.5
Type of donation			
Paid	164 (25.2)	191 (95.5)	128 (57.9)
Voluntary	486 (74.8)	9 (4.5)	93 (42.1)

*Three people did not give blood samples. We only had 218 samples from county blood bank B.
†Many blood donors were college students, so the average age was younger than the other 2 blood banks.

TABLE 3. Comparison by Category of Test Results Between Blood Center/Banks and NCCL, China, 2003

	NCCL								
	HBsAg			HCV			Syphilis		
	+	−	Total	+	−	Total	+	−	Total
City blood center									
+	12	0	12	0	0	0	6	0	6
−	7	631	638	1	649	650	1	643	644
Sum	19	631	650	1	649	650	7	643	650
County blood bank A									
+	0	0	0	0	0	0	0	0	0
−	0	200	200	0	200	200	3	197	200
Sum	0	200	200	0	200	200	3	197	200
County blood bank B									
+	2	0	2	0	0	0	0	0	0
−	2	214	216	2	216	218	0	218	218
Sum	4	214	218	2	216	218	0	218	218

county blood bank A, there were no HBsAg-positive samples; therefore, sensitivity could not be evaluated. In county blood bank B, 2 of the positive samples repeated positive, but there were 2 false-negative tests; thus, the sensitivity was only 50% (Table 4). The specificity in the city blood center and the 2 county blood banks was 100%.

Hepatitis C Virus

The city blood center failed to identify the single positive sample identified by the NCCL laboratory. County blood bank A had no HCV-positive samples, and county blood bank B failed to identify the 2 positive samples. The specificity in the city blood center and the 2 county blood banks was 100%.

Syphilis

The city blood center identified 6 of 7 positive samples; thus, sensitivity was 85.7%. County blood bank A missed all 3 positive samples (sensitivity = 0%), and county blood bank B had no positive samples. The specificity was 100% in all 3 facilities.

Composite Sensitivity and Specificity

Among the 650 samples from the city blood center, 27 were confirmed as positive, 9 of which had not been detected, rendering a sensitivity of 66.7% (Table 5). The specificity was 100%.

Among the 200 samples from county blood bank A, 3 were confirmed as positive, all of which were undetected (sensitivity = 0%). There were no false-positive samples; therefore, specificity was 100%.

Among the 218 samples from county blood bank B, 6 were confirmed as positive, among which 4 had not been detected (sensitivity = 33.3%). The specificity was 100%.

The composite sensitivity was 55.6% (only 20 of the 36 tests positive at the NCCL were identified by the local laboratories), and the specificity was 100%. Overall, 14 of every 1000 blood units (1.4%) labeled by the city blood center as pathogen-free would be expected to be contaminated with 1 of these 3 agents, as would 15 of 1000 (1.5%) from county blood bank A and 19 of 1000 (1.9%) from county blood bank B.

DISCUSSION

Exclusion of infectious donations from the blood supply is primarily dependent on accurate and reliable testing for transfusion-transmitted pathogens. Our study was designed to detect differences in donor test results between 3 identified blood centers and the laboratory designated as the authoritative laboratory for donor test confirmation by the Chinese Ministry of Health. Using the NCCLs as the standard for testing, our study reveals that there were serious problems with detecting HBsAg, HCV antibodies, and syphilis antibodies in the city blood center and in the 2 county-level blood banks. Retesting the city blood center samples identified the highest proportion of contaminated samples, 66.7%, which means that

TABLE 4. Assessment Indicators of Test Results by Laboratories for 3 Blood Center/Banks in Rural China, 2003

	Indicators	HbsAg (95% CL)	Anti-HCV (95% CL)	Antisyphilis (95% CL)
City blood center	Sensitivity	0.632 (0.386 to 0.828)	0.000 (0 to 0.945)	0.857 (0.420 to 0.992)
	Specificity	1.000 (0.992 to 1.000)	1.000 (0.993 to 1.000)	1.000 (0.993 to 1.000)
County blood bank A	Sensitivity	NA	NA	0.000 (0 to 0.690)
	Specificity	1.000 (0.977 to 1.000)	1.000 (0.977 to 1.000)	1.000 (0.976 to 1.000)
County blood bank B	Sensitivity	0.500 (0.092 to 0.908)	0.000 (0 to 0.802)	NA
	Specificity	1.000 (0.978 to 1.000)	1.000 (0.978 to 1.000)	1.000 (0.978 to 1.000)

CL, confidence limits.

TABLE 5. Assessment Indicators of Composite Test Results by 3 Blood Center/Banks in Rural China, 2003

Indicators	City Blood Center (95% CL)	County Blood Bank A (95% CL)	County Blood Bank B (95% CL)	All 3 Blood Center/Banks (95% CL)
Sensitivity	0.667 (0.460 to 0.828)	0.000 (0 to 0.690)	0.333 (0.060 to 0.759)	0.556 (0.383 to 0.717)
Specificity	1.000 (0.992 to 1.000)	1.000 (0.976 to 1.000)	1.000 (0.978 to 1.000)	1.000 (0.995 to 1.000)
Predictive value of positive	1.000	NA	1.000	1.000

they would have labeled almost one-third of the infected blood units as pathogen-free. County blood bank B would have labeled two-thirds of the contaminated units as pathogen-free, and county blood bank A, all of the contaminated units as pathogen-free. Because the prevalence of pathogens was low in the study populations, the calculation of the sensitivities was unstable, and the confidence limits for sensitivity and specificity were wide in some instances.

Accuracy and reliability of test results are a function of the sensitivity and specificity of test kits, quality of specimen, competency of testing personnel, and adherence to good laboratory practices. Our study was not designed to identify which of these factors was responsible for the discrepant results. We cannot say whether the apparently low sensitivity in the rural laboratories was due to the poor quality of test kits themselves, or due to test procedures by the laboratory technicians, or both. It is also possible, but less likely, that the results of the NCCLs, which we used as the "gold standard", were incorrect.

Our results do indicate that reliability of donor infectious disease screening performed at the 3 collection centers we studied is uncertain and that there is a need to assess to what degree this may be true throughout similar rural communities. In China, urban blood collection centers are generally staffed with trained laboratory professionals and are expected to have quality assurance measures in place. However, it is hard to recruit highly trained professionals to work in the rural areas, and quality assurance may be an unfamiliar concept.

As the prevalence of transfusion-transmitted disease increases in the population, the threat to the blood supply increases. Measures to standardize and improve donor infectious disease screening are urgently needed. These measures should include validation of test kits, better training, implementation of standardized quality control and quality assurance procedures, and periodic recertification of laboratory technicians. Most of these recommendations are already included in the official blood collection regulations[18–21] but are not uniformly enforced, especially in rural areas.

ACKNOWLEDGMENTS

The authors thank Professor Hongbo Zhang from Anhui Medical University and Dr. Guodong Mi from China CDC/NCAIDS; Drs. Jianmei He, Biyun Qin and Jun Zheng from Hunan CDC; and the collaborative research team staff from Changde City Center for Disease Control and Prevention, Changde City Blood Center, and 2 local county blood banks for their participation in the baseline survey. The authors also thank Dr. Jinming Li and his staff for performing laboratory tests at the NCCL in Beijing, and Wendy Aft for editing assistance.

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Genetic and Epidemiologic Characterization of HIV-1 Infection In Liaoning Province, China

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Background: Although many studies of HIV-1 in China have focused on high-risk injecting drug users and former blood donors in high prevalence regions, little is known about HIV-1 in relatively low prevalence provinces. Here, we compare the epidemiologic and genetic profile of HIV-1 in Liaoning—a low prevalence province—with those identified in China's most severely affected provinces.

Materials and Methods: Two hundred eight HIV-1–positive subjects from all major cities in Liaoning province were recruited between 2000 and 2008. 2.6 kilobase gag-pol sequences were amplified from plasma viral RNA and sequenced directly. The HIV-1 sequences obtained were analyzed using phylogenetic and recombinant approaches.

Results: We have shown that in recent years, although HIV-1 prevalence in Liaoning has remained low, the rate of new infection has increased rapidly, particularly among men who have sex with men and heterosexual risk individuals (together comprising >54% of infected individuals in 2007). Furthermore, phylogenetic analysis has identified all major subtypes/circulating recombinant forms of HIV-1 in Liaoning previously identified in high prevalence provinces. Our study also shows close relationships between HIV-1 subtype/circulating recombinant form and certain risk behaviors. Notably, men who have sex with men and heterosexual risk individuals harbor most divergent strains of HIV-1 from multiple high-risk groups.

Conclusions: Our study suggested that HIV-1 continues to spread to the general population through sexual contact; Liaoning, therefore, serves as the critical base for the introduction and spread of HIV-1 in northeast China. We believe the transmission patterns suggested herein will help guide public health workers in reducing further spread of HIV-1 within China.

Key Words: HIV type I, injecting drug users, men who have sex with men, China

(*J Acquir Immune Defic Syndr* 2010;53:S27–S33)

INTRODUCTION

The HIV-1/AIDS epidemic in China is at a critical juncture. Although HIV-1 infection has historically been largely confined to high-risk groups such as injecting drug users (IDUs) and former commercial blood and plasma donors (FBDs) in rural areas,[1,2] the rate of HIV-1 infection has been increasing rapidly in urban settings among men who have sex with men (MSM) and female sex workers. This is a worrisome trend previously seen in other Asian countries.[3,4]

The current epidemic in China can be broadly classified into 2 major risk groups. The first major risk group arose from injecting drug use and needle sharing in Yunnan province, and along drug-trafficking routes to the neighboring provinces of Guangxi, Guizhou, and Sichuan and to the far northwest province of Xinjiang.[3] The second group arose from illegal and unsanitary blood collection and transfusion practices among FBDs in Henan and neighboring provinces.[1,2] This typically involved the pooling of blood from several donors of the same blood type, followed by the removal of plasma and the reinfusion of cells back into the original donors to reduce anemia.[1,2] Contamination of these pooled samples with HIV-1, along with needle reuse and unsterilized equipment, greatly enhanced viral transmission. Epidemiologic and molecular genetic studies indicate that both of these 2 epidemic groups stemmed from the initial infection of Dai and Jingpo ethnic minority IDUs in southwest Yunnan province in the late 1980s.[5–11] IDUs and FBDs represent the first and worst affected populations in the HIV-1 epidemic in China.

Although there exist many HIV-1 epidemiologic and genetic studies of these 2 major groups,[3,7–16] little is known

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Supported by mega projects of national science research for the 11th Five-Year Plan (2008ZX10001-001), 973 program about the development of national significant elementary research to H.S. and L.Z. (2006CB504206), National Natural science Funds (30800969) and High-Level Scholars Program of the Liaoning Province Institutions of Higher Education [2008]90.

The work was conducted without any conflict of interest.

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about the situation in relatively low prevalence provinces. As such, we aim to study the epidemiologic and genetic features of HIV-1 in a low prevalence region—Liaoning province of northeast China—and compare with those identified in China's most severely affected provinces. We believe that our study will not only help to monitor the transmission patterns of HIV-1 from high to relatively low prevalence areas but also assist public health workers in implementing measures to curb the spread of HIV-1 within China.

MATERIALS AND METHODS

Study Subjects and Specimens

A total of 208 HIV-1–positive subjects from all major cities in Liaoning province were recruited between 2000 and 2008 by the First Affiliated Hospital China Medical University in Shenyang, Liaoning Province, in northeastern China. These included 109 cases from Shenyang, 31 from Huludao, 20 from Dalian, 16 from Dandong, 6 from Fushun, 4 cases from Chaoyang, Panjin, Tieling, and Yingkou, 3 cases from Anshan and Liaoyang, 2 cases from Jinzhou, and 1 case from Benxi and Fuxin (Fig. 1). This study was approved by the institution's ethical committee, and the study participants were interviewed by clinicians to determine their epidemiologic background, using questionnaires designed by the UNAIDS HIV-1 characterization network. This information was then verified with that from the HIV patient management database in the Hospital. Study subjects included 70 individuals with heterosexual risk, 52 FBDs or transfusion recipients, 10 IDUs, 75 male homosexuals, and 1 child born to an HIV-infected mother. Two hundred six of 208 subjects were adults (>15 years old), including 165 males and 41 females. Adult subject age data were obtained for 93.4% males (range: 19–69 years; mean: 36.4 ± 10.1 years) and 92.3% females (range: 18–58 years; mean: 35.1 ± 10.4 years). The 2 subjects <15 years old (4 and 14 years old) were males. All 208 specimens were serologically determined as HIV-1 positive with no evidence of HIV-2 infections. Baseline $CD4^+$ T-cell count was obtained for 95.2% male subjects (mean: 356 ± 243 cells/μL) and 100% female subjects (mean: 405 ± 243 cells/μL), and baseline HIV-1 viral load was obtained for 73% male subjects (mean: 4.68 ± 0.95 × 103 lgcopies/mL) and 92.3% female subjects (mean: 4.65 ± 0.95 × 103 lgcopies/mL). All patients were treatment-naive at the point of sample collection.

RNA Purification, Polymerase Chain Reaction Amplification, Sequencing, and Phylogenetic Analysis

HIV-1 RNA was extracted from plasma by a column purification method (QIAamp. Viral RNA Mini Kit; Qiagen, Hilden, Germany) and subjected to reverse transcription-nested polymerase chain reaction (PCR). The nucleotide sequence of the 2.6 kilobase *gag* reverse transcriptase (RT) gene (nucleotide position relative to HXB2 genome: 790–3421) was determined by direct sequencing (ABI PRISM. 3130 Genetic Analyzer, Applied Biosystems, Foster City, CA). The PCR primer-binding sites for the ampilcon were based on published sequences of geographical variants and were as highly conserved as possible. Codon alignment of query sequences with various HIV-1 reference subtypes and circulating recombinant form (CRFs) from the HIV database (http://hiv-web.lanl.gov/) was performed. Selected HIV-1 subtypes/CRFs of geographical importance were also included in the alignment. Phylogenetic and molecular evolutionary distances were estimated using the neighbor-joining method and the Kimura 2-parameter model with a transition–transversion ratio of 2.0. The reliability of the branching orders was tested by bootstrap analysis of 1000 replicates. Bootscanning, similarity plots and informative site analysis were performed using SimPlot v3.5 to define the recombination structure. All RNA extractions and PCR amplifications were carried out with appropriate negative

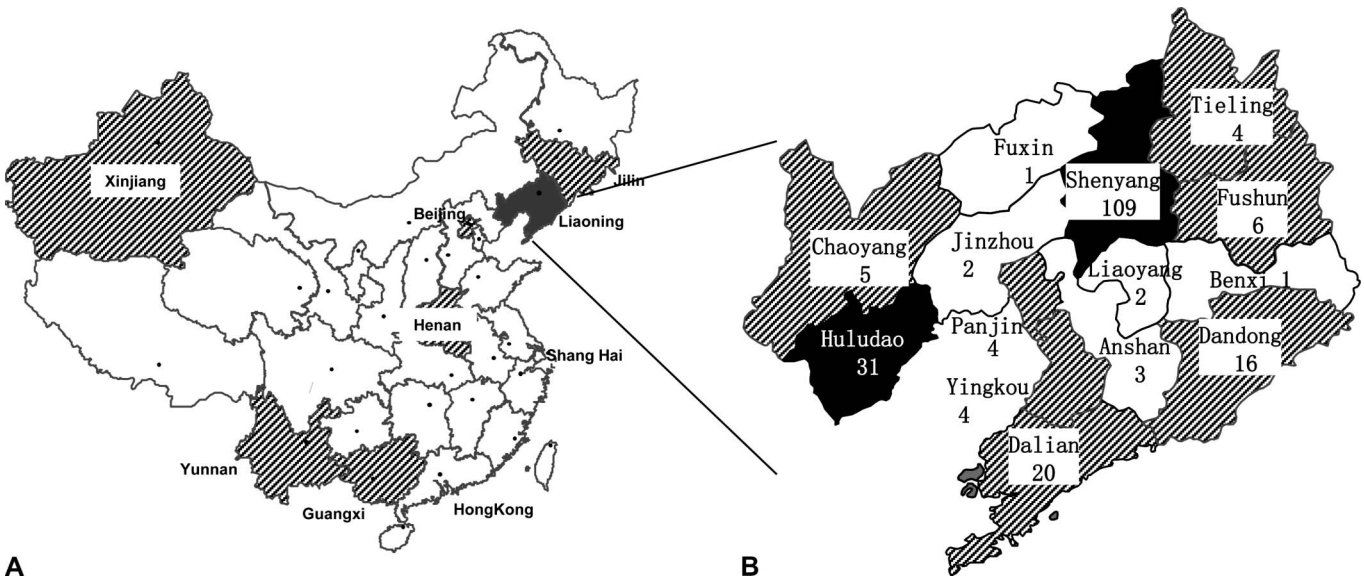

FIGURE 1. Map of the People's Republic of China (A) and Liaoning province (B), and the geographic distribution of studied HIV-1–infected cases in Liaoning.

controls to detect possible contamination during the procedure. To check for potential contamination, before analysis, the sequences obtained were compared with all known sequences in the HIV database by a Basic Local Alignment Search Tool (BLAST) search (http://hiv-web.lanl.gov/content/index).

Nucleotide Sequence Accession Numbers

The Genbank accession numbers of nucleotide sequences reported in this article are EF122502-EF122594, AY548279, and FJ531381-FJ531481.

RESULTS

The HIV-1/AIDS Epidemic in Liaoning

Liaoning province is located in the northeastern part of China (Fig. 1), the region traditionally referred to as Manchuria. Its geographic proximity to the Yellow Sea, the Bohai Gulf, and the Yalu River has made it an important base for industry and trade and it serves as the closest gateway to the Korean Peninsula. Administratively, Liaoning has a total of 14 counties and cities, of which the capital Shenyang is the largest (Fig. 1). Liaoning has an estimated population of 42 million, with Han as the ethnic majority (84%), followed by Manchu (13%), and Mongol (2%). The remaining 1% consists of Hui, Korean, and Xibo minorities.

Since the first HIV case was identified in Liaoning in 1991, a total of 990 HIV/AIDS cases had been reported by 2007. Although the cumulative number of HIV/AIDS cases remains relatively small, the rate of new case identification has increased rapidly in recent years. Although only 77 cases were found in 2004, 159 cases were identified in 2005, 216 cases in 2006, and 305 cases in 2007 (Fig. 2). This translates to an average annual rate of increase of approximately 60% over the last 3 years. Based on these reported cases, it is estimated that the total number of infected cases in Liaoning is about 5239, with province-wide prevalence rate of 0.0125%.

The recent increase in reported cases is also characterized by dramatic changes in risk factor distribution among infected individuals. Most notably, the proportion of cases transmitted through homosexual contact increased to 22% between 2005 and 2007 compared with less than 1% in the previous years (Fig. 2, inset). On the other hand, the proportion of cases transmitted through blood donation and transfusion decreased from 34% to 8% during the same period. Other risk factors such as injection drug use (IDU), mother to child transmission, and heterosexual contact have contributed relatively stable proportions to the total. Of note, individuals with unknown risk factors have contributed a substantial proportion of the total throughout the years (Fig. 2, inset).

The rapid increase in MSM-related infections is a significant feature of the changing epidemiologic profile of HIV-1 in Liaoning. Although the HIV-1 prevalence rates among the IDU, female sex worker, and STD (out patients attending sexually transmitted disease clinics) groups remain relatively low and stable (below 0.5%) between 1999 and 2007, there is a 6-fold increase for MSM in 2006 and 2007, according to data from the Disease Control and Prevention center of Liaoning Province. Furthermore, more than 65% of infected cases are male. On average, >80% of infected individuals have been aged 20–40 years.

Although such dramatic increases in reported HIV/AIDS cases are primarily due to the active testing initiative launched by national and provincial health authorities in 2004, these could also indicate an expansion of the epidemic in Liaoning. Indeed, differentiating new infections from newly identified chronic infections will require more sophisticated techniques.

Different Risk Groups Dominated by Distinct Subtypes of HIV-1

To study the pattern of distribution of HIV-1 genotypes, we obtained 208 nucleotide sequences encompassing the *gag* RT gene. A phylogenetic approach was used to study the relationships among HIV-1 strains within Liaoning and with those from outside. The most obvious and consistent result from phylogenetic analysis was that there are 3 major subtypes and/or CRFs of HIV-1 currently circulating in Liaoning. They are those clustering closely with reference sequences CRF01_AE (01 AE.TH.90.CM240) or CRF15_01B (15 01B. TH.99.MU2079); those with subtype B (B.FR.83HXB2-LAI-IIIBBRU) or B' (B.CN.RL42); and those with subtype C

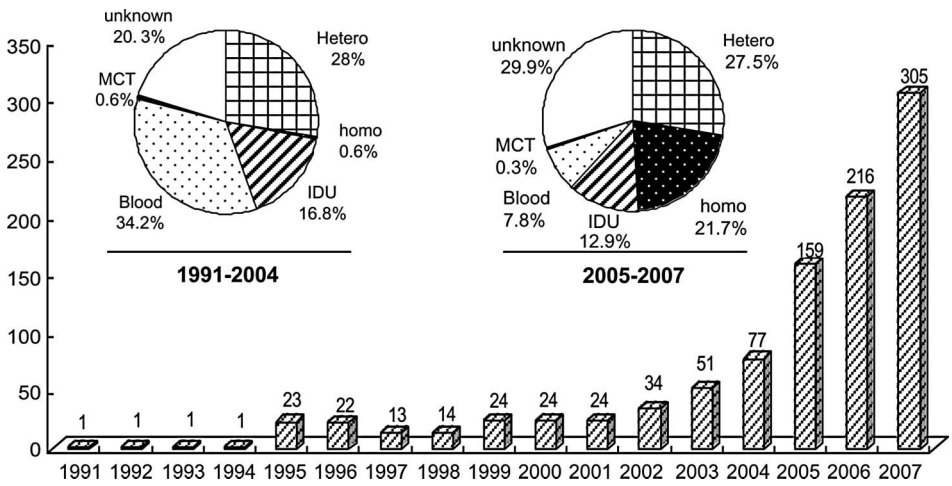

FIGURE 2. Accumulative reported HIV-1–infected cases in Liaoning between 1991 and 2007.

(C.IN.95.21068) or reference sequences CRF07_BC (07 BC.CN.97.CN54) or CRF08_BC (08 BC.CN.97.GX 6F). Approximately 43.3% of collected sequences were found in the CRF01_AE/CRF15_01B group, 41.3% in the subtype B/B' group, and 9.6% in the C/CRF07_BC/CRF08_BC group. The remaining 5.8% belong to other subtypes such as A1 or A2 or unknown recombinants. Of note, about 90.0% of infected IDUs had C/CRF07_BC/CRF08_BC viruses, whereas 92.3% of infections acquired through blood donation had subtype B or B', and 81.3% of MSM had CRF01_AE (Fig. 3A). The heterosexual contact risk group showed a variety of subtypes, with 37.1% subtype B or B', 12.9% CRF07_BC or CRF08_BC, 37.1% CRF01_AE, and the remaining 12.9% other subtypes (Fig. 3A). Furthermore, more than 96% of CRF01_AE infections were acquired through sexual transmission (67.8% MSM, 28.9% heterosexual risk) (Fig. 3B). Subtypes B and B', on the other hand, are strongly associated with blood donation (55.8%) and heterosexual contact (30.2%) and only weakly so with MSM (14.0%). Lastly, CRF07_BC and CRF08_BC are dominant in both the heterosexual contact (45.0%) and IDU (45.0%) risk groups (Fig. 3B).

Close Genetic Relationship Between HIV-1 Found in Liaoning and Those in High Prevalence Provinces and Regions

We have generated independent phylogenetic trees for the 3 major Liaoning HIV subtypes and CRFs; each of which is indicated by symbols corresponding to their known risk factor: homosexual (open triangle), heterosexual (closed triangle), IDU (closed square), and PBD/BT (closed circle). For clarity, only a few representative sequences from each risk groups are shown, together with reference sequences from different HIV-1 subtypes (http://hiv-web.lanl.gov/content/index). As shown in Fig. 4, sequences identified in Liaoning have a close genetic relationship with those previously found in Henan, Guangxi, and Yunnan provinces. For instance, sequences in the AE group are interdigitized with those identified in Guangxi (01 AE.CN.97.GX2F) and in neighboring Thailand (01 AE.TH.90.CM240). Although those found in heterosexual contact (closed triangle) are spread along many branches, most MSM (open triangle) sequences stem from a single branch, suggesting a close relationship among MSM in Liaoning (Fig. 4). This group contains sequences from both MSM and heterosexual risk individuals. The genetic distance within this group is as low as 0.027, suggesting the MSM and heterosexual contact groups are tightly linked. This finding perhaps relates to the fact that most of the MSM in China are bisexual and married with family.

Sequences in the subtype B/B' group are mostly clustered with B' sequences previously identified in China. Of the 2 groups of B' sequences, 1 group is related to the more recent sequences identified in Henan (B.CN.02.HNsq4) and Hubei (B.CN.05.HBdw111), whereas the other group is related to early epidemic sequences found in Yunnan (B.CN.x.RL42). As in the AE group, individuals infected through heterosexual contact have sequences scattered along many branches in both B and B' groups, whereas those from FBD are derived from a single branch, suggesting the tight relationship among blood donors in Liaoning and their genetic relatedness with those from those high prevalence provinces. In addition, sequences from blood donors are tightly grouped with those from heterosexual risk individuals (Fig. 4), and their genetic distance is as low as 0.038. This result may indicate that HIV-1 has begun to spread from the traditionally high-risk blood donor population to some in the general public through heterosexual contact. Lastly, some MSM were also found to have subtype B sequences similar to typical North American strains such as B.FR.83.HXB2-LAI-IIIB-BRU.

Sequences in the BC groups fall into 2 previously identified recombinant forms, CRF07_BC and CRF08_BC (Fig. 4). They are predominately comprised of IDUs (closed square) and heterosexual risk individuals (closed triangle) and are genetically indistinguishable from those previously identified in Yunnan (07 BC.CN.97.CN54), Guangxi (08 BC.CN.97.GX.6F), and India (C.IN.95.21068) (Fig. 4). One sequence loosely groups with subtype C, and its true subtype assignment needs to be further verified.

Recombinant Forms of HIV-1 Found in Liaoning Similar to Those Found in High Prevalence Provinces and Regions

We analyzed 62 HIV-1 sequences from Liaoning spanning the entire 2.6 kilobase *gag* RT gene (nucleotide

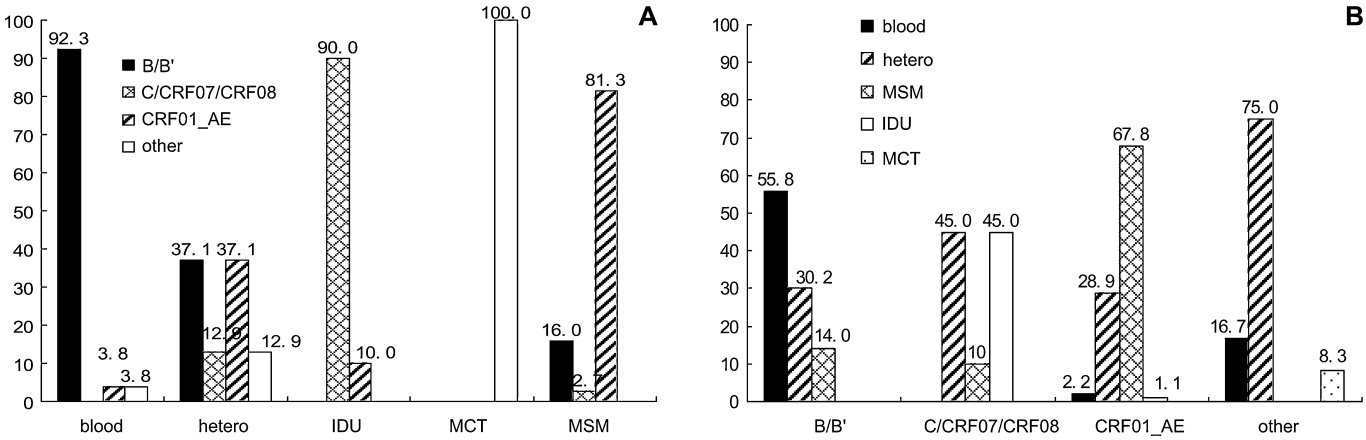

FIGURE 3. Correlation between risk factors and HIV-1 subtypes and CRF. A, Percentage of viral subtypes and CRF in each of risk group studied; and B, Percentage of risk groups in each of the viral subtype and CRF.

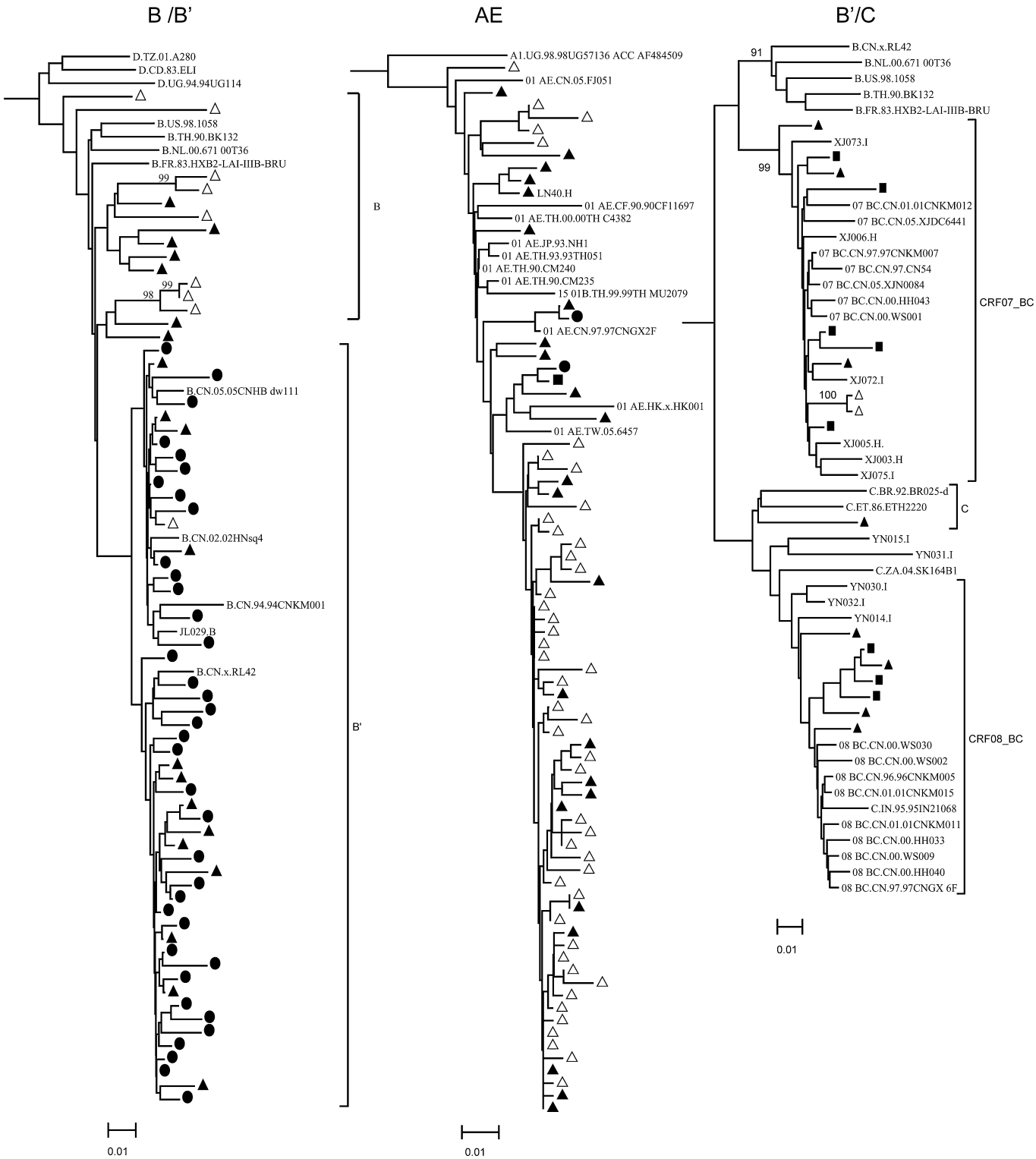

FIGURE 4. Neighbor-joining trees showing the 3 major circulating HIV-1 subtypes and CRF in Liaoning and their genetic relationship with those identified in high prevalence provinces. Individual sequences are indicated by symbols corresponding to their known risk factor: homosexual (open triangle), heterosexual (closed triangle), IDU (closed square), and FBD (closed circle). For clarity only a few representative sequences from each risk groups are shown, together with reference sequences from different HIV-1 subtypes (http://hiv-web.lanl.gov/content/index). The bootstrap values of 1000 replicates are labeled on the major branches.

position relative to HXB2 genome: 790–3421). Consistent with phylogenetic analysis, all CRF08_BC or CRF07_BC viruses had typical recombination features similar to those previously reported from Guangxi and Yunnan (Fig. 5). None of the CRF01_AE sequences showed any intersubtype recombination in the fragment studied. However, 1 sequence was found that is likely a new subtype CRF01_AE/B recombinant (Fig. 5). Further studies will be needed to characterize this strain in the context of full viral genome.

DISCUSSION

In this report, we have characterized the epidemiologic and genetic features of HIV-1 infection in relatively low prevalence Liaoning province. We believe this is the first time that comparative studies have been conducted between HIV-1 in high and low prevalence provinces in China. We have shown that in recent years, although HIV-1 prevalence in Liaoning has remained low, the rate of new infection has increased rapidly. The most astonishing finding is a dramatic increase in HIV-1 infection among MSM, accounting for more than 26% of the entire infected populations in 2007. In addition, the component of infections through heterosexual contact has reached 28%. In other words, sexual contact has become the dominant mode of HIV-1 transmission (26% + 28% = 54%) among infected cases.

Furthermore, major subtypes and CRFs of HIV-1 previously identified in Henan, Guangxi, and Yunnan have all been identified in Liaoning. Although there are some reports trying to illustrate the temporal and spatial relationship between HIV-1 in high and low prevalence provinces and regions,[17,18] it is impossible to describe exactly the chain of transmission events that led to the current epidemiologic picture in Liaoning. Nevertheless, our results provide some evidence that the HIV-1/AIDS epidemic in Liaoning is the result of multiple introductions of various HIV-1 strains from high prevalence provinces and regions. Liaoning, therefore, serves as the most critical base for the introduction and subsequent spread of HIV-1 in northeastern China.

As in high prevalence regions, there are close relationships between HIV-1 subtypes/CRFs and certain risk behaviors in Liaoning. For example, subtype B' and B sequences are predominantly found in paid blood donors, CRF07_BC and CRF08_BC mainly in IDU, and CRF01_AE in MSM, indicating that these viruses were introduced to Liaoning through their respective risk behaviors. However, such correlation has been compromised to a large extent in Liaoning compared with that in the original high prevalence provinces. Notably, multiple subtypes and CRFs have been identified within the heterosexual risk group, suggesting that HIV-1 strains from historically high-risk groups have been transmitted to the general population via heterosexual contact. Furthermore, the dramatic expansion of HIV-1 infection among MSM is comprised largely of CRF01_AE sequences. The strong genetic relatedness among CRF01_AE viruses demonstrates the rapid and perhaps recent dissemination of viruses within the MSM group in Liaoning.[19] This hypothesis is consistent with epidemiologic data showing 2006 as the turning point when there was a significant increase in HIV-1 prevalence among MSM. Lastly, as multiple subtypes and

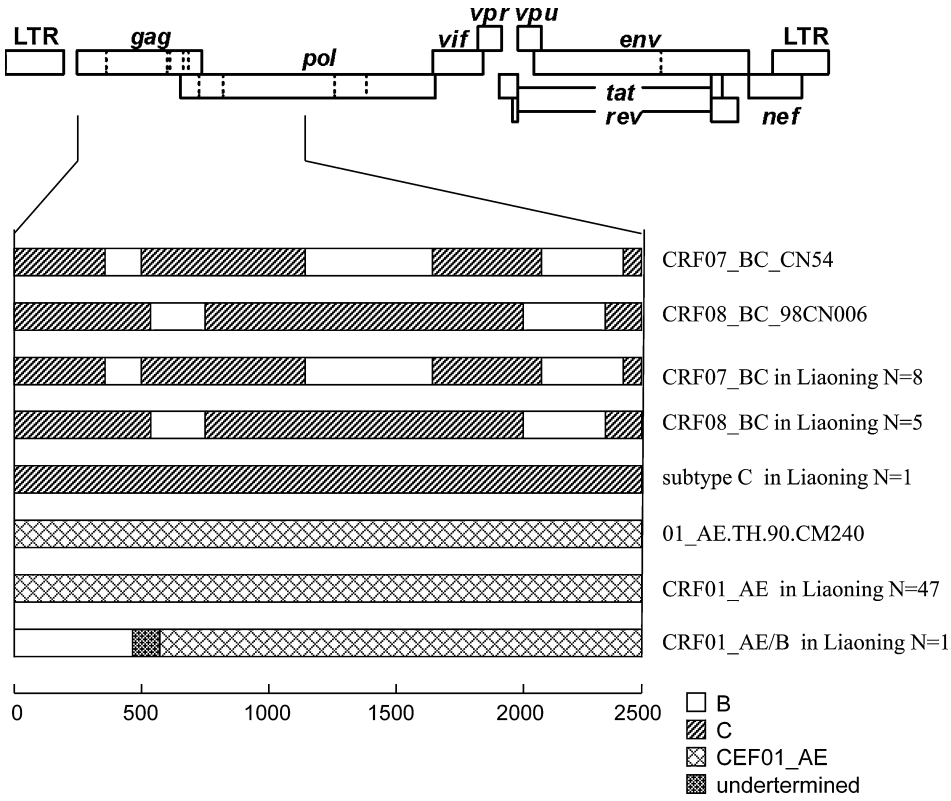

FIGURE 5. Bootscanning Analysis of HIV-1 gag-reverse transcriptase Sequences of 62 study participants. Participants included 8 CRF07_BC virus, 5 CRF08_BC virus, 1 pure subtype C viruses 47 CRF01_AE, and 1 new CRF01_AE and B recombinant virus 02CNRL42. The boostrap values are based on 500 replicates using the neighbor-joining method, with window: 200 basepairs, step 20 basepairs, Gapstrip:on, Kimura(2 parameter), T/t:2.0.

CRFs are circulating within the same population in geographic proximity, it is expected that further recombination events are likely to occur and generate novel recombinants. Indeed, in this instance, we have identified a new recombinant between CRF01_AE and B', although this must be further verified.

In summary, we have for the first time conducted province-wide epidemiologic and genetic studies on HIV-1 in low prevalence Liaoning province. Our data strongly indicate the close relationship between HIV-1 sequences in Liaoning and those in high prevalence regions. HIV-1 has therefore been able to overcome our preventive measures and continues to spread from the high prevalence southwest to the low prevalence northeast region of China. As the epidemic continues to spread, it is expected that viral genetic diversity will increase, which will inevitably pose more challenges to vaccine, drug, and microbicide development. It is high time to implement more effective and integrated measures to reduce the further dissemination of these viruses—in low prevalence areas like Liaoning and throughout the world's most populous nation.

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The HIV Epidemic in Yunnan Province, China, 1989–2007

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Objective: To investigate the characteristics and trends in the HIV epidemic in Yunnan province, China, between 1989 and 2007.

Methods: Statistical analysis of serological data from voluntary testing and counseling sites, medical case reports, mass screenings, sentinel surveillance, and other sources.

Results: By 2007, a cumulative total of 57,325 cases of HIV infection were reported in Yunnan, and unsafe drug injection practices and unsafe sexual behaviors were identified as the dominant modes of transmission. HIV affects injecting drug users most, particularly in Jingpo, Dai, and Yi ethnicities, more than 40% in 7 counties. HIV prevalence rates among female sex workers (FSWs) increased from 0.5% in 1995 to 4.0% in 2007; among men who have sex with men, from 4.0% in 2005 to 13.2% in 2007; among male clients of FSWs, from 0% in 1995–1997 to 1.8% in 2007; among male sexually transmitted disease clinic attendees, from 0% in 1992 to 2.1% in 2007; among pregnant women from 0.16% in 1992 to 0.5% in 2007; and among blood donors, from 0.0075% in 1992 to 0.084% in 2007.

Conclusions: The HIV epidemic in Yunnan has progressed to a concentrated epidemic. Future efforts must focus on not only groups at risk for primary infection (injecting drug users, men who have sex with men, and FSWs) but also on their low-risk sexual partners.

Key Words: case report, China, epidemiology, HIV/AIDS, sentinel surveillance

(*J Acquir Immune Defic Syndr* 2010;53:S34–S40)

INTRODUCTION

The HIV epidemic in Yunnan first appeared in 1989 with the discovery of 146 infected injecting drug users (IDUs) in Ruili, a town bordering Myanmar and situated along the drug trafficking routes channeling heroin into China from Southeast Asia's opium-producing "Golden Triangle" region.[1] Although this region has a long history of opium use, the advent of using injection needles as a common form of drug administration in the late 1980s created an efficient transmission mode that spread HIV among IDUs. Surveillance data shows HIV had appeared in geographically disparate groups of IDUs beginning around 1995 and has since spread with increasing momentum. Within several years, 8 counties were reporting HIV prevalence rates of more than 40%. By 1999, all 16 prefectures of Yunnan had reported HIV infections, and despite making up only 3% of the national population, Yunnan's reported cases of HIV accounted for 34.8% of total HIV cases in China.[2] Moreover, prevalence rates among some high-risk groups have already reached crisis proportions in certain areas; rates as high as 74.5% were reported among IDUs[2] and was approximately 10% among female sex workers (FSWs).[3–4]

In 1992, the provincial government began using a sentinel surveillance system to track the epidemic. As a result, Yunnan's HIV epidemic is one of the most consistently and thoroughly tracked in China, providing valuable insight into long-term trends and characteristics.[4–6] Additionally, many of China's earliest pilot studies testing intervention methods occurred in Yunnan.[7–9]

Yunnan has been described as a "key HIV epicenter in China,"[10] and an in-depth analysis of its long-term epidemiological trends provides a lens of examining how HIV is spread in Chinese settings. Yunnan can also act as a regional case study to which other regions can compare their own epidemiological trends and use Yunnan's experience to inform their choice of intervention methods.

METHODS

Two types of data were used in this article: sentinel surveillance data and reported cases of HIV infection via multiple strategies of HIV testing.

Sentinel Surveillance

In 1992, a standardized HIV sentinel surveillance system was established to consolidate information at the provincial level.[10] By 2007, 89 sentinel sites were set up conducting regular surveillance among IDUs (18 sites; sample size: 100–200 per site), FSWs (33 community-based sites and 1 women

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Supported by the Tenth 5 Years of Key Technologies Research and Development Program (2004BA719A14-1) and the China Multidisciplinary AIDS Prevention Training Program with NIH Research Grant # U2R TW 006917 and U2R TW 006918, funded by the National Institutes of Health, the Fogarty International Center, the National Institute of Drug Abuse, and the National Institute of Mental Health (China ICOHRTA, with Principal Investigator Z. Wu).

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re-education center site; sample size: 400 per site), male clients of FSWs (1 male re-education center site; sample size: 300–400 per site), sexually transmitted disease (STD) clinic attendees (12 sites; sample size: 300–400 per site), men who have sex with men (MSM) (one site; sample size: 300), male migrant workers (4 sites; sample size: 400 per site), pregnant women (18 sites; sample size: 800 per site), and tuberculosis (TB) patients (1 site; sample size: 800). Subjects of every category provided a 2–3 mL of blood sample for HIV antibody testing and participated in an anonymous interview to collect information on demographic details and HIV transmission–related risk behaviors.

Other Forms of HIV Case Detection

Testing in Medical Settings

All positive HIV cases found in any medical setting were reported directly to the provincial Centers for Disease Control and Prevention (CDC). Tests were conducted under any of the following conditions: presurgical screening, antenatal screening for pregnant women, physician-recommended testing for individuals exhibiting AIDS-related symptoms, the screening of blood donors, or as part of standard medical exams.

Testing in Other Settings

Voluntary testing and counseling (VCT) in China is offered by the national, provincial, prefectural, and county-level CDCs. CDC-certified hospitals and specialized medical centers also provided VCT services. VCT is also recommended for couples applying for marriage certificates.

In 2004, the national Ministries of Health, Justice, and Public Security passed a joint resolution requiring HIV testing of all individuals admitted to a detention center for the first time. By definition, "detention centers" include prisons, drug detoxification centers, re-education through labor camps, and detention centers for commercial sex offenders (commercial sex workers and clients) and for other types of offenses.

Key Changes in Testing Strategies

The introduction of new testing strategies in the mid-2000s resulted in dramatic changes to reported HIV cases as the number of people tested increased significantly, explaining the sharp increase in the number of reported HIV/AIDS cases beginning during that period (Fig. 1). The initiation of testing for detainees increased the number of tested individuals but inevitably also sampled groups particularly vulnerable to HIV infection, resulting in an upward bias in the reported number of HIV/AIDS cases. In addition, timeliness of case reporting improved in 2005, dictating all detected cases from various health facilities be directly reported to the National CDC within 24 hours, in contrast to previously aggregating HIV cases on a quarterly basis.[11] Finally, since 2005, all Yunnan couples who registered for marriage were recommended premarital screening.

HIV Testing Laboratory Procedures

In 1992, the China State Food and Drug Administration approved the use of enzyme-linked immunosorbent assay–testing method, confirmed by Western Blot analysis.[12] Rapid testing has also since become available for testing populations who benefit the most from fast notifications of test results, such as pregnant women for the prevention of mother-to-child-transmission, and for mobile populations who are less likely to return for their test results (eg, FSWs, STD clinic patients, migrant workers, and MSM).

In 1995, Yunnan began using alternative HIV testing methods (without using Western Blot for confirmation) recommended by the Joint United Nations Program on HIV/AIDS and the World Health Organization for developing countries.[13–15] Alternative testing strategies are most commonly used for testing IDUs in Yunnan.

Statistical Analysis

All statistical analysis for this report was conducted using the SPSS 12.0 statistical analysis software package (SPSS Inc. Chicago, IL, USA). Comparisons of characteristics between groups were conducted using χ^2 tests and results with P values of 0.05 or less were considered statistically significant. Cumulative results from the first year of available sentinel surveillance data were used for systematic

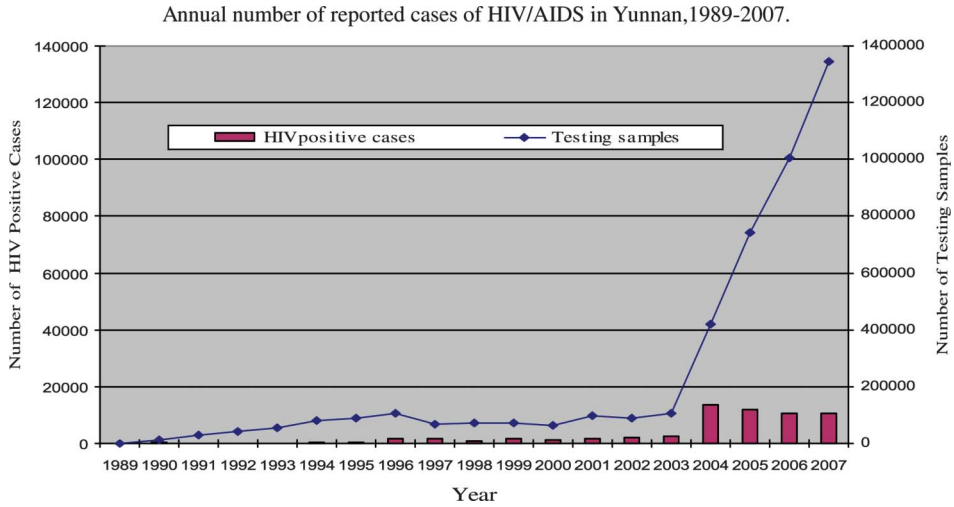

FIGURE 1. Annual number of reported cases of HIV/AIDS in Yunnan, 1989–2007.

comparisons. Surveillance sites with the longest operating and continuous data available were included.

RESULTS

By the end of 2007, Yunnan had recorded 57,325 cases of HIV infection (including 2077 foreign nationals) among which 7630 had progressed to AIDS. A cumulative total of 4525 deaths among HIV/AIDS-infected individuals was recorded, of whom, 1949 died of AIDS-related causes. Most reported HIV infections (29,458 cases, 51%) were identified in medical setting, followed by VCT (10,087 cases, 18%) (Table 1).

Trends Reflected in Reported Cases of HIV

Data collected from nonsurveillance settings between 1989 and 2007 revealed the following trends:

- The severity of the epidemic varies widely across regions, with reported cases in the prefectures of Dehong, Honghe, Dali, Lincang, Wenshan, and the municipality of Kunming, making up 78.2% of all reported cases in the province by the year 2007 (Fig. 2).
- The proportion of women among people living with HIV/AIDS (PLWHA) is increasing. The ratio of men to women has fallen from 40:1 in 1989 to 1.7:1 in 2007 (Fig. 3).
- The age distribution of PLWHA individuals has gradually increased over time. The proportion of 20-year to 29-year olds has fallen from 52.4% in 1989 to 36.6% in 2007; whereas the proportion of 30-year to 39-year olds has increased from 28.8% in 1989 to 43.2% in 2007.
- HIV transmitted through needle-sharing behaviors has drastically decreased from 100% in 1989 to 42.5% in 2007. Sexual contact and mother-to-child-transmission transmission now account for 47.4% and 1.3% of total infections, respectively.
- In 1989, the share of PLWHA among rural residents was 93.8%, among unemployed persons was 4.1%, and among persons with other forms of employment was 2.1%. By 2007, this had changed to 46.4%, 24.3%, and 29.3%, respectively.
- The ethnic background among PLWHA has also changed since 1989, from 75.3% Dai, 16.4% Jingpo, 5.7% Han, and 2.3% of other ethnicities, to 10.5%, 5.7%, 63.2%, and 20.6%, respectively in 2005.

TABLE 1. Testing Mode and Numbers Tested in Cumulative Numbers of Reported Cases of HIV

Testing Mode	Numbers Tested	HIV+
IDU	58,861	6763
Detention centers	235,838	2237
Contact tracing	3541	1488
ANC testing	850,292	2829
Premarital screening	410,413	2068
FSW screening	228,484	609
STD clinics	8065	1108
VCT	331,660	10,087
Blood donor screening	1,010,661	377
Immigration officers	129,535	302
Routine/medical	963,749	29,458
Total	4,231,099	57,325

ANC, antenatal clinic.

Trends in Sentinel Surveillance Data

Between 1992 and 2007, a total of 268,978 subjects were tested for HIV in sentinel surveillance program. The number of subjects tested in each subgroups breakdowns as follows: 31,138 IDUs; 34,049 FSWs; 4944 male migrants; 4501 male clients of FSWs; 68,038 STD clinic patients; 123,036 pregnant women; 2963 TB patients; and 309 MSM. The prevalence of HIV infection change over time among IDUs, FSWs, male clients of STD clinics, and pregnant women, as given in Figure 4.

Trends Among IDUs

In 1989, IDU infections accounted for 70% of total HIV cases. The provincial average prevalence rate among IDUs increased from 1992 to 2004 (2.7% in 1992, 15.0% in 1995, 30.0 % in 1999, 32.4% in 2004) and decreased to 28.4% in 2007. In 7 counties (Yingjiang, Longchuan, Luxi, Kaiyuan, Dali, Lincang, and Yanshan), HIV prevalence rates among IDUs has surpassed 40%.

Characteristics of HIV infection among IDUs could be summarized as follows. First, HIV prevalence rates among male IDUs' have remained significantly higher than those of female IDUs (22% vs. 15%; $\chi^2 = 52.83$, $P < 0.01$). Second, there is a recent downward trend in HIV prevalence among IDUs who were 24 years or younger. Third, HIV prevalence among IDUs with only primary schooling or less were significantly higher than those who had completed secondary schooling or more (22.7% vs. 15.9%; $\chi^2 = 59.7$, $P < 0.01$). Finally, HIV prevalence among IDUs was higher for ethnic minorities than for the Han ethnic group, even after controlling for different levels of education across ethnicities.

Trends Among FSWs

FSW surveillance data from the Kunming detention center and the community-based testing sites were analyzed separately. Until 1994, FSWs in the Kunming detention center had a 0% HIV prevalence rate, but this rate steadily increased over the years: 0.5% in 1995, 1.5% in 1997, 2.9% in 2006, and 4.0% in 2007. For FSWs tested in community sites, average provincial prevalence rates in 2005, 2006, and 2007 were 1.5% (range: 0%–4.5%), 1.5% (range: 0%–3.7%) and 1.9% (range: 0%–5.3%), respectively. In 2007, 14 additional surveillance sites were established across 10 prefectures to improve monitoring HIV epidemic among this group. Regional diversity characterized infections in this group; sites in Honghe, Dehong, and Lingchang prefectures have all recorded HIV prevalence rates >5%, whereas Zhaotong (Zhaoyang District) has not found any cases of HIV infection for the 3 consecutive years, 2005–2007.

Drug use (DU) had a profound impact on HIV among FSWs; DU FSWs had HIV prevalence rates as high as 35.5% compared with non-DU FSWs (1.9%, $\chi^2 = 897.4$, $P < 0.01$).

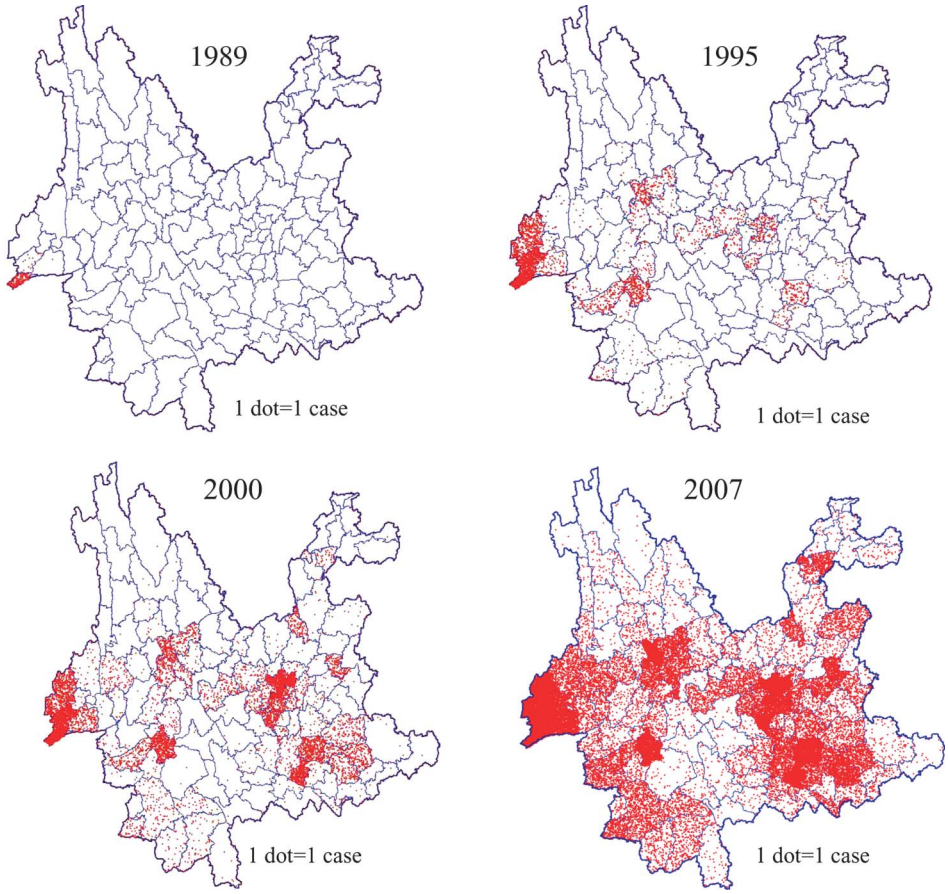

FIGURE 2. Geographical distribution of cumulative reported cases in Yunnan since 1989.

Further analysis among non-DU FSWs found that those with primary schooling or less had significantly higher HIV prevalence than those with secondary schooling or more (2.7% vs. 1.6%; $\chi^2 = 14.0$, $P < 0.01$) or as compared with DU FSWs with high school education or more (1.5%; $\chi^2 = 7.1$, $P < 0.01$). Similarly, average HIV prevalence rates among non-Han FSWs are higher than Han FSWs (2.3% vs. 1.7%; $\chi^2 = 5.3$, $P < 0.05$); ethnic minority groups rank in the following descending order of prevalence rates: De'ang 20.6% ($\chi^2 = 135.7$, $P < 0.01$), Jingpo 5.9% ($\chi^2 = 8.86$, $P < 0.01$), Wa 4.2% ($\chi^2 = 4.4$, $P < 0.05$), Miao, 3.8% ($\chi^2 = 2.9$, $P < 0.05$), Zhuang: 3.1% ($\chi^2 = 1.2$, $P > 0.10$), and Hani 2.8% ($\chi^2 = 2.29$, $P > 0.10$). HIV prevalence rates among local FSWs (registered residents of Yunnan) were significantly higher than those from other provinces (2.2% vs. 0.9%; $\chi^2 = 23.1$, $P < 0.01$). Street-based FSWs were also found to have higher HIV prevalence rates than establishment-based FSWs (3.7% vs. 1.7%; $\chi^2 = 23.6$, $P < 0.01$).

Trends Among MSM

HIV was first detected in MSM in 1999; recent surveillance in Kunming recorded prevalence rates of 4.0% in 2005 and 13.2% in 2007.

Trends Among Male Clients of FSWs

Surveillance sites targeting male clients of FSWs in Kunming have recorded the following prevalence rates: 0%, between 1995 and 1997; 0.3% in 1998; 0.3%–1.8% between 1999 and 2004; and 0.8 %–1.8% between 2005 and 2007.

Trends Among Male STD Clinic Attendees

The average HIV prevalence rate among male STD clinic attendees were: 0% in 1992; 0%–0.6% between 1993 and1995; 1.2%–2.3% between 1996 and 2000; 1.7%–3.1% between 2001 and 2004; and 2.0%–2.1% between 2005 and 2007. Non-Han ethnicities have higher prevalence rates than Han (3.1% vs. 1.9%; $P < 0.01$), among whom Jingpo and Dai had the highest rates at 6.3% ($\chi^2 = 10.2$, $P < 0.01$) and 5.1% ($\chi^2 = 50.6$, $P < 0.01$), respectively.

Trends Among the Male Migrant Population

Beginning in 2005, 4 HIV sentinel surveillance sites among male migrant workers were established, and they monitored workers on a road project, at a hydropower plant, at a coal mine, and at a building construction site. In 2005, 2006, and 2007, the average HIV prevalence rates among these 4 groups were 0.55% (range: 0%–1.8%), 0%, and 0.13% (range: 0%–0.25%), respectively. Of these migrants, non-Han had a higher HIV prevalence than Han (0.45% vs. 0.12%, $\chi^2 = 4.8$, $P < 0.05$).

Trends Among Pregnant Women

The provincial average HIV prevalence rate among pregnant women was: 0.16% in 1992; 0.14%–0.25% between

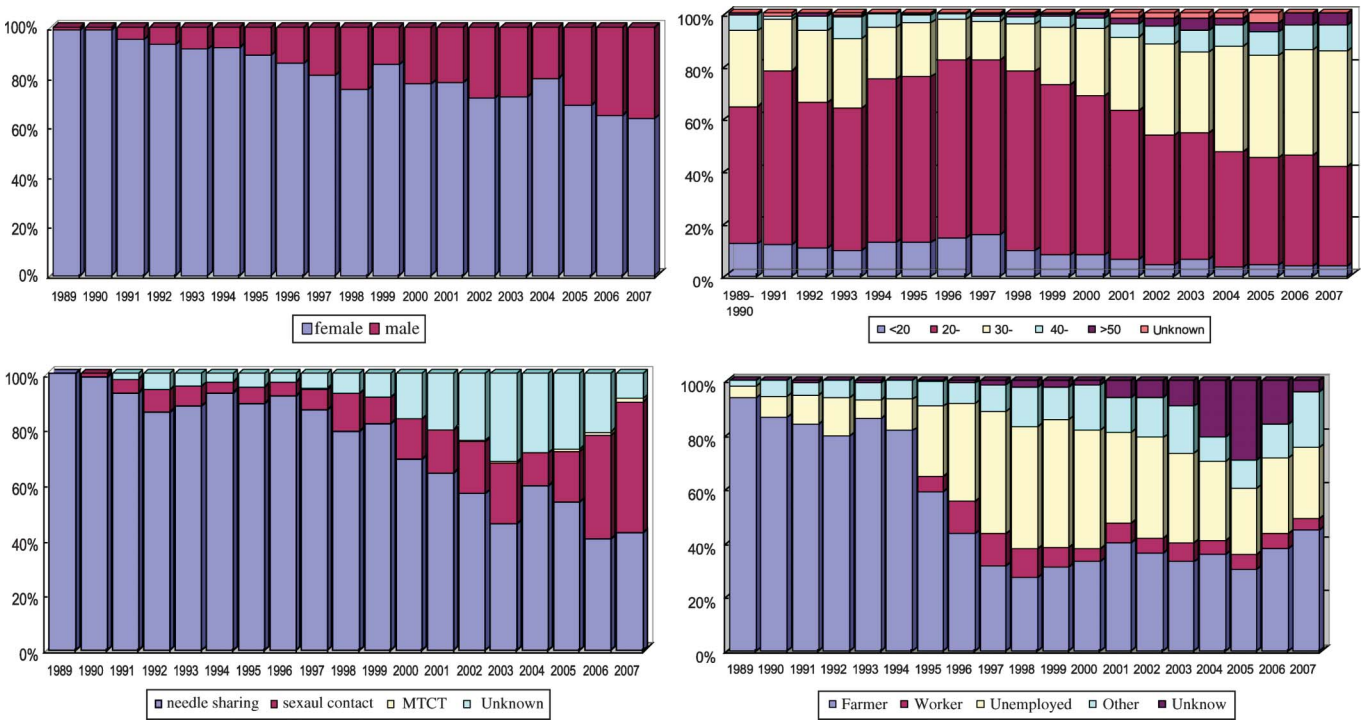

FIGURE 3. Reported HIV cases by sex, age groups, transmission route, and employment in Yunnan, 1989–2007.

1993 and 2002; 0.37% in 2003; 0.38% in 2004; 0.39% in 2005; 0.43% in 2006; and 0.50% in 2007. In the counties of Ruili, Yingjiang, Longchuan, Kaiyuan, Gejiu, Linxiang, Dali, and Wenshan, HIV prevalence in antenatal clinics has surpassed 1%. Non-Han pregnant women have a higher HIV prevalence than Han (0.33% vs. 0.24%, $\chi^2 = 157.8$, $P < 0.01$).

Trends in Other Populations

HIV surveillance testing for TB patients began in 2002, with the following prevalence rates: 1.6% in 2002; 1.5% in 2003; 0.8% in 2004; 1.2% in 2005; 1.6% in 2006; and 0.7% in 2007.

Screening of potential blood donors began in Kunming in 1992 and recorded HIV prevalence rates since are: 0%–0.0075% between 1992 and 2000; 0.015% in 2001; 0.029% in 2002; 0.056% in 2003; 0.072% in 2004; 0.127% in 2005; 0.098% in 2006; and 0.084% in 2007.

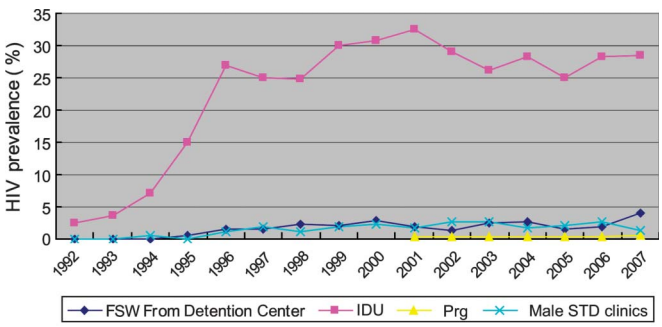

FIGURE 4. HIV prevalence rates among IDU, FSWs, male clients of STD clinics, and pregnant women from sentinel surveillance in Yunnan Province, 1992–2007.

DISCUSSION

More cases of HIV infection have been reported from Yunnan than any other province in China, showing both the severity of the epidemic and the strength of the long established HIV surveillance system. The defining characteristics of the Yunnan HIV epidemic are the key role played by injecting drug use (IDU) and the overall makeup of the infected population: young, male, rural, and unemployed. Wide regional variations in the severity of the epidemic correlate strongly with local IDU habits; 78.2% of cumulative reported cases have come from the prefectures of Dehong, Honghe, Lincang, Dali, Wenshan, and the city of Kunming, where heroin use is high. Several conclusions can be drawn from the trends detected in surveillance data and in the changing profile of the HIV-infected populations, as listed below.

Interpreting the Trends: Older IDUs

HIV prevalence is increasing among older IDUs and falling among younger IDUs. This may be due to lower IDU initiation by younger people or at least safer injection behaviors practiced by younger IDUs. Alternatively, testing rates among older IDUs at greater risk of infection may have increased with the introduction of a nationally subsidized antiretroviral therapy treatment program in 2004, thus inflating the number of infected IDUs from previously undetected infections. Furthermore, the mass roll out of treatment services has kept older, infected IDUs alive longer, resulting in an increase in the average age of infected IDUs.

Interpreting the Trends: Growth of a Sexual Epidemic

HIV surveillance data suggest sexual transmission through high-risk behaviors, particularly commercial sex, began in the mid-1990s. This trend had the most pronounced impact on FSWs and their male clients, MSM, and sexual partners of IDUs. All sexual epidemics originated in areas with prevalent IDU, suggesting an important link between the IDUs and sexual epidemics. A growing body of research supports a conceptual framework of a threshold prevalence rate among IDUs having a "seeding effect" in the development of larger sexual epidemics.[16,17] In Yunnan, there is strong evidence that male IDUs who visit FSWs and FSWs who inject drugs have played a crucial role in the transition of the epidemic from being primarily IDU-driven to sexually driven.[18]

Two vulnerable groups of particular concern in the sexual epidemic are street-level FSWs and MSM. These groups are not only at risk for both primary and secondary infections to their partners but are also difficult to access because of their underground behaviors and mobile lifestyles. Future prevention efforts must identify new ways of interacting with these groups to better analyze their behaviors and develop measures for effective behavioral interventions.

Interpreting the Trends: Spread to General Population

Increasing prevalence among blood donors and pregnant women indicate that HIV has begun to spread among the general low-risk population. HIV prevalence rates among these groups in Yunnan are above the national average and are increasing annually. In 8 counties, prevalence rates reported by antenatal clinics have already reached or passed 1%.

Interpreting the Trends: Impact on Ethnic Minorities

The HIV epidemic in Yunnan has disproportionately impacted ethnic minorities. Surveillance data show that among IDUs, the Jingpo, Dai, and Yi minorities have the highest prevalence rates; that among FSWs, the De'ang, Jingpo, Zhuang, Hani, Miao, Yi, and Zhuang ethnicities have high prevalence, and that among male STD patients, the Jingpo and Dai groups have the highest prevalence rates. HIV prevalence rates of ethnic minorities among pregnant women and male migrants are also high. The significant impact on these populations is thought to be associated with these communities' long exposure to heroin through their proximity to the Golden Triangle region. This exposure, coupled with limited access to health care and lower public health awareness, has fueled the spread of HIV within these subpopulations.

LIMITATIONS AND CHALLENGES

This study faces several data limitations. First, analysis of trends in reported cases of HIV is useful for understanding the changing profile of HIV-infected individuals but is limited in its ability to capture changes in the actual infected population. The representativeness of the tested population is affected by policy changes that either encouraged voluntary testing, such as in 2004, when free VCT services and nationally subsidized ARV treatment became available, or required compulsory testing of previously undocumented populations (who are often more vulnerable), as in 2005 when China began testing persons admitted to incarceration centers. Sampling bias can be reduced by introducing policy changes across the administrative area, but it is impossible to remove the time impact which must at least be acknowledged in any analysis of case reporting data.

Sentinel surveillance data must also acknowledge biases introduced though sampling methods and assumptions made about the generalizability of certain groups. For instance, the earliest sentinel surveillance stations often oversampled groups from high prevalence areas, which in turn would overestimate actual prevalence rates. Furthermore, the behaviors of populations thought to represent the general low-risk populations, such as blood donors, STD clinic patients, and pregnant women, may have systematic differences from the general population. For example, STD patients and pregnant women may have come from a sector of the population with above average rates of unprotected sex, or people with a history of blood donation may have had lower socioeconomic backgrounds, less public health awareness and/or health-seeking practices than the general population.

CONCLUSIONS

Future efforts in the prevention of HIV in Yunnan must focus on several key areas. First, the epidemic is still spreading among IDUs and prevention efforts must continue to target this group to prevent primary and secondary infections among them and their sexual and needle-sharing partners. Second, the association between HIV infection, poverty, and low levels of education indicates the need for strengthening public health awareness among underserved communities and also highlights the relationship between economic/social development and long-term public health goals. Third, there is a critical need for a better understanding of the characteristics and behaviors of street-level FSWs and MSM who are particularly vulnerable to getting infected and are also difficult to be reached. Last but not least, proven intervention programs that reduce risk behaviors and the transmission of HIV must be scaled up to improve coverage rates. Such interventions may include harm reduction or condom use programs and those that address multiple risk behaviors or that utilize a comprehensive approach to controlling HIV through programs that link prevention and treatment efforts.

ACKNOWLEDGMENTS

The authors thank Naomi Juniper and Adrian Liau for their editing assistance.

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HIV Among Plasma Donors and Other High-Risk Groups in Henan, China

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Objective: To describe the characteristics and changes of HIV/AIDS epidemic in different areas and high-risk populations in Henan, China.

Methods: Serological surveys were conducted among former plasma donors (FPDs), female sex workers, drug users, sexually transmitted disease clinic attendees, men who have sex with men, and long-distance truck drivers in different areas of Henan Province. Data originated from the sentinel surveillance surveys conducted between 2004 and 2006, a special epidemiological study of HIV among FPDs in 2004 and the HIV/AIDS case-reporting system were analyzed.

Results: By December 2006, a total of 35,232 HIV cases had been reported from 159 counties in Henan. HIV prevalence among FPDs was 8.6% (range: 0.09%–13.0%). Sentinel surveillance data collected between 2004 and 2006 indicated HIV prevalence from 0% to 0.80% in female sex workers; 0% to 0.86% in drug users; 0% to 1.39% in sexually transmitted disease clinic attendeess; 0% to 1.35% in long-distance truck drivers; and 0.88% to 2.67% in men who have sex with men.

Conclusions: HIV/AIDS epidemic in Henan is primarily centered among FPDs infected before 1996. Sexual transmission of HIV is increasing among other risk groups. Condom use and HIV testing and counseling need to be promoted to stop the spread of HIV.

Key Words: case reporting, epidemiology, former plasma donors, HIV/AIDS, sentinel surveillance

(*J Acquir Immune Defic Syndr* 2010;53:S41–S47)

INTRODUCTION

HIV-1 has spread rapidly in China since 1995.[1,2] By the end of 2007, there were an estimated 700,000 people living with HIV nationwide.[3] Henan province, located in central eastern China (Fig. 1), is one of the worst affected provinces in terms of HIV/AIDS. Henan's first HIV/AIDS cases were identified in 10 foreign students from Zimbabwe in 1989. In early 1995, the first local HIV cases were reported after an HIV outbreak among plasma donors. Around the same time, HIV also began to spread via sexual and vertical transmission.[4,5]

HIV infection through plasma donation has been reported in China and other developing countries.[6–8] Between 1990 and 1994, thousands of small commercial plasma collection centres were established in rural areas of China. Plasma donors were paid to donate blood, the plasma removed with the red blood cells reinfused into donors to prevent anemia. Frequency of plasma donation, combined with the reuse of tubing and the mixing of plasma from multiple donors during collection and the subsequent reinfusion of mixed red blood cells, led to thousands of HIV infections among plasma donors in China, particularly in Henan province.

The spread of HIV via plasma donation was interrupted in 1996 with the introduction and enforcement of laws banning the commercial collection of blood and blood products. At the same time, the government of Henan strengthened the management of blood supplies, effectively containing the transmission of HIV via blood collection, donation, and transfusion.[9] Since 1998, 100% of blood used in clinical settings in Henan has come from voluntary donors.[10]

In 1995, 2 national sentinel surveillance sites were established in Henan that focused on sexually transmitted disease clinic attendees (STDCAs) and female sex workers (FSWs). Since then, coverage has expanded to 46 sentinel surveillance sites in 2006. These sites currently monitor drug users (DUs), men who have sex with men (MSM), long-distance truck drivers (LDTDs), pregnant women, and hospital outpatients who have blood samples collected for reasons other than HIV testing.

Since 1995, various surveys[4,5,11–13] have been conducted among former plasma donors (FPDs) to measure the prevalence of HIV infection among FPDs and their children. These initial studies found the HIV prevalence rates ranged from 9.1% to 17.0% among FPDs and 2.1% among FPDs' nondonor spouses, and the rate of vertical transmission ranged from 28.9% to 38.4%. These initial surveys were limited in their ability to reflect the true HIV prevalence among FPDs in Henan because most FPD spouses and/or main sexual partners

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Supported by the Chinese Government AIDS Program and partly supported by the China Multidisciplinary AIDS Prevention Training Program with NIH Research Grant #U2R TW06918 funded by the Fogarty International Center, the National Institute on Drug Abuse, and the National Institute of Mental Health (China ICOHRTA, with Principal Investigator Z.Wu.).

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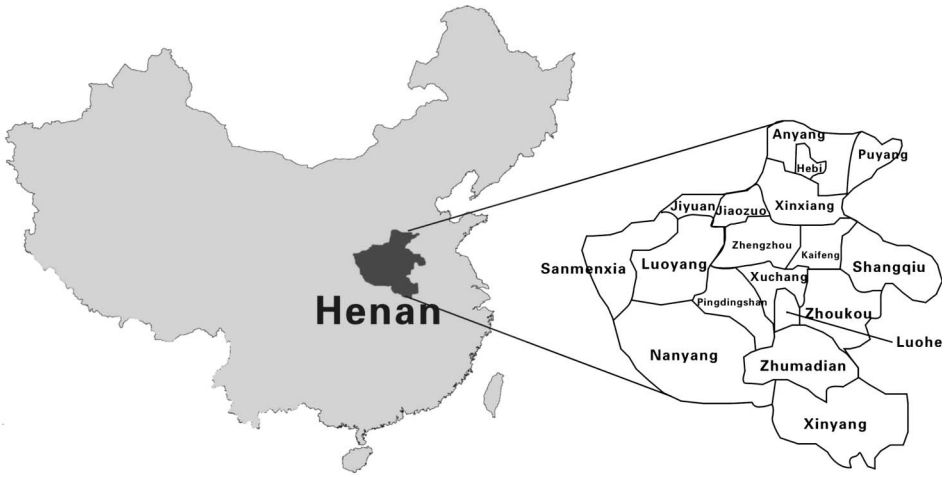

FIGURE 1. Geographic position of Henan in China, and Henan's 18 prefectures.

were not tested and because participants in these surveys were not randomly sampled nor were the survey locations representative of the FPD population.

To gain a more accurate understanding of the HIV burden among FPDs, the Henan provincial government introduced a new HIV-testing policy in 2004 designed to actively seek out certain groups believed to be at high risk of HIV infection.[14] From June to August of 2004, an HIV testing campaign was conducted among FPDs, the spouses of all HIV-positive FPDs and their children. Between 2004 and 2006, a substantial body of data were generated describing HIV infection in different populations in Henan. In this article, we present and discuss the results of HIV survey among FPDs and of HIV sentinel surveillance from 5 high-risk populations: FSWs, STDCAs, DUs, MSM, and LDTDs.

METHODS

Data came from 3 different sources in Henan: HIV sentinel surveillance; a special survey of HIV among FPDs; and the HIV/AIDS case-reporting system. All data were collected between 2004 and 2006.

Sentinel Surveillance

Sentinel surveillance surveys to assess HIV prevalence among high-risk populations, including FSWs, STDCAs, DUs, and LDTDs, were undertaken twice in 2004; since 2005, these surveys have been conducted annually. Data collection followed China's national HIV sentinel surveillance protocol. This protocol specifies when surveys are to be conducted (annually over the 2-month period from April 1 to May 31); sampling methods (cluster sampling method); and sample size (sampling is done until a sample size of 400 is reached; if a sample size of 400 is unobtainable, a sample of 250 is attempted and the sampling period extended by 1 month as necessary to recruit more respondents).

Respondents are interviewed anonymously using a standardized questionnaire to collect basic demographic and behavioral information. Respondents are also screened for HIV antibody by enzyme-linked immunosorbent assay (ELISA). Samples that test positive are retested by ELISA. All sentinel surveillance data are entered into a database created using EpiData 3.1 software (The EpiData Association, Odense, Denmark).

Special Survey of FPDs

A special HIV testing campaign among FPDs was conducted throughout Henan in 2004 to assess the HIV situation among FPDs and to link HIV-positive FPDs and their family members to government services. It is believed that almost all known FPDs were enrolled in the campaign, with the exceptions of those who denied having sold plasma in the 1990s, those who had left the province permanently, and those who had migrated out of the province temporarily.

FPDs participating in the campaign were tested for HIV, and a questionnaire was administered to collect demographic and risk behavior information; information on health status and health services utilization; and information about the HIV status of the respondents' spouse/sex partner and children. All new HIV/AIDS cases identified through the testing campaign were entered into the national HIV/AIDS case-reporting system.

HIV/AIDS Case-Reporting System

All newly identified HIV/AIDS cases in China undergo confirmatory HIV testing via Western Blot, and these cases are then entered into the national HIV/AIDS case-reporting system. Information collected in the national case-reporting system on newly identified cases includes demographic information (name, Chinese ID number, age, gender, marital status, area of residence, and occupation); disease status (HIV or AIDS); risk-behavior information (injecting drug use, experience of heterosexual or homosexual sex, plasma donation, blood transfusion/received blood products, surgical history, mother HIV positive, spouse/sexual partner HIV positive, occupational exposure to HIV); and laboratory test results and test dates.

The national HIV/AIDS case-reporting system requires public health professionals to follow up each reported HIV case every 6 months until the onset of AIDS, after which patients are visited every 3 months. Medical professionals from the county Centers for Disease Control and Prevention conduct patient follow-up either via a phone call or face-to-face interview. Data collected during follow-up include

demographic information and clinical information (disease status, $CD4^+$ T-lymphocyte test results, antiretroviral therapy status, and whether or not any clinical symptoms of AIDS have presented in the interval since the last medical follow-up).

The complete database of all Henan provincial HIV/AIDS patients up to December 31, 2006, in the national HIV/AIDS case-reporting system was downloaded from the Comprehensive Response Management Information System of the China Information System for Disease Control and Prevention website on January 1, 2007.

HIV Testing

Serum samples were screened by HIV rapid testing (Dainabot Company Limited, Tokyo, Japan) or ELISA (bioMérieux, Craponne, France). If a sample screened HIV positive, confirmatory testing was done using a Western blot assay (Genelabs Diagnostics Pte Ltd, Cavendish, Singapore).

Data Analysis

Data were analyzed using Visual FoxPro 7.0 (Visual FoxPro 7.0 for windows; Microsoft, Redmond, WA) and SPSS 13.0 (SPSS 13.0 for windows; SPSS Inc, Chicago, IL). HIV infection was the outcome variable. For categorical exposure variables, data were analyzed as frequency and percent. The Pearson χ^2 test and Fisher exact test were used to evaluate differences of proportions and prevalence among different years.

RESULTS

Sentinel Surveillance

HIV prevalence by risk groups and sites is presented in Table 1. HIV prevalence among FSWs, STDCAs, DUs, and LDTDs was low and remained low throughout the surveillance period. There is only 1 sentinel surveillance site in Henan monitoring HIV among MSM, and it was established in 2005 in the provincial capital, Zhengzhou City. HIV prevalence among MSM surveyed rose from 0.88% in 2005 to 2.67% in 2006; however, this change was not statistically significant ($P = 0.415$).

Special Survey of FPDs

During the HIV testing campaign among FPDs, 280,307 FPDs were identified and invited to participate in the survey; 269,246 subjects (96.1%) participated and were tested for HIV; and 23,157 were confirmed HIV positive (8.6%). Among those who tested HIV positive, 12,159 serodiscordant couples were identified. Of all HIV infections among FPDs, 35.9% came from Zhumadian prefecture, where HIV prevalence among FPDs was 10.9%. HIV prevalence among FPDs across Henan 18 prefectures ranged from 0.09% to 13.0%. In 5 prefectures, the prevalence was more than 10%; in 2 prefectures, it was between 5% and 10%, whereas in 6 prefectures, it was between 1% and 5%. The remaining 5 prefectures' HIV prevalence rate among FPDs was less than 1%.

National HIV/AIDS Case-Reporting System

The national HIV/AIDS case report system covers all HIV/AIDS cases, which have tested HIV positive with confirmatory tests. From the start of the HIV epidemic through the end of 2006, 35,232 cases covering all 18 prefectures of Henan were reported via the case-reporting system. In Henan, 8 prefectures reported more than 1000 cases: Zhumadian, Zhoukou, Nanyang, Shangqiu, Kaifeng, Xinyang, Luohe, and Zhengzhou. Of the total cases, 92.4% were residents of these 8 prefectures. The lowest HIV burden was found in the prefectures of Sanmenxia, Hebi, Jiyuan, and Puyang; each of these prefectures reported no more than 100 cases and together accounted for just 0.7% of all cases. Among the 35,232 cases reported, 7107 (20.2%) had died and 21,828 (61.7%) were AIDS patients. Among those with AIDS, 15,386 (70.5%) were receiving antiretroviral therapy.

The demographic characteristics of HIV-positive individuals in the case-reporting system are presented in Table 2. The majority of those infected were married (77.5%), between the ages of 30 and 49 years (~70%), working as farmers (90.8%), and had a primary school education or were illiterate (58.4%).

Modes of transmission are presented in Table 3. Most reported cases were infected through paid plasma donation in the 1990s, but this route of transmission fell from 85.6% in 2004 to 38.4% in 2006. Sexual transmission increased from 4.8% in 2004 to 22.4% in 2006 ($\chi^2 = 6124.3$, $P < 0.001$). Mother to child transmission (MTCT) also increased somewhat, rising from 2.9% in 2004 to 4.3% in 2005 but falling to 3.9% in 2006.

By the end of 2006, there were 1030 HIV-positive children in Henan who were infected via MTCT, accounting for 2.9% of the total HIV/AIDS cases in Henan. Of the total MTCT cases, 199 (19.3%) were under 5 years of age. The reported number of MTCT cases identified between 2004 and 2006 decreased from 601 in 2004 to 197 in 2005 and further decreased to 152 in 2006.

DISCUSSION

Understanding of the HIV epidemic in Henan, especially among FPDs, has improved in recent years as sentinel surveillance efforts have been stepped up and special surveys have been conducted.[11,15,16] The HIV epidemic among FPDs is believed to have started in the mid-1990s.[4,6,11,13,17,18] Henan was the worst affected province in China, and PLWHA in Henan are mainly FPDs who sold plasma and/or blood before 1996. Results from the HIV testing campaign in 2004 indicated that the average prevalence of HIV infection among FPDs in Henan was 8.6%; however, the prevalence in different prefectures ranged widely from 0.09% to 13.0%. Yan et al[12] and Zheng et al[11] also reported high HIV prevalence rates of 9.1% and 17.0% among FPDs in 2 different unspecified counties in 1999 and 2000, respectively, though these studies drew on smaller sample sizes and did not specify the study location.

In Henan, it is most likely that recently reported cases of HIV/AIDS among FPDs and people who received contaminated blood transfusions/blood products do not represent new infections, but rather the detection of those who were infected in the 1990s. This is suggested by the sizeable proportion of HIV cases who have already progressed to AIDS and the proportion of reported cumulative HIV cases who have died.

TABLE 1. HIV Sentinel Surveillance by Risk Groups and Sites in Henan, 2004–2006

	2004 Round 1			2004 Round 2			2005			2006		
Risk Groups and Sites	**n**	**HIV+**	**%**	**n**	**HIV+**	**%**	**n**	**HIV+**	**%**	**n**	**HIV+**	**%**
FSW												
Erqi district	251	2	0.80	—*	—	—	250	0	0	450	0	0
Kaifeng	252	0	0	222	0	0	257	0	0	405	0	0
Xinxiang	231	1	0.43	255	0	0	236	0	0	487	0	0
Xinyang	250	0	0	251	0	0	260	0	0	260	0	0
Anyang	—†	—	—	—†	—	—	270	0	0	527	0	0
Hebi	—†	—	—	—†	—	—	250	0	0	285	0	0
Wolong district	—†	—	—	—†	—	—	360	0	0	307	0	0
Shangqiu	—†	—	—	—†	—	—	274	0	0	276	0	0
Yuanyang county	—†	—	—	—†	—	—	250	0	0	240	0	0
Queshan county	—†	—	—	—†	—	—	128	1	0.78	276	0	0
Jiaozuo	—†	—	—	—†	—	—	—†	—	—	404	0	0
Luohe	—†	—	—	—†	—	—	—†	—	—	221	0	0
Puyang	—†	—	—	—†	—	—	—†	—	—	442	0	0
Sanmenxia	—†	—	—	—†	—	—	—†	—	—	313	1	0.32
Zhumadian	—†	—	—	—†	—	—	—†	—	—	237	1	0.42
Total	984	3	0.30	728	0	0	2535	1	0.04	5130	2	0.04
STD clinic attendees												
Jinshui district	250	3	1.20	202	1	0.50	327	0	0	400	2	0.50
Guancheng district	250	0	0	252	0	0	250	0	0	—*	—	—
Pingdingshan	188	0	0	183	0	0	252	0	0	—*	—	—
Puyang	255	0	0	253	0	0	277	0	0	207	0	0
Kaifeng	—†	—	—	—†	—	—	257	0	0	252	0	0
Luoyang	—†	—	—	—†	—	—	333	0	0	140	0	0
Xihua county	—†	—	—	—†	—	—	257	0	0	237	0	0
Xuchang	—†	—	—	—†	—	—	—†	—	—	191	0	0
Anyang	—†	—	—	—†	—	—	—†	—	—	258	2	0.78
Xinxiang	—†	—	—	—†	—	—	—†	—	—	—*	—	—
Jiaozuo	—†	—	—	—†	—	—	—†	—	—	216	0	0
Luohe	—†	—	—	—†	—	—	—†	—	—	273	0	0
Zhoukou	—†	—	—	—†	—	—	—†	—	—	106	0	0
Nanyang	—†	—	—	—†	—	—	—†	—	—	124	1	0.81
Jiyuan	—†	—	—	—†	—	—	—†	—	—	287	4	1.39
Total	943	3	0.32	890	1	0.11	1953	0	0	2691	9	0.33
DUs												
Xuchang	282	0	0	256	1	0.39	342	0	0	336	1	0.30
Lingbao county	—*	—	—	—*	—	—	—*	—	—	191	0	0
Zhengzhou	251	0	0	232	0	0	250	2	0.80	250	1	0.40
Pingdingshan	205	0	0	156	0	0	254	0	0	—*	—	—
Jiaozuo	268	1	0.37	290	0	0	263	0	0	288	1	0.35
Luoyang	260	1	0.38	232	2	0.86	133	0	0	—*	—	—
Zhumadian	—†	—	—	—†	—	—	—†	—	—	119	0	0
Total	1266	2	0.16	1166	3	0.26	1242	2	0.16	1184	3	0.25
LDTD‡												
Zhoukou	450	1	0.22	—	—	—	391	1	0.26	414	0	0
Zhenping county	265	0	0	—	—	—	263	0	0	252	0	0
Yuanyang county	222	3	1.35	—	—	—	245	1	0.41	250	0	0
Jiyuan	252	0	0	—	—	—	350	0	0	400	0	0
Total	1189	4	0.34	—	—	—	1249	2	0.16	1316	0	0
MSM												
Zhengzhou	—†	—	—	†	—	—	113	1	0.88	187	5	2.67

*Data were not displayed and analyzed because the sample sizes were less than 100.
†Data were not displayed because they were not sentinel surveillance sites in those years.
‡According to the guidelines, the LDTD sites conducted only 1 round of surveillance in 2004.

TABLE 2. Demographic Characteristics of Reported HIV/AIDS Cases in Henan, 2004–2006

	2004		2005		2006		Cumulative Total	
	n	%	n	%	n	%	n	%
Total	20,376	—	4593	—	3935	—	35,232	—
Gender								
Male	11,008	54.0	2540	55.3	2098	53.3	18,983	53.9
Female	9368	46.0	2053	44.7	1837	46.7	16,249	46.1
Age group								
0–9	483	2.4	147	3.2	107	2.7	751	2.1
10–19	335	1.6	180	3.9	171	4.3	876	2.5
20–29	722	3.5	361	7.9	287	7.3	1359	3.9
30–39	7733	38.0	1893	41.2	1450	36.8	12,354	35.1
40–49	6947	34.1	1190	25.9	1110	28.2	11,795	33.5
50–59	3562	17.5	612	13.3	614	15.6	6589	18.7
60–69	551	2.7	210	4.6	196	5.0	1359	3.9
Unknown	43	0.2	0	0.0	0	0.0	149	0.4
Marital status								
Married	16,099	79.0	3315	72.2	2939	74.7	27,315	77.5
Never-married	1675	8.2	630	13.7	485	12.3	3289	9.3
Others	2579	12.7	615	13.4	471	12.0	4	12.7
Unknown	23	0.1	33	0.7	40	1.0	158	0.4
Occupation								
Farmer	19255	94.5	3846	83.7	3168	80.5	32,001	90.8
Student	524	2.6	205	4.5	178	4.5	1055	3.0
Worker	141	0.7	158	3.4	188	4.8	660	1.9
Others	411	2.0	286	6.2	329	8.4	1368	3.9
Unknown	45	0.2	98	2.1	72	1.8	148	0.4
Education level								
Illiterate	3110	15.3	499	10.9	441	11.2	5147	14.6
Primary	9491	46.6	141	37.9	1467	37.3	15,439	43.8
Secondary	7157	35.1	1673	36.4	1395	35.5	12,332	35.0
High	362	1.8	193	4.2	204	5.2	939	2.7
College or over	49	0.2	26	0.6	33	0.8	126	0.4
Unknown	207	1.0	461	10.0	395	10.0	1249	3.5

Public awareness of the routes of HIV transmission and of the benefits of HIV counseling and testing have improved in Henan,[19] resulting in more people getting tested for HIV. Many people who contracted HIV/AIDS via transfusions and blood products have been detected in recent years through HIV voluntary counseling and testing (VCT) services.[19,20]

Although most HIV-infected individuals in Henan province are FPDs, the case-reporting system shows that after more than 10 years, HIV is now spreading via sexual transmission and MTCT. Li et al[21] and Wang et al[5] have confirmed this finding. The proportion of FPDs among total reported cases is decreasing, and the proportion of cases infected via sexual transmission seems to be on the rise.

TABLE 3. Changes in Patterns of HIV Transmission Routes Among Reported HIV/AIDS Cases in Henan, China, 2004–2006

	2004		2005		2006		Cumulative Cases	
Transmission	n	%	n	%	n	%	n	%
FPD	17,441	85.6	2265	49.3	1512	38.4	26,528	75.3
Blood tranfusion/blood products	1223	6.0	1087	23.7	951	24.2	3934	11.2
Sex	973	4.8	816	17.8	883	22.4	2807	8.0
Heterosexual	973	4.8	812	17.7	875	22.2	2795	7.9
Homosexual	0	0	4	0.1	8	0.2	12	0.0
IDU	6	0.0	21	0.5	12	0.3	48	0.1
Mother to child	601	2.9	197	4.3	152	3.9	1030	2.9
Unknown	132	0.6	207	4.5	425	10.8	885	2.5
Total	20,376	100	4593	100	3935	100	35,232	100

Sentinel surveillance results indicate that HIV prevalence among DUs, STDCAs, and LDTDs remains low though high-risk behaviors, such as low rates of condom use, having multiple sexual partners, or having extramarital sexual partners, are common among these groups.[22] HIV prevalence may be increasing among MSM in Henan.[9] Sentinel surveillance indicated that HIV prevalence among MSM was 2.7% in Zhengzhou in 2006, similar to rates in 2006 observed in Harbin (2.2%)[23] in north eastern China, but lower than HIV prevalence among MSM in Beijing (5.9%).[24] Self-reported condom-use rates among MSM are low; when asked if they had used a condom in the during anal intercourse with a man in the past 6 months, only 27.9% of MSM reported that they had.[22] This low rate of condom use, although higher than Zeng et al's survey in Shenzhen (22.7%)[25] and lower than Zhang et al's survey in 6 large cities of mainland China (32.5%),[26] confirms that condom use among MSM is not common practice in China. Other researchers have found that MSM in Zhengzhou had an average of 5 multiple male sexual partners, and 78.6% reported having had insertive and/or receptive anal intercourse in the previous 6 months.[22] Yang et al[27] investigated 1000 MSM in an unspecified Chinese city, and in the past 6 months, 43.6% of them had 3 or more male sexual partners and 53.6% had unprotected anal intercourse with men. In addition, some MSM in Zhengzhou report having concurrent male sexual partners and female sexual partners.[22] The conditions exist for the rapid transmission of HIV in this high-risk group if effective interventions are not implemented.

Those infected via sexual transmission include the spouses/sexual partners of HIV-infected individuals, FSWs, clients of FSWs, and MSM. Through the end of 2006, there were 2795 cumulative cases infected via heterosexual HIV transmission. Henan has monitored almost all identified serodiscordant couples and HIV-positive reproductive aged women to prevent new infections via sexual transmission and MTCT.

In October 2001, prevention of mother to child transmission (PMTCT) of HIV was initiated in 2 counties of Henan with high HIV prevalence. In 2003, this was expanded to 31 counties in 10 prefectures. After the "Four Frees and One Care" policy was announced in 2005, PMTCT was expanded to all prefectures in Henan.

To efficiently use limited resources, PMTCT services are differentiated in Henan depending on the HIV prevalence rate. In the 31 high prevalence counties, all HIV-positive women aged from 20 to 49 are provided with counseling and condoms on a monthly basis. In addition, all pregnant women who are unaware of their HIV status are given a free HIV test as part of routine prenatal care. HIV-positive pregnant women are offered free or subsidized PMTCT services. In low prevalence counties, all known HIV-positive women aged 20–49 also receive monthly counseling and condoms; however, free HIV testing services are not offered. HIV antibody screening is standard practice for hospital deliveries across Henan, and if a delivering mother tests HIV positive, PMTCT services are offered as quickly possible. PMTCT services in Henan include free abortion services if the woman decides to terminate the pregnancy. If she chooses to proceed with the pregnancy, free services will be obtained, which include follow-up during pregnancy and delivery; antiretroviral drugs for mother and child; alternative infant-feeding formula for 18 months; and HIV antibody screening for infants aged 18 months.

The case-reporting system shows that of the total MTCT cases, only 199 children (19.3%) were younger than 5 years. This suggests that the majority of MTCT infections took place before 2002. Furthermore, studies[28,29] carried out in Henan confirmed that multiple prevention methods are successful and can effectively decrease the HIV MTCT transmission rate.

In addition to expanding HIV VCT services, the government in Henan has also taken actions to prevent the further spread of HIV via sexual transmission and MTCT. These measures include providing free condoms and HIV testing services for discordant couples; using multiple methods to interrupt MTCT; carrying out behavioral intervention programs among high-risk populations (eg, 100% condom use programs for FSWs; HIV testing and behavioral interventions targeting MSM; and methadone maintenance treatment for DUs); and large-scale HIV/AIDS education programs.

CONCLUSIONS

The HIV/AIDS epidemic in Henan is still primarily centered among FPDs infected before 1996 and is much lower than originally thought. Transmission between discordant couples and from infected FPDs mother to child will have a limited widespread HIV role. Although HIV prevalence remains low among groups such as FSWs and DUs, rates of high-risk sexual behaviors are high. More attention must be paid to MSM in particular; surveillance data indicate rising HIV prevalence among MSM in Henan and high levels of risky sexual behaviors. HIV surveillance, VCT, and intervention programs should be further strengthened to stop the additional spread of HIV among MSM and other vulnerable groups in Henan.

ACKNOWLEDGMENTS

We are grateful to Naomi Juniper, Katharine Poundstone, Sheena G. Sullivan, and Adrian Liau for editing the many drafts of this article.

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Prevalence of HIV and STIs and Associated Risk Factors Among Female Sex Workers in Guangdong Province, China

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Objectives: To assess the prevalence of HIV and sexually transmitted infections (STIs) and associated factors among female sex workers (FSWs) in Guangdong, China.

Methods: Respondent-driven sampling was used to recruit 320 FSWs. The recruited participants were interviewed face-to-face using a structured questionnaire and tested for HIV, syphilis, gonorrhea, and Chlamydia.

Results: The prevalence of syphilis, gonorrhea, and Chlamydia were 8.0% (4.6%–12.2%), 9.5% (5.6%–14.3%), and 3.9% (1.7%–6.2%), respectively, and of any STIs was 19.7% (13.9%–26.2%). None of the participants were HIV positive. The median number of clients during the previous week was 5. The proportion of consistent condom use with the clients during the previous week was 58.0% (50.4%–65.5%), use with regular nonpaying partners and nonregular nonpaying partners were much lower than that with clients. Multivariate analysis indicated that years of education and perception of HIV risk were protective factors. Awareness of HIV/AIDS; regular sex partners deciding about condom use when having sex; recruiting clients at hotels, hair/beauty salons, or streets instead of massage parlors; and higher charge for last sexual service were associated with STI infection.

Conclusions: Future intervention programs should not only address personal risk factors but also empower FSWs to require condom use by both clients and nonpaying partners.

Key Words: behavior, China, HIV/AIDS, sex workers, STD

(*J Acquir Immune Defic Syndr* 2010;53:S48–S53)

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Supported by NIH Fogarty International Center training grant D43 TW000013.

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INTRODUCTION

China is experiencing a rapidly expanding HIV epidemic. The most common modes of HIV transmissions are through heterosexual contact and sharing contaminated needles among injection drug users (IDUs). Heterosexual transmission has been rising in recent years and has become the major driver of the HIV epidemic in China. According to the estimation conducted jointly by Ministry of Health of China, UNAIDS, and World Health Organization in 2007, there were about 700,000 people living with HIV/AIDS at the end of 2007, among whom heterosexual transmission accounted for 40.6%.[1] The results from HIV sentinel surveillance also showed that HIV prevalence among the sex workers has increased in recent years.[2] Guangdong Province is experiencing the same trend. The proportion of heterosexual transmission among the reported HIV/AIDS cases in Guangdong Province was 4.89% in 2001, 6.53% in 2002, 26.9% in 2006 and 37.9% from January to October 2007.[3,4]

The epidemic of STDs has expanded concurrently with the resurgence of the sex industry in China since the late 1970s. Results from the national STD surveillance system reveal that although the incidence of STDs was 12.32 per 100,000 population in 1989, by 1998, it had increased 4-fold to 50.68 per 100,000 population. The average annual increase in incidence for all STDs during the period from 1989 to 1998 was about 17.3%.[5]

Effective intervention strategies are urgently needed to control the transmission of HIV from IDUs to female sex workers (FSWs) and then to their clients. However, due to the illegal status of sex workers in China, little is known about the HIV/AIDS/STD epidemic situation and the related risk behaviors among FSWs. Surveillance for HIV and STDs and studies done among FSWs are mainly focused on the FSWs in the reeducation centers. Some research programs tried to recruit FSWs in the community using convenience sampling or chain referral sampling.[6–8] A representative sample from the community was needed to understand the risk behaviors and HIV/AIDS and STD status and to better evaluate the potential roles of FSWs in the spread of HIV/AIDS.

Respondent-driven sampling (RDS) is a new method of chain-referral sampling for obtaining a more representative sample from a hidden population. It has been applied in many research programs to sample hard-to-reach and hidden

populations such as IDUs and men who have sex with men[9–13] Those studies demonstrated that RDS was a feasible strategy for surveying hard-to-reach populations. However, the RDS method has not been widely applied for recruiting FSWs. The Vietnamese Ministry of Health conducted a survey using RDS to assess HIV prevalence, risk factors, and service utilization among FSWs in 2004. The program demonstrated that RDS could reach the less visible FSWs and, thus, may provide better estimates for the population.[14]

The present study was conducted to estimate HIV and STD prevalence and to identify predictors of infection among FSWs in Guangdong Province, China. RDS was used to obtain a probabilistic sample and to get a less biased estimate for the population.

METHODS

Participants and Procedures

The source population was the FSWs who lived or worked in the study county. FSWs were defined as those who had exchanged sex for money or goods in the past 6 months. It excluded those who exchanged sex for gifts or some other material rewards from their boyfriends or sweethearts. It also excluded those who were younger than 18 years.

RDS was used to recruit subjects into the study. Four seeds were recruited through local key informants or pimps to participate in the study. After the seeds completed the interview, each of them was given 3 coupons for recruiting their peers into the study. All new recruits were offered a dual incentive: one for completing the interview and one for successfully recruiting up to 3 peers into the study.

An office in the local Dermatology and STD Hospital was set up for the interviews. When the seeds or the participants with the referral coupon came to the office, screening was conducted to confirm their eligibility. An oral consent was obtained before the interview. The eligible participants underwent a face-to-face interview with a standardized questionnaire. The questionnaire was divided into 2 parts. The first part included questions dealing with knowledge and attitudes about HIV/AIDS and some basic information. The second part was about sexual-related and/or drug use-related behaviors. For the second part, the participants had the option to be interviewed face-to-face by the interviewer or to use a CD player to listen to prerecorded questions and put their answers on an answer sheet, which contained neither the questions nor identifying information.[15] The interviews were anonymous, no identifying information was collected.

After each interview, a free gynecological examination was conducted by a female gynecologist at the outpatient clinic of the hospital. A cervical swab was collected for testing for gonorrhea and Chlamydia. A 5-mL blood sample was also collected for testing for HIV and syphilis.

Testing Methods

Blood samples were collected for testing for HIV and syphilis. Serum samples were screened for antibodies to *Treponema pallidum* by the rapid plasma reagin test (Rongsheng Biotechnical Company, Shanghai, China). Positive specimens were confirmed by *T. pallidum* hemagglutination. Syphilis infection was defined as being positive on both rapid plasma reagin and *T. pallidum* hemagglutination tests. HIV antibody testing was done by enzyme-linked immunosorbent assay (Gibiai Biotechnical Company, Beijing, China). If a test was positive, 2 further assays (the original assay plus a different assay) were conducted in parallel. If both were negative, the result was recorded as HIV negative. If both were positive or there was discordance in the results, the specimen was sent to the confirmatory laboratory for Western blot testing.

Cervical swabs were collected for testing for gonorrhea and Chlamydia. The specimen was rolled on the culture plate and incubated in a CO_2 jar at 37°C for 24 hours. Thayer–Martin selective culture media was used for culturing *Neisseria gonorrhea*. For confirmatory tests, oxidase and sugar fermentation tests were done. Typical colonies of oxidase-positive gram-negative diplococci on Thayer–Martin culture media with a positive glucose fermentation test were used as the criteria for the identification of *N. gonorrhea*. Chlamydia was diagnosed by the enzyme immunoassay tests.

All the tests were conducted in the laboratory of the Zhaoqing Dermatology and STD Hospital. The blood samples were also sent to the HIV Confirmatory Center in Guangdong Centers for Disease Control and Prevention for HIV antibody tests (enzyme-linked immunosorbent assay; Organon Teknika, Netherlands).

Data Analysis

The data were double entered, using Epidata, by 2 researchers independently and were checked to assure accuracy and completeness.

Inconsistent condom use was defined as not using condoms 100% of the time for all sex acts during the last week, including any type of sex (oral, vaginal, or anal) with any kind of partner (clients, regular nonpaying, or nonregular nonpaying partners). STD infection was defined as any positive test for gonorrhea, Chlamydia, and/or syphilis.

The prevalence of STD and the potential predictors were described by measuring the frequency distribution. The frequency distribution was measured as the crude population proportion and the estimated population proportion (EPP) using RDS Analysis Tool, which was designed for analyzing RDS data adjusting for the long-chain referral recruitment design based on the linkage of the recruiters and recruitees and the participants' network sizes to produce population estimates.

Multivariate logistic regression was used to examine the associations of independent variables and the outcome (STD infection), simultaneously adjusting for potential confounders using statistical analysis system (SAS). The individualized weights generated for the dependant variable using RDS Analysis Tool were used to weight the data set for multivariate analysis.[16] Variables were selected into the multivariate model based on the prior knowledge of the relationship between them and inconsistent condom use. If there was no prior knowledge, variables were selected depending on how much their presence/absence affected the confidence intervals of other variables in the model. The cut-off level of change of the

confidence intervals of these variables of interest was predefined to be 10%.

RESULTS

Introduction of Recruitment Process (RDS)

A total of 320 participants, including the 4 seeds, were recruited for the study in 5 months. Each of the 4 seeds from street-based sex workers, massage parlor–based sex workers, hotel-based sex workers, and hair/beauty salon–based sex workers recruited 65, 209, 3, and 39 participants into the study, respectively. The longest recruitment tree had 16 recruitment waves. In total, 864 recruitment coupons were distributed, among which 316 (36.6%) were returned and 548 (63.4%) were not. Overall, the equilibriums with respect to the social and demographic characteristics were obtained after 2–10 waves.

Characteristics of Sample and EPP

Table 1 presents the characteristics of the FSWs. The median age of the 320 participants was 26 years. Most of the participants were Han (China's majority ethnic group) and had a junior middle school education (9 years of education). Over half of the participants (59.2%) had been married. Most of the participants were from Guizhou, Hunan, Sichuan, and Guangxi Provinces.

The FSWs were classified into 4 types according to the places where they are recruiting their clients or their working places: (1) massage parlor, karaoke bar, and drinking bar–based FSWs; (2) resort center and hotel-based FSWs; (3) hair/beauty salon–based FSWs; and (4) street, park, mall, construction site, rented apartment, and restaurant-based FSWs. FSWs from the above 4 places accounted for 25.3%, 22.6%, 25.6%, and 26.4%, respectively, of the total.

TABLE 1. Demographic Characteristics of the 320 Recruited FSWs

Characteristics	SPP (%)	EPP (%)	95% CI for EPP (%)
Age group			
18–29	71.6 (229/320)	66.5	(56.6 to 76.4)
30–48	28.4 (91/320)	33.5	(23.6 to 43.4)
Nationality			
Han nationality	96.6 (309/320)	97.1	(95.2 to 98.8)
Minorities	3.4 (11/320)	2.9	(1.2 to 4.8)
Education			
Illiteracy	3.1 (10/319)	5.6	(2.3 to 9.1)
Primary school (1–6 yrs)	27.3 (87/319)	35	(28.5 to 42.7)
Junior middle school (7–9 yrs)	58.9 (188/319)	51.1	(42.9 to 58.9)
High school (10–12 yrs)	9.7 (31/319)	7.9	(4.5 to 11.4)
Higher (more than 12 yrs)	0.9 (3/319)	0.4	(0.0 to 1.1)
Registered residence			
Guangdong	7.2 (23/320)	7.8	(3.2 to 14.1)
Not Guangdong	92.8 (297/320)	92.2	(85.9 to 96.8)
Marital status			
Ever married	51.4 (164/319)	59.2	(50.5 to 67.4)
Never married	48.6 (155/319)	40.8	(32.6 to 49.5)
Living status			
Living with partner	42.3 (132/312)	39.6	(32.0 to 46.5)
Not living with partner	57.7 (180/312)	60.4	(53.5 to 68.0)
Supporting family			
Supporting family	85.3 (273/320)	85.2	(80.9 to 89.5)
Not supporting family	14.7 (47/320)	14.8	(10.5 to 19.1)
Working places			
Type 1	34.3 (109/318)	25.3	(16.7 to 35.0)
Type 2	22.3 (71/318)	22.6	(16.1 to 29.8)
Type 3	19.2 (61/318)	25.6	(17.8 to 33.5)
Type 4	24.2 (77/318)	26.4	(18.6 to 34.7)

CI, confidence interval; SPP, sample population proportion; Type 1, massage parlor, karaoke bar, drinking bar-based sex workers; Type 2: resort center and hotel-based sex workers; Type 3: hair/beauty salon-based sex workers; Type 4: street-based, rented apartment-based and restaurant-based sex workers.

Sexual-Related Behaviors

Age at first sex experience ranged from 10 to 27 years, the median age was 19 years (Table 2). The age for initiating commercial sex ranged from 16 to 47 years, and the median age was 23 years.

The charge for the last commercial sex ranged from 10 ($1.25) to 2000 RMB ($250) Chinese Yuan. The median was 150 Yuan (about $19). The number of paying clients during the last week ranged from 0 to 30 with a median of 5. The EPP who had regular nonpaying partners and nonregular nonpaying partners during the last week was 46.6% (40.1–53.2) and 11.0% (6.9–16.1), respectively.

Condom Use With Sex Partners

Table 3 presents condom use with paying clients and nonpaying partners among the FSWs. 93.5% (90.7% to 96.5%) of the participants used a condom the last time they had sex with a client although 6.5% (3.6% to 9.5%) of them did not. The proportion of consistent condom use with clients during the last week was 58.0% (50.4% to 65.5%).

Incorrect condom use including using condoms just before ejaculation, rupture or breaking of the condoms, or not using the condoms during the entire sex act was not unusual among the FSWs. The proportion using condoms incorrectly during the previous month was 39.8% (33.0% to 46.6%).

70.9% of the participants used a condom the last time they had sex with a nonregular nonpaying partner. The proportion of consistent condom use with nonregular nonpaying partners during the last week was 43.1% (19.8% to 64.4%).

Only 38.7% of the participants used a condom the last time they had sex with a regular nonpaying partner. The proportion of consistent condom use with regular nonpaying partners during the last week was 20.5% (13.6% to 28.7%).

Drug Use

None of the participants used heroin, cocaine, or valium. 9.75% (31 of 318) had used the drug "ecstasy". Six participants had used drugs in the past 6 months. 1 of 28 (3.57%) of the participants had exchanged sex for drugs.

HIV and Sexually Transmitted Infection Prevalence

None of the participants was HIV positive. The adjusted prevalence of syphilis, gonorrhea, and Chlamyida was 8.0%

TABLE 2. Sex-Related Characteristics and the Numbers of Sex Partners of FSWs

	SPP (%)	EPP (%)	95% CI for EPP (%)
Age at first intercourse	19 (10–27)*	—	—
Age at first commercial sex	23 (16–47)*	—	—
Duration of being a CSW	2 years (1 month to 16 years)*	—	—
Charge for commercial sex	150 (10–2000) Chinese Yuan*	—	—
No. sex partners	—	—	—
No. clients last week	5 (0–30)*	—	—
No. regular non-paying sex partners last week			
0	51.9 (165/318)	53.4	(46.8 to 59.9)
1–2	48.1 (153/318)	46.6	(40.1 to 53.2)
No. nonregular nonpaying partners last week			
0	91.8 (292/318)	89.0	(83.9 to 93.1)
1–3	8.2 (26/318)	11.0	(6.9 to 16.1)

*Median (range).
CI, confidence interval; CSW, commercial sex worker; SPP, sample population proportion.

(4.6% to 12.2%), 9.5% (5.6% to 14.3%), and 3.9% (1.7% to 6.2%), respectively. The adjusted prevalence of any STD was 19.7% (13.9% to 26.2%).

Predictors for STD Infection

The multivariate logistic regression model indicated that years of education and self-perception of the risk of HIV infection were protective factors independently associated with STD infection. Awareness of HIV/AIDS, regular sex partners deciding condom use when having sex, recruiting clients at hotels, hair/beauty salons, or streets instead of massage parlors, and higher charge for commercial sex last time were risk factors independently associated with STD infection (Table 4). Other factors such as the number of sex partners, condom use, and drug use were not found to be associated with STD infection.

DISCUSSION

This study found that none of the participants were HIV positive, suggesting that the HIV epidemic in Guangdong Province is still concentrated among IDUs and had not expanded to general FSWs in the study county. The expansion of the HIV epidemic from IDUs to the FSWs relies on the overlap of the 2 populations; that is, the FSWs who are also IDUs or who have drug using clients. Tran et al[17] reported a prevalence of HIV of 12% among FSWs in Hanoi. The HIV prevalence among IDU-FSWs was 33%, 3.9% among non-injecting drug user-FSWs, and 1.6% among nondrug–using FSWs. Thus, sharing injecting equipment was the primary cause of the rapid increase of HIV infection among the FSW population in Hanoi. In his study population, there was a high proportion of drug use (that 38% used drugs, up to 83% of whom injected drugs). In our study, none of the participants were found to be IDUs, and only a few reported drug use by their sex partners. This may be the main reason for the low level of HIV observed among this population.

HIV sentinel surveillance among FSWs was conducted in the reeducation centers. It has been reported that incarcerated FSWs had a higher risk of HIV infection. In our study, we found, in the field assessment, that the FSWs who used drugs were more likely to be arrested and sent to a reeducation center. Only 2 of our participants had been arrested, and none of them had been sent to reeducation centers. The HIV prevalence in the sentinel surveillance which was conducted in the reeducation centers was higher than that in the comprehensive behavioral surveillance which was conducted in the community. The comprehensive behavioral surveillance in Guangdong Province found no HIV-positive cases in 2005 and 2007, whereas the HIV prevalence observed in the sentinel surveillance in 2005 and 2007 was 0.27% and 0.21%, respectively.[3]

The study found the prevalence of syphilis, gonorrhea, and Chlamydia to be 8.0% (4.6% to 12.2%), 9.5% (5.6% to 14.3%), and 3.9% (1.7% to 6.2%), respectively. The prevalence of syphilis and gonorrhea was much higher than among female market vendors (1.31% and 1.36%, respectively) in Fuzhou, China, as reported by Wu et al.[18] However, Wu et al[18] reported a higher prevalence of Chlamydia (11.2%) among the female market vendors in Fuzhou. Although the HIV prevalence among the FSWs in our study was 0%, the prevalence of STDs in our study population was relatively high, which is an indicator of high frequency of risk behaviors. Condom use was low among this population. Though the proportion of condom use for last sex with clients was high (93.5%), the proportion of consistent condom use with clients during the last week was only 58.0%. Condom use with nonpaying partners was even lower.

The study indicated that years of education and self-perception of the risk of HIV infection were protective factors independently associated with STD infection. Awareness of HIV/AIDS; regular sex partners deciding condom use; recruiting clients at hotels, hair/beauty salons, or streets instead of massage parlors; and higher charge for commercial sex last time were risk factors independently associated with STD infection.

Baltazar et al[19] reported that illiteracy was associated with acquiring a sexually transmitted infection and/or

TABLE 3. Condom Use With Clients and Nonpaying Sex Partners of FSWs

	SPP (%)	EPP (%)	95% CI of EPP (%)
Condom use with clients last time			
Yes	93.4 (296/317)	93.5	(90.7 to 96.5)
No	6.6 (21/317)	6.5	(3.6 to 9.5)
Frequency of consistent condom use with clients last week			
Used condoms consistently	58.1 (182/313)	58.0	(50.4 to 65.5)
Did not use condoms consistently	41.9 (131/313)	42.0	(34.5 to 49.6)
Incorrect condom use with clients in the past month*	42.9 (135/315)	39.8	(32.9 to 46.2)
Suggestion of condom use when having sex with clients usually			
The FSWs decide	53.6 (170/317)	50.2	(43.3 to 57.3)
The clients decide	4.4 (14/317)	5.0	(2.4 to 8.2)
Both sides decide	42.0 (133/317)	44.8	(38.1 to 51.0)
Condom use with nonregular nonpaying partners last time			
Yes	71.4 (20/28)	70.9	(54.0 to 87.2)
No	28.6 (8/28)	29.1	(12.8 to 46.0)
Frequency of condom use with nonregular nonpaying partners last week			
Used condoms consistently	44.8 (13/29)	43.1	(19.8 to 64.4)
Did not use condoms consistently	55.2 (16/29)	56.9	(35.6 to 80.2)
Suggestion of condom use when having sex with nonregular nonpaying partners usually			
The FSWs decide	33.3 (11/33)	37.3	(19.1 to 59.5)
The partners decide	24.2 (8/33)	21.0	(5.4 to 35.6)
Both sides decide	42.4 (14/33)	41.7	(20.8 to 62.6)
Condom use with regular nonpaying partners last time			
Yes	38.2 (86/225)	38.7	(32.3 to 46.2)
No	61.8 (139/225)	61.3	(53.8 to 67.7)
Frequency of condom use with regular nonpaying partners last week			
Used condoms consistently	17.4 (29/167)	20.5	(13.6 to 28.7)
Did not use condoms consistently	82.6 (138/167)	79.5	(71.3 to 86.4)
Suggestion of condom use when having sex with regular nonpaying partners usually			
The FSWs decide	29.0 (62/214)	30.9	(23.1 to 39.5)
The partners decide	19.1 (41/214)	18.6	(13.9 to 25.3)
Both sides decide	51.9 (111/214)	50.4	(41.5 to 57.5)

*Incorrect condom use includes using condoms just before ejaculation, rupture or breaking of the condoms, or not using the condoms during the entire sex act.
CI, confidence interval; SPP, sample population proportion.

reproductive system infection among FSWs. Tran et al[17] reported that being a low social economic FSW, having higher income compared with peers, and perception of self being at low risk for HIV were associated with HIV infection among noninstitutionalized FSWs. These reported risk factors for HIV were quite similar to those we found for STD infections, which suggested that HIV infection and STD infection share some common risk factors.

TABLE 4. Factors Associated With STIs—Results from Logistic Regression

Independent Variables	AOR	95% CI for OR	*P*
Years of education	0.825	(0.710 to 0.959)	0.01
Self perception of the risk of HIV infection	0.384	(0.152 to 0.969)	0.04
Aware of HIV/AIDS	4.749	(1.572 to 14.349)	<0.01
Amount charged for commercial sex last time	1.119	(1.032 to 1.213)	<0.01
The regular nonpaying partners deciding whether to use condoms	4.876	(1.774 to 13.398)	<0.01
Type 2 working place (resort center and hotel-based sex workers)*	8.949	(1.468 to 54.564)	0.02
Type 3 working place (hair beauty salon–based sex workers)*	18.859	(2.980 to 119.361)	<0.01
Type 4 working places (Street, rented apartment and restaurant-based sex workers)*	12.886	(2.205 to 75.294)	<0.01

STD infection: gonorrhea, syphilis, and/or Chlamydia.
The model controlled for marriage status, whether living with partners, period of living in the study county, consistent condom use with clients last week, 100% success persuading the clients to use condoms, number of clients last week, having regular nonpaying partners during the past week, and having nonregular nonpaying partners during the past week.
*The reference group was type 1 working place (massage parlor-based, karaoke bar-based, drinking bar-based sex workers).
AOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio; STI, sexually transmitted infection.

Regular nonpaying partners deciding condom use was independently associated with having an STD infection after controlling for confounders in our study. This suggested that lack of power in condom use decision making was a risk factor for STD infection, which suggested that future interventions not only need to target FSWs but also need to target their clients.

RDS was used to recruit FSWs in this study. It is a new method of chain-referral sampling utilizing an incentive for being interviewed and another incentive for recruiting peers to be interviewed. Heckathorn[20] asserted "RDS produces samples that are independent of the initial subjects from which sampling begins; and RDS reduces the biases resulting from voluntarism and masking and provides means for controlling the biases resulting from differences in the sizes of personal networks."[20] An underlying assumption of RDS is that the long-chain recruitment represents a first-order Markov process that reaches a dynamic equilibrium between the tendencies of persons with similar characteristics to associate with each other, relative network sizes, and underlying makeup of the target population. By tracking the linkage of the recruiters and recruitees and by recording the relative network sizes of participants, the biases inherent in the referral recruitment can be quantified and adjusted for in the analysis. Data for the adjusted analyses are sufficient when the sample reaches "equilibrium". In this program, the overall equilibriums with respect to the social and demographic characteristics were obtained after 2–10 waves. This study is the first using RDS to recruit subjects among FSWs in China. It showed that RDS was feasible among FSWs in China and provided a probabilistic sample for understanding the risk behaviors and HIV/STDs among FSWs. However, the number of the participants was very different from the 4 seeds ranging from 3 to 209. The results are dominated by the disproportionately large seed recruiting 209 participants. Another limitation in this study was that only 36.6% of the potential subjects returned with the distributed coupons. The subjects who did not return with the coupons may have different risk behaviors.

This study found a high prevalence of STD in spite of finding no HIV-positive in FSWs. It also revealed a high proportion of inconsistent condom use especially when having sex with nonpaying partners. This indicates the high potential for HIV transmission if the epidemic spread to FSWs and their clients. We found little overlap of FSWs and IDUs. This indicates that now is an excellent time to introduce intervention programs to reduce HIV transmission from IDUs to STDs general population through FSWs. Therefore, effective intervention programs for FSWs in this area should be implemented immediately.

ACKNOWLEDGMENTS

The authors thank Feng Deng, Ruiheng Xu, and Yurun Zhang for their valuable support. We are grateful to the staff of the Institute of HIV/AIDS Control and Prevention, Guangdong Provincial Center for Disease Control and Prevention, the staff of the Zhaoqing Dermatology and STD Hospital and Center for Disease Control and Prevention of Zhaoqing prefecture for their contributions to the conduct of the study and to Wendy Aft for assisting in the preparation of this article.

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HIV-1 and STIs Prevalence and Risk Factors of Miners in Mining Districts of Yunnan, China

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Objective: To assess HIV/sexually transmitted infection (STI) prevalence and associated risk factors among miners in Yunnan, China.

Methods: A cross-sectional study was conducted among 1798 miners in 2 townships of Gejiu City, Yunnan, from March to May 2006. Standardized interviewer-administered questionnaires were completed and specimens collected for HIV/STI testing.

Results: The prevalence of HIV, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, syphilis, herpes simplex virus-2, and any STIs among all miners was 0.7%, 4.8%, 0.8%, 1.8%, 9.6%, and 14.9%, respectively. One fifth of miners reported patronizing female sex workers (FSWs) at least once, and of these, 72% never used a condom with a FSW. Miners who visited FSWs had a higher prevalence of HIV (1.8% vs. 0.5%) and any STI (23.2% vs. 4.3%), including *C. trachomatis* (6.9% vs. 4.3%), *N. gonorrhoeae* (2.1% vs. 0.5%), and herpes simplex virus-2 (14.9% vs. 8.4%), and higher rates of illegal drug use compared with miners who visited no FSWs.

Conclusions: High prevalence of HIV/STIs among miners in Gejiu warrants special attention to this population, and vigorous interventions should address both sexual and drug use–related risk.

Key Words: China, HIV, miner, sexually transmitted infection

(*J Acquir Immune Defic Syndr* 2010;53:S54–S60)

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Supported by the Comprehensive Integrated Programs for the Research on AIDS funded by the National Institute of Allergy and Infectious Diseases, the United States National Institutes of Health with grant number U19AI51915, and by the China Multidisciplinary AIDS Prevention Training Program with NIH Research Grant #U2R TW 006918, funded by the National Institutes of Health, the Fogarty International Center, the National Institute of Drug Abuse, and the National Institute of Mental Health (China ICOHRTA, with Principal Investigator Z. Wu).

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INTRODUCTION

Heterosexual transmission has become the leading route of transmission of new HIV cases in China, surpassing intravenous drug use (IDU) for the first time since China's HIV epidemic began in the late 1980s.[1] Due to high rates of unprotected sex and drug use behaviors, China's "floating population" of migrant workers "liudong renkou" is at risk for HIV/sexually transmitted infections (STIs) and may play a critical role in the spread of HIV in China[2–5] as has been observed in other contexts.[6] Largely because of China's gender imbalance and economic reforms over the last 20 years, an estimated 100–150 million migrants from the countryside who are mostly male, young, poor, and uneducated have migrated to urban centers in search of work.[7] As mobility has increased and the economy has grown, the commercial sex industry has boomed and STI rates have risen.[8,9] Separated from home and working long hours in difficult conditions, male migrants may patronize female sex workers (FSWs), increasing their risk of HIV and helping to fuel epidemics of HIV and STIs.[4] Though China's HIV epidemic is still concentrated in high-risk groups, some regions of Yunnan province already have generalized epidemics with more than 1% of pregnant women in antenatal clinics testing HIV positive.[10,11] Clients, especially in provinces such as Yunnan, may subsequently "bridge" these infections through unprotected intercourse with both sex workers and regular partners.

To our knowledge, this is the first study to examine HIV/STI prevalence and the associated risk behaviors among a large sample of miners in China. Only one other study has examined HIV risk among male migrant clients in China.[12] Attention, however, has been given to HIV/STIs in migrant workers in China, with variable results. For instance, STIs were detected in 18% of market vendors of Eastern China[13] and 20% of a community sample of migrant workers in Beijing, Shanghai, and Nanjing reported a history of STIs.[12] Studies in Zhejiang[14] and Shanghai,[15] however, found minimal cases of STIs and no HIV. Still, behavioral studies in China have found that migrant populations have high-risk sexual behaviors, including multiple sex partners, engagement in commercial sex, and scarce condom use.[3,16]

Mining townships around Gejiu City in Yunnan, like other mining communities studied in Africa,[17–19] have great potential for HIV/STI spread. Gejiu City, known as the "tin capital" of China, has a population of 453,300, not including an estimated 67,900 migrant workers from rural areas, most of whom are miners. Development of the local mining industry

and the influx of single migrant miners have contributed to the expansion of the local commercial sex industry. The first HIV infection in Gejiu was reported in an injecting drug user in 1996, but by December 2004, a total of 1774 HIV cases were confirmed in Gejiu.[20] Though IDU still accounts for the majority of HIV infections in Yunnan,[20] the percentage of cases associated with sexual transmission has risen steadily from 5.3% in 1996 to 11.8% in 2004.[11,21] There are indications that Gejiu City is moving toward a generalized HIV epidemic; in 2003, HIV prevalence among women receiving antenatal care was 0.8%.[10] A pilot study conducted in 2005 among 232 miners in Laochang and Kafeng mining townships outside of Gejiu indicated that almost all (94.8%) were not local residents; 9.4% reported sex with FSWs; and the prevalence of HIV, gonorrhea, and chlamydia was 0.5%, 0.5%, and 9.3%, respectively.[22] Our study assessed HIV and STI prevalence and risk factors among a large sample of miners in Gejiu City.

METHODS

Study Population

Laochang and Kafang are 2 mining townships located approximately 20 and 25 kilometers from Gejiu, respectively. They have a combined population of 13,000. Five mines were selected as study sites based on the following criteria: (1) short distance from the entertainment facilities in town with transportation readily available; (2) private ownership; and (3) employment of ethnic minority miners. There were approximately 2000 miners working in the 5 selected mines.

All miners enrolled in the study were: (1) employed in 1 of the 5 selected mines; (2) aged 16 or above; and (3) willing and able to provide informed consent.

Data Collection

A cross-sectional study was conducted in the 5 selected mines of Laochang and Kafang townships from March to May 2006. Every effort was made to include all potential subjects. Subjects who met the above selection criteria and signed the informed consent forms were assigned a personal identification number. Study staff explained to every eligible participant the purpose of the study, the procedures, and the risks and benefits of study participation. The informed consent process, interviews, and specimen collection were all conducted in private rooms at the hospital or clinic in each of the 5 mining districts. Each participant was interviewed face-to-face by an interviewer of the same gender to collect information on sociodemographics, sexual behaviors, drug use, HIV/AIDS-related knowledge, and STI symptoms.

Individual pretest counseling sessions were provided to each participant before specimen collection. A 5-ml void urine sample and 7-ml venous blood specimen was collected from each participant and labeled only with a personal identification number. All participants were requested to return in 4 weeks to receive testing results and posttest counseling by trained study staff.

Laboratory Procedures

All specimens were collected and processed according to the manual of procedures approved by the National Institutes of Allergy and Infections Diseases and the Chinese Center for Disease Control and Prevention (CDC). Blood specimens were sent to the Gejiu CDC laboratory, where the plasma was separated for HIV testing by enzyme-linked immunosorbent assay (ELISA). Specimens found positive for HIV antibody by ELISA were confirmed by 2 additional ELISA tests and 1 Western blot test at the Yunnan Provincial CDC reference laboratory.

The Gejiu CDC laboratory performed herpes simplex virus (HSV-2) antibody testing and *Treponema pallidum* antibody testing by rapid plasma reagin (RPR). Positive RPR specimens were confirmed by *T. pallidum* particle assay at the Yunnan Provincial CDC laboratory. Syphilis cases were identified by positive *T. pallidum* particle assay and RPR. Urine specimens were tested with morphine gold conjugate test strip (ACON MOP) for morphine in the Gejiu CDC laboratory.

Data Management and Statistical Analysis

All data collected were transmitted via the DataFax system to the data management team in Beijing. The final data received via DataFax were manually entered into the SAS database for analysis. Sociodemographics, HIV/STI prevalence, knowledge, and attitudes were analyzed for all miners and compared between miner clients and miner nonclients.

Statistical analysis of data was performed with SAS version 9.1 (SAS Institute Inc, Cary, NC). The proportions between groups were compared by using χ^2 test or Fisher exact probability. The means between groups were compared by using Student t test. Univariate and multivariate logistic regression were used to estimate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for associations between HIV and STIs and variables of interest. Risk factors associated with HIV infection were adjusted for confounding variables and were fitted to a logistic regression model using a forward stepwise regression method. For multivariate analysis, variables were only retained if they were statistically significant at the level of $P < 0.05$ or if the coefficients of regression of the other variables in the same computation were substantially changed by their inclusion in the model.

Ethical Considerations

The study protocol was approved by the institutional review boards of the National Center for AIDS/STD Control and Prevention, Yunnan Provincial CDC, and the Division of AIDS Prevention Science Review Committee at the US National Institutes of Health.

RESULTS

Participant Recruitment

A total of 1804 miners were identified and screened and 1798 enrolled. Reasons for not participating included age less than 16 (n = 1); refused to participate (n = 3); and withdrawal from the study after giving informed consent (n = 2). Of all the enrolled miners, 1796 completed the questionnaire, 1760 provided a blood specimen, and 1773 provided a urine specimen.

Sociodemographic Characteristics

Miners ranged in age from 16 to 58, with an average age of 28.5 (±7.4) years. There was no significant difference in the mean ages of the miners enrolled from the 2 townships (P = 0.17). Among the 1796 miners who completed questionnaires, 81.6% were <35 years; 65.1% attended school for ≤6 years; 14.3% never attended school; 60.9% were married; and of those married, 36.4% lived apart from their spouses. Forty-two percent (42.6%) were Han (the major ethnic group in China accounting for 90% of the total Chinese population), 44.8% were Hani, and 12.6% were from other ethnic groups. Most miners (92.8%) had a "hukou" (residence permit) from outside Gejiu, only 7.2% had a Gejiu hukou. Most (84.7%) with a hukou from outside Gejiu were from elsewhere in Yunnan, with only 8.1% from other provinces. A significant proportion (41.3%) had stayed at the study site for <1 year. Before mining in Gejiu, many miners were farmers (64.8%), and others were miners (11.0%), students (8.4%), factory workers (2.1%), construction workers (7.1%), or other (6.6%).

Three hundred thirty-nine miners (339 of 1796; 18.9%) reported a history of patronizing FSWs. Comparison of sociodemographic characteristics between client and nonclient miners are presented in Table 1.

TABLE 1. Sociodemographic Characteristics and HIV and STI Prevalence of Miners by Client Status (Numbers are Percentages)

Variables	Miners		
	Clients (n = 339)	Not Clients (n = 1457)	*P*
Sociodemographic			
Mean age (SD) (yrs)*	27.5 (6.7)	28.7 (7.6)	0.0023
Han ethnic group	36.0	44.1	0.0063
Married	56.6	64.5	0.0068
Schooling >6 yrs	38.1	34.1	0.1701
Living with regular partners	36.3	39.3	0.3001
Residing locally ≤2 yrs	52.1	64.0	<0.0001
Born locally	7.7	7.0	0.6663
Income >800 Yuan/month	50.2	45.4	0.1171
Travel time to the township center ≤15 min	71.4	64.5	0.0153
Resident permit (hukou)			
Gejiu	8.0	7.1	0.5667
Yunnan but non Gejiu	88.5	83.8	0.0285
Other province	3.5	9.1	0.0007
Drinks alcohol	77.3	65.8	<0.0001
Smokes	91.2	87.0	0.0367
HIV and STI prevalence			
HIV infection†	1.8	0.5	0.0127
Syphilis†	2.4	1.6	0.3371
HSV-2†	14.9	8.4	0.0003
N. gonorthoea‡	2.1	0.5	0.0029
C. trachomatis‡	6.9	4.3	0.0496
Total STIs infection	23.2	12.9	<0.0001

*Mean age and (standard deviation of age) in years.
†Thirty-six subjects did not provide blood specimen for HIV, Syphilis, and HSV-2.
‡Twenty-three subjects did not provide urine specimens for *N. gonorrhoea* and *C. trachomatis*

HIV and STI Prevalence

Thirteen miners (0.7%) (95% CI: 0.3% to 1.1%) were HIV positive. The relative prevalence of syphilis, HSV-2, *Neisseria gonorrhea*, and *Chlamydia trachomatis* were 1.8% (95% CI: 1.2% to 2.4%), 9.6% (95% CI: 8.2% to 10.9%), 0.8% (95% CI: 0.4% to 1.2%), and 4.8% (95% CI: 3.8% to 5.8%). Prevalence of any STI was 14.9% (95% CI: 13.2% to 16.5%). There was a statistically significant difference in prevalence of syphilis (P = 0.02), *C. trachomatis* (P = 0.01), and HSV-2 (P = 0.01) between Kafang and Laochang townships.

Miner clients had a significantly higher prevalence of HIV (1.8% vs. 0.5%, $P < 0.05$), HSV-2 (14.9% vs. 8.4%, $P < 0.001$), *N. gonorrhea* (2.1% vs. 0.5%, $P < 0.01$), *C. trachomatis* (6.9% vs. 4.3%, $P < 0.05$), compared with nonclients (Table 1). There was no difference in syphilis (P = 0.05) based on client status. Prevalence of any STI was also significantly higher in clients (23.2% vs. 4.3%, $P < 0.0001$).

Awareness of HIV and Other STIs Knowledge

Misconceptions about HIV transmission were high. Only 66.9% had heard of HIV/AIDS; 84.5% believed that mosquitoes can transmit HIV; and 73.0% believed that sharing bathroom facilities with others could transmit HIV. Only 4.1% knew the correct routes of HIV transmission. In addition, only 43.9% of miners knew that people living with HIV/AIDS may seem healthy.

Miner clients in general had higher knowledge and awareness of HIV/STIs compared with nonclients (Table 2). Significantly, more clients had heard of HIV/AIDS (82.3% vs. 63.3%, $P < 0.0001$), had heard of condoms (75.8% vs. 54.6%, $P < 0.0001$), and knew HIV can be sexually transmitted (76.4% vs. 59.4%, $P < 0.0001$). In general, more clients than nonclients knew the correct routes of HIV transmission; more clients believed that there is a risk of HIV transmission from sexual intercourse (67.6% vs. 48.5%, $P < 0.0001$), a risk from sharing injection needles (65.5% vs. 47.4%, $P < 0.0001$), and a risk from blood transfusion (68.7% vs. 49.1%, $P < 0.0001$). However, only 9.1% of clients and 3.8% of nonclients believed that they were at risk for HIV.

Sexual Behavior and Drug Use

High-risk sexual behaviors were frequent among miners. Eighty-seven percent (87.3%) of all miners reported having sexual intercourse, and 34.0% reported having 2 or more sex partners in the past 12 months. One fifth of miners (18.9%) reported having purchased sex, and of these, 45.1% had visited FSWs twice or more in the past 12 months (range: X–70 visits). Reported condom use with FSWs was very low, 72.0% reported never using condoms with FSWs. Levels of drug use among miners were low, with 19 miners (1.1%) reporting previous illegal drug use, and 4 of these 19 (21.1%) reporting injecting drug use. Sixteen miners tested positive for morphine in their urine (0.09%).

In general, miner clients had more risk behaviors but higher knowledge and perceived risk of HIV/STIs (Table 2). Significantly more miner clients than nonclients reported

TABLE 2. HIV/STI Risk Behaviors, Knowledge, and Attitudes of Miners by Client Status

Variables	Miners		P
	Clients (n = 339)	Not Clients (n = 1457)	
Risk behaviors			
Illegal drug use	3.5	1.3	0.0044
Tattoo	9.4	6.0	0.0240
Surgical operation history	8.9	6.5	0.1290
Frequents karaoke halls in leisure time	36.9	11.1	<0.0001
Circumcised	1.2	0.3	0.0241
Reported STIs symptoms in the last 12 months	19.5	3.0	<0.0001
Age of first sexual experience <16 yrs	15.9	21.8	0.0158
>1 partner in past 12 months	65.8	14.5	<0.0001
>3 partner in past 12 months	33.6	6.0	<0.0001
Never used a condom with regular partner	56.3	61.5	0.0804
Never used a condom with FSW	72.3	NA	NA
Knowledge and attitudes of HIV/STIs			
Ever heard of condoms	75.8	54.6	<0.0001
Ever heard of HIV/AIDS	82.3	63.3	<0.0001
Disease can be transmitted through sexual behavior	76.4	59.4	<0.0001
Someone with HIV can look normal and healthy	47.2	35.2	<0.0001
No HIV risk from dining with others commensally	30.4	19.9	<0.0001
No HIV risk from shaking hands with others	32.7	24.4	0.0017
No HIV risk from sharing tools with others	35.1	26.0	0.0008
No HIV risk from sharing bathroom facilities with others	23.3	16.8	0.0051
No HIV risk from mosquitoes bites	13.6	9.6	0.0311
Risk of HIV transmission from sexual intercourse	67.6	48.5	<0.0001
Risk of HIV transmission from sharing injection needles	65.5	47.4	<0.0001
Risk of HIV transmission from mother to child	55.2	42.3	<0.0001
Risk of HIV transmission from sharing shaving paraphernalia with others	49.6	32.3	<0.0001
Risk of HIV transmission from blood transfusion	68.7	49.1	<0.0001
Believes self to be at risk of HIV	9.1	3.8	<0.0001
Believes self to be at risk of STIs	15.6	3.4	<0.0001
AIDS can not be cured	34.2	23.5	<0.0001

illegal drug use (3.5% vs. 1.3%, $P < 0.01$). They also reported more STI symptoms in the last 12 months (1.2% vs. 0.3%, $P < 0.001$), multiple sexual partners (>3 partners in the last 12 months, 65.8% vs. 14.5%, $P < 0.0001$), early age of sexual debut (<16 years old, 21.8% vs. 15.9%, $P < 0.05$), and frequenting karaoke halls in leisure time (36.9% vs. 11.1%), a common work venue for FSWs. There was no significant difference in condom use with regular partners or FSWs and tattoo or surgical operation history.

HIV/STI Risk Factors

Risk factors for HIV and STIs by client status significant in univariate and multivariate analyses are presented in Table 3. HIV infection in miner clients was independently associated with illegal drug use (adjusted OR: 266.9, 95% CI: 13.3 to 999.9, $P < 0.01$), tattoo history (adjusted OR: 42.3, CI: 3.6 to 502.1, $P < 0.01$), and 3 or more FSW partners in the past 12 months (adjusted OR: 24.0, CI: 2.1 to 276.9, $P < 0.01$). HIV infection in nonclients was independently associated with illegal drug use (adjusted OR: 11.5, CI: 1.3 to 105.3, $P < 0.05$) and 3 or more sexual partners in the last 12 months (adjusted OR: 5.9, CI: 1.2 to 31.7, $P < 0.05$).

STI infection in miner clients was independently associated with illegal drug use (adjusted OR: 3.5, CI: 1.1 to 11.3, $P < 0.05$) and reported STI symptoms in the last 12 months (adjusted OR: 2.5, CI: 1.4 to 4.5, $P < 0.01$). STI infection in nonclients was independently associated with being an ethnic minority (adjusted OR: 2.6, CI: 1.8 to 3.6, $P < 0.01$) and living with a spouse (adjusted OR: 1.6, CI: 1.2 to 2.2, $P < 0.01$). Going to a karaoke hall frequently in leisure time, however, was independently protective of STIs in miner nonclients (adjusted OR: 0.5, CI: 0.3 to 0.9, $P < 0.05$).

DISCUSSION

Mining communities are high-risk areas for HIV and STI transmission, largely due to the temporary nature of the work and the associated disruption of social ties.[17–19] Mining areas often do not provide accommodation for spouses or families, and most miners migrate alone (only 36% of married miners lived with spouses). Mining districts, perceived to be thriving economically, also attract female migrants who engage in sex work.[18]

The miners in our study were primarily young ethnic minority migrants with low educational attainment and except for their ethnic minority status match the demographic

TABLE 3. Univariate and Multivariate Analysis of HIV/STI Infection and Selected Sociodemographic and Risk Behavior Variables by Client Status

	Miner Clients (n = 336)					
	HIV Positive (n = 6)			STI Positive (n = 78)		
Variables	No. (%)	OR (95%CI)	Adjusted OR (95% CI)	No. (%)	OR (95% CI)	Adjusted OR (95% CI)
Age >27 yrs	5 (3.1)	5.5 (0.6 to 47.7)	—	44 (27.2)	1.5 (0.9 to 2.6)	—
Ethnic minority	2 (0.9)	0.3 (0.1 to 1.5)	—	50 (23.3)	1.0 (0.6 to 1.7)	—
Married	2 (1.1)	0.4 (0.1 to 2.1)	—	45 (23.6)	1.0 (0.6 to 1.7)	—
Schooling >6 yrs	4 (3.1)	3.3 (0.6 to 18.2)	—	27 (20.9)	0.8 (0.5 to 1.4)	—
Illegal drug use‡	3 (25.0)	35.7 (6.3 to 201.6)*	266.9 (13.3 to 999)*	6 (50.0)	3.5 (1.1 to 11.2)†	3.5 (1.1 to 11.3)†
Tattoo	3 (9.4)	10.4 (2.0 to 53.8)*	42.3 (3.6 to 502)*	5 (15.6)	0.6 (0.2 to 1.6)	—
Smoking	6 (2.0)	1.3 (0.1 to 23.1)	—	74 (24.1)	2.0 (0.7 to 5.9)	—
Drinks alcohol	5 (1.9)	1.4 (0.2 to 12.6)	—	62 (23.8)	1.1 (0.6 to 2.1)	—
Frequents karaoke halls in leisure time	5 (4.1)	9.0 (1.0 to 77.8)†	—	29 (23.6)	1.0 (0.6 to 1.7)	—
Living with spouse	1 (0.8)	0.3 (0.1 to 3.0)	—	33 (26.8)	1.4 (0.8 to 2.3)	—
Time living in the local township >2 yr	5 (3.1)	5.5 (0.6 to 47.7)	—	44 (27.2)	1.5 (0.9 to 2.6)	—
Age of first sexual experience <16 yr	2 (3.8)	2.7 (0.5 to 15.3)	—	9 (17.0)	0.6 (0.3 to 1.4)	—
Age of first sexual experience with FSW <16 yr	1 (10.0)	7.1 (0.8 to 67.5)	—	1 (10.0)	0.4 (0.1 to 2.9)	—
Reported STIs symptoms in the past 12 months	4 (6.1)	8.6 (1.5 to 48.3)†	—	25 (37.9)	2.5 (1.4 to 4.5)*	2.5 (1.4 to 4.5)*
No. FSW partner in the past 12 months >3	3 (5.2)	5.0 (1.0 to 25.4)†	24.0 (2.1 to 277)†	14 (24.1)	1.1 (0.5 to 2.1)	—
No. sexual partner in the past 12 months >3	3 (2.7)	2.0 (0.4 to 10.1)	—	28 (24.8)	1.1 (0.6 to 1.9)	—
Never used condom with FSWs	2 (1.3)	0.6 (0.1 to 3.4)	—	34 (22.7)	0.9 (0.6 to 1.6)	—

	Miner Nonclients (n = 1421)					
	HIV Positive (n = 7)			STI Positive (n = 185)		
Variables	No. (%)	OR (95% CI)	Adjusted OR (95% CI)	No. (%)	OR (95% CI)	Adjusted OR (95% CI)
Age >27 yrs	4 (0.5)	1.1 (0.2 to 5.0)	—	110 (14.2)	1.3 (0.9 to 1.7)	—
Ethnic minority	6 (0.8)	4.7 (0.6 to 39.0)	—	138 (17.3)	2.5 (1.8 to 3.6)*	2.6 (1.8 to 3.6)*
Married	6 (0.7)	3.4 (0.4 to 28.0)	—	133 (14.6)	1.5 (1.1 to 2.1)†	—
Schooling >6 yrs	1 (0.2)	0.4 (0.1 to 2.7)	—	48 (9.9)	0.6 (0.5 to 0.9)	—
Illegal drug use‡	1 (5.3)	12.9 (1.5 to 112.9)†	11.5 (1.3 to 105)†	3 (15.8)	1.3 (0.4 to 4.4)	—
Tattoo	1 (1.2)	2.6 (0.3 to 21.6)	—	10 (11.5)	0.9 (0.4 to 1.7)	—
Smoking	7 (0.6)	2.3 (0.1 to 40.0)	—	168 (13.6)	1.6 (0.9 to 2.6)	—
Drinks alcohol	6 (0.6)	3.1 (0.4 to 26.0)	—	136 (14.5)	1.5 (1.1 to 2.1)†	—
Frequents karaoke halls in leisure time	1 (0.6)	1.3 (0.2 to 11.2)	—	11 (7.0)	0.5 (0.2 to 0.9)†	0.5 (0.3 to 0.9)†
Living with spouse	4 (0.7)	2.1 (0.5 to 9.2)	—	93 (16.6)	1.7 (1.2 to 2.3)*	1.6 (1.2 to 2.2)*
Time living in the local township >2 yr	3 (0.6)	1.4 (0.3 to 6.1)	—	72 (14.2)	1.2 (0.9 to 1.6)	—
Age of first sexual experience <16 yr	0 (0.0)	0.2 (0.0 to 4.1)	—	26 (8.3)	0.5 (0.3 to 0.8)*	—
Age of first sexual experience with FSW <16 yr	NA	NA	—	NA	NA	—
Reported STIs symptoms in the past 12 months	0 (0.0)	0.5 (0.0 to 8.5)	—	10 (23.3)	2.1 (1.0 to 4.3)†	—
No. FSW partner in the past 12 months >3	NA	NA	—	NA	NA	—
No. sexual partner in the past 12 months >3	2 (2.3)	6.3 (1.2 to 33.1)†	5.9 (1.1 to 31.7)†	16 18.6	1.6 (0.9 to 2.8)	—
Never used condom with FSWs	NA	NA	—	NA	NA	—

*$P < 0.0$.
†$P < 0.05$.
‡Illegal drug use indicates the status found via self-reporting or the positive status from urine morphine testing. HIV and STI association with IDU was not calculated because IDU sample was too small.
NA, not applicable.

characteristics of China's so-called "surplus males."[7] These migrant surplus men may be helping to fuel the HIV epidemic in China through unprotected sex with multiple partners or through IDU behaviors.[5] HIV-related risks among FSWs (often also migrants) have been more widely studied in China,[23–30] than those of migrant surplus men.

HIV among the participating miners (0.7%) was 10 times higher than China's last national HIV estimate among the general population (0.05%, end of 2007).[1] Comparisons with other migrant population studies should be made with caution given their diversity across China; however, HIV prevalence among miners in this study was much higher than recent

studies of migrants in eastern China[13–15] and slightly higher than a smaller convenience sample of miners in the same area (0.5%).[22] *N. gonorrhea* and *C. trachomatis* rates in our miners were also greater than in a population-based study of 20-year-old to 64-year-old Chinese male adults (0.02% and 2.1%)[31] and among migrant workers in Shanghai (0.5% and 3.5%).[15]

HIV/STI rates may be higher in our study because of increased heterosexual risks. More than 2 times more males (18.9%) reported ever patronizing FSWs compared with a study of male adults aged 20–64 years old in China (9.4%)[32] and migrants in Shanghai (3.2%).[15] Other sexual risks (multiple sexual partners, young age at sexual debut, STI symptoms) were higher among clients compared with nonclients. This is consistent with a recent study of male migrant clients in China, in which multiple sex partners and history of STIs were associated with client status.[12]

Clients also had higher HIV rates (1.7% vs. 0.5%) and overall STI rates (23.3% vs. 4.3%). Yunnan CDC data show a relatively high HIV prevalence among FSW clients (0.3%–1.8%, 2003),[33] and a study in southwest China of FSW male clients reported an STI prevalence of 37.8%.[34] Multiple encounters with FSWs (≥3) conferred an independent HIV risk for clients in our study; and even for nonclients, multiple sex partners was associated with HIV. Though never using a condom with FSWs was not associated with HIV/STIs, condom use among clients was very low (only 13.3% reported always using condoms with FSWs) placing them at high risk of acquiring HIV/STIs. One interesting finding was that many clients were of an ethnic minority. It is possible that certain ethnic minority cultures facilitate liberal sexual norms, such as 2 Hani holidays when it is customary for men to have extramarital sexual contacts. Ethnic minorities in our study were twice more likely to be STI infected (OR: 2.1).

Drug use was an important factor in HIV/STI risk among miners and was strongly associated with HIV and STIs among clients (OR: 266.9 and 3.5, respectively) with half (3 of 6) of the HIV-positive clients being drug users (2 of 3). Clients were also more likely to be drug users than nonclients (3.5% vs. 1.3%, $P < 0.05$), a finding consistent with those of another study of male migrant clients in China.[12] Although multiple sex contacts with FSWs may increase HIV/STI risk among miner clients, those clients infected with HIV by IDU and with inconsistent condom use may simultaneously put FSWs at risk. Some international studies have proposed that HIV/STI transmission occurs from the "core" group of sex workers to "bridging" groups of clients who may transmit to the general population.[35,36] Similar to Africa,[17,37] our findings suggest in mining communities both FSWs and miner clients may be both "core" and "bridging" groups for HIV/STI transmission to the general population. Mining districts as a whole may be considered high-risk places, and interventions targeting the entire mining community should be considered, such as those proposed in a study of a Tanzanian mining community.[17]

Several limitations to this study should be noted. First, as this was a cross-sectional study, causality cannot be confirmed. For instance, as both drug use and multiple encounters with FSWs were independent risk factors for HIV in miner clients, it is not known how infection occurred. It is also unclear whether risky behaviors preceded migration or were encouraged by it. Second, as sexual behavior is a sensitive topic and data were collected by a face-to-face interview, participants likely under-reported commercial sex and other risk behaviors. Even with under-reporting, however, rates of patronizing FSWs, HIV, and STIs were higher in this population compared with the previously mentioned studies. Third, although this was a large sample of miners, results should not be extrapolated to all miners in China due to important regional differences in terms of demographics, economic conditions, and illicit drug availability and use.

Despite these limitations, this study demonstrates that miners who patronize FSWs are at substantial risk of contracting HIV/STIs and potentially escalating these epidemics in China. Although targeting mobile populations can be a major challenge,[38] some mining communities have reported declining STIs after prevention, education, and systematic treatment of miners and FSWs.[39] Workplace-based peer education, improvement of STI services, condom promotion, and community-based voluntary testing and counseling has also proven effective in other migrant communities. HIV/STI treatment options should not be reliant on a local residence permit, therefore, other methods of health care delivery should be made available.

In conclusion, miners in Gejiu constitute a high-risk population that may bridge HIV/STIs to both FSWs and regular partners and subsequently to the general population. Future studies should explore the availability and effectiveness of HIV/STI prevention and treatment programs in this high-risk community.

ACKNOWLEDGMENTS

Authors thank Gejiu CDC, Yunnan Provincial CDC, and the National Center for STD Control in Nanjing for their aid in laboratory testing and their enthusiastic help and support throughout the project. Authors also thank all the study participants and Naomi Juniper for editing drafts of this article.

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HIV Prevalence Among Pulmonary Tuberculosis Patients in Guangxi, China

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Objective: To determine the HIV prevalence rate among tuberculosis (TB) patients in Guangxi, China.

Methods: Stratified cluster sampling and systematic sampling methods were used to select 16 clinics from which pulmonary TB patients were recruited to participate in this study. Two thousand three hundred pulmonary TB patients provided information on sociodemographic characteristics, HIV-related knowledge and high-risk behaviors, and method of TB diagnosis. Five-milliliter blood sample from the regular TB check up was retained and tested for HIV antibody.

Results: HIV prevalence among pulmonary TB patients was 0.5% (12 of 2300). There was statistical difference in HIV prevalence neither between urban and rural nor between male and female patients; however, TB patients from higher HIV prevalence areas had a higher rate of HIV infection than TB patients from a lower HIV prevalence areas for both rural or urban areas (0.8% vs. 0, $\chi^2 = 7.49$, $P < 0.01$).

Conclusions: HIV prevalence is higher among pulmonary TB patients than among the general population in Guangxi. Program to address the dual infections of HIV/TB are needed.

Key Words: China, coinfection, HIV, tuberculosis

(*J Acquir Immune Defic Syndr* 2010;53:S61–S65)

INTRODUCTION

Immunosuppression as a result of HIV infection increases the frequency and speed of progression from latent tuberculosis (TB) infection to active TB.[1,2] According to the World Health Organization, TB is one of the major causes of death among HIV-infected people, and TB/HIV coinfection has been found to reduce the effectiveness of directly observed therapy treatment of TB.[3,4] Concern over growing HIV-driven epidemics of TB has galvanized global consensus on this issue; however, large-scale implementation of public health strategy to jointly address HIV/TB coinfection.[5,6]

China has been identified as one of the countries where a rapidly increasing HIV epidemic could fuel an epidemic of TB.[6,7] China is one of 22 countries with a high TB burden and has a growing HIV epidemic. In 2000, it was estimated that approximately 9% (range: 7%–12%) of all new TB cases in adults worldwide (of which 31% were in Africa and 26% in the United States) were attributable to HIV infection, as were 12% of the 1.8 million deaths from TB, crippling already overburdened health care resources.[6,8]

A 2000 national TB epidemiology survey conducted in China reported overall TB prevalence of 367 cases per 100,000 (0.0036%), with an estimated 4.5 million active pulmonary TB patients and 1.5 million new infections a year.[9,10] At present, the HIV epidemic in China continues to gain momentum after the first detection of a group of infected injecting drug users in southern China in 1989; by 1998, HIV infection had been detected in every province and by 2007, an estimated 700,000 people were thought to be living with HIV/AIDS.[11] Although HIV in China disproportionately affects groups such as commercial sex workers and their clients, injecting drug users and men who have sex with men,[11] people infected with TB tend to be from poor socio-economic backgrounds with limited access to information and adequate health services, such as farmers or laborers.[12] The overlap among the populations vulnerable to HIV and TB infections points to the systematic challenges in controlling the twin epidemics, which must address issues of health care access and provision of information on prevention methods.

Should the TB/HIV coinfection rate increase, it is anticipated that providing comprehensive HIV/AIDS care and support to HIV-positive TB patients such as antiretroviral therapy, and the monitoring and management coinfection cases,[13] will be made more difficult. On top of this, health care services in poor areas of China suffer from a lack of infrastructure, aging equipment, and a shortage of adequately trained healthcare workers, resulting in additional overburdening of already strained health care institutions.[14]

HIV prevalence in TB patients can be used as an indicator of the degree of spread of HIV into the general

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Supported by fund from the National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and Prevention; and Liyan Wang was supported by the China Multidisciplinary AIDS Prevention Training Program with NIH Research Grant # U2R TW06918 funded by the Fogarty International Center, National Institute on Drug Abuse, and the National Institute of Mental Health (China ICOHRTA, with Principal Investigator Z. Wu).

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population. This information is also important for the provision of comprehensive HIV/AIDS care and support.[13] A routine TB-HIV integrated surveillance system to monitor and evaluate the implementation of HIV testing and provision of HIV care to TB patients needs to be established. China does not have such surveillance and will require basic information to establish this system. As such, there is little published or existing data available on HIV infection rates among TB patients in China.

Guangxi Autonomous Region bears an unusually high burden of pulmonary TB and HIV/AIDS in China. In 2000, Guangxi had a TB prevalence rate of 650 of 100,000,[15] and the HIV prevalence in 2003 was 0.1% of the general population.[16] The purpose of this article is to determine the HIV prevalence rate among TB patients in Guangxi.

METHODS

Data Collection

Data were collected between December 2005 and February 2006, and a total of 2300 participants were recruited as study subjects. A stratified cluster sampling method was used for selecting pulmonary TB patients. Counties were stratified into 4 types according to whether an area was urban or rural and whether the number of cumulative reported HIV/AIDS cases was above or below the 2004 provincial-wide by-county median figures for respective type of county (rural, urban). As can be seen in Figure 1, area 1 sites were identified as rural with above average HIV; area 2 sites were rural with below average HIV; area 3 sites were urban with above average HIV; and area 4 were urban areas with below average HIV (Fig. 1). Of a total of 86 TB treatment clinics administered by the Guangxi Center for TB Prevention and Control, 36 were identified in area 1, 36 in area 2, 7 in area 3, and 7 in area 4.

The second stage of sampling consisted of selecting clusters of patients from each area. Six clinics were systematically sampled from each of areas 1 and 2, and 2 clinics were from each of areas 3 and 4 (Fig. 1), for a total of 16 clinics. Consecutive sampling methods were used within the cluster to enroll patients. Trained clinicians at each selected clinic screened newly diagnosed and existing pulmonary TB patients for study eligibility. Eligible patients who consented to participate in the study answered questions regarding socio-demographic characteristics, medical history, and HIV/AIDS-associated knowledge. Each subject also provided a blood sample for HIV testing.

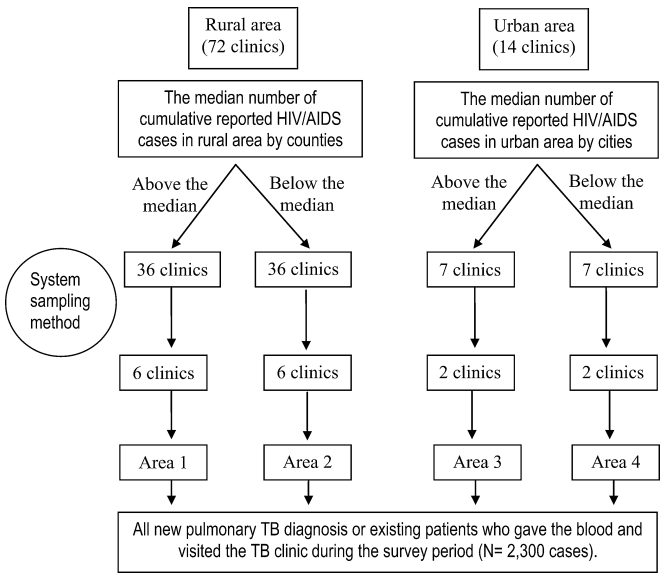

FIGURE 1. Flow chart of the sample selection process.

Pulmonary TB patients were diagnosed in at least 1 of the following ways: (1) sputum TB tested positive (smear examination or bacillus incubation); (2) sputum tested TB negative, but active TB symptoms were identified through X-RAY; (3) pathological diagnosis of TB; (4) suspected pulmonary TB patient if other pulmonary diseases were ruled out after a follow-up X-RAY; and (5) person suffered from TB-related pleuropneumonia (except for thorax hydrocele, which can be caused by other infections).[17]

During a regular follow-up visit, blood specimen is taken to test hepatofunction and hemogram. The remainder of the blood sample was used to test for HIV. HIV-positive cases were confirmed by Western blot method (test kit made by Genelabs Technologies Inc, Cavendish, Singapore) after testing positive for HIV antibody using 2 different types of enzyme-linked immunosorbent assays (the first enzyme-linked immunosorbent assay test kit was made by Beijing WANTAI Biological Pharmacy Company, Beijing, China, and the second was made by Livzon Group Reagent Factory, Zhuhai, China). All samples were prepared according to Genelabs Technologies Inc's instructions and blind tested at the Guangxi Center for Disease Control and Prevention (CDC) using Microsoft Excel (Microsoft, Redmond, WA) for automated test result interpretation.[18]

Data Analysis

All survey data were double entered at the Guangxi CDC and validated using Epidata 3.0 (The EpiData Association, Odense, Denmark). Data analysis was conducted with SPSS10.0 for Windows (SPSS Inc, Chicago, IL). All descriptive data were described using frequencies and median values. χ^2 tests of association were conducted to compare categorical variables.

Quality Control

Standardized protocols and questionnaires were used in each study site by the interviewers to collect data during the survey period. The interviewers were TB clinic doctors and were given interview training by TB and HIV experts from the China CDC (National) and the Guangxi CDC (Provincial). During the survey, 2 supervisors from the China CDC and the Guangxi CDC periodically monitored data collection either in person or via the telephone.

Ethics

The study protocol was approved by the institute review board at the National Center for AIDS/STD Control and Prevention, Chinese CDC.

RESULTS

Sociodemographic Characteristics

A total of 2300 participants were recruited. The mean age was 41.8 (SD, 17.6) years (Table 1). The majority were male (68.7%), of Han ethnicity (69.2%), married or living with their regular partner (72.2%), and had at least 9 years of schooling (72.3%). The most common occupations were farmers and laborers.

HIV/AIDS-Related Behaviors and Knowledge

Among the 2300 subjects, 17 (0.7%, 95% CI: 0.4% to 1.2%) participants reported a history of injecting drug use, and 53 (2.3%, 95% CI: 1.7% to 3.0%) participants reported at least 1 lifetime commercial sex experience (either as a sex worker or a client). Sixty-nine (3.0%, 95% CI: 2.3% to 3.8%) participants had ever received blood transfusions, and 57 participants (2.5%, 95% CI: 1.9% to 3.2%) had ever received blood products. Five men (0.3%, 95% CI: 0.1% to 0.7%) reported sex with other men.

The United Nations General Assembly Special Session on HIV/AIDS indicators were used to test knowledge of HIV prevention methods. Participants were assigned a score based on the percentage of questions answered correctly. Using this composite indicator, 39 (1.7%) received a score of 100%; and the percentage of respondents with perfect scores for areas 1, 2, 3, and 4, were 1.4%, 1.1%, 3.4%, and 1.4%, respectively (Table 2).

TABLE 1. Demographic Characteristics of Participants by Different Areas Among Pulmonary TB Patients, Guangxi, 2005

	Area 1 (%)	Area 2 (%)	Area 3 (%)	Area 4 (%)	Total (%)
No.	979	742	440	139	2300
Gender					
Male	71.1	69.5	64.1	62.6	68.7
Female	28.9	30.5	35.9	37.4	31.3
Age (yrs)					
<15	0.4	0.4	3.3	0.0	1.0
15–19	6.3	7.8	4.5	4.7	6.4
20–29	22.9	26.5	23.8	18.6	24.0
30–39	17.4	18.9	17.9	17.8	18.0
40–49	16.0	14.4	10.5	20.9	14.7
50–59	14.4	15.5	16.9	22.5	15.8
60–69	11.3	10.0	12.1	13.2	11.1
≥70	11.3	6.4	11.0	2.3	9.1
Mean age, years (SD)	42.9 (18.0)	40.0 (16.7)	42.3 (18.8)	42.5 (14.7)	41.8 (17.6)
Ethnicity					
Han	81.4	55.4	71.8	48.2	69.2
Zhuang	17.9	41.4	25.7	49.6	28.9
Others	0.7	3.2	2.5	2.2	2.0
Marital status					
Single	25.5	27.1	23.6	16.5	25.1
Regular partner	0.8	0.5	2.5	0.0	1.0
Married	71.4	71.4	66.8	82.0	71.2
Divorced/separated	0.4	0.3	0.7	0.0	0.4
Widowed	1.8	0.7	6.4	1.4	2.3
Occupation	4.0	2.7	8.8	11.5	4.9
Agriculture worker	77.0	84.5	49.5	44.6	72.2
Laborer	2.5	2.2	6.2	10.1	3.5
Public servant	3.3	3.9	8.8	5.0	4.6
Student	6.4	2.7	12.9	20.1	7.3
Merchant/business owner	6.9	4.1	13.8	8.6	7.4
Others	4.0	2.7	8.8	11.5	4.9
Education					
Never attended school	10.3	12.8	21.6	9.4	13.2
Primary (5–6 yrs)	35.4	38.0	26.8	25.2	34.0
Secondary (8–9 yrs)	40.9	41.2	29.1	33.1	38.3
Secondary (11–12 yrs)	11.2	6.3	15.9	23.0	11.3
College degree or more	2.1	1.6	6.6	9.4	3.3

The median is based on the number of cumulative reported HIV/AIDS cases above or below the 2004 Guangxi county median figures.
Area 1, rural, above the median; area 2, rural, below the median; area 3, urban, above the median; area 4, urban, below the median.

TABLE 2. HIV Related High-Risk Behaviors and Knowledge Among Pulmonary TB Patients, Guangxi, 2005

	Area 1		Area 2		Area 3		Area 4		Total	
	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)
No. people		979		742		440		139		2300
HIV knowledge*	14	1.4 (0.8 to 2.4)	8	1.1 (0.5 to 2.0)	15	3.4 (1.9 to 5.6)	2	1.4 (0.2 to 5.1)	39	1.7 (1.2 to 2.3)
HIV high-risk behaviors										
IDU	14	1.4 (0.8 to 2.4)	0	—	1	0.2 (0.006 to 1.3)	2	1.4 (0.2 to 5.1)	17	0.7 (0.4 to 1.2)
Commercial sex	41	4.2 (3.0 to 5.6)	8	1.1 (0.5 to 2.0)	2	0.5 (0.06 to 1.6)	2	1.4 (0.2 to 5.1)	53	2.3 (1.7 to 3.0)
Blood transfusion	29	3.0 (2.0 to 4.2)	20	2.7 (1.6 to 4.1)	14	3.2 (1.8 to 5.3)	6	4.3 (1.6 to 9.2)	69	3.0 (2.3 to 3.8)
Blood product use	28	2.9 (2.0 to 4.1)	18	2.4 (1.4 to 3.8)	1	0.2 (0.006 to 1.3)	9	6.5 (3.0 to 11.9)	57	2.5 (1.9 to 3.2)
MSM	2	0.3 (0.03 to 1.0)	1	0.2 (0.005 to 1.0)	2	0.7 (0.09 to 2.5)	0	—	5	0.3 (0.1 to 0.7)

*UNGUASS indicator.
Area 1, rural, above the median; area 2, rural, below the median; area 3, urban, above the median; area 4, urban, below the median; IDU, injecting drug use; MSM, men who have sex with men.

HIV Prevalence

Twelve participants tested positive for HIV, for a study sample prevalence rate of 0.5% (95% CI: 0.3% to 0.9%). There was no significant difference in HIV prevalence between urban (0.5%, 95% CI: 0.1% to 1.5%) and rural (0.5%, 95% CI: 0.2% to 1.0%) participants. However, HIV prevalence among pulmonary TB cases selected in the 2 areas where the cumulative number of HIV/AIDS cases was above the provincial median (0.8%, 95% CI: 0.4% to 1.5%) was higher than the cases selected from the areas where the cumulative number of HIV/AIDS cases was below the provincial median (0, one sided 97.5% CI: 0% to 0.4%), $\chi^2 = 7.49$, $P < 0.01$). This finding indicates that TB patients in high HIV settings are more likely to have HIV than TB patients in low HIV settings. No significant difference was found with regard to other variables, including ethnicity, gender, age, or occupation (Table 3).

Among the 12 coinfection cases, 11 were males with ages ranging 20–49. Ten of the cases were either from the Han ethnic group, had completed less than 9 years of education, or were farmers. Seven of the cases (58.3%) were married. Nine coinfected participants (75%) were diagnosed with pulmonary TB with sputum negative or no sputum tests (Table 3). This result implies that when HIV-positive people are screened for pulmonary TB, diagnosis should not focus solely on sputum-positive or incubation-positive methods of diagnosis.

DISCUSSION

The 0.5% HIV prevalence found among pulmonary TB patients is markedly higher than the provincial average of 0.1% in Guangxi. This finding is consistent with results reported in African countries.[19,20] The HIV/TB coinfection rate in our study is lower than the national HIV/TB coinfection rate of 4.3% in Vietnam, a neighboring country with a similar national HIV prevalence rate as China but with a higher TB rate. The same rate was even higher in the capital of Ho Chi Minh City: TB patients were found to have HIV prevalence of 9.8% in 2005.[21,22]

The finding of 0.5% HIV prevalence among TB patients is comparable with similar surveys conducted among TB patients in Hunan and Henan, where HIV/TB coinfection rates of 0.96% and 0.39%, respectively, were found among TB patients.[23,24] A study conducted in 4 counties of Hebei,

TABLE 3. HIV Prevalence Among Pulmonary TB by Different Categories, Guangxi, 2005

	No. Pulmonary TB Cases	No. HIV Positive	HIV (%) (95% CI)
Age group			
<50	1496	11	0.7 (0.4 to 1.3)
≥50	804	1	0.1 (0.003 to 0.7)
Gender			
Male	1581	11	0.7 (0.3 to 1.2)
Female	719	1	0.1 (0.003 to 0.8)
Ethnicity			
Han	1581	10	0.6 (0.3 to 1.2)
Zhuang	662	2	0.3 (0.04 to 1.1)
Occupation			
Merchant/ business owner	165	2	1.2 (0.1 to 4.3)
Agriculture	1645	10	0.6 (0.3 to 1.1)
Others*	490	0	0.0 (0 to 0.8)‡
Area type			
Urban	579	3	0.5 (0.1 to 1.5)
Rural	1721	9	0.5 (0.2 to 1.0)
Reported HIV/AIDS cases over median‡	1419	12	0.8 (0.4 to 1.5)
Reported HIV/AIDS cases below median	881	0	0.0 (0 to 0.4)†
Area 1	979	9	0.9 (0.4 to 1.7)
Area 2	742	0	0.0 (0 to 0.5)†
Area 3	440	3	0.7 (0.1 to 1.2)
Area 4	139	0	0.0 (0 to 2.6)†
Diagnosis methods			
Sputum positive	971	3	0.3 (0.06 to 0.9)
Sputum negative	1 231	8	0.6 (0.3 to 1.3)
No sputum	98	1	1.0 (0.03 to 5.6)
Guangxi Total	2300	12	0.5 (0.3 to 0.9)

*includes labor, student, and government staff.
†One sided, 97.5% confidence interval.
‡Test difference between 2 groups with cumulative HIV cases over or below the provincial median using χ^2-test, $\chi^2 = 7.49$, $P < 0.01$.

a province with lower HIV but high TB prevalence, found 0% HIV infection among its TB patients, although another conducted in a county in Henan found this same rate to be 5.1%.[25,26]

According to the results of this study, HIV/TB coinfection prevalence is 0% in Guangxi in areas with a HIV prevalence rate below the provincial median for rural and urban areas. This suggests the most efficient use of resources would be to establish TB/HIV coinfection sentinel surveillance sites in high HIV prevalence areas, as such sites will be more efficient at finding coinfections.

This study had several limitations. First, the nonprobability sampling methods may have resulted in a biased sample; however, some researchers have found bias from cluster sampling to be minor compared with estimates derived using simple random sampling.[27,28] Second, "self-reporting" bias may have underestimated more sensitive information such as drug use and commercial sex.

HIV-related TB not only fuels the world-wide TB epidemic and increases the burden of TB control and prevention, but TB has also become the leading cause of death in people living with HIV/AIDS. The World Health Organization suggests countries with limited resources and in the planning stages of establishing a HIV/TB sentinel surveillance system should periodically conduct HIV screening among pulmonary TB patients.[3] However, this study suggests the coinfection prevalence of TB and HIV in Guangxi is not as high as other countries with high HIV and TB burdens where coinfection rates between 1.5% and 9% have been reported.[29] Our study findings suggest TB/HIV coinfection sentinel surveillance sites among pulmonary TB patients should be limited to the areas with a high HIV prevalence in China.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the help of Qiuying Zhu, Weijiang Lu, and all the other public health officers in Guangxi. CDC, who participated in this survey and the doctors in 16 TB clinics for assisting in collecting the data. We would also like to thank Naomi Juniper and Adrian Liau for reviewing and editing the article.

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Prevalence and Correlates of HIV and Syphilis Infections Among Men Who Have Sex With Men in Seven Provinces in China With Historically Low HIV Prevalence

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Objectives: To assess HIV and syphilis infection among men who have sex with men (MSM) in Chinese regions with historically low HIV prevalence.

Method: A cross-sectional survey was conducted in 20 cities or districts across 4 provinces, 2 autonomous regions, and a municipality. Socioeconomic/behavioral risk factors were measured. Blood samples were tested for HIV via enzyme-linked immunosorbent assay and Western blot confirmation and syphilis via rapid plasma reagin and passive particle agglutination test for detection of *Treponema pallidum* Antibodies.

Results: Of 4983 MSM participants, 2.9% were HIV infected (range: 0%–15.1%) and 9.8% were syphilis infected (1.3%–29.3%). Syphilis infection was associated with older age [adjusted odds ratio (AOR) = 2.9; 95% confidence interval (CI): 2.0 to 4.3], not being married or cohabiting (AOR = 0.7; 95% CI: 0.5–0.9), less education (AOR = 1.3; 95% CI: 1.0 to 1.7), inconsistent condom use during anal sex with men (AOR = 1.4; 95% CI: 1.0 to 1.8), and living in inner Mongolia (AOR = 23.9; 95% CI: 9.7 to 58.6), Jilin (AOR = 7.9; 95% CI: 3.4 to 18.3), Heilongjiang (AOR = 7.1; 95% CI: 3.1 to 16.6), Liaoning (AOR = 6.1; 95% CI: 2.6 to 14.2), or Chongqing (AOR = 5.9; 95% CI: 2.5 to 13.9). HIV infection was associated with older age (AOR = 3.7; 95% CI: 2.0 to 6.7), less education (AOR = 2.9; 95% CI: 1.8 to 4.7), inconsistent condom use during anal sex with men (AOR = 1.9; 95% CI: 1.2 to 3.2), syphilis infection (AOR = 2.1; 95% CI: 1.3 to 3.4), and living either in Liaoning (AOR = 8.2; 95% CI: 1.1 to 61.4) or Chongqing (AOR = 57.2; 95% CI: 7.9 to 414.4).

Conclusions: HIV and syphilis have reached alarming rates in China's MSM population, thus, appropriate responses are urgently needed.

Key Words: China, drug abuse, HIV, MSM, sexual behavior, syphilis

(*J Acquir Immune Defic Syndr* 2010;53:S66–S73)

INTRODUCTION

The HIV epidemic in China continues to grow, expanding beyond injection drug users.[1–3] Half of all new cases in 2007 were transmitted sexually.[2,4] Of particular concern is increasing transmission among men who have sex with men (MSM). HIV prevalence in this group is estimated between 1% and 5%.[4–7] Between 2005 and 2007, the cumulative reported HIV cases attributed to MSM increased from 0.4% to 3.3%.[2] Unsafe sex between men accounted for 11% of the estimated new HIV cases in 2007, which is an increase from previous years.[2] Given that MSM in China are not a highlighted high-risk group, this trend is worrisome. Emerging data suggest that MSM are increasing risky activities. Massive internal migration from rural areas to urban cities has occurred, resulting in MSM being more visible and socially connected.[2,4,7,8] This is especially true in large-sized and medium-sized cities with large concentrations of migrants.[2,4,7,8] This social transformation has been associated with higher risk for HIV infection in MSM.[2,4,7–9]

In addition to rising HIV prevalence, high syphilis prevalence (~10%) has been documented in urban MSM.[4–7,10–13] High prevalence of both of these infections can be attributed to high-risk behaviors in MSM. For example, 70% of urban MSM reported having sex with more than 1 partner in the past 6 months.[2] Only 30% used condoms for anal sex, and about half reported not using condoms when having paid sex with a male.[2] A significant number (>25%) of MSM have also had sex with females.[4] These prevalent high-risk behaviors, coupled with increasing syphilis prevalence, make MSM a particularly vulnerable risk group for HIV. Sexually transmitted infections (STIs), particularly, for example, syphilis and herpes, are strongly associated with HIV acquisition.[14–17] Recognition and treatment of syphilis are crucial to both HIV and syphilis control and prevention. Without decisive action, MSM could become the second highest prevalent risk group, behind injection drug users, for HIV infection in China.[18]

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Supported partly by the China Global Fund AIDS Program Round Five, the National Center for AIDS/STD Control and Prevention, the Chinese Center for Disease Control and Prevention, and the Institute for Global Health and Department of Pediatrics, Vanderbilt University School of Medicine.

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Most studies examining HIV, STIs, and risk behaviors among MSM were conducted in large Chinese cities, particularly Beijing,[4,6,19] Shanghai,[20] and Guangzhou.[21] Few studies have been conducted in provinces/autonomous regions in China with historically low HIV prevalence, due to difficulties in accessing and enrolling MSM for both surveillance and epidemiological studies.[1,22,23] This prevents the creation of evidence-based policies for HIV and STI risk reduction. To effectively guide and evaluate prevention programs, systematic data on MSM throughout China is needed. We sought to examine prevalence of HIV and syphilis and their socioeconomic/behavioral risk factors among MSM in 4 provinces, 2 autonomous regions and a municipality where data on HIV and syphilis infections is limited. Despite their distinction in status, we will refer to provinces, autonomous regions, and municipalities as "provinces" in this article because China's public health system treats them similarly.

METHODS

Study Sites

This study was conducted in 20 large and mid-sized urban cities (or districts) across 7 provinces (Fig. 1). These cities (or districts) are located in Western and Northern China and were previously regarded as low HIV prevalence regions. MSM have gradually become more visible in the urban cities of these regions, but insufficient information about this risk group has resulted in a lack of MSM public health programs before 2006. Surveys in other Chinese cities have suggested that HIV prevalence among MSM is on the rise, indicating a need for the present survey.

Participants

A cross-sectional survey was conducted among MSM in 7 provinces from July to September 2006. The sizes of MSM populations were estimated in each community, and site recruitment venues were mapped. Participants were recruited by trained staff through venue-based recruitment, complemented by internet advertisement, community outreach, and peer referral using "snowball" techniques. Participants were recruited from gay-oriented venues including clubs, bars, parks, and bathhouses. All potential participants were invited to eligibility assessments and interviews in community-based voluntary counseling and testing centers or STI clinics. Survey information was collected anonymously and remained confidential. The enrollment criteria were: male, 14 years of age or older, reported having had oral or anal sex with another male in the past year, willing to finish the study, and provided written informed consent. The study was approved by the institutional review board of Vanderbilt University.

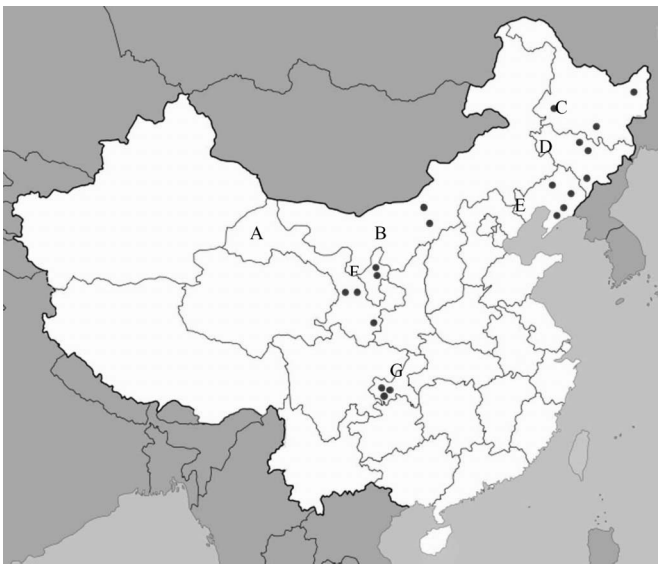

FIGURE 1. Study sites—20 cities (districts) were selected from 7 provinces in China. The 7 provinces include Gansu = A; inner Mongolia = B; Heilongjiang = C; Jilin = D; Liaoning = E; Ningxia = F; and Chongqing = G. Each dot represents a study city or district.

Measures and Test

Questionnaire-based interviews were used to provide socioeconomic and behavioral information. Socioeconomic characteristics included age, marital status, residency, ethnicity, education, and sexual orientation. Behavioral information was gathered about sexual activities and HIV risk behaviors. Assessing a subject's awareness of 3 major transmission routes for HIV was done by categorizing 3 questions identifying modes of transmission. Blood samples were collected for HIV and syphilis tests. Two screening tests were used to diagnose HIV: an enzyme-linked immunosorbent assay (Vironostika HIV Uni-Form II Ag/Ab; BioMérieux Corporate, Marcy l'Etoile, France) and a confirmatory test using the HIV-1/2 Western blot assay (HIV Blot 2.2 WB; Genelabs Diagnostics, Singapore). Syphilis seropositivity was determined using rapid plasma reagin and a Passive Particle Agglutination Test for Detection of Antibodies to *Treponema pallidum* (*Treponema pallidum* Antibodies; Rong Sheng Biostix Inc, Shanghai, China).

Statistical Analysis

Data were double entered and evaluated for congruency using EpiData software (version 6.4; EpiData Association; Odense, Denmark). SPSS software (Version 16.0; SPSS Inc, Chicago, IL) was used for analysis. χ^2 or T tests were employed for bivariate analysis of sociodemographic and behavioral variables. Multivariable logistic regression model were constructed using a stepwise backward sequence. Variables with $P < 0.05$ in bivariate analysis were considered statistically significant and included in the multivariable model.

RESULTS

General Description of Participants

Of the 5442 participants enrolled in this study, 459 (9.2%) were excluded from analysis due to missing survey responses (Table 1). The remaining 4983 eligible participants were included in the study. The age of participants ranged from 15 to 68 with a mean age of 28.4 years. Nearly three-quarters of participants were local residents of their study site, 19.0% lived in other cities in the same province, and 7.8% resided in a different province. The majority (92.0%) belong to the Han ethnic group. Among 4657 participants who reported their

TABLE 1. Demographic Characteristics of Self-Identified Sexual Orientation Among MSM in 7 Provinces of China (n = 4657)

Factors	Homosexual (%)	Bisexual/ Heterosexual (%)	Total (%)
Age (± SD)	27.3 ± 7.7	30.6 ± 9.0	28.5 ± 8.3
Age (yrs)			
15–22	921 (30.9)	337 (20.2)	1258 (27.0)
23–35	1596 (53.5)	866 (51.8)	2462 (52.9)
36–68	468 (15.7)	469 (28.1)	937 (20.1)
Marital status			
Single	2299 (77.0)	793 (47.4)	3092 (66.4)
Married/cohabitate	498 (16.7)	746 (44.6)	1244 (26.7)
Separated/divorced/widowed	187 (6.3)	133 (8.0)	320 (6.9)
Residency			
Local	2169 (74.4)	1201 (73.5)	3370 (74.0)
Other city (same province)	541 (18.6)	291 (17.8)	832 (18.3)
Other city (different province)	206 (7.1)	143 (8.7)	349 (7.7)
Ethnicity			
Han	2752 (92.2)	1534 (91.7)	4286 (92.0)
Other	233 (7.8)	138 (8.3)	371 (8.0)
Education			
Junior high school or lower	622 (20.8)	424 (25.4)	1046 (22.5)
Senior high school	1088 (36.4)	699 (41.8)	1787 (38.4)
College or higher	1275 (42.7)	549 (32.8)	1824 (39.2)
Study sites			
Gansu	258 (8.6)	176 (10.5)	434 (9.3)
Inner Mongolia	94 (3.1)	66 (3.9)	160 (3.4)
Heilongjiang	589 (19.7)	199 (11.9)	788 (16.9)
Jilin	686 (23.0)	419 (25.1)	1105 (23.7)
Liaoning	735 (24.6)	396 (23.7)	1131 (24.3)
Ningxia	42 (1.4)	27 (1.6)	69 (1.5)
Chongqing	581 (19.5)	389 (23.3)	970 (20.8)

Among 4983 eligible participants, 326 did not indentify their sexual orientation and are missing from this table.

sexual orientation, 64.1% self-identified as homosexual, 34.3% bisexual, and 1.5% heterosexual.

Sexual Behavior

Among the participants, 60% had their sexual debut at less than 18 years old, with one-third having had their first sexual encounter with a female. Most participants (82.1%) reported having anal sex with a man in the past 6 months, and 39.2% reported greater than 3 sexual partners in the past 3 months. In the previous 6 months, 27.8% reported always using a condom during anal sex with a man. A quarter reported having had sex with a woman in the past 6 months, and only 18.2% reported always using a condom. Additionally, 5.9% reported paid sex with a man in the past 6 months, and 38.1% reported always using a condom.

Prevalence Rates of HIV and Syphilis Infections

HIV infection was observed in 2.9% of participants (range by site: 0%–15.1%), and 9.8% were syphilis infected (1.3%–29.3%). Coinfection with HIV and syphilis was found in 31 participants. HIV was more common among participants with syphilis [adjusted odds ratio (AOR) = 2.1, 95% confidence interval (CI): 1.3 to 3.4] (Table 2).

Predictors for Syphilis Infection

In multivariate analysis, factors associated with syphilis infection were middle and old age (AOR = 1.5; 95% CI: 1.1 to 2.0; 25–35 vs. <22 years of age and AOR = 2.9; 95% CI: 2.0 to 4.3; 36–68 vs. <22 years of age), not being married or cohabiting (AOR = 0.7; 95% CI: 0.5–0.9; married or cohabited vs. single), less than junior high education (AOR = 1.3; 95% CI: 1.0 to 1.7), inconsistent condom use during anal sex with a man in the past 6 months (AOR = 1.4; 95% CI: 1.0 to 1.8), and HIV infection (AOR = 2.4; 95% CI: 1.5 to 3.8). When compared with Gansu, the province with the lowest syphilis prevalence, living in inner Mongolia (AOR = 23.9; 95% CI: 9.7 to 58.6), Jilin (AOR = 7.9; 95% CI: 3.4 to 18.3), Heilongjiang (AOR = 7.1; 95% CI: 3.1 to 16.6), Liaoning (AOR = 6.1; 95% CI: 2.6 to 14.2), or Chongqing province (AOR = 5.9; 95% CI: 2.5 to 13.9) was significantly associated with increased syphilis risk (Table 3).

Predictors for HIV Infection

Significant factors associated with HIV and included in the model were middle and old age (adjusted odds ratio AOR = 2.3; 95% CI: 1.3 to 4.0; 23–35 vs. <22 years of age and AOR = 3.7; 95% CI: 2.0 to 6.7; 36–68 vs. <22 years of age), less education (AOR = 2.9; 95% CI: 1.8 to 4.7; junior high school or lower vs. college or higher), syphilis seropositivity (AOR = 2.1; 95% CI: 1.3 to 3.4), and inconsistent condom use during anal sex with a man in the past 6 months (AOR = 1.9; 95% CI: 1.2 to 3.2; sometimes vs. always). When compared with Gansu, living either in Liaoning (AOR = 8.2; 95% CI: 1.1 to 61.4) or Chongqing (AOR = 57.2; 95% CI: 7.9 to 414.4) province was significantly associated with increased HIV risk (Table 2).

DISCUSSION

To our knowledge, this is the first large population-based HIV survey conducted among MSM in China. We demonstrate that HIV prevalence is high within this population. We provide additional information about the syphilis epidemic among MSM and risk factors for HIV and syphilis transmission among this high-risk group.

HIV was detected in 2.9% (range by site: 0%–15.1%) of MSM in 7 provinces with historically low HIV prevalence. This overall prevalence is similar to prevalence seen in large Chinese cities, for example, Beijing (3.1%–5.8%)[4,6,24] and Shanghai (3.0%),[24] but it greatly exceeds other reports examining this risk group.[5,7,10,12,21] We also found an astonishingly high HIV prevalence of 15.1% in Yuzhong, a district in Chongqing Municipality.

Syphilis prevalence was also high, with a mean prevalence of 9.8% (range by site: 1.3%–29.3%). This is comparable to the prevalence observed in 4 other studies and a systematic review examining syphilis infection among high-risk and low-risk groups in China.[5,10,20,21,25] However, syphilis prevalence varied greatly between provinces. Inner Mongolia

TABLE 2. Risk Factors for HIV Infection Among MSM in 7 Chinese Provinces (N = 4983)

Factors	% Positive	Total, N[1]	OR[2] (95% CI)[3]	AOR[4] (95% CI)
Age				
15–22	1.7	1366	1.0	1.0
23–35	2.6	2608	1.5 (1.0 to 2.5)	2.3 (1.3 to 4.0)†
36–68	5.5	1009	3.4 (2.1 to 5.5)‡	3.7 (2.0 to 6.7)‡
Marital status				
Single	2.4	3298	1.0	—
Married/cohabited	3.5	1354	1.4 (1.0 to 2.1)	—
Separated/divorced/widowed	5.5	330	2.3 (1.4 to 3.9)†	—
Residency				
Local	2.8	3567	1.0	—
Other city (same province)	2.0	923	0.7 (0.4 to 1.1)	—
Other city (different province)	6.3	378	2.3 (1.5 to 3.7)†	—
Ethnicity				
Han	3.1	4582	1.0	—
Others	1.0	401	0.3 (0.1 to 0.9)*	—
Education				
College or higher	2.0	1946	1.0	1.0
Senior high school	2.8	1887	1.4 (0.9 to 2.1)	1.6 (1.0 to 2.5)
Junior high school or lower	4.6	1150	2.4 (1.6 to 3.6)‡	2.9 (1.8 to 4.7)‡
Sexual orientation				
Homosexual	2.9	2985	1.0	—
Bisexual/heterosexual	3.3	1672	1.2 (0.8 to 1.6)	—
Study site				
Gansu	0.4	477	1.0	1.0
Inner Mongolia	0.0	167	—	—
Heilongjiang	0.7	809	1.8 (0.4 to 8.8)	2.7 (0.3 to 22.4)
Jilin	0.8	1211	2.0 (0.4 to 9.0)	1.7 (0.2 to 15.5)
Liaoning	1.9	1243	4.5 (1.1 to 19.0)*	8.2 (1.1 to 61.4)*
Ningxia	0.0	76	—	—
Chongqing	10.4	1000	27.6 (6.8 to 112.2)‡	57.2 (7.9 to 414.4)‡
Awareness of 3 major HIV transmission routes				
No	2.1	1355	1.0	—
Yes	3.2	3628	1.5 (1.0 to 2.3)*	—
Age at sex debut (yrs)				
<18	2.7	3003	1.0	—
≥18	3.3	1980	1.2 (0.9 to 1.7)	—
Sexual debut partner				
Male	2.3	3188	1.0	—
Female	4.1	1664	1.8 (1.3 to 2.5)†	—
Anal sex with man in P6M				
No	1.5	863	1.0	—
Yes	3.2	3970	2.2 (1.2 to 3.9)†	—
Frequency of anal sex with man in P6M				
≤3	2.9	2507	1.0	—
>3	3.7	1613	1.3 (0.9 to 1.9)	—
Condom use during anal sex with man in P6M				
Always	2.1	1102	1.0	1.0
Sometimes	3.6	2316	1.8 (1.1 to 2.8)*	1.9 (1.2 to 3.2)†
Never	4.0	552	1.9 (1.1 to 3.5)*	1.3 (0.7 to 2.6)
Paid sex with men in P6M				
No	3.1	3912	1.0	—
Yes	3.7	246	1.2 (0.6 to 2.4)	—

(*continued on next page*)

TABLE 2. (*continued*) Risk Factors for HIV Infection Among MSM in 7 Chinese Provinces (N = 4983)

Factors	% Positive	Total, N[1]	OR[2] (95% CI)[3]	AOR[4] (95% CI)
Condom use during paid sex with men				
Always	4.3	93	1.0	—
Sometimes	3.4	117	0.8 (0.2 to 3.3)	—
Never	0.0	35	—	—
Sex for money with men in the P6M				
No	3.1	3861	1.0	—
Yes	3.4	295	1.1 (0.6 to 2.1)	—
Condom use during sex for money with men in the P6M				
Always	1.4	138	1.0	—
Sometimes	3.9	128	2.8 (0.5 to 14.5)	—
Never	7.7	26	5.7 (0.8 to 42.2)	—
Sex with women in P6M				
Yes	2.9	1298	1.0	—
No	2.9	3651	1.0 (0.7 to 1.5)	—
Condom use during sex with women in P6M				
Always	3.9	231	1.0	—
Sometimes	1.3	551	0.3 (0.1 to 0.9)*	—
Never	4.3	484	1.1 (0.5 to 2.5)	—
Drug use				
No	2.8	4883	1.0	—
Yes	7.6	79	2.8 (1.2 to 6.6)*	—
Syphilis status				
Negative	2.5	4493	1.0	1.0
Positive	6.3	490	2.6 (1.7 to 3.9)‡	2.1 (1.3 to 3.4)‡

[1]Total N for each subgroup may not equal to the number of 4983 because of missing data. [2]OR, odds ratio; [3]95% CI, 95% confidence interval; [4]AOR, adjusted odds ratio.
*$P < 0.05$.
†$P < 0.01$.
‡$P < 0.001$.

had syphilis prevalence of 29.3%, whereas prevalence in the remaining provinces ranged from 1.3% to 12.8%.

This study found that age, junior high education or less, inconsistent condom use during anal sex with men in the past 6 months, syphilis infection, and study province were all independently associated risk factors for HIV infection. Similar risk factors were also associated with increased syphilis risk and included age, junior high education or less, inconsistent condom use during anal sex with men in the past 6 months, HIV infection, and study province.

We also demonstrated a correlation between HIV and syphilis infection. HIV prevalence was higher among participants with syphilis infection (6.3%) than those without infection (2.5%; $P < 0.01$). Although not unexpected, these findings are worrisome. Syphilis is a marker for engaging in high-risk sexual practices (eg, unprotected sex with multiple partners), and syphilis is known to facilitate HIV transmission.[14–17] High prevalence of potential risk factors concurrently with the high prevalence of syphilis suggest that MSM in these provinces are at increased risk for HIV infection.

Our data indicate that 1.6% of participants use illicit drugs and that drug use was associated with HIV infection (odds ratio = 2.8; 95% CI: 1.2 to 6.6, $P < 0.05$), but this increased risk was not significant in multivariate analysis. This is consistent with other studies, suggesting drug use is not a significant contributor to HIV transmission among Chinese MSM.[7] Overall, a small proportion of MSM reported illicit drug use with one-third having injected in the past 6 months. Previous studies found even less drug use among MSM.[4] What is alarming, however, is high illicit drug use in 2 districts in Chongqing; these districts also had the highest HIV prevalence. In Jiulongpo and Yuzhong, illicit drug use was reported in 5.8% and 9.4% of participants, and HIV prevalence was 9.4% and 15.1%, respectively. These findings suggests that although illicit drug use is not a significant risk factor for HIV, increased illicit drug use amongst MSM in China could result in the HIV epidemic beginning to resemble that of western countries where drug use is a major risk for HIV transmission among MSM.[4,26,27]

Knowledge about HIV transmission routes was high (72.8%), suggesting partial success of HIV education programs. However, high-risk behavior coupled with high HIV and syphilis prevalence among this population suggest that education is not translating into behavior modification. This suggested that risk reduction education alone cannot help MSM make lasting behavioral changes. In addition to providing accurate and up-to-date information on risky behaviors, effective community-based prevention programs not only make condoms available and accessible but also focus on enhancing individuals' motivation to change their

TABLE 3. Risk Factors for Syphilis Seropositivity Among MSM in 7 Chinese Provinces (N = 4983)

Factors	% Positive	Total, N[1]	OR[2] (95% CI)[3]	AOR[4] (95% CI)[3]
Age				
15–22	6.6	136	1.0	1.0
23–35	9.2	2608	1.4 (1.1 to 1.9)*	1.5 (1.1 to 2.0)*
36–68	15.8	1009	2.7 (2.0 to 3.5)†	2.9 (2.0 to 4.3)†
Marital status				
Single	8.8	3298	1.0	1.0
Married/cohabited	10.9	1354	1.3 (1.0 to 1.6)‡	0.7 (0.5 to 0.9)*
Separated/divorced/widowed	15.5	330	1.9 (1.4 to 2.6)†	0.8 (0.5 to 1.2)
Residency				
Local	9.8	3567	1.0	—
Other city (same province)	10.4	923	1.1 (0.8 to 1.4)	—
Other city (different province)	10.1	378	1.0 (0.7 to 1.5)	—
Ethnicity				
Han	9.8	4582	1.0	—
Other	10.7	401	1.1 (0.8 to 1.5)	—
Education				
College or higher	8.3	1946	1.0	1.0
Senior high school	10.2	1887	1.3 (1.0 to 1.6)‡	1.1 (0.8 to 1.5)
Junior high school or lower	11.9	1150	1.5 (1.2 to 1.9)*	1.3 (1.0 to 1.7)‡
Sexual orientation				
Homosexual	9.7	2985	1.0	—
Bisexual/heterosexual	9.6	1672	1.0 (0.8 to 1.2)	—
Study site				
Gansu	1.9	477	1.0	1.0
Inner mongolia	29.3	167	21.6 (10.3 to 45.2)†	23.9 (9.7 to 58.6)†
Heilongjiang	9.8	809	5.6 (2.8 to 11.3)†	7.1 (3.1 to 16.6)†
Jilin	12.8	1211	7.6 (3.9 to 15.1)†	7.9 (3.4 to 18.3)†
Liaoning	8.4	1243	4.7 (2.4 to 9.5)†	6.1 (2.6 to 14.2)†
Ningxia	1.3	76	0.7 (0.1 to 5.6)	—
Chongqing	9.3	1000	5.3 (2.7 to 10.7)†	5.9 (2.5 to 13.9)†
Awareness of 3 major HIV transmission routes				
No	11.3	1355	1.0	—
Yes	9.3	3628	0.8 (0.7 to 1.0)‡	—
Age at sex debut (yrs)				
<18	10.7	3003	1.0	—
≥18	8.6	1980	0.8 (0.6 to 1.0)‡	—
Sexual debut partner				
Male	9.1	3188	1.0	—
Female	10.9	1664	1.2 (1.0 to 1.5)‡	—
Anal sex with man in P6M				
No	10.3	863	1.0	—
Yes	9.4	3970	0.9 (0.7 to 1.2)	—
Frequency of anal sex with man in P6M				
≤3	9.4	2507	1.0	—
>3	10.3	1613	1.1 (0.9 to 1.4)	—
Condom use during anal sex with man in P6M				
Always	7.4	1102	1.0	1.0
Sometimes	10.5	2316	1.5 (1.1 to 1.9)*	1.4 (1.0 to 1.8)‡
Never	9.9	552	1.4 (1.0 to 2.0)	1.2 (0.8 to 1.8)‡
Paid sex with men in P6M				
No	9.6	3912	1.0	—
Yes	8.9	246	0.9 (0.6 to 1.4)	—

(*continued on next page*)

TABLE 3. (*continued*) Risk Factors for Syphilis Seropositivity Among MSM in 7 Chinese Provinces (N = 4983)

Factors	% Positive	Total, N[1]	OR[2] (95% CI)[3]	AOR[4] (95% CI)[3]
Condom use during paid sex with men				
Always	8.5	93	1.0	—
Sometimes	5.9	117	0.7 (0.2 to 1.9)	—
Never	22.9	35	3.2 (1.1 to 9.2)‡	—
Sex for money with men in the P6M				
No	9.4	3861	1.0	—
Yes	10.8	295	1.2 (0.8 to 1.7)	—
Condom use during sex for money with men in the P6M				
Always	10.9	138	1.0	—
Sometimes	13.3	128	1.3 (0.6 to 2.6)	—
Never	3.8	26	0.3 (0.0 to 2.6)	—
Sex with women in P6M				
Yes	8.9	1298	1.0	—
No	10.1	3651	1.1 (0.9 to 1.4)	—
Condom use during sex with women in P6M				
Always	10.8	231	1.0	—
Sometimes	7.8	551	0.7 (0.4 to 1.2)	—
Never	9.5	484	0.9 (0.5 to 1.4)	—
Drug use				
No	9.8	4883	1.0	—
Yes	7.6	79	0.8 (0.3 to 1.8)	—
HIV status				
Negative	9.5	4838	1.0	1.0
Positive	21.4	145	2.6 (1.7 to 3.9)†	2.4 (1.5 to 3.8)†

[1]Total N for each subgroup may not equal to the number of 4983 because of missing data; [2]OR, odds ratio; [3]95% CI, 95% confidence interval. [4]AOR, adjusted odds ratio.
*$P < 0.05$.
†$P < 0.01$.
‡$P < 0.001$.

behavioral patterns, teaching concrete strategies, and behavioral skills to reduce risk, providing tools for risk reduction, and reinforcing positive behavior change.

Since 2005, the Chinese government has made efforts to scale up intervention programs for MSM, which include condom promotion, counseling and testing, peer education, STI services, and follow-up outreach and care services for HIV-infected individuals.[2] The government has also developed national guidelines on HIV prevention and control for MSM.[2] However, based on the results of this study, these efforts are not translating into the behavior modification needed to reduce STI and HIV risk. Only 18.9% of participants reported having an HIV test, and only 77.8% received pretest counseling. Less than one-third reported seeking treatment for an STI at an appropriate clinic with 10.4% seeking no treatment at all for symptomatic STIs. Less than half (46.3%) reported having received educational information about HIV through free posters and brochures. Additionally, third quarter national statistics in 2007 showed that 88,082 MSM were reached by comprehensive HIV prevention interventions, which represents only 8.2% of the MSM population (MOH, unpublished data, October 2007). Although widespread stigma hinders MSM from seeking HIV-related and STI-related services, additional efforts are needed to ensure that targeted messages reach a high proportion of MSM to prevent HIV and STI transmission. Increasing access to both STI clinics and education is also necessary to ensure that those infections, which increase HIV risk, are properly diagnosed and treated. Without appropriate health messages and support, many MSM will continue to engage in risky sexual behavior and fail to seek treatment when needed.

HIV and other STI transmission through male homosexual sex is increasing dramatically[1,2,28,29]; however, MSM have not been effectively targeted in China. This group has been largely ignored by both social and public health structures for too long, given their highly disproportionate HIV burden.[30] Discrimination and stigmatization against MSM also continue to fuel the epidemic, resulting in under-representation in prevention/care programs and surveillance systems.[30] Increased efforts are needed to target MSM for these services and ensuring their inclusion in surveillance systems.

Strengths of this study include its substantial sample size, geographic diversity of recruitment venues, and geographic mapping of the targeted population with population size estimation. Our study subjects may represent a wider spectrum of MSM in China than previous studies, which relied on convenience sampling.[10,12,24] The study also has limitations. The cross-sectional nature of the study prevents ascertainment of causal associations between variables of interest. Additionally, an analysis of the role of social and sexual networks was not conducted. MSM typically have multiple sex partners and are highly mobile. An analysis of these networks

would have enabled us to better understand the role of MSM in HIV/STI transmission within and beyond this population. Our study only interviewed urban MSM and therefore might not be representative of the MSM population. However, MSM tend to congregate in urban areas, even if they live in rural areas, suggesting that our study can be representative of more than just urban MSM. Finally, our study does not examine all sociodemographic and behavioral characteristics that could be risk factors for both HIV and syphilis. Additional studies need to be conducted to increase our understanding of current syphilis and HIV epidemics among Chinese MSM. A better understanding of the epidemic is crucial for successful prevention.

Both HIV and syphilis infections have reached alarming rates in China's MSM population, even in previously low prevalence regions. Although awareness of HIV transmission routes is high, suggesting successful dissemination of HIV education, potential risk factors are extremely prevalent, indicating that more needs to be done. Both HIV and syphilis control is deserving of China's highest priority. Increased testing for HIV and STIs, particularly for MSM, should be considered a necessary component of the prevention strategy, along with better targeted education programs and greater access to treatment. Combined syphilis and HIV control is essential among MSM in Chinese cities not hitherto perceived to be in the epidemic mainstream. This study should serve as a call to redouble our efforts in increasing access to testing, prevention, and treatment programs for MSM in China.

ACKNOWLEDGMENTS

Authors thank Dr. Kenneth James Drake and Ms. Meredith Bortz from Vanderbilt University for help preparing the article.

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HIV/STD Prevalence Among Men Who Have Sex With Men in Chengdu, China and Associated Risk Factors for HIV Infection

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Objective: To assess the prevalence of HIV and selected sexually transmitted diseases (STDs) among men who have sex with men (MSM) in Chengdu, China, and the risk factors associated with HIV infection.

Methods: A cross-sectional study using a snowball sampling method was conducted from March to July 2007. Participants were asked to complete a questionnaire about sexual history, high-risk behaviors, STD infection history, HIV knowledge and testing, and an assessment of depression. Blood samples were taken for antibody testing for HIV, herpes simplex virus 2 (HSV-2), and syphilis.

Results: A total of 538 MSM were recruited, and 513 (95.4%) consented to complete the questionnaire. HIV, HSV-2, and syphilis prevalence were 9.1%, 24.7%, and 28.1%, respectively. The rate of consistent condom use was low and varied by types of sexual partners. The highest was with casual male partners (38.6%), and the lowest was with wife or girl friend (17.8%). Money boys were 6 times more likely to be infected with HIV compared with clerks/students. Infection with either HSV or syphilis increased the risk of HIV infection more than 4-fold.

Conclusions: The prevalences of HIV and STDs were high among MSM in Chengdu. To prevent HIV/STDs, campaigns promoting condom use are needed not only to boost the frequency of condom use but also to educate MSM about proper condom use.

Key Words: China, HIV, men who have sex with men, prevalence, STD

(*J Acquir Immune Defic Syndr* 2010;53:S74–S80)

INTRODUCTION

Men who have sex with men (MSM) have been harshly and disproportionately impacted upon by HIV and continue to be a major driver of the HIV/AIDS epidemic in the world. In the United States, MSM accounted for approximately 45% of newly reported HIV/AIDS diagnoses in 2006 and nearly 54% of cumulative AIDS diagnoses.[1] In Australia, New Zealand, and most western European countries, MSM accounted for as much as 70% of all HIV infections.[2] In Indonesia, MSM represent 15% of reported AIDS cases, 29% in Singapore, 32% in Hong Kong, and 33% in the Philippines.[3]

By 2007, the major groups infected with HIV in China were injection drug users (IDUs; 38.5%), former blood donors (19.3%), and promiscuous heterosexuals (17.8%).[4] However, recent data indicated an emerging epidemic among MSM in the main cities.[5–8] According to the China Ministry of Health, 2%–4% of adult males in China are primarily homosexual in their sexual behaviors which corresponds to 5–10 million men.[9] By the end of 2005, it was estimated that 47,000 MSM were living with HIV/AIDS, accounting for 7.3% of the total number of estimated HIV cases in China.[10]

Surveys among MSM have been rare in China. In Beijing, an increasing HIV prevalence among MSM has been observed in the past 3 years, from 0.4% in 2004 to 4.6% in 2005 and to 5.8% in 2006.[7] This trend agreed with the results of another study in a northern city of China that showed a slight increase of HIV prevalence among MSM from 1.3% in 2002 to 2.2% in 2006.[5] Studies across China have reported high levels of sexually transmitted disease (STD) infections, a high prevalence of multiple sexual partners, and low consistent condom use.[5,7,11–14] In a study conducted in 6 large cities in China, only 32.5% of 1389 participants had always used condoms when having anal intercourse. The average number of their male sex partners was 5.7, including 4.4 unfamiliar sex partners in the past 6 months, 11.6% had participated in group sex in the past 6 months.[12]

Limited data on HIV among MSM in Sichuan indicated that high-risk behaviors occur within this population. One survey reported that 84.7% MSM had had sex with male partners in the past 6 months and that the median number of partners for anal sex and oral sex were 4.4 and 4.2, respectively. About 62% of those who engaged in anal sex reported having 3 or more partners in the past 6 months and 20% of them had paid for sexual services during the same period. Condom use with different male partners varied significantly.

Received for publication September 30, 2009; accepted October 20, 2009.

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Supported by the US National Institutes of Health Fogarty International Center research training grant D43 TW000013.

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The proportions of consistent condom use with regular, casual, and commercial male partners were 15.8%, 16.3%, and 32.3%, respectively. Only 18.3% of participants reported having been tested for HIV antibody in the past 12 months.[15,16]

With support of the China–United Kimgdom HIV/AIDS Prevention and Care Project and the Sichuan Center for Disease Control and Prevention, the Chengdu Gay Community Care Organization (CGCCO) has provided HIV voluntary counseling and testing and high-risk behavior surveillance among MSM in Chengdu since 2002. Data indicated that HIV prevalence surged from 0.64% in 2003 to 6.58% in 2006, and the percentage of consistent condom use when having anal sex remained at about 40% after the 4-year intervention effort.[17] A cross-sectional survey was conducted from March to June 2007 in Chengdu to update the prevalence of HIV and STDs among MSM and the factors associated with HIV infection.

METHODS

Study Design and Sampling

The snowball sampling method was used to recruit participants from the Chengdu MSM community. According to the formative study carried out before the quantitative survey, the major venues for MSM activities in Chengdu included internet chatrooms, bars, tea bars, money boy (MB) brothels, public restrooms, public bathhouses, and parks. Fifteen seeds were selected to cover all types of venues. Because some seeds "died out" soon after the survey started, 4 more seeds were recruited later in the process using the same procedure. All seeds were MSM at least 18 years old, fluent in both Mandarin and the Chengdu dialect, and had patronized MSM venues frequently.

MSM eligible for the study were at least 18 years, had been living in Chengdu in the past 3 months, and had had oral or anal sex with other men. All of the participants were given the option of either completing the written questionnaire by themselves or undergoing a face-to-face interview in either the Mandarin or Chengdu dialects. The information collected in the questionnaire included demographic characteristics, sexual history with other men and women including unprotected anal intercourse, commercial sex, self-reported STD infection history and specific symptoms of STD infections in the genital track or anus in the past 6 months, past HIV testing, HIV knowledge and attitudes, and assessment of depression [Center for Epidemiologic Studies Depression Scale (CES-D)].

At the beginning of the survey, the interviewer briefly introduced himself and the study, then went through a series of formalities with the participant including the importance and nature of confidentiality, issues related to the collection of information, the right not to participate and to withdraw from participation without penalty, incentive distribution, referral information related to sexual health issues, and access to the final report. Participants were not asked to sign the informed consent form to maintain the anonymity of this study. After the interview, a 2.5-mL blood sample was drawn from each participant for HIV, herpes simplex virus 2 (HSV-2), and syphilis testing.

Laboratory Testing

Collected specimens were tested by the Sichuan Provincial Center for Disease Prevention and Control for antibodies to HIV, HSV-2, and syphilis. Antibody to HIV was detected by the enzyme-linked immunosorbent assay (ELISA; Livzon Group Reagent Factory, Zhuhai, China), and positive results were confirmed by Western blot (Singapore MP Biomedical Asia Pacific Ltd Singapore). IgG antibody to syphilis was tested by ELISA (Beijing Kinghawk Pharmaceutical Co, Ltd Beijing, China). HSV-2 IgG was also tested for ELISA using the only reagent approved by Food and Drug Administration (Focus Technologies, Cypress, CA).

Ethical Considerations and Incentives

The survey was anonymous, no names or other personal identifying information were collected from the participants. Each participant was assigned a unique study number and identified only by this number during the process. A private room in the CGCCO office was used for the interviews. Participants were given a prenumbered card with an appointment date for receiving their test results and posttest counseling. Referral for treatment for the positives was provided as needed. Fifty Chinese Yuan (US $6.5) was given to the participants as compensation for their time or the equivalent value in condoms and lubricants.

The study protocol was reviewed and approved by the Institutional Review Board of the University of California, Los Angeles and the Chinese Center for Disease Control and Prevention (China CDC).

Statistical Methods

Descriptive analyses were conducted to describe the demographic characteristics of the sample, prevalence of HIV and STDs, and the risk factors for HIV infection. Univariate and multivariate logistic regressions analyses were used to assess the associations between the risk factors and HIV infection. Variables in the multivariate analysis were selected based on the results of univariate analysis and prior knowledge. When variables were significantly correlated, only those variables best explaining the relationships were used for model fitting. All statistical analyses were performed using the Statistical Analysis System, version 9.1.3 for Windows.

RESULTS

A total of 538 MSM were recruited to the study among whom 513 (95.4%) completed the questionnaire. All 538 blood samples were tested for HIV and HSV-2, although only participants who finished the questionnaire were tested for syphilis. The HIV (confirmed only), HSV-2, and syphilis prevalences of the total sample were 9.1% [49 of 538; 95% confidence interval (CI): 6.7% to 11.5%], 24.7% (133 of 538; 95% CI: 21.1% to 28.4%), and 28.1% (144 of 513; 95% CI: 24.2% to 32.0%), respectively. Prevalences of both HIV and HSV-2 were higher among those who refused to respond to the questionnaire (HIV: 16.0% vs. 8.8%; HSV-2: 32.0% vs. 24.4%). However, because the sample size was small and no personal information was collected for nonrespondents, no further conclusions could be made.

Demographic Information

Because no information was obtained from those who refused to answer the questionnaire, only 513 participants were included in the final analysis. The age of the participants ranged from 16.8 to 44.5 years, with a median age of 24 years. More than half (57.5%) were younger than 25 years, and 48.2% had some college or higher education. The majority (80.8%) of the sample had never been married. The primary reason for getting married was to satisfy their parents' wishes (54.4%) followed by the desire to conceal their homosexual orientation (27.9%). Some participants indicated that they did not know their sexual orientation before getting married. For those who had never married, 50.5% wanted to be married in the future. Approximately, 70% of them thought the most important reason to marry would be to satisfy their parents' wishes. The second most important reason was that they also loved females (26.8%). Only 12.2% reported that the most important reason to be married was to conceal their sexual orientation.

Almost two-thirds (63%) of the participants identified themselves as either absolutely homosexual or bisexual. Forty-three (8.4%) did not state their sexual orientation or "did not know." However, when asked which gender(s) they preferred to have sex with, 9 of the 43 preferred only males, 15 preferred mostly males, 13 both equally, 4 mostly female, and 2 only females. Sexual orientation of those who did not reveal their sexual orientation was defined according to these preferences.

The most popular strategy to find male sexual partners was the internet (63.1%), followed by through friends (51.9%), in bars (19.5%), and in public bathhouse (10.6%). When asked which *one* above had been used most, 54.2% of participants selected internet and 27.6% through friends.

High-Risk Sexual Behaviors and Condom Use

The median age at first sex (oral, anal, and/or vaginal) was 19 years. More than 60% of the participants' first sexual partners were male (62.1%). Some of the participants started their sexual activities as early as 8 years old, although a few had their first anal intercourse with a male in their 40s. Table 1 shows the numbers of male sex partners with whom the participants had had oral or anal sex and female sex partners. More than half (55.5%) of the participants had had sex with female partners in their life.

A boyfriend (BF) was defined as somebody with whom the participant had had sex and desired a long-term relationship. The majority of the participants had only 1 or no BFs in the past 6 months. The numbers of BFs or female sex partners in the past 6 months were similar between HIV-positive and HIV-negative participants. However, HIV-positive participants tended to have more casual male partners (Table 1).

The most preferred sexual behavior with male partners was anal sex (82.7% with BFs and 77.7% with casual male partners). About half (44%) of the participants had always or almost always been insertive, whereas 32% were always receptive, and 22% were about the same for both.

In the past 6 months, 26 participants (5.1%) had paid for sex with FSWs, and 52 (10.2%) with "MBs," whereas 10 (2.0%) had sold sex to female clients and 93 (18.3%) to male clients. The number of participants who had sold sex was higher than those admitting to be MBs, indicating that some of them might have been selling sex only occasionally.

TABLE 1. Number of Lifetime Sexual Partners and Partners in Past 6 Months

	HIV Positives, n = 45		HIV Negatives, n = 468		
	n	%	n	%	*P*
No. lifetime male sex partners (oral sex)					
1–5	7	16.7	176	39.4	<0.01
6–10	8	19.0	128	28.6	
11–50	20	47.6	106	23.7	
>50	7	16.7	37	8.3	
No. lifetime male sex partners (anal sex)					
1–5	9	21.4	197	44.8	<0.01
6–10	7	16.7	111	24.8	
11–50	20	47.6	110	24.6	
>50	6	14.3	29	6.5	
No. lifetime female sex partners					
0	13	30.2	205	45.9	0.01
1	12	27.9	145	32.4	
1–5	10	23.3	65	14.5	
>5	8	18.6	32	7.2	
No. BFs in past 6 months					
0	13	28.9	140	29.9	0.51
1	19	42.2	227	48.5	
>1	13	28.9	101	21.6	
No. casual male partners in past 6 months*					
0	4	8.9	122	26.1	<0.01
1	11	24.4	82	17.6	
2–5	14	31.1	190	40.7	
>5	16	35.6	73	15.6	
No. female sex partners in past 6 months					
0	33	73.3	344	73.5	0.91
1	7	15.6	80	17.1	
>1	5	11.1	44	9.4	

*Fisher exact test.

The rate of consistent condom use (always used condoms when having sex) varied by type of sexual partners. The highest use was with casual male partners (38.6%), and the lowest was with wives or girlfriends (17.8%). About two-thirds (67%) had had anal sex as their most recent encounter, and condom use for the most recent sexual intercourse was 57.5% (289 of 503, 95% CI: 53.1% to 61.8%). The primary means to avoid HIV/STD infection when not using a condom was washing after sexual intercourse (52.9%) and avoiding having anal sex (28.3%).

Five questions were used to assess participants' knowledge of condom use (Table 2). Only 120 men (23.4%) gave the right answers to all 5 questions. One third (33.7%) of the participants thought that condoms could be tested for safety before sex by filling them with water, and 26.3% believed that HIV/STDs could be prevented by putting a condom on just before ejaculation.

Knowledge about HIV/AIDS was generally low (Table 2). No critical questions were answered correctly by more than

TABLE 2. Knowledge of HIV/AIDS and Condom Use

	Yes		No		Unsure	
	n	%	n	%	n	%
Knowledge about HIV/AIDS						
A person with HIV/AIDS can look as healthy as other people	337	66.3	106	20.9	65	12.8
Persons with STDs are more likely to be infected with HIV	326	63.9	87	17.1	97	19.0
HIV/AIDS currently is curable	48	9.5	351	69.6	105	20.8
People with HIV cannot transmit the virus to others if not symptomatic	73	14.5	340	67.7	89	17.7
Doing physical exercises can prevent infection with HIV	316	62.6	138	27.3	51	10.1
Eating more nutritious food can prevent HIV infection	231	45.7	211	41.8	63	12.5
Washing after having sex can prevent HIV infection	286	56.3	171	33.7	51	10.0
Knowledge about how to use a condom use						
Need to check expiration date before use	457	89.3	17	3.3	38	7.4
Need to test condoms for safety by filling with water before use	172	33.7	241	47.3	97	19.0
Squeeze the tip of condom gently till so no air is trapped inside, and hold the tip to unroll the condom along the length of the penis	418	82.1	32	6.3	59	11.6
Condoms can prevent people from being infected with HIV/STDs if put on just before ejaculation	133	26.3	315	62.3	58	11.5
Withdraw penis when it is still hard	303	60.4	107	21.3	92	18.3

70% of the participants, including "a person with HIV/AIDS can look as healthy as other people" (66.3%), "persons with STDs are more likely to be infected with HIV" (63.9%), and "people with HIV cannot transmit the virus to others if not symptomatic" (67.7%).

Using lubricant when having anal sex prevents small tears and lesions in the anus lining reducing the risk of HIV transmission. In our study, 258 participants (50.4%) used only water-based lubricants when having anal sex, 60 (11.7%) used only oil-based lubricant, and 112 (21.9%) used both. When not having lubricant available, 218 (42.6%) avoided having anal sex, and 239 (46.7%) used other material for lubrication such as saliva, toothpaste, or oil.

Other Risk Behaviors

One fifth (21.6%) of participants often consumed alcohol before having sex among whom, 51 admitted to being drunk a few times. One quarter (124; 24.2%) of participants had used illegal drugs. The most popular was Ketamine (112 of 124, 91.1%) followed by amphetamine (68 of 124, 55.3%). Only 4 participants had used heroin of whom 2 had injected. Only 14 (2.7%) of participants had used drugs before having sex.

Sexually Transmited Diseases

One fifth (20.3%) of participants reported having been diagnosed as being infected with a STD. Only half (53.5%) received treatment in a regular clinic or hospital. Among those who denied being diagnosed with a STD, 24.2% had had symptoms in the genital track or anus 1–2 weeks after having oral, anal, or vaginal intercourse. According to the results of testing for HSV-2 and syphilis, 195 participants (36.2%) were infected with at least 1 STD of whom 74 (37.9%) had both HSV-2 and syphilis infections.

Depression Assessment

The shortened version of the CES-D was used to assess participants' mental health status. The CES-D is a 20-item, self-reporting depression scale. Items refer to the frequency of symptoms during the past week. The score for each person is calculated based on the answers to the questions. A score below 15 indicates that the participant does not seem to be experiencing high levels of depressive symptoms at that time. Scores between 15 and 21 indicate mild to moderate depression and more than 21 indicate possible major depression. In this study, 237 participants (46.3%) scored less than 15, 82 participants (16.0%) between 15 and 21, and 193 participants (37.7%) more than 21.

Risk Factors for HIV Infection

In the total sample, students comprised 14.8%, but none were found to be infected with HIV. Thirty HIV-infected participants (66.7%) were self-employed or in a service business and seven HIV-positive participants were MBs. HIV-positive persons tended to have had more lifetime sexual partners than negatives.

The possible risk factors for HIV infection were assessed by logistic regression. Because HSV-2 and syphilis infections were correlated in the sample (OR = 6.59, 95% CI: 4.24 to 10.24), STD infection was defined as either one of them or both. Table 3 shows the results of univariate and multivariate logistic regression. After controlling for other variables, participants who had a college or higher education level were 3 times more likely to be infected with HIV (OR = 3.17, 95% CI: 1.44 to 6.97). Those who had a history of being infected by either HSV or syphilis were more than 4 times more likely to be HIV positive (OR = 4.48, 95% CI: 2.02 to 9.96). Not knowing how to use condoms properly also significantly increased the risk for HIV infection (OR = 2.65, 95% CI: 1.27 to 5.54). Compared with clerks or students, the risk of HIV infection for MBs was 6 times higher (OR = 6.43, 95% CI: 1.54 to 28.86). For those who had lived in Chengdu for more than 5 years, the risk of HIV infection was 2.5 times higher (OR = 2.47, 95% CI: 1.06 to 5.76).

TABLE 3. Factors Associated With HIV Infection Among MSM in Chengdu

		Univariate			Multivariate		
	n	OR	95% CI	*P*	OR	95% CI	*P*
Age (yrs)							
<25 (ref)	295	1	—	—	—	—	—
25–35	142	1.62	0.81 to 3.28	0.18	—	—	—
>35	76	2.08	0.93 to 4.66	0.07	—	—	—
Education							
Senior high school or lower (ref)	206	1	—	—	1	—	—
College or above	247	1.03	0.56 to 1.91	0.92	3.17	1.44 to 6.97	<0.01
Occupation							
Clerk/student (ref)	240	1	—	—	1	—	—
Self-employed/service business	224	4.52	2.03 to 10.10	<0.01	4.11	1.68 to 10.06	<0.01
MB	47	5.12	1.76 to 14.90	<0.01	6.43	1.54 to 28.86	0.01
Marital status							
Never married	404	1	—	—	—	—	—
Married/divorced	96	1.66	0.82 to 3.36	0.16	—	—	—
Income (yuan/month)							
<500	93	0.48	0.18 to 1.27	0.14	—	—	—
500–2000 (Ref)	274	1	—	—	—	—	—
>2000	127	0.65	0.30 to 1.40	0.27	—	—	—
Sexual orientation							
Homosexual (ref)	347	1	—	—	—	—	—
Bisexual	130	1.08	0.53 to 2.17	0.84	—	—	—
Heterosexual	36	0.96	0.28 to 3.32	0.95	—	—	—
From urban or rural area							
Urban (ref)	410	1	—	—	—	—	—
Rural	103	1.92	0.98 to 3.77	0.06	—	—	—
Time of living in Chengdu							
≤5 years (ref)	193	1	—	—	1	—	—
>5 years	320	2.59	1.22 to 5.51	0.01	2.47	1.06 to 5.76	0.04
No. lifetime male partners for anal sex							
≤10 (ref)	324	1	—	—	1	—	—
>10	165	3.60	1.87 to 6.93	<0.01	2.76	1.32 to 5.78	<0.01
No. BFs in past 6 months							
0 (ref)	153	1	—	—	—	—	—
1	246	0.90	0.43 to 1.88	0.78	—	—	—
>1	114	1.39	0.62 to 3.12	0.43	—	—	—
No. casual male sex partners in past 6 months							
0 or 1 (ref)	219	1	—	—	—	—	—
2–5	204	1.01	0.47 to 2.14	0.99	—	—	—
>5	89	3.00	1.41 to 6.36	<0.01	—	—	—
No. lifetime female sex partners							
≤1 (ref)	375	1			—	—	—
>1	115	2.60	1.36 to 4.96	<0.01	—	—	—
Condom use during the last intercourse							
No (ref)	214	1	—	—	—	—	—
Yes	289	1.54	0.81 to 2.93	0.19	—	—	—
Condom use with BF in past 6 months							
Never	53	0.95	0.31 to 2.90	0.92	—	—	—
Sometimes	221	1.28	0.67 to 2.44	0.45	—	—	—
Always (ref)	84	1			—	—	—
Condom use with casual male partners in past 6 months							
Never	44	0.61	0.14 to 2.70	0.51	—	—	—
Sometimes	193	1.73	0.92 to 3.25	0.09	—	—	—
Always (Ref)	149	1	—	—	—	—	—

TABLE 3. (*continued*) Factors Associated With HIV Infection Among MSM in Chengdu

		Univariate			Multivariate	
	n	OR	95% CI	*P*	OR	95% CI	*P*
Correctly answered questions about condom use							
≥4/5 (Ref)	261	1	—	—	1	—	—
≤3/5	252	2.22	1.16 to 4.23	0.02	2.65	1.27 to 5.54	<0.01
Lubricant use							
No (ref)	82	1	—	—	—	—	—
Yes	430	1.04	0.45 to 2.41	0.93	—	—	—
Preferred sexual behaviors							
Anal sex	277	1.06	0.57 to 1.96	0.86	—	—	—
Others (ref)	233	1	—	—	—	—	—
Diagnosed STD during lifetime							
No (ref)	396	1	—	—	—	—	—
Yes	104	1.30	0.63 to 2.67	0.47	—	—	—
Either HSV or syphilis							
No (ref)	318	1	—	—	1	—	—
Yes	195	5.19	2.61 to 10.33	<0.01	4.48	2.02 to 9.96	<0.01
Illegal drug use							
Yes	124	0.77	0.36 to 1.64	0.50	—	—	—
No (ref)	389	1	—	—	—	—	—
CES-D							
<15 (ref)	237	1	—	—	—	—	—
15–21	82	1.21	0.48 to 3.04	0.68	—	—	—
>21	193	1.59	0.81 to 3.10	0.18	—	—	—

DISCUSSION

Chengdu is one of the largest city in southwest China. Studies have estimated that Chengdu has more than 71,000 MSM among whom at least 10,000 are sexually active.[18] Surveillance data among MSM in Chengdu indicated that the HIV prevalence has increased dramatically from 0.64% in 2003 to 6.58% in 2006[17] and was 9.11% in our study in 2007.

HSV-2 and/or syphilis infection significantly increased the risk of being infected with HIV. After controlling for other risk factors, participants who had been infected with either HSV or syphilis were 4 times more likely to be infected by HIV. In our study, about 20% of participants self-reported having had a diagnosed STD infection in the past, but only half had been treated in a regular clinic.

High-risk behaviors were common in this population. Only half of the participants used a condom during their last sexual intercourse. Consistent condom use was low even with casual male sex partners (38.6%). Only 23% of participants were able to correctly answer all the questions about how to use condoms properly. When not using a condom during sex, more than half of them just washed after sex to avoid being infected with HIV/STDs.

MBs were 6 times more likely to be infected with HIV compared with government employees, clerks, or students. Some participants who did not identify themselves as MB also reported occasional behaviors of selling sex for extra money. Among those who were self-employed or worked in a service business, 18.1% had engaged in commercial sex with male clients in the past 6 months, which was higher than among clerk/government employees (3.7%) or students (2.7%), putting this group at higher risk of HIV infection.

MSM living in Chengdu for more than 5 years were twice as likely to be infected with HIV compared with those living there a shorter time. This may reflect a shorter cumulative exposure time. The internet has become the most popular method for MSM seeking sexual partners, followed by through friends. In addition to focusing on the venues patronized by MSM, such as bars, parks, and bathhouses, intervention activities targeting MSM should target the internet and personal networks. Programs also need to reach MSM with STDs who do not attend STD clinics.

By the end of 2007, the major HIV transmission mode in Sichuan was still injection drug use. In our study, about one fourth of the participants had tried illegal drugs. However, drug use was not found to be a risk factor for HIV infection in our study, possibly because most of them used Ketamine or amphetamine instead injecting heroin. Thus, the HIV epidemic among MSM and IDUs seemed to be independent, so far.

Limitations of This Study

Because of the biases associated with the snowball sampling method, participants in this study were not likely to have been a representative sample of MSM in Chengdu. Possible bias may also derive from the choice of the initial seeds because most of them were volunteers from the Chengdu Gay Care Organization, were young, and had a college degree or higher level of education. Participants wanting to hide their sexual orientation such as those who were married or had

a high social status were probably less likely to be recruited to this study. Therefore, compared with the entire MSM population in Chengdu, our sample might have been younger, better educated, and less likely to be married. The IgG antibodies of syphilis were tested by an ELISA assay and were not confirmed by treponema pallidum hemagglutination assay (TPHA) testing. Therefore, the syphilis prevalence in this study might be overestimated. A positive result of syphilis testing only indicated a history of infection, not necessarily active syphilis.

CONCLUSIONS

HIV prevalence among MSM in Chengdu has been increasing rapidly in the past few years. STD infections were also very high in this population and significantly increased the risk for being infected with HIV. To prevent HIV/STDs, promotion campaigns of condom use are needed not only to boost the frequency of condom use but also to educate MSM about proper condom use. Certain subpopulations, such as those infected with STDs or who engage in commercial sex, require more attention and intervention. To reach the most sexually active MSM, more efforts should target the internet and the personal networks in this population.

ACKNOWLEDGMENTS

The authors are grateful to the people who participated in this study. We especially thank CGCCO for their heartily assists and helpful input in this study. Appreciation also goes to Dr. Abdelmonem Afifi, Dr. Thomas Coates, Dr. Li Li, Dr. Pamina Gorbach, and Dr. Marc Bulterys for their review, comments, and inspiring suggestions.

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Sexual Risk Behaviors and HIV Infection Among Men Who Have Sex With Men Who Use the Internet in Beijing and Urumqi, China

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Objectives: To assess HIV and syphilis infections among men who have sex with men who use the internet (MSMUI) and their risk behaviors.

Methods: In 2007, 429 MSMUI were recruited via the internet in Beijing and Urumqi, China. A questionnaire was administered, and a blood specimen was collected and tested for HIV and syphilis.

Results: Median age of participants was 25 years. Median number of lifetime sexual partners was 10. 90.7% ever had sex with a cyber friend. Rates of condom use in the last oral, insertive, and receptive anal sex were 9.1%, 66.3%, and 60.4%, respectively. Infection rates of HIV, syphilis, and HIV/syphilis coinfection were 4.8%, 11.4%, and 1.7%, respectively. Factors associated with HIV infection were being ≤24 years [odds ratio (OR) = 2.85, 95% confidence interval (CI): 1.05 to 7.75], syphilis positive (OR = 4.78, 95% CI: 1.68 to 13.58), used non–water-based liquid as lubricant (OR = 8.03, 95% CI: 1.03 to 62.52), and having bleeding gums or oral ulcers during condom-free oral sex (OR = 3.17, 95% CI: 1.13 to 8.88).

Conclusions: MSMUI engage in high-risk sexual behaviors and have a high prevalence of HIV and syphilis infections. The internet is the predominant venue for the majority of MSMUI to find sexual partners. It is urgent to implement effective intervention programs targeting this group.

Key Words: China, HIV, internet, men who have sex with men, syphilis

(*J Acquir Immune Defic Syndr* 2010;53:S81–S87)

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Supported by the China Multidisciplinary AIDS Prevention Training Program with NIH Research Grant #U2R TW 006918, funded by the National Institutes of Health, the Fogarty International Center, the National Institute of Drug Abuse, and the National Institute of Mental Health (China ICOHRTA, with Principal Investigator Z. Wu).

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INTRODUCTION

In most developed countries, men who have sex with men (MSM) were the first group affected by HIV/AIDS and they still account for a large proportion of reported HIV/AIDS cases.[1,2] China's HIV/AIDS epidemic has progressed differently with intravenous drug users and former commercial blood donors accounting for more than 62% of accumulated HIV/AIDS cases between 1985 and 2006.[3] HIV transmission through blood transfusion has been stopped; and methadone maintenance treatment, needle exchange programs, and health education have helped reduce the spread of HIV among drug addicts in China.[4,5] Studies indicated rapid rising rates of HIV infection among MSM in China. In 2005, MSM accounted for 7.3% of China's estimated 650,000 people living with HIV/AIDS, however, by 2007, this figure had increased to 12.2% of the estimated 700,000 HIV/AIDS cases.[3] The proportion of MSM in reported cases of HIV/AIDS in the China national notifiable disease system has dramatically increased from 0.4% in 2005 to 3.3% in 2007.[3,6]

Various determinants increase the likelihood MSM have large numbers of multiple lifetime sexual partners and engage in high-risk sexual behaviors rendering them more vulnerable to HIV and sexually transmitted infections (STIs).[7,8] If appropriate and effective actions are not taken, China may face a significant increase in HIV infection among MSM.

According to the China Internet Network Information Center, by September 2007, nearly 71 million urban adult males were using the internet.[9] It is estimated that 10%–15% of adult males in China have had lifetime male/male sexual experiences including kissing, fondling, mutual masturbation, and oral and anal sex.[10]

MSM are increasingly using the internet to look for sex, and significant associations between internet sex-seeking and high-risk sexual behaviors have been reported.[11–13] There are growing numbers of international studies indicating sexual intercourse with male partners met online increases HIV/STIs risk,[12,14] however, the characteristics of Chinese men who have sex with men who use the internet (MSMUI) have not yet been well documented. The nature of the internet makes it an ideal venue for recruiting understudied, at-risk groups,[14] such as Chinese MSM who might be less willing to respond to more conventional research approaches. To better understand MSMUI in China, we conducted a cross-sectional survey of 429 MSMUI in 2 cities in China in 2007.

METHODS

Participants, Recruitment, and Fieldwork Sites

In this study, MSM refers to men who have already had, or intent to have, oral or anal sex with other men and if not specified, sexual partners refers to male sexual partners. For 2 weeks before survey commencement (June 11 to July 11 in Beijing; July 16 to August 17 in Urumqi) and during the survey, identical banners containing information concerning our study were placed on the main pages of a national gay website and a Beijing-based MSM volunteer website inviting MSM to participate in our study. Contact information was also posted on 3 major national gay partner-seeking websites and 1 Xinjiang-based gay online chat room for recruiting participants.

Qualified participants met the following criteria: (1) ever had or likely to have sex with a man; (2) 18 years or older; (3) accessed gay information on the internet in the 3 months before study commencement. All participants were invited to come to the 2 voluntary counseling and testing (VCT) centers between 6 PM and 10 PM local time during the survey period. To ensure cohort compliance with enrollment requirements, the survey designer and an MSM community member were present at the VCT centers to screen participants for the duration of the study.

The study was based off-line in 2 VCT site, 1 in Beijing Xicheng District Center for Disease Control and Prevention (CDC) in Beijing and 1 in Xinjiang Uighur Autonomus Region CDC in Urumqi (the capital city of Xinjiang Uighur Autonomous Region).

Survey Content

Consenting participants were interviewed face-to-face by trained interviewers. Qualified HIV/STI counselors gave HIV counseling and provided referrals for social support or medical services as needed. A 5 mL of intravenous blood sample was collected for HIV and syphilis testing. All participants who completed questionnaires received 50 Chinese yuan renminbi (RMB) (about US $7.5) and some small gifts (condoms, lubricant, MSM health booklet) for their participation. Participants were surveyed on their sociodemographic characteristics, internet use, and HIV-related risk behaviors.

Specimen Test

Blood samples were tested for HIV antibody using an enzyme-linked immunosorbent assay (Bio-Merieux, Boxtel, Netherlands), and positive results were confirmed by a HIV-1/2 Western Blot (HIV Blot 2.2 WB, Genelabs Diagnostics, Cavendish, Singapore). Syphilis antibodies were screened by enzyme-linked immunosorbent assay (Shanghai Kehua Bio-logic Production Company, Shanghai, China). Reactive samples were confirmed by a passive particle agglutination test for detection of antibodies to *Treponema pallidum* (Serodia TPPA; Fuji-rebio Inc, Tokyo, Japan).

Ethics

Trained investigators explained to participants the aim, process, benefits, and potential risks of study participation before obtaining informed consent. Participants were informed survey participation was anonymous and voluntary, and they had the right to discontinue participation at any time. Ethical approval was obtained from the institutional review board of the National Center for AIDS/STD Control and Prevention, China CDC, Beijing.

Data Analysis

EpiData software (EpiData 3.0 for Windows; The EpiData Association, Odense, Denmark) was used to double enter and validate the data. Statistical Analysis System (SAS 9.1 for Windows; SAS Institute Inc, Cary, NC) was used to analyze the data. A χ^2 test was performed to assess whether proportions of key indexes between MSMUI from the 2 locations had any statistically significant differences. Logistic regression analysis was performed to assess potential risk factors related to HIV infection.

RESULTS

A total of 429 MSMUI were recruited; of whom, 153 were recruited from responding to the banners, 176 from collected contact details posted online, and 70 were referred by friends who had participated in the study. Of the 429 participants, 420 provided a blood specimen (of the 9 who did not provide a blood specimen, 6 were hematophobic and 3 believed they had no risk for infection and thus refused to provide a sample) and 399 completed a questionnaire (30 participants went to the VCT clinics when investigators were not present, so they did not complete the questionnaire but provided a blood sample and basic sociodemographic information). HIV/syphilis infection rates were based on data of the 420 men who provided a blood specimen. Logistic regression of potential factors influencing HIV infection was based on data of the 390 men who both provided a blood specimen and completed a questionnaire. Other statistics were based on data of the 399 men who completed a questionnaire. χ^2 tests showed that there were no significant differences in proportions of key indexes (age, $\chi^2 = 0.95$, $P = 0.33$; ethnicity, $\chi^2 = 0.31$, $P = 0.58$; HIV infection rate, $\chi^2 = 0.29$, $P = 0.59$) between samples from the 2 cities. Analysis was based on the data from the 2 cities combined together.

Most articipants were young, educated, never married, and identified as homosexual (Table 1). Infection rates of HIV, syphilis, and HIV/syphilis coinfection were 4.8% (20 of 420), 11.4% (48 of 420) and 1.7% (7 of 420), respectively. MSM who had a low education level (senior high school or less) had a higher HIV rate (11.2%) compared with those who had a high education level (having some college or above, HIV rate of 2.47%, $P = 0.001$). Local resident had a lower HIV infection (1.5%) compared with non–local resident (6.6%, $P = 0.043$).

Lifetime Sexual Behaviors

The median number of lifetime sex partners was 10 (range: 0–1000) (Table 2). Rates of condom use in the last oral, insertive, and receptive anal sex were 9.1% (35 of 385), 66.3% (220 of 332) and 60.4% (200 of 331), respectively. Nearly 40% of participants consistently used condoms in both insertive and receptive anal sex in the past 6 months. Nearly half (164 of 399) ever had sex with a female partner and 42.1% (69 of 164) used condoms in the last such sex. The average age of sexual

TABLE 1. Sociodemographic Characteristics of MSMUI

Characteristics	Questionnaire n (%)*	Biological Specimen		
		No. Subject	HIV+ (%)†	Syphilis (%)†
Age, yrs (median age = 25 yrs)				
18–24	171 (42.9)	166	11 (6.6%)	17 (10.2)
25–29	123 (30.8)	122	2 (1.6)	15 (12.3)
30–39	88 (22.1)	86	5 (5.8)	11 (12.8)
40–56	17 (4.3)	16	1 (6.3)	4 (25.0)
Marital status				
Never married	334 (83.7)	326	14 (4.3)	38 (11.7)
Currently married	46 (11.5)	45	3 (6.7)	4 (8.9)
Separated/divorced	19 (4.8)	19	2 (10.5)	5 (26.3)
Education				
Junior high school or less	16 (4.0)	16	6 (37.5)‡	5 (31.3)
Senior high school	93 (23.3)	91	6 (6.6)	8 (8.8)
Some college	244 (61.2)	238	7 (2.9)	33 (13.9)
Postgraduate or more	46 (11.5)	45	0 (0.0)	1 (2.2)
Beijing/Urumqi local resident				
Yes	135 (33.8)	131	2 (1.5)‡	14 (10.7)
No	264 (66.2)	259	17 (6.6)	33 (12.7)
Ethnicity				
Han	362 (90.7)	353	17 (4.8)	41 (11.6)
Other§	37 (9.3)	37	2 (5.4)	6 (16.2)
Salary (RMB)‖				
<500	84 (21.1)	83	3 (3.6)	6 (7.2)
500–	40 (10.0)	38	4 (10.5)	4 (10.5)
1000–	119 (29.8)	116	7 (6.0)	19 (16.4)
2000–	156 (39.1)	153	5 (3.3)	18 (11.8)
Self reported sexual orientation				
Homosexual	283 (70.9)	278	13 (4.7)	38 (13.7)
Bisexual	1 (0.3)	1	1 (100.0)	1 (100.0)
Heterosexual	74 (18.5)	72	3 (4.2)	5 (6.9)
Undecided	41 (10.3)	39	2 (5.1)	3 (7.7)
Occupation				
Office clerk	149 (37.3)	142	5 (3.5)	24 (16.9)
Student	93 (23.3)	92	2 (2.2)	5 (5.4)
Civil servant	20 (5.0)	20	2 (10.0)	3 (15.0)
Other	120 (30.1)	119	8 (6.7)	12 (10.1)
Unemployed	17 (4.3)	17	2 (11.8)	3 (17.6)

*Proportions were analyzed based on data of the 399 men who completed a questionnaire.

†HIV+ and syphilis refer to HIV and syphilis infection, respectively, % refers to infection rate, as some participants did not provide blood specimen, the denominators in this column do not necessarily equal to subjects who completed questionnaire survey.

‡Senior high school or less compared with college or above, Fisher exact $P = 0.001$; local resident compared with nonlocal resident, Fisher exact $P = 0.043$.

§Other ethnicities included Uighur, Kazak, Hui, and Man.

‖The currency exchange rate was 7 RMB equaled approximately 1 US Dollar at the time of the study.

debut was 21, and the average absolute duration between realization of sexual orientation and first sex with a male was 3 years. No statistical difference was found in any of sexual behavioral variables for HIV and/or syphilis infections.

Internet-Related Sexual Behaviors

The internet was the most popular venue to find sexual partners with 82.2% (328 of 399) using it, followed by cafés or bars (14.8%, 59 of 399), bath houses (14.3%, 57 of 399), and parks and toilets (13.3%, 53 of 399) (Table 3). 13.8% (55 of 399) did not use the internet to find sexual partners but did use more traditional venues. Fifteen participants did not respond and 1 had never had sex with a man. Among MSMUI who were 24 years or younger, 83.6% (143 of 171) used the internet to find sexual partners. The next most common venue used by this group was bars (19.9%, 34 of 171). Among MSMUI older than 24 years, 81.1% (185 of 228) used the internet to find sexual partners. The next most common venue used by this group was bath houses (19.7%, 45 of 228).

Almost all (382 of 399) had ever met a male cyber friend (initial contact made online) offline and (362 of 399) had ever had sex with a cyber friend, with 69.1% (257 of 362) having

TABLE 2. Lifetime Sexual Behaviors of MSMUI*

Characteristics	Questionnaire n (%)*	Biological Specimen		
		No. Subject	HIV (%)†	Syphilis (%)†
No. male sex partners				
0	1 (0.3)	1	0 (0.0)	0 (0.0)
1	16 (4.0)	15	0 (0.0)	2 (13.3)
2–10	221 (55.4)	214	8 (3.7)	17 (7.9)
11–500‡	161 (40.4)	160	11 (6.9)	28 (17.5)
Condom use in last oral sex				
Yes	35 (9.1)	34	1 (2.9)	4 (11.8)
No	350 (90.9)	343	18 (5.2)	41 (12.0)
Condom use in last insertive anal sex				
Yes	220 (66.3)	215	12 (5.6)	34 (15.8)
No	112 (33.7)	110	4 (3.6)	8 (7.3)
Condom use in last receptive anal sex				
Yes	200 (60.4)	195	11 (5.6)	29 (14.9)
No	131 (39.6)	129	8 (6.2)	13 (10.1)
Frequency of condom use in insertive anal sex in past 6 months				
Never (=0%)	29 (10.3)	29	0 (0.0)	0 (0.0)
Occasionally (≤50%)	55 (19.6)	55	4 (7.3)	6 (10.9)
Often (>50%)	87 (31.0)	85	5 (5.9)	11 (12.9)
Always (100%)	110 (39.1)	108	4 (3.7)	17 (15.7)
Frequency of condom use in receptive anal sex in past 6 months				
Never	32 (11.9)	32	0 (0.0)	0 (0.0)
Occasionally	56 (20.7)	56	4 (7.1)	5 (8.9)
Often	75 (2.8)	72	4 (5.6)	15 (20.8)
Always	107 (39.6)	105	7 (6.7)	16 (15.2)
Perception of risk of HIV infection				
Not at all	70 (17.5)	66	2 (3.0)	6 (9.1)
Very low (<50%)	167 (41.9)	161	6 (3.7)	19 (11.8)
Possibly (50%)	65 (16.3)	65	2 (3.1)	8 (12.3)
Very likely (>50%)	13 (3.3)	13	3 (23.1)	3 (23.1)
Don't know	84 (21.1)	84	6 (7.1)	11 (13.1)
Ever tested for HIV				
Yes	191 (47.9)	185	8 (4.3)	34 (18.4)
No	208 (52.1)	205	11 (5.4)	13 (6.3)
Ever had STIs				
Yes	105 (26.3)	102	8 (7.8)	19 (18.6)
No	294 (73.7)	288	11 (3.8)	28 (9.7)
Ever had sex with a woman				
Yes	164 (41.1)	161	10 (6.2)	22 (13.7)
No	235 (58.9)	229	9 (3.9)	25 (10.9)
Condom use in last vaginal/anal sex with a female partner				
Yes	69 (42.1)	66	5 (7.6)	11 (16.7)
No	95 (57.9)	95	5 (5.3)	11 (11.6)

*Proportions were based on data of the 399 men who completed a questionnaire.

†HIV+ and syphilis refer to HIV and syphilis infection, respectively, % refers to infection rate, as some participants didn't provide blood specimen, the denominators in this column do not necessarily equal to subjects who completed questionnaire survey.

‡Can be disaggregated into 11–20 (18.3%, 73 of 399), 21–50 (12.5%, 50 of 399), and 51–1000 (9.5%, 38 of 399).

1–10 sexual cyber friends and 29.0% (105 of 362) having 11 or more such partners. More than half (220 of 398) met their first male sexual partner online. Percentages of condom use in the last oral sex, insertive anal sex, and receptive anal sex with cyber friends were 7.2% (25 of 349), 69.6% (201 of 289), and 68.7% (202 of 294), respectively. Most (270 of 382) never inquired about the HIV infection status of a newly met cyber friend.

No statistical difference was found in any of internet-related sexual behavioral variables for HIV and/or syphilis infections.

Perception of HIV/STIs Risk, Condom Use, and HIV/STIs Testing

Nearly half (47.9%, 191 of 399) had ever tested for HIV, and 26.3% reported at least 1 type of lifetime STI. A majority (59.5%, 237 of 399) of participants still perceived themselves to be at no or little risk of HIV infection and 21.1% (84 of 399) could not define their perception of risk. Within the ≤24 age group, rates of constant condom use during insertive and receptive anal sex within the past 6 months, respectively, were 47.1% (33 of 70) and 46.1% (35 of 75) for those who perceived no or little risk of HIV infection, 17.6% (3 of 17) and 9.5% (2 of 21) for those who perceived high or very high risk of HIV infection, and 34.8% (8 of 23) and 16.7% (5 of 30) for those who could not define their level of risk.

Nearly all (94.2%, 180 of 191) who ever tested for HIV knew the result of their last test, however, more than half (59.4%, 237 of 399) believed they were at no or low risk for HIV. More than half (59.6%, 28 of 47) of the syphilis-positive MSM who completed the questionnaire reported no STIs. Among those reporting a history of HIV/STIs, after diagnosis, almost all (99.0%, 104 of 105) reported using at least 1 method to reduce transmission of HIV/STIs, of which 57.1% (60 of 105) reduced the number of sexual partners, 29.5% (31 of 105) decreased penetrative sexual behaviors, 83.8% (88 of 105) used condoms on a regular basis, and 37.1% (39 of 105) started to test for HIV.

Factors Influencing HIV Infection

Table 4 shows logistic regression analysis of risk factors for HIV infection. Being 24 years or younger [odds ratio (OR) = 2.85, 95% confidence interval (CI): 1.05 to 7.75], being syphilis positive (OR = 4.78, 95% CI: 1.68 to 13.58), having used saliva as a substitute for lubricant (OR = 8.03, 95% CI: 1.03 to 62.52), and having bleeding gums or oral ulcers during oral sex (OR = 3.17, 95% CI: 1.13 to 8.88) were associated with HIV infection. However, the number of male sexual partners (OR = 1.00, 95% CI: 0.995 to 1.01) and being circumcised (OR = 0.73, 95% CI: 0.19 to 2.81) were not associated with HIV infection.

DISCUSSION

MSMUI had a high level of education as nearly three quarters had an education of some college or more, this is similar to other studies surveying MSM via the internet in China.[10,15] With nearly a quarter of the MSMUI in our sample being students, education campaigns targeting student MSM websites may be valuable in controlling HIV/syphilis infection among this subpopulation of MSMUI.

MSMUI in China tend to be younger than MSM samples recruited offline. The median age of this sample (25 years) was

TABLE 3. Internet Use and Sexual Risk Behaviors of MSMUI

Internet Use and Risk Behaviors	Questionnaire n (%)*	Biological Specimen		
		No. Subject	HIV (%)†	Syphilis (%)†
Ever met a male cyber friend				
Yes	382 (95.7)	373	18 (4.8)	45 (12.1)
No	17 (4.3)	17	1 (5.9)	2 (11.8)
Met your first sexual partner via the internet				
Yes	220 (55.8)	213	6 (2.8)	18 (8.5)
No	179 (44.2)	177	13 (7.3)	29 (16.4)
No. male sex partners known via the internet				
0	37 (9.3)	37	3 (8.1)	3 (8.1)
1	46 (11.5)	41	2 (4.9)	2 (4.9)
2–10	211 (52.9)	208	9 (4.3)	22 (10.6)
11–380‡	105 (26.3)	104	5 (4.8)	20 (19.2)
Condom use in oral sex with a newly met cyber friend?				
Yes	25 (7.2)	25	0 (0.0)	4 (16.0)
No	324 (92.8)	317	15 (4.7)	38 (12.0)
Condom use in insertive anal sex with a newly met cyber friend?				
Yes	201 (70.0)	198	7 (3.5)	30 (15.2)
No	86 (30.0)	84	4 (4.8)	9 (10.7)
Condom use in receptive anal sex with a newly met cyber friend?				
Yes	202 (68.7)	198	9 (4.5)	29 (14.6)
No	92 (31.3)	90	5 (5.6)	10 (11.1)
Frequency of watching online gay porn				
Often (once a week or more)	129 (32.3)	126	3 (2.4)	14 (11.1)
Occasionally (once a month or more)	176 (44.1)	171	11 (6.4)	21 (12.3)
Seldom (less than once a month)	94 (23.6)	93	5 (5.4)	12 (12.9)
Ever watched gay porn before meeting a male cyber-friend				
Yes	211 (53.1)	205	7 (3.4)	29 (14.1)
No	186 (46.9)	183	12 (6.6)	17 (9.3)
Watching gay porn increases the possibility of sexual risk behaviors				
Yes	135 (33.8)	132	5 (3.8)	8 (6.1)
No	264 (66.2)	258	14 (5.4)	39 (15.1)
Meeting a cyber friend in which time to span most likely results in unsafe sex				
8–12 AM	7 (1.8)	7	2 (28.6)	3 (42.9)
12–18 AM	11 (2.8)	11	1 (9.1)	1 (9.1)
18–24 AM	242 (61.4)	237	9 (3.8)	29 (12.2)
24–8 AM	134 (34.0)	130	7 (5.4)	13 (10.0)
Do you support online HIV/STIs counseling?				
Yes	385 (96.5)	376	19 (5.1)	45 (12.0)
No/whatever	14 (3.5)	14	0 (0.0)	2 (14.3)
Who do you think are optimal counselors?				
Clinical doctors	187 (46.9)	182	10 (5.5)	25 (13.7)
CDC staff	219 (54.9)	214	13 (6.1)	27 (12.6)
MSM	164 (41.1)	162	11 (6.8)	25 (15.4)
Psychologist/psychiatrist	218 (54.6)	213	11 (5.2)	30 (14.1)

*Proportions were based on data of the 399 men who completed a questionnaire.

†HIV+ and syphilis refer to HIV and syphilis infection, respectively, % refers to infection rate, as some participants did not provide blood specimen, the denominators in this column do not necessarily equal to subjects who completed questionnaire survey.

‡This section can be disaggregated into 11–20 (14.3%, 57 of 399) and 21–380 (12.0%, 48 of 399).

younger than noninternet samples.[7,8,10] Younger MSMUI tend to engage in more high-risk sexual behaviors than older MSM[16,17] and greater frequency of high-risk sexual behaviors is related to higher rates of HIV infection.[18,19] This relative youth may have implications for HIV/syphilis infection as the results indicate MSMUI ≤24 years have a higher HIV infection rate than those >24 years. Reasons for this might be: (1) they are sexually active, (2) they lack awareness of the concept of self-protection while having sex, and (3) they are comparatively passive in their sexual contacts with older partners and thus are in a disadvantaged position to protect themselves. China may face a widespread HIV epidemic

TABLE 4. Potential Factors Related to HIV Infection Among MSMUI*

Variable	HIV Infection			
	Crude OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Age				
>24	1	—	1	—
≤24	1.03 (0.96 to 1.10)	0.45	2.85 (1.05 to 7.75)	0.04
Syphilis infection				
Negative	1	—	1	—
Positive	4.83 (1.80 to 12.97)	0.002	4.78 (1.68 to 13.58)	0.003
Bleeding gums/oral ulcer during oral sex				
Never	1	—	1	—
Ever	3.02 (1.14 to 7.99)	0.026	3.174 (1.13 to 8.88)	0.028
Used saliva as lubricant in sex				
Never	1	—	1	—
Ever	7.68 (1.01 to 58.20)	0.049	8.03 (1.03 to 62.52)	0.047

*Analysis performed on the data of the 390 men who completed a questionnaire and provided a blood specimen.

†Number of sexual partners and circumcision were included in the logistic regression but were not associated with HIV infection, and data were not shown.

among young MSMUI without timely interventions targeting this population. As the internet can be used effectively to provide sex education to young people in China,[20] websites targeting student MSMUI may be used to provide health and sexual information.

The internet has become an important venue for MSM in China to find sex partners.[15] A possible reason for the popularity of the internet as a sex partner seeking venue is that it offers some anonymity, allowing them to make contact with other MSM or to find specific types of partners, without negative social consequences in a time-efficient manner.[11,13,21] This may explain why the median number of lifetime sexual partners of MSMUI was higher than that of non–internet-using MSM in China with a similar median age.[7,8,22] Public health efforts to communicate with MSMUI must use the internet as this population may not be reached by traditional outreach methods.

A study in 6 US cities found young MSM with a low-risk perception reported considerable high-risk behaviors.[23] This study found within the ≤24 years group, rates of constant condom use during insertive and receptive anal sex within the past 6 months were considerably higher among those who perceived no or little risk of HIV infection than among those who perceived high or very high risk of HIV infection (47.1% and 46.7% vs. 17.6% and 9.7%). MSMUI might consider more condom use equals decreased risk and therefore perceive less risk when condoms are used more often.

A study in San Francisco showed MSM continued to engage in risky sexual behaviors when diagnosed STI negative.[24] Most participants were unaware of their STIs status as nearly 60% of syphilis-positive MSMUI reported no STIs. There are significant barriers for MSM in China to receive timely STI diagnosis and treatment: the price for diagnosis and treatment of STIs is high; MSM experience discrimination from clinic doctors and nurses; it takes days to receive test results; and the quality of clinical laboratory testing is not high and physicians often misdiagnose STIs.[25] MSM in our study craved trustworthy and effective gay-friendly STIs clinics where they can receive appropriate therapy at a reasonable price. They preferred a MSM community member with a medical and psychological background to provide online HIV/STI counseling. Efforts should be made to expand coverage of HIV/STIs testing among MSMUI so as to increase their awareness of their serostatus. This may also have the effect of encouraging safer sexual practices as almost all (99.0%, 104 of 105) participants who reported HIV/STIs history tried to use at least 1 way to avoid transmitting HIV/STIs to others.

Most MSM who use the internet are in urban areas as internet coverage in the countryside is still limited. Two-thirds of participants in out study were not local residents of the study cities. This confirms the results of a qualitative study conducted in Shanghai.[9,26] Nonresident MSM in China have a higher rate of sexual risk behaviors and HIV/STIs infection than resident MSM,[7,10,22] which our study confirms as 85.0% (17 of 20) of HIV carriers and 68.8% (33 of 48) of syphilis carriers were nonlocal residents. Nonresident MSM faced difficulties in maintaining long-term relationships partly due to economic instability and the lack of a private dwelling. This subgroup is in immediate need of psychological support and HIV/STIs services.

Although the sampling methods used avoid the shortcomings of traditional sampling methods and surveys completed online,[2,12] they have their limitations. MSM who use the internet only represent a portion of the MSM population in China, and the results of our study can not be generalized to all MSM in China. The results may not be generalizable to MSMUI in all cities in China, as it is possible there are behavioral differences in different regions. In addition, internet-use behaviors change rapidly China, so the results may only be applicable to the study period. Participants may have confused the purposes of the research with the provision of clinical care as testing for HIV/Syphilis was provided, therefore, a representative sample of MSMUI may not have been obtained.

CONCLUSIONS

We found that MSMUI engage in high-risk sexual behaviors and have high infection rates of HIV/Syphilis. More efforts are needed to enhance HIV/STIs counseling, testing, and treatment services. Online counseling facilitated by scaled-up online public health campaigns might be an effective manner of benefiting this population.

ACKNOWLEDGMENTS

The authors are grateful to health officials and MSM community members in Beijing and Urumqi who supported the study and to subjects who participated in the study.

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A Pilot Intervention to Increase Condom Use and HIV Testing and Counseling Among Men Who Have Sex With Men in Anhui, China

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Objective: To test the feasibility of a peer-driven behavioral intervention and to evaluate efficacy in reducing HIV-related risk among men who have sex with men (MSM) in China.

Methods: Twelve seeds were recruited from traditional MSM venues and a total of 218 MSM were enrolled into 12 intervention groups participating in 4 intervention sessions. The intervention was conducted from May to October 2006 in Anhui Province. Reported condom use and HIV testing were used as outcome indicator to evaluate effectiveness of intervention.

Results: Average age was 25.5 years old, 64.2% reported homosexual orientation, and 22.5% bisexual orientation. 77.9% of participants were followed up 3 months after intervention completion. Self-reported condom use measured as use in last 3 episodes of anal intercourse with another man increased from 55.3% at baseline to 65.2% postintervention, whereas HIV testing increased from 10.0% at baseline to 52.4% postintervention. No significant reduction in the number of male sexual partners occurred; however, number of female sexual partners decreased significantly.

Conclusions: Interventions are effective in increasing condom use and HIV testing but not in reducing the number of sexual partners. Expansion of such intervention needs to be further explored.

Key Words: China, HIV testing, intervention, men who have sex with men, sexual behavior

(*J Acquir Immune Defic Syndr* 2010;53:S88–S92)

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Supported by the China Multidisciplinary AIDS Prevention Training Program with NIH Research Grant U2RTW006917 and U2RTW006918, funded by the National Institutes of Health, the Fogarty International Center, the National Institute of Drug Abuse, and the National Institute of Mental Health (China ICOHRTA, with Principal Investigator Z. Wu).

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INTRODUCTION

Global and regional trends in the HIV/AIDS pandemic exhibit 2 distinct patterns: generalized and concentrated epidemics. In Latin America, North America, and Western Europe, concentrated epidemics of sex between men is the dominant mode of HIV transmission.[1,2] Moreover, transmission has been found to spread rapidly among men who have sex with men (MSM). In Thailand alone, HIV prevalence among MSM was found to have increased 11.3% between 2003 and 2005, and as much as 21% of estimated new infections in 2005 were attributed to unprotected sex among MSM.[3]

In 2005, a joint assessment report by the Chinese Ministry of Health and United Nation Theme Group on AIDS estimated that HIV infections among MSM accounted for 7.3% of the total number of the 650,000 estimated HIV cases in China.[4] The 2007 joint assessment report estimated that this proportion had increased to 11.0%; whereas of the estimated 50,000 HIV infections, MSM were thought to account for 12.2% of the total infections.[5] Other studies have also shown rapid increases in HIV prevalence among MSM. A study found a HIV prevalence of 0.4% in 2004, 4.6% in 2005, and 5.8% in 2006 in Beijing,[6] whereas another 2 studies conducted in southwestern China found prevalence rates as high as 10.6% in 2006[7] and 16.9% in 2007 among sampled MSM.[8] The results from the above surveys indicate that HIV epidemic among MSM in China has reached crisis proportions in certain areas and that MSM are a key target populations for future prevention efforts.

MSM in China is an understudied population. Limited studies show that Chinese MSM engage in high-risk sexual behaviors, including sex with multiple and different types of sexual partners, low condom-use rates, and low rates of HIV testing. For example, a national survey of 1124 MSM in 2001 indicated that unprotected oral and anal sex were common practices, approximately 13.7% had commercial sex and 44.0% were married to women.[9] A study of gay bars in Anhui Province found that in a 2-month recall period, 19.5% of respondents reported having engaged in casual, commercial, female and/or male primary sexual partners concurrently.[10]

Chinese MSM have also been found to have low rates of consistent condom use. A 2001 study conducted in Beijing found that 6.2% and 30.9% of MSM reported consistent condom use in oral and anal sex in the past 6 months, respectively.[11] Similarly, a national study in China found the rate of condom use for last recalled oral and anal intercourse

was 17.8% and 54.8%, respectively,[12] and surveys conducted among MSM in Shenzhen in the southeast and Hefei in eastern China revealed similar findings.[13,14]

Voluntary HIV testing services have been expanded rapidly in past a few years, most MSM are not aware of their own HIV serostatus.[9,10,15] In 2005, only 24.5% of MSM in Hefei reported ever being tested for HIV, and 31% of respondents were not aware of free voluntary counseling and testing services.[15]

Previous HIV interventions among MSM in China have largely consisted of distributing condoms and educational materials through MSM volunteers and often in MSM social venues.[16–18] To date, however, there has not been a scientific evaluation of the efficacy of these intervention efforts, making it imperative that behavioral interventions targeting MSM are designed to be rigorously assessed. This peer-driven intervention is designed as a group intervention that utilizes existing peer networks and focuses on the 3 goals of increasing condom use, increasing HIV testing, and reducing the number of sexual partners among MSM.

METHODS

Study Location and Participant Recruitment

The study was conducted during May to October 2006 in Hefei, Wuhu, and Fuyang, 3 cities in Anhui Province, where researchers were able to locate gay bars and contact participants through local MSM networks. Peer-driven referral was used to recruit potential study participants. Eligibility criteria included (1) age more than 18 years; (2) sex with other men in the past year; and (3) living in Hefei, Wuhu, or Fuyang during the study period.

Twelve "seed" MSM, a member of the targeted population widely respected by his peers, were recruited from our previous study to create seeds for this study.[19] In addition to the above eligibility criteria, seeds also had to consent to undergo leadership training, to recruit peers to take part in the intervention study, and to lead intervention activities for their peers. Each seed was asked to refer up to 3 peers, who in turn recruited 3 of his own peers, and so on. In this manner, a total of 218 MSM participants were recruited.

Intervention Design and Outcome Indicators

A peer-driven behavioral intervention was chosen to influence the MSM peer networks. Each intervention group consists of a seed and his referral chain made up of his peers. Confidentiality and informed consent were strictly observed in this study. Investigators explained the aims, significance, benefits, and potential risks of the study to all eligible MSM, and willing participants provided written consent before study commencement.

The intervention was based on the AIDS Risk Reduction Model[20] and consisted of 4 1.5-hour sessions with activities such as role playing, games, group discussions, brainstorming, and competitions to test knowledge. The first session focused on behavior labeling, (ie, identifying HIV high-risk behaviors, including assessing knowledge of HIV transmission and prevention) and evaluating individual high-risk behaviors. Participants were assessed on their knowledge of HIV transmission, prevention, and correct condom use. Evaluation of individual high-risk behaviors was comprised of discussions of usual MSM behaviors, ways to evaluate the risk of HIV infection and transmission, and methods to protecting themselves. In session 2, participants develop individualized plan to make a commitment to changing their high-risk behaviors. During this session, open discussions about happiness and well-being were encouraged to improve the desire of MSM to change their behaviors. Additionally, identifying obstacles and finding solutions were discussed for the intent of planning changes in behavior. This session also included training on communication skills about sexual topics. Session 3 emphasized taking action to change high-risk behaviors. This session discussed the obstacles to safe sex and the solutions to overcome these obstacles. Participants were given an opportunity to communicate personal experiences and provide mutual support. Each participant continued to work on his own behavior change plan. The final session addressed ways to deal with barriers to practicing safe sex. Participants shared their experiences of having safe sex and discussed any difficulties encountered. They described situations in which they failed to engage in safe sex and then discussed the factors related to the situation and provided suggestions. Through role-play, participants also learned skills about having safe sex. These include practicing how to put a condom on a penis (using a banana); practice negotiating the use of different types of condoms and discussing which ones were more stimulating (eg, flavored, ribbed, colored, etc.); and discussing the feelings of happiness and the sense of well-being experienced by engaging in safe sex between lovers.

Intervention efficacy and feasibility was evaluated comparing pretest and posttest indicators, including sexual behaviors, HIV-related knowledge, condom use, and HIV testing history. Self-reported condom use was measured as use in the last 3 episodes of anal intercourse with another man. Recall period for other behaviors at posttest is for the past 2 months. Information was collected through self-administered questionnaires administered at baseline and in the third month after the intervention.

Statistical Analysis

EpiData 3.0 (The EpiData Association, Odense, Denmark) software was used to input the original data and Statistical Product and Service Solution 10.01 (SPSS Inc. Chicago, IL) was used to analyze the data. χ^2 tests were used to compare preintervention and postintervention indicators, including rate of HIV testing, condom use in male anal sex, and the number of male sexual partners and to compare different patterns of condom use between sex with males and sex with females. Rates of HIV testing, condom-use habits, and sexual partnering behaviors were analyzed using paired χ^2 tests to determine behavior change since baseline among the 170 participants who were followed up 3 months after the end of the intervention program.

RESULTS

Study Subject Characteristics

A total of 218 eligible MSM participated in this intervention. The mean age was 25.5 (median 24.0; SD: 6.8;

range: 18–61), and 64.2% reported homosexual orientation, whereas 22.5% reported bisexual orientation. Heterosexual and undecided sexual orientations accounted for 0.9% and 12.4%, respectively. The majority had completed at least tertiary education (65.6%), and current students (university or vocational school) accounted for 35.3% of participants. Migrants from other areas of China comprised 9.6% of participants (Table 1).

All participants took part in the first and second intervention activities, 75.2% (164 of 218) attended the third and the fourth intervention activities, and 77.9% (170 of 218) participants were followed up for assessment in the third month after completion of the intervention. Comparing participants who dropped out of the study (n = 48) versus those who were followed up after the study (n = 170), 3 variables of age (26.3 ± 8.9 vs. 25.2 ± 6.0), education level at least college (51.1% vs. 69.6%), and condom use in anal sex last 3 times (59.5% vs. 55.6%), no significant differences were found between the 2 groups at the baseline.

Recruitment Chains and Number of Recruitment Waves

Twelve MSM from gay venues (gay bars, public parks, and toilets) were recruited as seeds. From the first recruitment wave to the fifth, 16.5% (36 of 218), 34.8% (76 of 218), 32.6% (71 of 218), 12.4% (27 of 218), and 3.7% (8 of 218) of participants, respectively, were recruited. Of the 12 seeds' recruitment chains, 7 reached 5 waves (Table 2).

TABLE 1. Sociodemographic Characteristics of Participants

Variable	Number	Percentage (%)
Age group		
18–24	121	55.5
25–29	51	23.4
30–34	22	10.1
<35	24	11.0
Education		
College or higher	143	65.6
High school	73	33.5
Primary school	2	0.9
Occupation		
Student	77	35.3
Self-employed	33	15.1
Service employee	31	14.2
Factory worker	20	9.2
Civil servant	19	8.7
Teacher	13	6.0
Others	25	11.5
Marital status		
Unmarried	173	79.4
Married	34	15.6
Divorced	11	5.0
Sexual orientation		
Homosexual	140	64.2
Bisexual	49	22.5
Heterosexual	2	0.9
Undecided	27	12.4
Local household registration (hukou)		
Yes	197	90.4
No	21	9.6

Effects of the Intervention

χ^2 tests comparing baseline and postintervention indicators found that the rate of HIV testing in the last 2 months increased significantly from 15.1% (33 of 218) to 52.4% (89 of 170) ($P < 0.01$). Reported condom-use rates also improved, with the percentage of subjects who never used condoms during sex with men in the last 2 months decreased from 25.0% (34 of 136) to 9.4% (12 of 128) ($P < 0.01$) and the percentage of subjects reporting consistent use in last 3 instances of anal intercourse with a man increased from 49.8% (326 to 654) to 59.8% (305 to 510) ($P < 0.01$). No change was found in the number of male sexual partners reported by study subjects over the course of the intervention (Table 3).

The rate of HIV testing increased from 10.0% at the baseline to 52.4% at the follow-up ($P < 0.01$). There were improved rates of condom use in the last 3 instances of anal intercourse (from 55.3% to 65.2%, $P < 0.05$), with a similar improvement in condom-use rates with casual male sexual partners (from 43.2% to 52.2%; $P < 0.05$) and regular sexual partners (from 41.9% to 60.9%; $P < 0.01$). Meanwhile, the rate of having female sexual partners in the last 2 months decreased significantly from 17.6% to 11.2% ($P < 0.01$). No changes in the rates of having 1 or more male casual sexual partners and having 2 or more male sexual partners in the last 2 months were found (Table 4).

DISCUSSION

With the increase of HIV infection among MSM in China, there is an urgent need to develop interventions to promote condom use and HIV testing.[5–7,21] The primary aim of this study was to test the feasibility and effectiveness of a peer-driven behavioral intervention to reduce HIV-related risk behaviors among MSM in China. The results of this study may have important implications for future HIV prevention efforts among MSM in mainland, China.

TABLE 2. Numbers of Participants in the Recruitment Waves

	No. Participants in Recruitment Waves					
Seeds	1st	2nd	3rd	4th	5th	Total
A	3	7	9	2	1	22
B	3	5	11	0	0	19
C	3	8	3	3	0	17
D	3	7	4	1	0	15
E	3	6	5	2	1	17
F	3	8	6	3	1	21
G	3	6	4	3	1	17
H	3	8	15	5	2	33
I	3	5	2	3	1	14
J	3	4	0	0	0	7
K	3	9	5	3	0	20
L	3	3	7	2	1	16
Total	36	76	71	27	8	218

TABLE 3. HIV Testing and Sexual Behaviors Between Baseline and Follow-Up

Variable	Baseline	Follow-up	χ^2	*P*
Rate of HIV testing in the last 2 months	15.1% (33/218)	52.4% (89/170)	61.37	0.000
No condom use in anal sex with man in last 2 months	25.0% (34/136)	9.4% (12/128)	11.19	0.001
Condom use in last 3 anal intercourses	49.8% (326/654)	59.8% (305/510)	11.44	0.001
Had 2 or more male sexual partners in last 2 months	39.4% (86/218)	41.2% (70/170)	0.12	0.73
Had 1 or more male casual sexual partner in last 2 months	33.0% (72/218)	34.1% (58/170)	0.05	0.82
Total	218	170	—	—

Regarding feasibility, this study found that "seeds" played a crucial role in assisting researchers by leading intervention sessions and to maintain contact with participants throughout the study. These are important findings in light of results of a recent study in Shanghai which found that many Chinese MSM still experience social discrimination from family members, peers, colleagues, and employers even in large metropolitan cities.[22] Such environments lead many MSM to hide their sexual orientation and drive their risk behaviors underground where public health officials cannot perform effective interventions.[19] Nor have MSM been a traditional target group of public health authorities in China, although this is slowly changing.

Results of this study suggest that our intervention is effective in promoting HIV testing and increase condom use and may also decrease the number of female partners among MSM in China. Based on our findings, public health authorities could incorporate the peer-driven behavioral intervention model to conduct a multilocation trial to test the feasibility of a nation-wide scale up of HIV control and prevention programs targeting MSM. This is particularly applicable in China where MSM often seek out sexual partners via the internet, in discreet gay venues (bars frequented by MSM, bathhouses, parks, and public restrooms, etc), or through personal social networks.[19] In light of Chinese social and cultural norms, MSM intervention efforts must consider how to access MSM in a discreet manner that respects their privacy. Intervention programs must also work with members of the target community to identify acceptable ways of effecting sustainable behavior change.

A limitation of this study is that it is a preintervention and postintervention comparison design and uses self-reported behaviors as indicators of intervention efficacy rather than measuring new cases of HIV or sexually transmitted infections. A long-term objective therefore is the need to more accurately determine whether the peer-driven behavioral intervention model actually does reduce the incidence of HIV infection. Future studies will need to consider using randomized controlled trial designs to effectively measure the effectiveness of an MSM-targeted intervention.

TABLE 4. HIV Testing and Sexual Behaviors Between Baseline and Follow-Up, Results from Paired χ^2 Test

Variable	Baseline	Follow-up	*P*
Rate of HIV testing in the last 2 months	10.0% (17/170)	52.4% (89/170)	<0.01
Condom use in last 3 anal intercourses with men	55.3% (262/474)	65.2% (319/489)	<0.01
Condom use in last 3 anal intercourses with male casual sexual partners	43.2% (153/354)	52.2% (194/372)	0.02
Using condom in last 3 male anal intercourses with regular male sexual partner	49.1% (218/444)	60.9% (296/486)	<0.01
Nonuse of condoms in last anal sex with male casual sexual partners	35.3% (70/170)	27.1% (46/170)	0.04
No condom use in last intercourse with male or female regular sexual partner	45.3% (70/170)	31.2% (53/170)	<0.01
Had female sexual partner in the last 2 months	17.6% (30/170)	11.2% (19/170)	<0.01
Had 2 or more male sexual partners in the last two months	38.2% (65/170)	41.2% (70/170)	0.60
Have 1 or more male casual sexual partners in last 2 months	32.4% (55/170)	34.1% (58/170)	0.78
Total	170	170	—

CONCLUSIONS

Our study has found that peer-driven behavioral interventions are culturally and socially acceptable to Chinese MSM, can increase condom use and HIV testing among MSM in China, and can decrease the number of female sexual partners. Decreasing the numbers of male sexual partners may be more difficult than increasing condom use among MSM in China.

ACKNOWLEDGMENTS

The authors would like to thank Naomi Juniper and Adrian Liau for editing the article and Kumi Smith for her comments.

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Microbicide Acceptability and Associated Factors Among Female Sex Workers and Male Clients in Kaiyuan County, Yunnan Province, China

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Objectives: To determine microbicide acceptability and associated factors among female sex workers (FSWs) and their clients in Yunnan, China.

Methods: Kaiyuan County, with high rates of HIV in FSWs, in Yunnan Province was chosen as the study site. Establishments were selected using stratified sampling, and FSWs were recruited using random sampling. Male clients of FSWs were also recruited. In-depth interviews and anonymous questionnaires were used to collect data. An acceptance rate was calculated for each individual variable, and factors associated with acceptability were assessed using multivariate analysis.

Results: Four hundred FSWs and 200 male clients were recruited. Microbicides were acceptable if they prevented HIV transmission effectively and safely, were lubricating, effective up to 24 hours, and <10 China Yuan (CNY) (US $1.50) per use. Eighty-one percent of participants indicated future intention to use microbicides. Factors associated with potential microbicide use included age, establishment stratum, price, perception of risk behavior, and knowledge of AIDS/sexually transmitted infections.

Conclusions: The acceptablitiy of microbmicides is high among FSWs and their clients. Development of effective and affordable microbicides has great potential for controlling sexual transmission of the HIV epidemic in China.

Key Words: acceptability, China, FSWs, male clients, microbicides

(*J Acquir Immune Defic Syndr* 2010;53:S93–S97)

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Supported by the US Center for Disease Control and Prevention Global AIDS Program, 5U62PS022883-5.

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INTRODUCTION

The HIV epidemic continues to grow worldwide. Among the 39.5 million people living with HIV in 2006, new HIV infections accounted for 4.3 million, and 85%–90% of new HIV infections were contracted through heterosexual transmission.[1] Interacting synergistically with the HIV epidemic is the epidemic of other sexually transmitted infections (STIs), some of which can exacerbate the infectivity of HIV and the host's susceptibility to HIV infection.[2]

The effectiveness and use of male and female condoms are limited by the need for women to negotiate their use with their sexual partners.[3] Microbicides, which are self-administered prophylactic agents applied to the vagina or rectum in various formulations and by various delivery methods hold great promise for HIV prevention among sexually active people. Microbicides allow women to control its use, instead of depending on men for the use of condoms, can impede transmission of HIV and/or other sexually transmitted pathogens, and some may even provide contraceptive protection.[4,5]

Increasingly, the major mode of HIV transmission in China is through heterosexual sexual contact, and the burden of HIV infections is among women, especially in female sex workers (FSWs). Sentinel surveillance data indicated that the rate of HIV infection in FSWs increased from 0.02% in 1995 to 1% in 2005,[6] and in 2007, 44.7% of new HIV infections were due to heterosexual transmission.[7] The urgent need in using microbicides to assist in limiting the sexual spread of HIV in China is clear. This article is the first to present research on male clients of FSWs (herafter referred to as male clients) attitudes toward microbicides in China.

METHODS

Study Site

The Kaiyuan County located in Yunnna was selected as the study site. An HIV prevalence of 11.9% (89 of 747) was found among FSWs in Kaiyuan in 2006 that was much higher than both the national (1%)[6] and Yunnan provincial average (1.7%).[8] This implies great potential of HIV transmission via sexual intercourse.

Participants, Sampling, and Data Collection

Establishment-based FSWs and their clients were the study participants. These establishments were divided into 3 strata according to the price of sexual service: >60 China

Yuan (CNY) (about US $9)—stratum A; 30–60 CNY (about US $4.50 to US $9)—stratum B; <30 CNY (US $4.50)—stratum C. Fifteen establishments each were selected from strata A and B, and 10 establishments were selected from stratum C. FSWs in selected establishments were recruited through random sampling, and no more than 15 FSWs were selected from each establishment.

Male clients were recruited by 1 of 3 methods. The first method was through FSWs recommending their clients, with each FSW limited to recommending 3 male clients. Another method was through snowball sampling, using male clients as seeds referred by FSWs. A third method was through Kaiyuan Center for Disease control and prevention (CDC) employees recommending people they knew who patronized FSWs.

Eligibility was defined as having commercial heterosexual sexual intercourse in the last month, having lived for more than 6 months in Kaiyuan county, and not planning to leave in the next 12 months. Male drug users were excluded.

In-depth interviews and anonymous questionnaires were used to collect data. There were separate questionnaire versions and interview outlines for FSWs and for male clients. The FSW questionnaire comprised 5 parts as follows: (1) sociodemographic characteristics; (2) AIDS/STI knowledge (16 questions); (3) history of gynaecopathia intravaginal drug and lubrication use; (4) sexual history, and (5) attitudes toward microbicides. The male client questionnaires comprised 4 parts as follows: (1) sociodemographic characteristics; (2) AIDS/STI knowledge (14 questions); (3) sexual history, and (4) attitudes toward microbicides. A preliminary survey was conducted to assess the suitability of both the in-depth interview outlines and the questionnaires and were revised as necessary. Questionnaires were completed by all eligible participants, whereas interviews were completed by a subset of the participants.

Informed participant consent was obtained, and subjects were assured that participation was anonymous and all information provided would be confidential. The questionnaire was administered by trained interviewers. An in-depth interview was conducted on FSWs' reported history of engaging in sexual intercourse while using intravaginal drugs. A similar interview was conducted with male clients on their history of sexual intercourse with women using intravaginal drugs.

In total, 420 FSWs and 241 male clients were recruited; 20 FSWs (19 had stopped sex work and 1 was deaf) and 41 male clients (20 were drug users and 21 had never received commercial sexual services) were excluded. Of the eligible participants (400 FSWs and 200 male clients), none refused to participate, and all completed questionnaires. All of the 8 eligible FSWs and 43 eligible male clients completed in-depth interviews.

Data Analysis

The in-depth interviews were recorded by researchers, and the recorded data were transcribed. Using ATLAS.ti 5.0, researchers coded, compared, sorted, induced, and organized the data to obtain the results. Structured questionnaire data were entered into Epi Data 3.1 (The EpiData Association, Odense, Denmark) and were then analyzed by SPSS 13.0 (SPSS Inc, Chicago, IL) software for descriptive, univariate, and multivariate logistic regression methods to identify the factors associated with the acceptability of microbicides.

Ethics

The study protocol was approved by the Institutional Review Board of the National Center for AIDS/STD Control and Prevention of the Chinese Center for Disease Control and Prevention.

RESULTS

Characteristics of Participants

The demographic and risk characteristics of the 600 participants are reported in Table 1. The average age was 28 years for FSWs and 38 years for male clients. Education obtained was low for both FSWs and clients. The majority were single, separated, or windowed. More than half of FSWs reported previously using a vaginal product.

Participant Attitudes Toward Potential Microbicide Features

Most participants (73.67%) have never heard of microbicides and as an actual product is still currently unavailable;

TABLE 1. Demographic and Risk Characteristics of Participants

Characteristic	Female (n = 400)	Male (n = 200)
Establishment strata		
A	186	74
B	146	60
C	68	66
Median age (range)	28 (14–50)	38 (18–70)
Nationality, %		
Han	72.75	82
Education, %		
Primary school	35.3	33.5
Junior high school	54	43.5
Senior high school	10.5	23
Marital status, %		
Single/separated/widowed	78	64.5
Married/living with a partner	22	35.5
Monthly income, %		
Less than 500 CNY	14	17.5
500–1000 CNY	32.25	32.5
1000–2000 CNY	33	39.5
More than 2000 CNY	20.75	10.5
Condom use with commercial partners in the previous 6 months, %		
Every time	85.25	54.00
Often	12.25	22.50
Seldom	2.00	10.50
Never	0.50	13.00
History of STIs, %		
Yes	12	—
No	85.75	—
History of vaginal product use, %	57.75	—

CNY, China Yuan.

a description of microbicides was explained in detail to all participants.

Participants were asked to rank in descending order which features of the microbicide (contraception, disease prevention, pleasant to use, convenience, safety, comfort, and cleanliness) they considered to be the most important. Most participants (83.5%) regarded disease prevention, especially impeding the transmission of HIV, as the most important feature (Table 2).

More than half of participants (52.5%) hoped microbicides would be lubricating. Only female participants were asked about potential duration of microbicide effectiveness. The most frequently chosen duration was up to 24 hours (16.25%).

The range of price per application participants could choose was from 1 to 100 CNY. The most frequently chosen price (27.17%) was no more than 10 CNY per use.

Nearly three-quarters of female participants (70%) wanted to insert microbicides into the vagina using an applicator; 22 male clients with a history of anal intercourse also did not mind inserting microbicides into their partner's rectum with their fingers or with an applicator.

More than half of female participants (57.75%) would like microbicides to be available over the counte. Females thought the efficacy of microbicides was the most important feature (47.75%), whereas men were more concerned with the safety of microbicides (59.50%).

Acceptability of Microbicides

On the premise that microbicides are effective at preventing HIV and STIs, 90.17% of FSW participants were willing to accept changes in their vaginas after the insertion of microbicides, and 70% of male participants were able to accept leakage of microbicides.

The majority of participants (81%) (female and male) indicated that they would purchase and use microbicides in the future, and 78% of participants said they would use this product with their steady partner. After being informed that microbicides currently had an efficacy as low as 40% of the male condom for preventing HIV and STIs, 64% participants still thought it was necessary for China to import this product, whereas 36% of all participants (female and male) expressed that they did not want to use microbicides because they were worried about its safety and were uncomfortable with the idea of inserting something into their vagina/anus.

More than half of female participants (59%) indicated that they would use microbicides when they were unable to negotiate condom use with their commercial partner; however, if they were able to negotioate condom use, only 14.75% of female participants indicated that they would use microbicides in addition to condoms.

TABLE 2. Preferred Microbicide Features

Preferred Microbicides Features	No.	Percent (%)
Disease prevention	501	83.50
Lubrication	315	52.50
Duration of activity up to 24 hours*	65	16.25
<10 CNY per time	163	27.17
Insertion method		
Female		
Fingers	118	29.50
Applicator	280	70.00
Males (22) with history of anal sex		
Fingers	9	40.91
Applicator	10	45.45
Distribution		
Prescription	154	38.50
OTC	231	57.75
Preferred formulation*		
Suppository	225	56.25
Most concerned about		
Female (efficacy)	191	47.75
Male (safety)	119	59.50

*Female participants only questioned.
CNY, China Yuan; OTC, over the counter.

Influence of Microbicides on Sexual Behavior

Two-thirds of female participants (67.5%) thought the use of microbicides would not influence their sexual behavior, but a minority (3.75%) indicated the number of clients they currently had would increase. Meanwhile, nearly a fifth of women (18.25%) thought microbicides would lead to a decrease in condom use.

Among male participants, nearly half (44.5%) thought microbicides would result in a decrease in condom use and nearly a quarter (21%) thought their frequency of commercial sexual intercourse would increase. Among the 22 men who reported a history of anal intercourse, 8 indicated that they would increase their frequency of anal intercourse with microbicide use.

History of Intravaginal Drug Use

To understand attitudes pertaining to microbicide acceptability in greater detail, females with a history of sexual intercourse while using intravaginal drugs and males who had experienced sexual intercourse with a female using an intravaginal drug were interviewed in depth.

Among the 400 female participants, eight women (2%) had experienced sexual intercourse while using intravaginal drugs, and 2 (25%) reported no change in sensation, whereas 6 (75%) reported a change in sensation. The changed sensations included a feeling of coolness, increased lubrication, and discomfort. The reasons for these women using intravaginal drugs were to treat disease and for pain relief. FSWs who were using the intravaginal drugs were more likely to report having new male partners and/or steady partners.

Among the 200 male participants, 43 (21.5%) had experienced sexual intercourse with females using intravaginal drugs and 10 men (23.26%) reported that they were unaware of any change in sensation. Senstations used to describe the microbicides included the following: cool, sticky, increased lubrication, scorching, and uncomfortable. Almost all of the men (92.59%) were unaware before sexual intercourse that their female partner was using an intravaginal drug. The majority (88.89%) of their female partners were new partners.

Twenty-two of the 43 men (51.16%) accepted the practice of using intravaginal drugs although 21 (48.84%) did not.

Men who were more willing to accept the use of intravaginal drugs said that they did not feel any difference in their partners' vagina and that they did not mind whether their female partners used intravaginal drugs or not. Men who were less likely to accept this sexual practice suspected their female partners inserted drugs into their vagina because they were ill.

Factors Associated With Microbicides Acceptability

Based on the results of the univariate factor analysis, we used logistic regression methods to identify the factors associated with the acceptability of microbicides. The dependent variable was whether participants accepted microbicides or not. Ten independent variables were entered in the model. Gender, lubrication, price, and having taken measures to prevent STIs in the past 6 months were significant (Table 3). Although age, establishment strata, and score of relative AIDS/STI knowledge were not in the last equation, univariate factor analysis showed that they were also factors in microbicide acceptability.

Perception of risk behaviors affected the acceptability of microbicides among all participants (Table 4). Knowledge of STIs and AIDS was also a factor in affecting microbicide acceptability among female participants.

FSWs who scored more questions about STDs and AIDS correctly (at least 10 of 16 questions) (n = 319) had a higher acceptance rate of using microbicides (93%) than those who scored fewer questions correctly (n = 33, acceptance rate: 83%, $\chi^2 = 6.85$, $P = 0.03$).

TABLE 3. Results of Logistic Regression Analysis of Microbicide Acceptability

Factors	Wald	OR	OR (95% CI)	*P*
Gender				
Male*	—	1.00	—	—
Female	33.03	5.37	3.03 to 9.52	<0.01
Took measures to prevent STIs in the past 6 months				
No*	—	1.00	—	—
Yes	9.59	4.54	1.74 to 11.84	—
Lubrication				
No*	—	1.00	—	—
Yes	14.41	2.90	1.67 to 5.03	<0.01
Price of microbicides per use				
>10 CNY*	13.11	1.00	—	—
5–10 CNY	7.17	0.35	0.16 to 0.76	0.01
0–5 CNY	13.07	0.26	0.12 to 0.54	<0.01

*Represents reference group.

TABLE 4. Results of Comparison of Acceptability of Microbicides Among Participants With Different Perceptions of Risk Behavior

Perception of Risk Behavior	Accept Microbicides		χ^2	*P*
	N	%		
Reducing the number of partner to prevent STIs				
Yes	349	87.47	5.02	0.03
No	138	80.23	—	—
Know that only using condom before ejaculation is risky				
Yes	340	88.31	8.61	<0.01
No	147	79.03	—	—
Willing to use condom				
Yes	468	87.97	44.62	<0.01
No	19	48.72	—	—

DISCUSSION

Overall acceptability of microbicides was high, indicating the potential market for microbicides among people engaging in high-risk sexual behavior is good. Participants also believed that such products should be available to women if proven to be safe and effective.

Some participants indicated that they would decrease condom use if microbicides became available. If microbicides do lead to a decrease in condom use and become a method of soliciting customers, our results are likely to be discouraging. At present, microbicides have an efficacy as low as 40% of the male condom for preventing HIV and STIs[9]; therefore, even if their future efficacy is increased to 80%, microbicides should not be absolutely substituted for condoms. These results give an early warning that providers must deliver accurate messages to users and not exaggerate or hide the real efficacy of microbicides. At the same time, sex education should be improved among FSWs and male clients in order for informed decisions to be made.

The covert use of microbicides has been related to sexual partner type,[10] and women might be more inclined to use microbicides covertly with a new partner believing he would be less likely than a regular partner to notice anything unusual in the vagina.[3] However, in our study, men who engaged in sexual intercourse with new female partners using intravaginal drugs were aware of their use. They did not punish or censure these women because the men thought their relationship was casual and they did not want to spend energy arguing with the women. In view of this fact, microbicides can be a method through which FSWs can persist in getting protection when their male clients refuse to use a condom in casual relationships.

Younger participants were more likely to accept microbicides compared with older participants, and it has been reported that age is a factor in influencing choice regarding microbicide type.[11] The higher the price of microbicides, the lower the acceptability, although participants from higher priced establishments were more likely to accept microbicides than those from lower priced establishments. A positive perception of risky sexual behavior and a strong knowledge of STIs and AIDS were helpful for the acceptance of microbicides indicating sex education should be strengthened.

The efficacy of microbicides in preventing HIV was a critical factor influencing acceptability. This indicates that although each participant had different preferences concerning

the physical characteristics of microbicides, the efficacy of microbicides was the basis of its acceptability.

Compared with female participants, male participants exhibited more caution concerning microbicides. Caution among men and the impact of male condom use on female decisions showed that male attitudes were an important factor in deciding whether to take preventive measures or what type of preventive measures to take. Therefore, health education for men, especially for male clients, is extremely important.

Most participants choose to insert microbicides with an applicator, indicating both men and women hoped to have clean and safe insertion methods. The sensation of microbicides in the vagina is also a factor influencing acceptability of microbicides; therefore, insertion method and sensation of use will need to be carefully designed to encourage maximum acceptance of product use.

Our study was conducted in Kaiyuan county, Yunnan province, where the rate of HIV transmission through unprotected sexual intercourse is high, and many HIV/AIDS projects have been implemented. Therefore, these FSWs were likely to be more knowledgable about AIDS and were more eager to obtain preventive measures to protect themselves, resulting in high microbicide acceptability. Additionally, most FSWs wanted microbicides to be lubricating. This preference was related to FSWs habit of using lubricants during sexual intercouse. The acceptability of microbicides was also influenced by the local AIDS epidemic and female vaginal practices. These results are consistent with several international studies.[12–15]

As far as we know, this was the first time in Kaiyuan county and in Yunnan province that a group of male sexual clients was directly surveyed. We explored 3 recruitment methods. Of the 3 methods, recommendation of male clients was not reliable, whereas both methods of FSW and Kaiyuan CDC employee recommendation were more reliable. Nonetheless, the CDC employee recommendation method required more time than FSW recommendation as the participants recommended by the employees of Kaiyuan CDC were extremely concerned about potential exposure of their identity and insisted on being interviewed in locations they had suggested. From this perspective, CDC employee recommendation was not efficient and it does not lend itself to quality control. Therefore, for this study, FSWs' recommendation was the most efficient and reliable method of male client recruitment.

This study had a number of limitations. First, participants were assessed on the likelihood of a hypothetical microbicide; therefore, it is inevitable that some questions were answered subjectively. Second, the population of male clients has not been comprehensively described in Kaiyuan county, so our sampling methods were restricted, and random sampling was not possible. For this population, we used recruitment via personal recommendation. The shortcoming of such a method is that participants are familiar with the person who introduced them, and therefore, a representative sample of the male client population is unlikely to be obtained. Third, there are many factors influencing the acceptability of microbicides, and our study may not have investigated all factors. In addition, our study site was limited to 1 county with a high HIV/AIDS prevalence; therefore, it is possible that our results are not representative of other locations in China.

CONCLUSIONS

Our study found that microbicides is acceptable to both FSWs and their clients in Kaiyuan Yuanna, if they provide protection from HIV infection effectively and safely, and affordable. In view of China's large population and the increasing rate of HIV transmission via unprotected sex, the development of effective, safe, and affordable microbicides has a great potential in controlling sexual transmission of HIV epidemic.

ACKNOWLEDGMENTS

The authors would like to thank Naomi Juniper for her assistance in the preparation of this article and thank Adrian Liau for editing assistance.

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Evolution of Men Who Have Sex With Men Community and Experienced Stigma Among Men Who Have Sex With Men in Chengdu, China

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Objectives: To understand the stigma and discrimination experienced by men who have sex with men (MSM) in Chengdu, and to evaluate their impact on effective HIV prevention.

Methods: Focus group discussions and individual in-depth interviews were conducted from June to September 2006.

Results: Stigma and social pressure for MSM were reported to mainly arise from their families to get married and have children to protect family reputation and lineage. Few participants reported experiencing stigma and discrimination from friends, colleagues, or general society. Nevertheless, fear of being ostracized because of their sexual orientation was frequently expressed, and was a major barrier for participating in HIV/AIDS prevention programs. Fear of stigma and discrimination related to HIV infection from inside the MSM community was also identified as a major reason for MSM reluctance to seek HIV testing and treatment.

Conclusions: Stigma and discrimination related to homosexual activities and HIV/sexually transmitted disease infection have been major barriers for MSM seeking health services. HIV/AIDS programs must be sensitive to issues of stigma both from outside and inside the MSM community.

Key Words: men who have sex with men, stigma, discrimination, HIV, China

(*J Acquir Immune Defic Syndr* 2010;53:S98–S103)

INTRODUCTION

Stigma and discrimination have been identified as primary obstacles against effective HIV prevention.[1,2] As elsewhere, men who have sex with men (MSM) in China are suffering from stigma and discrimination.[3,4]

In the past 30 years, Chinese society has experienced dramatic sexual liberation concurrent with adoption of more liberal policies and economic reforms. These changes include increasing pre- and extramarital sex, development of a flourishing sex industry, internet and casual sex, and more openness regarding homosexual behaviors. Increasing numbers of people now regard sexuality as a basic human right, meaning that everyone has the right and freedom to pursue his or her own sexual happiness.[5–7] Sodomy, previously condemned as a form of hooliganism, was removed from legislation in 1997,[4] and homosexual behaviors were excluded from the *China Psychiatrics Classification and Diagnostic Criteria, Version 3*, as a psychosis in 2001, indicating an increasing acceptance of MSM in general society.[7]

Nevertheless, homosexuality is still regarded as deviation from social mores by mainstream society in China. A survey among 3000 college students across China in 1992 revealed that 82.0% of male students and 84.5% of female students believed that homosexual behaviors were a psychopathic disorder.[8] When asked how they would react if their best friend were homosexual, 67.5% responded that they would suggest to that friend that he seek treatment, and 11.2% would break off the friendship; if it were a relative, 30.4% said that they would feel ashamed, and 38.6% said that they would consider it to be a serious illness.[8] Another study among Chinese students in 2002 had similar results, in which 78.6% of men and 66.4% of women disapproved of the concept that homosexuality should be allowed.[6]

Due to discrimination against homosexuals, MSM remain a hidden population. Thus, it is difficult to reach MSM with information and intervention programs. Admitting to homosexuality reduces their quality of social life and family support, leads to low self-esteem, increases high-risk behaviors such as sexual aggression and drug or alcohol abuse, often resulting in poor psychologic and physical health.[3,9–12] They also have difficulty in negotiating safer sex. The pressure of strong Chinese tradition to marry and have children, intensified by the current 1-child policy, causes many MSM to hide their sexual orientation and get married, putting their wives and children at risk of HIV infection and sexually transmitted diseases (STDs).[13,14]

Chengdu, one of the major cultural and economic centers in southwest China, is noted for its tolerance and openness. The total number of sexually active MSM has been estimated to be as high as 71,000 in Chengdu.[15] The HIV prevalence among MSM increased dramatically from 0.6% in 2003 to 5.8% in 2006.[16]

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Supported by the National Institutes of Health Fogarty International Center research training grant D43 TW000013.

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To date, only a few studies have been carried out in China about the stigma and discrimination experienced by MSM. In this qualitative study, we document MSM activities and discrimination experienced in Chengdu.

METHODS

From July to September 2006, a qualitative study was conducted among MSM in Chengdu employing focus group discussions and in-depth interviews. The study protocol was reviewed and approved by the Institutional Review Board of the University of California, Los Angeles, and the Chinese Center for Disease Control and Prevention.

Focus group discussion provided information for mapping of MSM venues and understanding prevalent behaviors. A semistructured guide was used to ensure that the same basic lines of inquiry were pursued with each person interviewed. The information collected included basic demographic information, major venues for homosexual activities, knowledge about HIV/STD, HIV-related risk behaviors, and personal experiences with homophobia, stigma, and discrimination. Participants were recruited from different venues by volunteers from the Chengdu Gay Community Care Organization (CGCCO) or by personal reference. Participants were men, at least 18 years old, had been living in Chengdu in the last 3 months, and had had oral or anal sex with other males in the past. All the interviews were administered by male interviewers in a private room in the office of CGCCO. The conversations were audiorecorded and transcribed in Chinese.

The qualitative data collection and analyses yielded 2 types of findings: (1) high-quality, detailed descriptions of each case, which were useful for documenting uniqueness; and (2) important shared patterns and opinions that cut across cases.[17,18] A set of codes was developed to classify the words by categories, from which a matrix to display identified categories by groups of respondents was formulated. After summarizing the data, the shared patterns and opinions that significantly emerged from across cases were summarized into several major points to facilitate conclusions. A combination of direct quotes and paraphrases was used to convey the respondents' main points and representation of their own words. The analysis used ATLAS.ti for data storage, coding, retrieval, comparisons, and linking.

RESULTS

A total of 43 subjects were recruited, among whom 16 participated in the 3 FDG and 27 were interviewed in-depth; one subject was inebriated and withdrew voluntarily. Among the 26 participants in the in-depth interviews, 13 were originally from Chengdu. Their ages ranged from 19.5 to 52 years; 12 were younger than 25 years. Fifteen had at least college-level education. Only 2 participants were currently married, and 4 divorced or separated. Twenty self-identified as homosexual and 6 as bisexual.

MSM Venues in Chengdu

The typical venues for MSM in Chengdu in the 1980s included public squares and plazas, parks, tea bars, and public lavatories. The 2 most famous were the Labor's Culture Palace and the tea garden in Wenshu Temple, where many older MSM were introduced to and participated in homosexual social life. Both places were bulldozed and rebuilt. In the late 1990s, gay bars and money boy (MB) brothels started to appear in Chengdu. We found more than 25 venues, relatively numerous, considering the size of the city, providing many choices for meeting with other MSM.

China has recently experienced booming internet development, which has become one of the most important sources for MSM to find homosexual-related information and sexual partners. Most participants routinely used the internet at home and/or in their offices. Those who did not have a personal computer use low-cost internet cafés. Most online partner seeking has been done through instant chat software or chatrooms on websites. The internet provides anonymity, and is very easy and convenient to use. Three main chatrooms, always full, are typically used. There were also 3 web sites. One participant described the development of online chatrooms in the last few years:

■ *"MSM in Chengdu started to use chatrooms in about 2003. There was no chatroom in 2002, and only one website chatroom called 'Sunshine' was established in 2003. Not many people used it at that time. The chatroom had a capacity of 100 persons and it was not usually full. Now we have three, two for 175 persons and one for 100, and they are always jammed by visitors." (Focus group discussion 1).*

When asked why they started to use the internet, most participants cited convenience, anonymity, and safety.

■ *"The main reason to use internet was because of its convenience. Today you can get online anywhere, at home, in the office… You can stay online when you go to work. You don't need to show yourself, you can say what you want to say, and ask anything you want to know, like height, weight, age, and how he wants to do it, before you meet the person. Some questions you can hardly ask face-to-face." (Focus group discussion 1).*

Internet has also expanded the scope and sociality of MSM, and provided many more choices to find friends and sexual partners.

■ *"In bars, choices are limited. You can hang around with and talk to only a few persons. When you find somebody new, you cannot just go to him and say hello. Now it is very easy to add new persons to your QQ [one of the most popular instant online chat software programs in China]. You can communicate with many people at the same time. In traditional venues, you could get to know no more than 100 persons a year. But now, it is very easy to reach the limit of 500 persons for QQ in half a year." (Focus group discussion 2).*

Because of the internet, usual MSM venues in Chengdu are undergoing a transformation. Bars, tea bars, and most public parks are no longer places for hunting for sex partners, but for recreation with friends. MB brothels, public bathhouses, and lavatories are still serving as venues for commercial or quick sex. The price for having sex with MB dropped from 150–300 Yuan (US $20–40) in the late 1990s to 50 Yuan (US $6.5) in 2005. The number of the brothels increased to 7 in 2006, and the average price went up to 100 Yuan (US $15), indicating the increased demands

for commercial sex in the MSM community. In the last few years, blackmail occurred among MSM who went to public bathhouses and lavatories, so they are becoming less popular.

■ *"My friends and I used to visit those places (public lavatories) before. But later too many people from outside [of the MSM community] started to appear. Most of them were not homosexual, but wanted to use the gay community to earn a living. They went there and blackmailed people. Later my friends told me that internet was safer and more convenient, so I switched to use internet." (Focus group discussion 2).*

■ *"In my opinion, those places (public bathhouses and lavatories) are really dirty and dangerous. On the one hand, there are many bad people, cheating or even blackmailing others. On the other hand, it is very easy to catch diseases to have sex with people in there." (I14, single, 20 year-old, college-educated student).*

Because sexual activities in public places and commercial sex are illegal, MSM venues are occasionally subject to police inquiry. However, we noticed that there were public lavatories and MB brothels located near police stations. The explanation from a former owner of a MB brothel was

■ *"Nowadays, you cannot be arrested because of homosexuality if you don't do it in public places or announce it publicly. Nevertheless, there are many other menaces to homosexuals out there. If you stay close to the police station, other bad things like robbing or blackmailing are not likely happen to you." (I17, single, 41 year-old, high school-educated, self-employed, former MB brothel owner).*

Homosexual-Related Stigma and Discrimination

Participants' experiences of stigma and discrimination came mainly from 3 sources: general society, family, and within the MSM community.

General Society

Because most participants carefully conceal their sexual orientation not many reported discrimination from the general population. Only one participant reported an episode of being put in detention for a few days about 20 years before, and 2 episodes of discrimination from colleagues or the general population because of his feminine physical appearance. Nevertheless, most participants expressed fear of being socially ostracized if their sexual orientation were disclosed. Being single and past the usual age for marriage, having a feminine physical appearance, and/or being present in MSM venues raises suspicions.

■ *"Nobody knows about my status except my homosexual friends. Although it is not directly to me, I feel that discrimination against the MSM population does exist. There is one guy in our company who looks very feminine. I don't know if he is gay or not, but he is really isolated in the workplace… Of course I feel pressure being single. Most of my classmates and friends have girlfriends, some even already got married. Many times my colleagues asked me why I don't have a girlfriend and wanted to set up a date for me. Their enthusiasm really bothered me because I had to make up excuses to refuse their help. To be frank, I really care about how people see me. I don't want them to know (my status)." (Interview #10, single, 24 year-old, college-educated company employee).*

■ *"I keep my secret very deep and carefully. I never think of telling anybody else about that [homosexual orientation]. I seldom go to gay cruising spots because I don't want to be seen there. I don't want to do that and be under suspicion." (#19, single, 21 year-old college-educated, unemployed).*

Participants may divide their friends into 2 circles, those who are gay and those who are not, or even give up social life with their nongay friends. Some younger participants chose to tell the truth to trusted friends. There is a possibility that at least some of their close friends also know about their true sexual orientation, but do not confront them with it. In most cases, participants did not feel discrimination or estrangement from their friends after admitting to being gay.

■ *"I have two or three best friends who know about my situation. I told them myself. Before they knew about that, I had felt a gap between us. It was not a problem for them to accept it when I told them about my sexual orientation. Now we can even talk about some topics of homosexuality and make jokes about it." (Interview #7, single, 20 year-old, high school education, self-employed).*

■ *"Maybe one or two friends have suspected. I had brought a few close friends to gay bars to see performances. We've been friends for many years. I think they know about it, but they never asked me." (Interview #6, married, 52 years old, college-educated company employee).*

Although nobody in our study would willingly disclose their sexual orientation to the general population, many of them felt it would not have been a difficult situation to deal with if their friends or colleagues found out about their sexual orientation.

■ *"I think in the current situation in China, it is not a good idea to willingly disclose my status. However, it also does not matter if somebody finds out. I've had no experience of being discriminated against. But I think it is not a big deal. People at work judge me by my ability, not my sexual orientation. It might be used against me in some circumstances. Other than that, I do not think it is a problem." (Interview #12, divorced, 30 year-old, college-educated businessman).*

■ *"People outside my (gay) circle don't know my situation. I am an independent person. It doesn't matter what people think of me. It is good that people in my company don't like to probe into other people's lives. Everybody knows that I am single and have no intention of be married. But nobody should care about that. It is my own business." (Interview #8, single, 46 year-old, college-educated company employee).*

Stigma and discrimination from health care personnel has been identified as one of the major reasons MSM do not use health services.

■ *"It is embarrassing going [to the hospital or CDC] for testing. When you specifically ask for HIV testing, they think you must be a bad person or did something wrong. Last time I came here [CGCCO] for testing. Because we were all the same type of people, I did not feel strange at all." (Focus group discussion 2).*

Family Members

The primary source of pressure in China that MSM identified is the need to show filial piety and maintain the family lineage. Men who fail to fulfill this obligation are viewed not only as shameful but as selfish and shirking their family responsibilities. As a result, MSM who are not married at the proper age cause great concern to parents, especially in the rural areas. With the 1-child policy in China, the pressure for getting married and having children is greater than ever.

■ *"What I care about most is not the gossip about me, but the feelings of my parents. They raised me up to manhood. The only thing they wish from me is to be somebody and make them proud. I cannot be too selfish and let them down." (interview #10, single, 24 year-old, college-educated company employee).*

■ *"I have been thinking of telling my parents about my status lately. When I was young, I didn't think about that. My parents really want me to get married. The pressure from my family is getting too strong. I tried to find a girlfriend but it did not work out. I really have no interest in women and we just broke up a couple of days ago." (Interview #8, single, 25 year-old, college-educated teacher).*

As a response to pressure, MSM tend to postpone marriage to an inevitable point when they must choose between getting married or disclosing their true sexual orientation to their families. They usually choose to tell a sibling or other relative, usually female, rather than their parents.

■ *"I have told my sister. I was forced to. My parents had once set up a date for me and I refused to go. Since I had done this many times and I am the only son in my family, my mom got frustrated and started to cry. My sister came and asked me why I did not want a girlfriend, and demanded a reason. In that situation I had no choice but to tell her [that I am homosexual]. My sister was stunned. She turned around and left without saying a word. I did not dare to talk to her for two days. But she forgave me anyway and told me it was up to me what life I wanted to live. But there is no way that I can tell my parents. They are from the countryside and are not educated. They would never understand what homosexuality is." (Interview #11, single, 28 year-old, high school-educated service business worker).*

Compared with other family members, it was much harder for parents to accept the truth that their son is homosexual, and they therefore exert enormous pressure on MSM who reveal the truth to them.

■ *"I am the only son in my family. When I told my mom that I am a gay, she cried for almost a week. My mom said it was such shame for them. I told her I could save their face by killing myself. I knelt down before my mom and she got down on her knees too. We both cried. If I had been given another chance, I would never have told my family that I am gay. It was too painful… She still cannot accept this, and always thought that if I can go to find a girlfriend and have sex then I could be normal again." (Interview #5, single, 29 year-old, college-educated accountant).*

When MSM disclose to family members about their sexual orientation, they risk losing the respect and support of their families, which in some cases, leads to low self-esteem.

■ *"My parents have passed away and all my brothers knew about my status. One year during the lunar new year I met a person from Chongqing. It was very cold and he had just been cast out by his parents because they just found out [he was gay]. I felt pity for him and brought him to my oldest brother's house to celebrate the new year. My brother was very angry when I brought a stranger who was gay to his house, and he said something very awful. I got angry too and left with him. I have not spoken to my brother since then. Because I really care about the feelings of my family, I quit my job [which was good] and left Chengdu for many years. I did many bad things to survive, and was put in jail for theft for three years." (Interview #17, single, 41 year-old, high school-educated, self-employed, former MB brothel owner).*

Among those participants who had been married, 2 had told their wives about their sexual orientation before marriage. Both of them mentioned that their wife had the misconception that homosexual was a psychologic ailment that could be rectified by having a normal heterosexual relationship. Nevertheless, acceptance of the marriage by their wives was also an indication of the increased tolerance of homosexuality in the young generation.

■ *"I am divorced. I got married because of family pressure. My ex-wife had been an old friend for many years. She was beautiful and shared the same opinions with me on many things. We understood each other and communicated very well. This is something I don't have with my boyfriends. So I told her about my situation and asked her to marry me. Maybe at that time she thought she could change me, and so she agreed. We got married but it did not work out. Now we are just good friends." (Interview #12, divorced, 30 year-old, college-educated businessman).*

Within the MSM Community

Many participants expressed a negative attitude toward MSM. They felt that MSM are not trustworthy and that homosexual relationships are unreliable. MSM tend to build their own circle of friends based on age, social status, personal interests, etc. Normally there is not much communication and interaction between the different groups. There are certain subpopulations, such as MB, feminine-looking MSM, and those who go to certain places such as public lavatories or public bathhouses who provoke more negative attitudes than others.

■ *"I think it is normal [to be homosexual] as long as you don't think of yourself as a woman. I don't like those who act really*

girly. I don't like men who behave in feminine ways. I don't like that. (Interview #6, married, 52 year-old, college-educated company employee).

■ *"Those places [public lavatories and bathhouses] are really a mess. People go there only for sex. They definitely have no need for communication. They only want sex." (Interview #7, single, 41 year-old, high school-educated, self-employed, former MB brothel owner).*

Enormous stigma about HIV infection existed among the participants. Most participants thought that only those who had been self-indulgent and had sex with many partners could be the potential victims of HIV infection. Few expressed willingness to go for anonymous testing at the CGCCO because they feared people would know that they had come for HIV testing and would be suspicious. Many participants mentioned an incident that occurred in Chengdu, when a man willingly disclosed his positive result to seek help in the community but ended up committing suicide.

■ *"[People don't come to the CGCCO for HIV testing] because they are afraid that people in the [homosexual] community will learn their test results. If you go to other places for HIV testing, you can choose not to tell anybody regardless of the result. If you come here [CGCCO], many people will know you have been here and will ask about the result. Gossip travels very fast in this population. It will put great pressure on you." (Focus group discussion 2).*

DISCUSSION

In ancient times, Chinese culture was very tolerant about male homosexual behaviors. As early as the Zhou dynasty (1122–256 B.C.) homosexual activities had been common, at least in the upper class of society. There is an idiom "the passion of the cut sleeve" in Chinese, which is still used to refer to homosexuality. The story originates from a Han dynasty emperor who cut his sleeve on which his adored male lover was sleeping in order not to wake him. Tolerance of homosexuality persisted until the beginning of the last century, when social tolerance of homosexuality declined due to changes in social norms and philosophy, and only sex within marriage for reproductive purposes was accepted.[6,19]

Sex-related issues have become more private, and returned to the personal sphere in China, beginning in the late 1970s. Homosexual activities have become more visible and exempt from severe legal punishment.[4,5] This has given MSM more choices and freedom. Another important factor that has dramatically changed the lives of MSM is popularization of the internet, which provides information about homosexuality and the MSM community, and a source for seeking gay friends and sexual partners without the risk of discovery. The younger generation can simply go to the internet for information that may help them to accept their sexual identity, and to gain access to the MSM community.

Nonetheless, fear of discovery is still a major force that keeps the homosexual population hidden, denying them access to information and intervention programs. MSM tend to disguise their true identities when they are involved in community activities, making outreach more difficult.

Getting married and bearing children remain among the most solemn and important responsibilities for most Chinese men. Traditional beliefs still revile exclusive homosexuality because it interferes with continuation of the family lineage. A homosexual life-style without marriage is considered undutiful and is unacceptable to the family and society. Therefore, when they come out to their family, MSM may face not only the agony they cause in the family but also the possibility of losing support and respect from them and other relatives. Therefore, MSM tend to hide their homosexual activities, postpone getting married, move away from family, or try to find support from other family members, but eventually most get married, causing them to become a potential bridge for HIV transmission to the general population.

Since the late 1990s, HIV intervention programs have been trying to involve MSM. However, because of the distinctions among subgroups within the MSM community, only a portion of the population can usually be reached, even through MSM organizations; most marginalized subgroups such as MB and married MSM are excluded. Another major barrier for HIV prevention is the fear that HIV/STD testing will cause disclosure of both their sexual orientation and their HIV positivity.

Therefore, programs that target MSM must be sensitive to stigma related to both homosexuality and HIV infection. Programs should provide a mechanism to prevent HIV-infected MSM from being discovered not only by general society but also by the MSM community. In China, to get free treatment for AIDS, the patient must register using their real name and address. Considering the universal distrust of MSM for health care institutes, a more effective way of providing follow-up services to HIV-positive MSM might be through MSM organizations. However, for this to be effective, stigma within the MSM community toward HIV/AIDS must also be addressed.

Intervention programs also need to be able to reach the hidden or marginalized subpopulations among MSM such as MB. Programs among MSM in China seldom reach MB, especially those not working in brothels. To reach hidden subpopulations, intervention programs should create a supportive environment and provide relevant information and health services conveniently and confidentially.

Our study had several limitations. The participants were recruited from MSM venues or by personal reference. Therefore, they are not a random sample of MSM in Chengdu. Married MSM were probably under-represented. No participants were recruited directly from public lavatories or bathhouses, although several participants had been involved in MSM activities in such locations. More than half of the participants had college or higher education, and only one participant reported selling sex. Stigma and discrimination experienced by MSM in Chengdu might be different in other parts in China that are not as liberal as Chengdu.

CONCLUSIONS

Most MSM in China lead a double life and do not come out, due to stigma and discrimination. Thus, it is difficult to

estimate the number of MSM and to obtain adequate and accurate information about them.

Stigma and discrimination related to homosexual activities and HIV/STD infection have been the major barriers to MSM seeking health services. HIV/AIDS programs must be sensitive to issues of stigma both from outside and inside of the MSM community. Confidentiality and supportive follow-up services for HIV-positive MSM are among the first issues that need be guaranteed by HIV intervention programs to persuade more MSM to come for HIV testing.

ACKNOWLEDGMENTS

The authors are grateful to the people who participated in this study. We especially thank Mr. Xiaodong Wang, Jun Wang, and other members of Chengdu Gay Community Care Organization (CGCCO) for their enthusiastic assistance and helpful input for this study. Appreciation also goes to Drs. Abdelmonem Afifi, Thomas Coates, Li Li, Pamina Gorbach, and Marc Bulterys for their review, comments, and inspiring suggestions.

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The Situation of Children Affected by HIV/AIDS in Southwest China: Schooling, Physical Health, and Interpersonal Relationships

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Objective: To investigate the schooling, physical health and interpersonal relationships of children affected by HIV/AIDS in rural areas of southwest China.

Methods: Using a structured survey, quantitative data were collected on a total of 116 children and 114 of their caregivers.

Results: Parental illness or death adversely affected children's school attendance and school performance. Over one-third (36.2%) of children reported being ill for more than 3 days during the previous 6 months; more orphans were hospitalized during the latest illness than nonorphans, although the difference was not statistically significant. One-third (33.6%) of children were aware that their parents were HIV positive. Ten percent of orphans reported that their relationships with peers became worse after parental illness or death, which was significantly higher than nonorphans. Twenty-five percent of orphans reported they were teased by others compared with 1.9% of nonorphans.

Conclusions: HIV infection has impacted negatively on the children in terms of education, health, and peer association. These findings can be used as preliminary data supporting intervention strategies and activities to improve the general welfare of children affected by HIV/AIDS in China.

Key Words: HIV/AIDS, child health, parent, schooling, interpersonal relations, China

(*J Acquir Immune Defic Syndr* 2010;53:S104–S110)

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Supported by the China Multidisciplinary AIDS Prevention Training Program with NIH Research Grant #U2RTW006917 and U2RTW006918, funded by the US National Institutes of Health, the Fogarty International Center, the National Institute of Drug Abuse and the National Institute of Mental Health (China ICOHRTA, with Principal Investigator Z. Wu).

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INTRODUCTION

Approximately 33 million adults, most of them parents, are now living with HIV worldwide,[1] and more than 15 million children have been orphaned by AIDS.[2] As improved treatment strategies continue to prolong the lives of parents with HIV, more children will live with a chronically ill parent.[3] The most recent estimate indicates that as of the end of 2007, there were approximately 700,000 people living with HIV/AIDS in China.[4] Although HIV prevalence among the general population is still relatively low in China, high-prevalence rates have been reported in certain locations and populations.[4] Consequently, the situation of children with HIV-infected parents and children orphaned by AIDS has emerged as a serious issue in high-prevalence areas.[5]

Previous studies from Africa have shown that when a family member has AIDS, expenditure on health care quadruples, food consumption may drop by as much as 41%, savings are depleted, and families often go into debt to care for sick individuals.[6] The amount of resources available for a child's education decreases when parents are infected with HIV or die. As a result, children are more likely to dropout of school as tuition fees become unaffordable.[7] In addition, HIV/AIDS-related stigma in the classroom may also cause children to stop going to school, decreasing the quality and consistency of school attendance.[8] Children affected by HIV/AIDS may receive poorer care and supervision, may suffer from malnutrition, and may not have access to available health services, although there are conflicting data on the associations between nutrition and family HIV/AIDS status.[9–11] Affected and orphaned children tend to be traumatized and suffer a variety of psychological reactions to parental illness and death.[12,13]

The studies described above were largely conducted in African countries and limited data are available from other developing countries, such as China. Unlike Africa, in China, the HIV/AIDS epidemic has been largely driven by intravenous drug users. There are approximately 288,000 drug users living with HIV/AIDS in China, accounting for 44.3% of the country's total number of estimated HIV cases.[4] In provinces located along drug trafficking routes, drug use accounts for around 90% of HIV/AIDS cases.[4]

To date, there have been few studies conducted to explore the lives of children affected by HIV/AIDS in China. In a cross-sectional survey of 251 AIDS orphans conducted in 5 provinces, 61% of children lived with surviving parents and over 15% of children had lost both parents. One-quarter of the

orphans did not attend school.[14] Another study conducted in Yunnan Province indicated that in 266 randomly selected households with registered HIV-infected drug users, 40% of these children had lost at least one parent. Most of the children resided in a household with a low economic status and a high dependency ratio. Compared with orphans, nonorphans and their families in this study were less likely to receive social support from the community. Orphans and older children were less likely to attend school and more likely to be truant if enrolled in school.[5]

To address this knowledge gap and provide a basis for intervention planning, a cross-sectional study was undertaken to examine the quality of life of children affected by HIV/AIDS from August 2005 to September 2006 in Longchuan County, Yunnan Province, China, one of the regions most affected by HIV/AIDS.[17] In 2006, there were 2718 known cases of HIV, 75% of which were infected via intravenous drug injection. Four townships were selected to participate in the study. These four townships account for most (70%) of the registered HIV cases, and have approximately 80% of all children orphaned by HIV/AIDS in the county. This article presents quantitative results on the schooling, physical health, and interpersonal relationships of these children.

METHODS

Both qualitative and quantitative methods were used to investigate various aspects of the quality of life of children living in HIV/AIDS-affected families. Results of the qualitative studies have been published elsewhere.[15,16] This study was approved by the Institutional Review Board at the National Centre for AIDS/STD Control and Prevention, Chinese Centre for Disease Control and Prevention.

HIV/AIDS-affected families were eligible if they (1) had at least one child aged between 8 and 18 years old, (2) the child was HIV-negative, and (3) the child had at lease one HIV-positive parent or had lost one or both parents to AIDS. Within each household, one child aged 8–18 years old and one caregiver (the person actively involved with the child's daily care) were interviewed.

Measurements

Two sets of questionnaires were developed to collect information from children and caregivers, respectively.[15,16] Except for family sociodemographic characteristics, most questions were comprised of parallel child self-report and caregiver proxy-report formats, with the questions essentially identical and differing only in appropriate language.

Sociodemographic characteristic variables measured included caregiver's age, sex, education, marital status, ethnic group, and child's age and sex. The child's orphan status was identified using terms adopted from UNAIDS/United Nations Children's Fund (UNICEF)/the United States Agency for International Development (USAID).[18] Orphans were defined as children under the age of 18 years who had lost one or both biological parents. Children whose parents were both alive at the time of the survey were nonorphans.

Four variables assessed the children's physical health and illness. These included status of child's health during the previous 6 months (very good/good/fair/poor); incidences of illness longer than 3 days in the previous 6 months; duration of any illness in the previous 6 months; and severity of the last illness.

The status of the child's schooling was assessed by investigating school attendance, whether the family received external financial support for education from the government or other sources, and perceived changes in school performance after parental illness or death (became worse/became better/did not change/not sure).

The quality of the child's relationship with the caregiver was measured using 5 questions assessing whether caregivers knew about their child's school performance (yes/no); whether caregivers knew their child's friends (yes/no); whether the child had been informed about their parent's HIV/AIDS status (yes/no); average time caregivers spent with their child; and frequency of child–caregiver communication (always/often/sometimes/never). The peer relationship was measured by 2 questions assessing: (1) whether the child was teased by other children (yes/no); and (2) the change in their relationships with their peers after parental illness (ie, onset of AIDS) or death (became worse/became better/did not change/not sure).

Procedures

Study participants were recruited with the help of local health care workers who treat HIV-positive patients in the community. Eligible families who agreed to participate in the study met with an interviewer. Informed consent was obtained before the interview and potential participants were advised they could decide to quit the interview at any time if they wanted. For caregivers, written informed consent was obtained, and for children, caregivers provided consent. To ensure confidentiality, no identifiable personal information was collected and only research staff had access to the data.

The questionnaire was administrated by a qualified interviewer in the health care worker's clinic or in the participant's own house, depending on the participant's request. For illiterate participants, the questionnaires were administered under the supervision of a research assistant. Caregivers were interviewed first, after which they were asked for permission to their children being interviewed. If the caregiver agreed, the interviewer talked with the child about the study. The child's verbal consent was obtained and audio-recorded after it was determined that the child understood what he/she was consenting to. Children were given verbal information before completing questionnaires on their own under the supervision of a research assistant.

Data Analysis

For categorical variables, data were compiled as frequency and percent and the differences between orphans and nonorphans were compared using chi-square test. When one of the categories is ordinal, Wilcoxon rank-sum test was used. For continuous variables, data were calculated as mean ± SD and the 2 groups were compared by independent *t* test. The agreement between child self-report and caregiver proxy-report was determined through intraclass correlation coefficient.

RESULTS

Sample Characteristics

During August to September 2006, 126 families with eligible participants were approached. No adult was present at home for 8 families during 3 contact attempts and the remaining 2 families refused to participate in the study, resulting in a final sample of 116 families. One hundred fourteen caregivers and 116 children completed all items in the questionnaires. One caregiver agreed for her child to participate but did not answer the questions herself. Another caregiver was sick at home and could not be interviewed. Among the 116 children, 52 (44.8%) were nonorphans. Twenty-five (39.1%) orphans were living with their parents, 35 (54.7%) with their grandparents, 2 (3.1%) with their uncles and aunts, and 2 (3.1%) by themselves.

Table 1 summarizes the demographic variables of the caregivers and children. No statistically significant differences were found with respect to ethnic group, caregiver's education, child's age, and sex. Caregivers in the orphan group were significantly older (mean = 44.85 years; SD = 13.87) than those in the nonorphan group (mean = 36.94 years; SD = 5.32). Over 60.0% of caregivers in the orphan group were females, whereas 61.5% of caregivers in the nonorphan group were males. Around 40.0% of caregivers of orphans were widowed, which was significantly higher than caregivers of nonorphans (1.9%) ($P < 0.001$).

Schooling and School Performance

Three-quarters (75.0%) of children were currently attending school (Table 1). This rate is lower than the provincial (96.2% in 2004) and national (98.7% in 2005) level. No significant difference was found for school attendance rates between orphan groups. Further analysis showed that the school attendance rate was 93.3% (56/60) among children eligible to receive primary school education, and 53.6% (30/56) among children eligible to receive junior middle school education. In terms of school performance, 12% percent of children reported a drop of school performance after parental illness or death. More orphans received schooling support from the governments or other organizations (63.8%) than nonorphans (50.0%), but the difference was not statistically significant ($P = 0.74$).

TABLE 1. Demographic Characteristics of Children and Their Caregivers

Caregivers	Total (n = 114)	Nonorphan (n = 52)	Orphan (n = 62)	*P*
Age (yrs)*	41.25 (11.50)	36.94 (5.32)	44.85 (13.87)	<0.01
Sex†				<0.01
Male	52 (45.6)	32 (61.5)	20 (32.3)	
Female	62 (54.4)	20 (38.5)	42 (67.7)	
Ethic group†				0.92
Jingpo	65 (57.0)	29 (55.8)	36 (58.1)	
Dai	21 (18.4)	10 (19.2)	11 (17.7)	
Han	21 (18.4)	9 (17.3)	12 (19.4)	
Others	7 (6.2)	4 (7.7)	3 (4.8)	
Marital status†				<0.01
Unmarried	8 (7.0)	3 (5.8)	5 (8.1)	
Married	73 (64.0)	46 (88.5)	27 (43.5)	
Divorced	8 (7.0)	2 (3.8)	6 (9.7)	
Widowed	25 (22.0)	1 (1.9)	24 (38.7)	
Education†				0.75
Did not go to school	43 (37.7)	21 (40.4)	22 (35.5)	
Primary	60 (52.6)	27 (51.9)	33 (53.2)	
Junior middle or higher	11 (9.7)	4 (7.7)	7 (11.3)	
Relation with child†				<0.01
Parent	78 (68.4)	50 (96.2)	25 (40.3)	
Grandparent	34 (29.8)	2 (3.8)	35 (56.5)	
Uncle/aunt	2 (1.8)	0 (0.0)	2 (3.2)	
Children	(n = 116)	(n = 52)	(n = 64)	
Age (years)*	12.09 (2.62)	12.15 (2.67)	12.03 (2.59)	0.80
Sex†				0.94
Male	62 (53.4)	28 (53.8)	34 (53.1)	
Female	54 (46.6)	24 (46.2)	30 (46.9)	
Education†				0.85
Current school attendance	87 (75.0)	39 (75.0)	47 (73.4)	
School dropout	29 (25.0)	13 (25.0)	17 (26.6)	

*Data given as Mean (SD).
†Values presented as number (percentage).

Health and Illness

Table 2 reports the health and illness of children by orphan status, both for child self-report and caregiver proxy-report results. No statistically significant differences were found for health and illness between the 2 groups. Approximately 60% of children reported that their health was very good during the previous 6 months. Over one-third (36.2%) of children reported that they had been ill for more than 3 days in the previous 6 months, with an average of one episode of illness. Among those children who had been ill in the previous 6 months, 47.6% reported that they had to take medication and stay at home. Orphans reported less serious illnesses than nonorphans but this was not statistically significant. Caregivers of nonorphans reported more frequent illnesses than orphans and more orphans were hospitalized during the latest illness than nonorphans, but the differences were not statistically significant.

Family and Peer Relationships

One-third (33.6%) of children reported that they had been informed about their parent's HIV/AIDS status. Twice as many orphans (43.8%) as nonorphans (21.2%) were informed. Approximately 60.0% of children believed that their caregivers knew about their school performance and three-quarters of children believed that their caregivers knew their friends. No significant difference was found between orphans and nonorphans. However, more nonorphans' caregivers reported knowing about their child's school performance than orphan caregivers. In terms of child-caregiver communication, orphans reported communicating less with their caregivers than nonorphans ($P = 0.04$), whereas no significant difference was found for the caregiver proxy-report result ($P = 0.76$) (Table 3).

Eleven percent of orphans reported that their relationships with peers became worse after the illness or death of their parents, whereas 14% of orphan's caregivers reported that their child's peer relationships became worse after parental illness or death. One-quarter of orphans reported that they were teased by others, which was significantly higher than nonorphans ($P < 0.01$). Caregivers of orphans also reported significantly more teasing than those of nonorphans. It should also be noticed that caregivers tended to report more teasing occurrences than the children did.

Child/Caregiver Agreement

Table 4 shows the correlation between child self-report and caregiver proxy-report for some variables. Agreements are better on average for physical and illness items than personal association items. Orphans and their caregivers showed better agreements on most items than nonorphans and their caregivers.

DISCUSSION

In this study, the overall school attendance rate among school-aged children was lower than the provincial and national levels, similar with findings from previous studies.[5,14] However, no difference was noted for school attendance rate between orphans and nonorphans and is inconsistent with

TABLE 2. Physical Health and Illness of HIV/AIDS-Affected Children by Orphan Status: Child Self-Report and Caregiver Proxy-Report

	Child Self-Report				Caregiver Proxy-Report			
	Total (n = 116)	Nonorphan (n = 52)	Orphan (n = 64)	*P*	Total (n = 114)	Nonorphan (n = 52)	Orphan (n = 62)	*P*
Child's health during the previous 6 mo*								
Very good	66 (56.9)	30 (57.7)	36 (56.3)	0.69†	59 (51.8)	31 (59.6)	28 (45.2)	0.22†
Good	42 (36.2)	20 (38.5)	22 (34.4)		43 (37.7)	15 (28.8)	28 (45.2)	
Fair	7 (6.0)	2 (3.8)	5 (7.8)		10 (8.8)	5 (9.6)	5 (8.1)	
Poor	1 (0.9)	0 (0.0)	1 (1.6)		2 (1.8)	1 (1.9)	1 (1.6)	
Child has been ill for ≥3 d in the previous 6 mo?*								
Yes	42 (36.2)	18 (34.6)	24 (37.5)	0.75	35 (30.7)	17 (32.7)	18 (29.0)	0.67
No	74 (63.8)	34 (65.4)	40 (62.5)		79 (69.3)	35 (67.3)	44 (71.0)	
How many times have child been ill for ≥3 d in the previous 6 mo?‡	1.00 (1.00, 2.00)	1.00 (1.00, 3.00)	1.50 (1.00, 2.00)	0.92†	1.00 (1.00, 3.00)	2.00 (1.00, 3.00)	1.00 (1.00,3.00)	0.68†
How severe was the latest illness?*	(n = 42)	(n = 18)	(n = 24)	0.30†	(n = 35)	(n = 17)	(n = 18)	0.72†
Did not disturb schooling or normal life	18 (42.9)	6 (33.3)	12 (50.0)		15 (42.9)	7 (41.2)	8 (44.4)	
Took some medicine and stayed at home	20 (47.6)	10 (55.6)	10 (41.7)		15 (42.9)	9 (52.9)	6 (33.3)	
Was in hospital	3 (7.1)	1 (5.6)	2 (8.3)		5 (4.4)	1 (5.9)	4 (22.2)	
Has not got well till now	1 (2.4)	1 (5.6)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	

6 mo, 6 months; 3 d, 3 days.
*Values presented as number (percentage).
†Rank-sum test.
‡Data given as Median (25 percentile, 75 percentile).

TABLE 3. Family and Peer Relationships of HIV/AIDS-Affected Children by Orphan Status: Child Self-Report and Caregiver Proxy-Report

	Child Self-Report				Caregiver Proxy-Report			
	Total (n = 116)	Nonorphan (n = 52)	Orphan (n = 64)	*P*	Total (n = 114)	Nonorphan (n = 52)	Orphan (n = 62)	*P*
Caregiver knows about child's school performance*	69 (59.5)	31 (59.6)	38 (59.4)	0.98	78 (68.4)	42 (80.8)	36 (61.3)	<0.01
Caregiver knows who child's friends are*	87 (75.0)	39 (75.0)	48 (75.0)	1.00	85 (74.6)	41 (78.8)	44 (71.0)	0.34
Child informed of parental HIV/AIDS status*	39 (33.6)	11 (21.2)	28 (43.8)	0.01	43 (37.7)	18 (34.6)	25 (40.3)	0.53
Child teased by others*	17 (14.7)	1(1.9)	16 (25.0)	<0.01	52 (45.6)	7 (13.5)	45 (72.6)	<0.01
Average time of caregiver accompanying child (hours per day)†	3.00 (1.00, 4.00)	3.00 (2.00, 4.00)	3.00 (1.00, 4.50)	0.70	3.00 (2.00, 4.00)	3.00 (2.00, 4.75)	3.00 (1.00,4.00)	0.44
Child communicates with caregiver*								
Always	23 (19.8)	12 (23.1)	11 (17.2)	0.04‡	24 (21.1)	13 (25.0)	11 (17.7)	0.76‡
Often	17 (14.7)	3 (5.7)	14 (21.9)		27 (23.6)	9 (17.3)	18 (29.1)	
Sometimes	23 (19.8)	16 (30.8)	7 (10.9)		9 (7.9)	6 (11.5)	3 (4.8)	
Never	53 (45.7)	21 (40.4)	32 (50.0)		54 (47.4)	24 (46.2)	30 (48.4)	
Change of peer relations after parental illness or death*								
Became worse	9 (7.8)	2 (3.8)	7 (10.9)	<0.01§	9 (7.9)	0 (0.0)	9 (14.5)	<0.01§
Became better	6 (5.2)	0 (0.0)	6 (9.4)		0 (0.0)	0 (0.0)	0 (0.0)	
Did not change	74 (63.8)	30 (57.7)	44 (68.8)		32 (28.1)	14 (26.9)	18 (29.0)	
Not sure	27 (23.2)	20 (38.5)	7 (10.9)		73 (64.0)	38 (73.1)	35 (56.5)	

*Values presented as number (percentage).
†Data given as median (25 percentile, 75 percentile).
‡Rank-sum test.
§Fisher Exact test.

previous studies conducted in other countries.[19–21] One possible explanation for this finding is that after the implementation of the Regulations of AIDS Prevention and Treatment (Decree of the State Council of the PRC No. 457, issued in 2006), families with children orphaned by HIV/AIDS were more likely to receive free schooling from the local government or other organizations. Another may be due to the increased community empathy, especially in some minority communities in China, for families with AIDS orphans.[5] Neighbors may provide assistance to AIDS-affected families, including small amounts of money, food, clothes, medicine, and help with housework.[16] This may partially contribute to the equality seen in the economic status between orphan and nonorphan households.[13]

Although there is a lack of direct empirical data on the impact of being orphaned or made vulnerable on the performance of children in school, it has been suggested that these children might perform poorly in school.[22] AIDS-affected children face barriers to education over and above the effects of poverty.[23] These barriers include their need to care for sick parents[24]; emotional scarring related to parental death[25]; and discrimination within classrooms and the community.[8] For orphaned children, school-work is most likely supervised by an older sibling, or to be unsupervised, or less likely to be

TABLE 4. Correlations Between Child Self-Report and Caregiver Proxy-Report

	ICC		
	Total	Nonorphan	Orphan
Child's health during the previous 6 mo	0.40*	0.44*	0.36
Child ill for ≥3 d in the previous 6 mo	0.63**	0.67**	0.59**
Severity of the latest illness	0.76**	0.54*	0.92**
Caregiver knows about child's school performance	0.47*	0.22	0.59*
Caregiver knows about child's friends	0.39	0.39	0.39
Child informed of parental HIV/AIDS status	0.45*	0.38	0.49*
Child teased by others	0.48*	0.36	0.50*
Child communicates with caregiver	0.36	0.29	0.40*
Change of peer relations after parental illness or death	0.35	0.27	0.38

6 mo, 6 months; 3 d, 3 days.
*$P < 0.05$; **$P < 0.01$.

supervised by a caregiver,[26] which can also contribute to poorer school performance. Our findings indicated a 12% drop in self-reported school performance after parental illness or death. Appropriate interventions should be developed to promote the school performance of these children.

Regarding the association between family HIV/AIDS status and children's physical health, participants reported no significant differences in terms of severity or frequency of illness between orphans and nonorphans. One possibility may be that the data we collected were based on the participant's self-report of the general health, and no health indicators were measured. From our research, it was clear that most orphans were living with their grandparents and had heavier burdens of housework and farm chores than nonorphans. Orphans, compared with nonorphans, may feel greater responsibility to their families to do well at school and to do their household chores. Therefore, orphans might be less likely to report minor illness than nonorphans. An additional explanation may be that the small sample size was not powerful enough to detect a difference between the 2 groups. More research is therefore needed to explore the impact of a family HIV/AIDS status on children's physical health.

When HIV/AIDS begins to affect a household, family relationships provide the most immediate source of support. Consistent with findings from other countries,[27,28] the vast majority of children orphaned by HIV/AIDS in China continue to live with the surviving parent or their extended family. As our study shows, caregivers were well aware of their children's school performance and friends. However, both children and caregivers reported a low frequency of child-caregiver communication. Nonorphans reported more communication with caregivers than orphans. One explanation may be that many orphans silently bear the grief of parental loss and do not tell their caregivers; some believe that it is their responsibility to avoid mentioning it and making the family members sad.[16] Children who are able to communicate freely with their parents may be more likely to view their family positively and report fewer psychological problems.[25] Research has also shown that a strong positive relationship between parents and children is significantly related to lower rates of risk behaviors, including those associated with HIV infection.[29,30] Therefore, strategies to increase communication between affected children and their caregivers are needed.

According to the transactional theories of child development, peers play an important role in influencing children's cognition, behavior, and general personality characteristics.[31] Parents' influence tends to decrease as children enter middle childhood and adolescence.[32] The current study found that parental illness or death negatively affected children's relationships with their peers. It could be that children may suffer from discrimination or feel self-stigmatized due to parental HIV/AIDS, which results in self-isolation and impairs their relationships with their peers. Also, children who dropped out of school might feel lonely and isolated because the number of friends and the frequency of contact decreases. Peer support should therefore be incorporated in intervention programs.

Moderate agreement was found for variables between self- and proxy-report. To our knowledge, no such data have been previously reported. Agreement was better for physical health than for interpersonal relationships. One possibility may be that teenaged children are more likely to rebel against adults and are thus less likely to communicate with their caregivers, especially in terms of talking about their friends and any emotional problems they encounter. In addition, our results indicated that agreement was better between orphans and their caregivers than that of nonorphans and their caregivers. An explanation may be that after the tragedy of parental loss, caregivers of orphans may be more concerned about the children in their care compared with caregivers of nonorphans. This suggests the need to measure both the child's and the caregiver's perspectives when evaluating children's health status.

Results of this study may be limited by its generalizability to other families affected by HIV. For instance, the current study may be more applicable to an older population of children due to the literacy requirement. Also, information on nonparticipants was not available, In addition, all participants came from communities with a high ratio of drug use and some were ethnic minorities, so the findings of this study may not be applicable to other areas of China where the HIV epidemic and the ethnicity of the general population is different. Despite these disparities, the findings can still apply to most affected children and inform the development of intervention programs that promote care and support of children affected by HIV/AIDS.

ACKNOWLEDGMENTS

Authors are grateful to all the children and their caregivers who participated in this study. Our thanks also go to our collaborators at Longchuan County CDC and to Naomi Juniper and Adrian Liau for editorial assistance.

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Measuring Health-Related Quality of Life in Children Living in HIV/AIDS-Affected Families in Rural Areas in Yunnan, China: Preliminary Reliability and Validity of the Chinese Version of PedsQL 4.0 Generic Core Scales

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Objectives: To investigate the preliminary reliability and validity of the Chinese Mandarin version of the Pediatric Quality of Life Inventory (PedsQL) 4.0 Generic Core Scales in a sample of general children and children living in HIV/AIDS-affected families.

Methods: The PedsQL 4.0 was administered to 116 children aged 8–18 years from HIV/AIDS-affected families and 115 of their caregivers. The questionnaire was also administered to a control group of 109 children and 107 of their caregivers.

Results: Most of the self-report and proxy-report scales in both groups exceeded the reliability standard of 0.70, whereas the self-report emotional functioning and school functioning subscales were slightly less than 0.70. On average, children living in HIV/AIDS-affected families scored significantly lower than the control group. The level of agreement between self-reports and proxy reports was low. Correlations were higher on average for the younger age group than for the older age group.

Conclusions: The Chinese Mandarin version of PedsQL 4.0 is a valid and reliable instrument for use with children living in HIV families. The health-related quality of life for children living in HIV families is lower than children from ordinary families.

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Supported by the China Multidisciplinary AIDS Prevention Training Program with NIH Research Grant #U2RTW006917 and U2RTW006918, funded by the US National Institutes of Health, the Fogarty International Center, the National Institute of Drug Abuse, and the National Institute of Mental Health (China ICOHRTA, with Principal Investigator Z. Wu).

Presented as poster presentation in the XVII International AIDS Conference, August 3–8, 2008, Mexico City, Mexico; and the abstract was published in *AIDS*. 2008 CD ROM (No. CDD0064).

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Key Words: Children, Health, health-related quality of life, HIV/AIDS, PedsQL

(*J Acquir Immune Defic Syndr* 2010;53:S111–S115)

INTRODUCTION

An estimated 33 million adults globally, most of them parents, are now living with HIV,[1] and more than 15 million children have been orphaned by AIDS.[2] Attention has been given to the spectrum of the impact of HIV/AIDS on children worldwide.[3–5] There is documentation of the disadvantages faced by these children with respect to economic impact, child labor, education, health and nutrition, psychological impact, and long-term developmental impact.[6] Given the multidimensional impact HIV/AIDS has on children, it is necessary to develop an appropriate instrument to capture and evaluate the comprehensive nature of the health status of affected children. The health-related quality of life (HRQoL) is increasingly acknowledged as an important health outcome measure in clinical trials and health services research and evaluation. As a multidimensional assessment of the physical, psychological, and social functioning status, HRQoL is believed to be a good measure of studying health status.[7]

The Pediatric Quality of Life Inventory (PedsQL) is one of the more promising HRQoL measures for children. Developed in the United States, the advantages of PedsQL include brevity, availability of age-appropriate versions, and parallel forms for child and parent.[8,9] Recent reports confirm that PedsQL performs well in distinguishing healthy children from pediatric patients with either acute or chronic conditions if those conditions impact on the child's general HRQoL significantly.[10–12]

The most recent estimate indicates that as of the end of 2007, there were approximately 700,000 people living with HIV/AIDS in China.[4] The epidemic of children with HIV-infected parents, including children orphaned by AIDS, has emerged as an important issue.[5] However, limited information is available to understand the HRQoL of children living in HIV/AIDS-affected families. The aim of our study was to investigate the preliminary reliability and validity of the Chinese version of PedsQL 4.0 Generic Core Scales in a sample of general children and children living in HIV/AIDS-affected families.

METHODS

Participants

The study was conducted in 4 townships of Longchuan County, Yunnan Province, China. Institutional ethics approval to conduct the study was obtained from the Institutional Review Boards at National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and Prevention. Both HIV/AIDS-affected and HIV/AIDS-unaffected families were selected to participate in the study. Within each household, 1 child aged 8–18 years and 1 caregiver (1 that is actively involved with the child's day-to-day care) were interviewed. During August to September 2006, 126 affected families and 130 control families with eligible participants were approached. A sample of 116 affected families and 109 control families were recruited for the interviews. No adult was present at home for 8 affected and 16 control families during 3 contact attempts; the remaining 7 families refused to participate in the study.

Measurements

The 23-item PedsQL 4.0 Generic Core Scales encompasses the essential core domains for pediatric HRQoL measurement: (1) physical functioning (8 items), (2) emotional functioning (5 items), (3) social functioning (5 items), and (4) school functioning (5 items). It consists of parallel child self-report and parent proxy report format for ages 2–4, 5–7, 8–12, and 13–18 years. The items for each of the forms are essentially identical, differing in developmentally appropriate languages, or first or third person tense. A 5-point response scale is utilized across child self-report for ages 8–18 years and parent proxy report.

Items are reverse scored and linearly transformed to a 0–100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, and 4 = 0), so that higher scores indicate better HRQoL. Scale scores are computed as the sum of the items divided by the number of items answered (this accounts for missing data). In addition to the 4 subscales, 2 summary scores were computed. Physical health summary score (8 items) is the same as the physical functioning subscale, and psychosocial health summary score (15 items) is computed as the sum of the items divided by the number of items answered in the emotional, social, and school functioning subscales. User agreement was signed with Mapi Research Trust, Lyon, France, before using the questionnaires. The Chinese Mandarin version of the questionnaires was translated and validated by the research group from the Department of Statistics and Epidemiology, School of Public Health, Sun Yat-sen University, following the PedsQL Linguistic Validation Guidelines.[13]

Parents or caregivers of all children filled out an additional questionnaire on family sociodemographic characteristics, including caregiver's age, gender, education, marital status, ethnic group, and child's orphan status.

Procedures

Study participants were recruited through the help of local health service providers who treat HIV-positive patients in the community. Local health service providers approached eligible families and asked the parents or caregivers if they would like to participate in the study. The nearest neighbor households with no HIV-positive patients were also approached as the control families. If they agreed, potential participants were approached by interviewers and enrolled in the study.

The questionnaire interviews were conducted in the health service providers' or the participants' own houses, according to the participants' request. Informed consent was obtained before the interview. Caregivers were interviewed first, after which they were asked whether they would agree to their children participating in the study. If the caregiver agreed, the interviewer talked with the child about the study. The child's verbal consent was obtained and audio recorded after it was determined that the child understood what he/she was consenting to.

Data Analysis

For categorical variables, data were compiled as frequency and percent, and the differences between affected and control groups were compared by χ^2 test. The exception is when one of the categories in the contingency tables is ordinal (eg, child's education level), in which case, the Wilcoxon Rank-Sum test was employed. For continuous variables (ie, PedsQL 4.0 score), data were calculated as mean $\pm$ standard deviation, and the 2 groups were compared by independent t test. Internal consistency reliability for each scale was determined by calculation Cronbach's α coefficients. Scales with reliability coefficients equal to or greater than 0.70 were considered satisfactory. The validity was determined by comparing scale scores across groups. We anticipated that children in the control group would report higher PedsQL 4.0 scores than children living in HIV/AIDS-affected families. The consistency between child self-report and parent proxy report was determined through intraclass correlation.[14]

RESULTS

Sample Characteristics

Of the 109 control families, 107 caregivers and 109 children completed enough items on the parent proxy or child self-report measure to derive at least 1 subscale score and/or summary score. Of the 116 affected families, 115 caregivers and 116 children completed enough items to derive at least 1 subscale score and/or summary score to be included in the data tables. For the school functioning subscale, data were missing for those children who dropped out of school.

Table 1 summarizes the demographic variables of the caregivers and children in 2 groups. No statistically significant differences were found with respect to age, gender, education, marital status, and household income. In the control group, the average age of caregivers was 39.53 (SD = 9.5), and average age of children was 12.17 (SD = 2.7). In the affected group, the average age of caregivers was 41.17 (SD = 11.5), and the average age of children was 12.09 (SD = 2.6). About 60% of caregivers were females, and more than 50% of children were boys in both groups. Most children (80.7% in the control group and 84.5% in the affected group) were currently attending school. In terms of ethnic backgrounds, more

TABLE 1. Demographic Characteristics of Children and Their Caregivers

	Control Group	Affected Group	*P*
Caregivers	n = 107	n = 115	
Age*	39.53 (9.5)	41.17 (11.5)	0.25
Gender†			
Male	45 (42.1)	52 (45.2)	0.64
Female	62 (57.9)	63 (54.8)	
Ethic group†			
Jingpo	43 (40.2)	66 (57.4)	0.05
Dai	27 (25.2)	21 (18.3)	
Han	23 (21.5)	21 (18.3)	
Others	14 (13.1)	7 (6.1)	
Marital status†			
Unmarried	1 (0.9)	1 (0.9)	0.10
Married	90 (84.1)	81 (70.4)	
Divorced	5 (4.7)	8 (7.0)	
Widowed	11 (10.3)	25 (21.7)	
Education†			
Didn't go to school	32 (29.9)	44 (38.3)	0.54
Primary	60 (56.1)	60 (52.2)	
Junior middle	11 (10.3)	9 (7.8)	
Senior middle or higher	4 (3.7)	2 (1.7)	
Household income per year‡	3000	3000	0.37
Children	n = 109	n = 116	
Age*	12.17 (2.7)	12.09 (2.6)	0.80
Gender†			
Male	58 (53.2)	62 (53.4)	0.97
Female	51 (46.8)	54 (46.6)	
Education†			
School dropout	21 (19.3)	18 (15.5)	0.55
Current school attendance	88 (80.7)	98 (84.5)	

*Data given as mean (SD).
†Values are presented as number (percentage).
‡Data given as median.

affected families came from Jingpo, but this was not statistically significant ($P = 0.051$).

Internal Consistency Reliability

Internal consistency reliability alpha coefficients by age group are presented in Table 2. The majority of the child self-report scales and parent proxy report scales in both groups exceeded the minimum reliability standard of 0.70 required for group comparisons, whereas the child self-report emotional functioning and school functioning subscales were slightly less than 0.70.

Discriminate Validity

Table 3 contains the PedsQL 4.0 scores for children from the affected and control families. For child self-report, affected children scored significantly lower on total score ($t = 2.530$, $P = 0.006$), psychosocial functioning ($t = 2.430$, $P = 0.008$), emotional functioning ($t = 2.140$, $P = 0.017$), and school functioning ($t = 1.687$, $P = 0.047$) than children from the control group. For parent proxy report, caregivers of children from affected families reported lower scores on total score ($t = 2.760$, $P = 0.003$), psychosocial functioning ($t = 2.286$, $P = 0.012$), emotional functioning ($t = 2.953$, $P = 0.002$), and social functioning ($t = 2.205$, $P = 0.014$) than those from the control families.

TABLE 2. Cronbach's Alpha Coefficients for PedsQL 4.0 Generic Core Scales Child Self-Report and Parent Proxy Report for Affected and Control Groups

	Control group			Affected group		
Scale	8–12 yrs	13–18 yrs	Total	8–12 yrs	13–18 yrs	Total
Child self-report						
Total score	0.89	0.86	0.88	0.91	0.88	0.90
Physical health	0.87	0.89	0.88	0.89	0.84	0.87
Psychosocial health	0.83	0.70	0.79	0.85	0.81	0.84
Emotional functioning	0.63	0.56	0.60	0.58	0.71	0.64
Social functioning	0.74	0.65	0.71	0.81	0.81	0.81
School functioning	0.68	0.66	0.67	0.58	0.62	0.63
Parent proxy report						
Total score	0.89	0.91	0.91	0.90	0.87	0.89
Physical health	0.83	0.90	0.86	0.90	0.85	0.88
Psychosocial health	0.85	0.85	0.85	0.87	0.81	0.85
Emotional functioning	0.78	0.78	0.78	0.76	0.75	0.75
Social functioning	0.76	0.82	0.82	0.83	0.83	0.83
School functioning	0.79	0.85	0.85	0.77	0.75	0.76

Child/Caregiver Concordance

Table 4 shows the correlational consistency between self-report and proxy report. The level of agreement between self-report and proxy reports was low. Correlations were higher on average for the younger age group than for the older age group, especially on psychosocial health. Correlations were higher for the control group than for the affected group.

DISCUSSION

This article describes the psychometric properties of the Chinese Mandarin version of the PedsQL 4.0 Generic Core Scales (age 8–18 years) in a comparison of children living in HIV/AIDS-affected families to general controls. The performance of the scales was found to be similar to that reported for the original PedsQL 4.0. The Chinese PedsQL 4.0 total score for both self-report and proxy report approached or exceeded an alpha of 0.90, indicating the suitability of the total scale scores for the primary analysis of HRQoL outcome in this population. The physical functioning and psychological health summary scores exceeded 0.70, making them acceptable for group comparisons. The child self-report emotional functioning and school functioning scores did not achieve the standard of 0.70. As discussed in the original PedsQL 4.0 articles,[12] these subscales should be used for descriptive or exploratory analysis until further testing is conducted.

The PedsQoL 4.0 performed as hypothesized using the know-groups method. There were differences in HRQoL between HIV/AIDS-affected children and those from the control families for both self-report and proxy report, with the former significantly lower than the latter. However, our results

TABLE 3. Scale Descriptives for the PedsQL 4.0 Generic Core Scales Child Self-Report and Parent Proxy Report: Affected and Control Groups

	Control group			Affected group				
Scale	n	Mean	SD	n	Mean	SD	*t* Score	*P**
Child self-report								
Total score	88	78.15	12.18	98	73.39	13.35	2.530	0.006
Physical health	109	79.12	17.02	116	80.77	17.07	0.726	0.234
Psychosocial health	88	77.33	11.90	98	72.78	13.47	2.430	0.008
Emotional functioning	109	74.62	15.62	116	70.17	15.56	2.140	0.017
Social functioning	109	80.36	14.98	116	81.64	17.15	0.595	0.276
School functioning	88	72.44	15.40	98	68.52	16.19	1.687	0.047
Parent proxy report								
Total Score	82	81.62	12.53	88	76.57	11.32	2.760	0.003
Physical health	107	85.29	14.95	115	84.17	13.75	0.578	0.282
Psychosocial health	82	80.10	13.36	88	75.67	11.90	2.286	0.012
Emotional functioning	107	76.95	17.26	115	70.14	16.93	2.953	0.002
Social functioning	107	84.33	15.93	115	79.89	13.92	2.205	0.014
School functioning	82	72.43	17.69	88	73.11	17.60	0.251	0.401

*The differences are statistical significant if $P < 0.05$ (1 tailed).

show that the PedsQoL 4.0 is not sensitive enough to detect the difference of physical health between 2 groups of the present sample. The negative influence of family HIV/AIDS status on children is embodied mainly in their psychological health, which is consistent with related studies investigating the impacts of HIV/AIDS on children.[15,16] One possibility of this finding may be that families with children affected by HIV/AIDS, especially those with AIDS orphans, tend to receive more assistance from neighbors.[5] Many of these assistances include providing money, food, clothes, medicine, and helping with housework.[17] This contributes partially to the equality in household economic status between the affected and control group, with the impact of household economic status mostly embodied in the physical health of children. An additional explanation may be due to the small sample size that was not powerful enough to detect a difference between the 2 groups. This finding suggests that children's psychological health be made a priority when developing and conducting intervention programs.

Consistent with previous studies, the caregiver–child agreement on the PedsQL 4.0 was low,[14,18] which confirms the need to measure both child and caregiver perspectives when evaluation pediatric HRQoL. Lack of agreement between caregivers and children may result from differences in perception of the same situation and also differences in interpretation of different items.[19] Differences in levels of caregiver–child correlation were found when analysis were performed separately by age group, domain type, and participating group. Across both control and affected groups, caregiver–child correlation for the younger age group was higher on psychosocial health but lower on physical health than for the older age group. This result is contrary to the findings of another study, which found that parent–child agreement for the younger age group was higher on physical health and lower on psychosocial health than for the older age group.[14] One explanation may be the "psychological reactance" that children in the stage of adolescency are less likely to communicate with their caregivers about their problems, especially psychological and emotional problems. Differences in levels of caregiver–child correlations were also found between affected and control group. Correlations were good for the control group on most subscales than those for the affected group. One possibility of

TABLE 4. Intraclass Correlation Between PedsQL 4.0 Generic Core Scales Child Self-Report and Parent Proxy Report for Affected and Control Groups

	Control Group			Affected Group		
Scale	8–12 yrs (n = 56)	13–18 yrs (n = 47)	Total (n = 103)	8–12 yrs (n = 57)	13–18 yrs (n = 43)	Total (n = 100)
Total score	0.58*	0.16	0.48*	0.41*	0.14	0.29
Physical health	0.36	0.41	0.39	0.22	0.47*	0.29
Psychosocial health	0.63*	0.09	0.54*	0.38	0.09	0.26
Emotional functioning	0.54*	0.09	0.35	0.38	0.04	0.24
Social functioning	0.40	0.39	0.40	0.16	0.46*	0.28
School functioning	0.75*	0.33	0.65*	0.60*	0.41	0.51*

*Correlations are significant at the $P < 0.05$ level (2 tailed).

this finding may be that children from HIV/AIDS-affected families are less likely to communicate with their caregivers than those from the ordinary families.[20] Many children silently bear the grief of parental loss and do not tell their caregivers; some hold it as their responsibility to avoid mentioning it and making the family members sad.[21] Studies have shown that children who are able to communicate freely with their parents about HIV/AIDS issues view their family positively and report fewer psychological problems.[22] Therefore, stronger effort has to be made to increase communication between affected children and their caregivers.

The present study has several potential limitations. Test-retest reliability and responsiveness are not reported. However, it can be argued that test-retest reliability may be less useful than internal consistency reliability in HRQoL instrument development. In addition, the number of cases was limited by availability of children living in HIV/AIDS-affected families as some eligible families refused to have their children participate in the study. Generalizability issues include lack of information on nonparticipants and participants from communities with intense exposure to drug use and ethnic minorities. Despite the disparities, the findings are still applicable and can inform the development of future interventions that promote care and support of children living in HIV/AIDS-affected families.

CONCLUSIONS

The study demonstrates the preliminary reliability and validity of the Chinese Mandarin version of PedsQL 4.0 for the first time with a HIV/AIDS-affected population. The findings suggests that the PedsQL 4.0 is generally a valid and reliable instrument, replicating some of the earlier findings for the original version. This is the first study of its kind to provide evidence that the HRQoL of children living in HIV/AIDS-affected families is lower than the HRQoL of children from ordinary families.

ACKNOWLEDGMENTS

We would like to thank Prof Varni for permission to use the PedsQL 4.0 Generic Core Scales. We are also grateful to all the children and their caregivers who so willingly participated in this study. We thank Adrian Liau for editing the article.

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Quality of Life of Outpatients in Methadone Maintenance Treatment Clinics

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Objective: To explore the quality of life (QOL) changes in methadone maintenance treatment (MMT) clinic outpatients in the first 3 months of treatment.

Methods: A cohort study was conducted in 5 MMT clinics for more than 3 months, and the QOL of outpatients was measured by the QOL instrument for drug addicts at days 1, 30, and 90 to explore QOL changes. Repeated measurement analysis method was used for data analysis.

Results: One hundred seventy-two outpatients in 5 MMT clinics were recruited, and 142 (82.65%) remained in treatment at day 90. The Cronbach α coefficient of the QOL instrument for drug addicts used in our study is 0.96, with a range of 0.74–0.94 for all subscales. The QOL scores of drug addicts improved from day 1 to day 30 ($\bar{X}_{\text{beginning}} = 51.92$, $\bar{X}_{\text{first month}} = 74.83$, $P < 0.01$), and all subscale scores improved significantly ($P < 0.01$). However, QOL improved little from day 30 to day 90, ($\bar{X}_{\text{first month}} = 74.83$, $\bar{X}_{\text{third month}} = 75.99$, $P < 0.01$). Physical health and mental health improved significantly during the second and third month, whereas all other subscale scores did not ($P > 0.05$).

Conclusions: MMT is helpful in improving the QOL of outpatients in MMT clinics in China.

Key Words: addiction outpatient, China, methadone maintenance treatment, quality of life

(*J Acquir Immune Defic Syndr* 2010;53:S116–S120)

INTRODUCTION

Drug addiction resurged in China in the early 1980s and spread quickly in the 1990s. From 1990 to 2000, the numbers of registered drug abusers increased more than 11-fold from 70,000 to 860,000.[1] There were 957,000 registered drug abusers in 2007[2]; however, the real number of drug abusers is estimated to be much higher. Heroin remains the major drug of abuse (78%) in China, and nearly three-quarters of heroin users (72.5%) are injecting drug users (IDUs),[2] and 40% of IDUs are estimated to share needles or syringes.[3]

Drug abuse is a complex issue and is linked to many social, economic, criminal, and health challenges facing different societies, one of which is HIV/AIDS. Globally, IDUs account for approximately 10% of the estimated 4.3 million new HIV infections that occur each year.[4] Of the estimated 700,000 HIV people living with HIV/AIDS, in China in 2007, approximately 38.1% (266,700) were infected via injecting drug use.[3] Although sexual intercourse is now the main HIV/AIDS transmission route in China, injecting drug use is still a major HIV transmission route and accounted for 42% of new HIV cases in 2007.[3]

In terms of the reduction of heroin use, criminal activity, and protection against HIV infection, methadone maintenance treatment (MMT) has been proven an effective therapy for heroin abuse.[5–7] After initial trials, MMT clinics were established by the Chinese government in 2004. According to an evaluation of the effectiveness of the first 8 pilot MMT clinics in 2007,[8] from baseline to 6 months, the proportion of drug use by clinical patients dropped rapidly (69.1% vs. 8.9%), injection frequency was reduced (90 times vs. twice per month), and self-reported criminal activities decreased sharply (20.7% vs. 3.6%). In addition, 95.9% of outpatients were satisfied with clinical services provided. Later studies of MMT in China have found results consistent to the evaluation of the 8 pilot MMT clinics.[9–12] Consequently, MMT is being scaled up rapidly in China and by the end of 2007, there were 503 clinics providing treatment for more than 50,000 outpatients per day.

To improve the effectiveness of MMT clinics, it was suggested that MMT clinics provide comprehensive services to outpatients in addition to MMT, such as providing free HIV and hepatitis C virus (HCV) testing. Although a comprehensive services model has not been developed, all MMT clinics provide at least 1 of the following services in China: antiretroviral therapy for eligible clients, psychological counseling, rehabilitation programs with social support, and life skills and employment skills training.[13,14]

To determine the impact of MMT on the lives of MMT clinic outpatients in China, a culturally appropriate quality of life instrument for drug addicts[15] was used to assess quality of life changes of MMT clinic outpatients during the first 3 months of treatment.

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Supported by the China Multidisciplinary AIDS Prevention Training Program with NIH Research Grant # U2R TW 006917 and U2R TW 006918, funded by the National Institutes of Health, the Fogarty International Center, the National Institute of Drug Abuse, and the National Institute of Mental Health (China ICOHRTA, with Principal Investigator Z. Wu).

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METHODS

Study Sites

Xi'an, the capital city of Shannxi province, has 8.2 million citizens, of which approximately 9000 are registered drug addicts and 69 are people living with HIV/AIDS. There are 5 MMT clinics in Xi'an, 4 of which were established 1 month before study commencement. These 5 MMT clinics offer HIV/HCV testing and psychological counseling provided by doctors from these clinics.

Participant Recruitment, Informed Consent, and Confidentiality

Participants were outpatients from the 5 MMT Clinics in Xi'an, who began treatment between November 15 and December 15, 2006. To be eligible, participants must be 20 years or above; have at least primary school education; can self-administer the questionnaire; and do not have a serious mental illness. The participant criteria was given to the chief medical officer of each clinic, who then checked all patient records and made a list of eligible potential participants (n = 176). All eligible potential participants were approached by the chief medical officer to see if they were interested in participating in the study. The purpose and processes of the study and the potential risks and benefits were explained by the researcher to each participant. It was emphasized that participation was confidential, and their daily treatment would not be affected whether or not they participated in the study. All except 4 outpatients (2.2%) agreed to participate, and verbal informed consent was obtained.

Quality of Life Instrument

The quality of life instrument for drug addicts used in our study was developed by Xiao et al[15] in 2006. The instrument was developed to test the quality of life of drug addicts and is composed of 61 items covering following 6 dimensions: physical health, mental health, family relationships and social support, living condition (economic status and ability to participate in various social activities), drug dependence, and satisfaction with life. The Cronbach α coefficient was 0.958, test-retest reliability was 0.917, and half-split reliability was 0.844. Six dimensions accounted for 53.68% of variance. The loading of each item on expected factors was 0.433–0.853. The comparative fit index was 0.95, and the standardized root mean residual was 0.07. In addition, the instrument had good content validity when tested on drug addicts using a cognitive study, indicating each item is perceived by drug addicts and the instrument designer as having a similar meaning. Therefore, it has robust psychometric properties.[15]

Study Design

A cohort study was conducted. Outpatients in MMT clinics were followed for 3 months (Fig. 1). After informed consent was obtained, quality of life scores of outpatients were measured by the quality of life instrument for drug addicts at treatment day 1, day 30, and day 90.

Permission to undertake the study was granted by the Institutional Review Board of the National Center for STD/AIDS Control and Prevention, Chinese Center for Disease Control and Prevention.

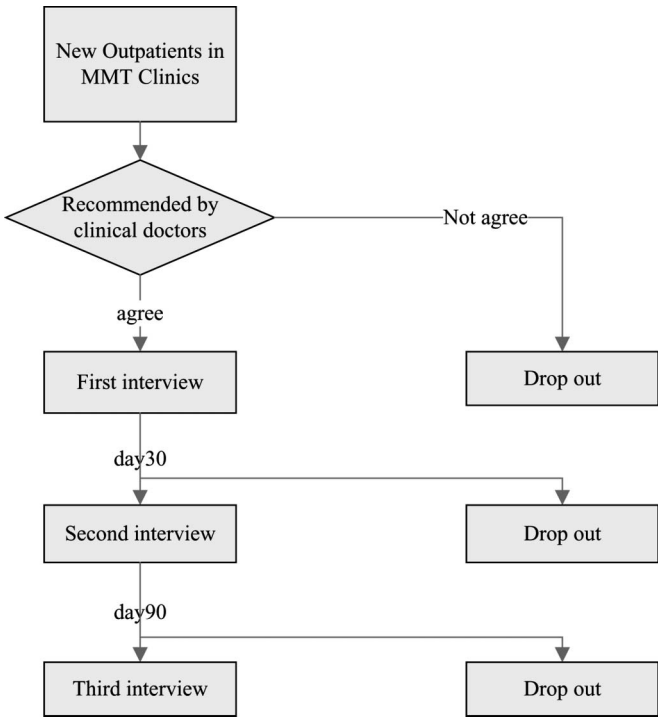

FIGURE 1. Study design flowchart.

Interview

After informed consent was given, a self-administered questionnaire was completed by participants in a separate private room. The researcher responded to interviewees' questions and checked the integrity of the completed questionnaires. If any missed item was unintentional, this was immediately corrected.

Statistical Analysis

To ascertain whether or not sociodemographic characteristics were confounders in the comparison of quality of life for drug addicts, χ^2 test and analysis of variance (ANOVA) were used to compare the sociodemographic characteristics of participants on day 1, day 30, and day 90. The reliability of the quality of life measurement was calculated. ANOVA for repeated measurement data was used to analyze the difference between drug addicts' quality of life scores on day 1, day 30, and day 90. If the data did not accord with Feldt–Huynh condition, Greenhouse–Geisser adjusted result was used.

RESULTS

Sociodemographic Characteristics of Participants

One hundred and seventy-two outpatients were recruited. On day 30, 163 (94.77%) outpatients remained and this dropped to 142 (82.56%) outpatients on day 90. During the course of the study, most participants were male (~85%),

unemployed (~ 76%), Han Chinese (~90%), intravenous drug users (~76%), and HCV positive (~73%). The sociodemographic characteristics of participants at each data collection time point are listed in Table 1.

The sociodemographic characteristics of participants at day 1, day 30, and day 90 were compared, and no significant difference was found between the different time points ($P > 0.05$). Thus, sociodemographic characteristics were not confounders for comparison of the quality of life scores for drug addicts between day 1, day 30, and day 90.

Reliability of the Quality of Life Instrument

In our study, the reliability of the quality of life of instrument was calculated, and the results are as follows: Cronbach α coefficient was 0.96 for the overall instrument and was 0.91 for physical health, 0.94 for mental health, 0.86 for family relationship and social support, 0.74 for living condition, 0.81 for drug dependence, and 0.86 for satisfaction with life. The Spearman–Brown split-half reliability coefficient was 0.86 overall and was 0.83 for physical health, 0.89 for mental health, 0.82 for family relationship and social support, 0.72 for living condition, 0.83 for drug dependence, and 0.83 for satisfaction with life. According to Fayer and Hays,[16] reliabilities of an instrument exceeding 0.70 are acceptable for group comparison and should be larger than 0.8 for individual evaluation. This indicates the quality of life instrument used in this study has sufficient reliability.

TABLE 1. Sociodemographic Characteristics of Participants

Variables	Day 1 (172)	Day 30 (163)	Day 90 (142)
Gender (%)			
Male	146 (84.9)	138 (84.7)	121 (85.2)
Female	26 (15.1)	25 (15.3)	21 (14.8)
Age (yrs)	38.0 ± 5.43	37.8 ± 5.39	37.9 ± 5.25
Marital status (%)			
Single	67 (39.0)	65 (39.9)	59 (41.5)
Married	80 (46.5)	75 (46.0)	63 (44.4)
Divorced	24 (14.0)	22 (13.5)	20 (14.1)
Widow/widower	1 (0.6)	1 (0.6)	0 (0.0)
Employment			
Unemployed	133 (77.3)	124 (76.1)	108 (76.1)
Farmer	4 (2.3)	4 (2.5)	2 (1.4)
Employer	12 (7.0)	12 (7.4)	11 (7.7)
Laborer	12 (7.0)	12 (7.4)	11 (7.7)
Waiter	8 (4.7)	8 (4.9)	7 (4.9)
Office clerk	3 (1.7)	3 (1.8)	3 (2.1)
Ethnicity			
Han	154 (89.5)	147 (90.2)	126 (88.7)
Hui	17 (9.9)	15 (9.2)	15 (12.6)
Zhuang	1 (0.6)	1 (0.6)	1 (0.7)
Education (%)			
Primary school and illiterate	17 (9.9)	17 (10.4)	14 (9.9)
Junior high school	96 (55.8)	91 (55.8)	80 (56.3)
Senior high school	51 (29.7)	47 (28.8)	40 (28.2)
College and	8 (4.7)	8 (4.9)	8 (5.6)
Drug use (yrs)	9.6 ± 4.881	9.7 ± 4.86	9.59 ± 4.724
Drug administration method (%)			
Inhaled	39 (22.7)	36 (22.1)	31 (21.8)
Intravenous injection	131 (76.2)	125 (76.7)	109 (76.8)
Muscular injection	1 (0.6)	1 (0.6)	1 (0.7)
Mixed	1 (0.6)	1 (0.6)	1 (0.7)
HIV (%)			
Yes	0 (0.0)	0 (0.0)	0 (0.0)
No	161 (93.6)	157 (96.3)	137 (96.5)
Unknown	11 (6.4)	6 (3.7)	5 (3.5)
HCV (%)			
Yes	122 (70.9)	119 (73.0)	106 (74.6)
No	39 (22.7)	38 (23.3)	31 (21.8)
Unknown	11 (6.4)	6 (3.7)	5 (3.5)

Quality of Life for Outpatients Receiving MMT

Table 2 and Figure 2 show the changes of quality of life score and subscale scores of outpatients receiving MMT at treatment initiation, day 30 and day 90.

As the ANOVA for repeated measurement data indicates, quality of life scores of outpatients in MMT clinics differed between days 1, 30, and 90 ($F = 469.15$, $P < 0.05$). The quality of life score on day 30 was higher than day 1 ($F = 550.44$, $P < 0.05$), and only a minor increase was measured from day 30 to day 90 ($F = 191.34$, $P = 0.05$). This indicates MMT is helpful in improving the quality of life of outpatients in clinics, especially in the first month.

Physical Health

The physical health subscale score increased from day 1 to day 30 ($F = 191.71$, $P < 0.05$), and from day 30 to day 90 ($F = 6.32$, $P < 0.05$) indicating that the physical health of outpatients receiving MMT improved gradually over the 3 month period.

Mental Health

The score of mental health increased significantly from day 1 to day 30 ($F = 324.65$, $P < 0.05$) and also did so from day 30 to day 90 ($F = 5.77$, $P < 0.05$).

Family Relationship and Social Support

The subscale score for family relationship and social support of outpatients on day 30 improved over day 1 ($F = 163.54$, $P < 0.05$). This was the only subscale to register a decrease from day 30 to day 90, although this decrease was not significant ($F = 0.85$, $P > 0.05$).

Living Condition

The subscale score on day 30 is much higher than that on day 1 ($F = 124.34$, $P < 0.05$); however, there was no significant change between day 30 and day 90 ($F = 1.55$, $P > 0.05$), indicating that outpatients' living conditions improved rapidly in the first month and then remained stable for the following 2 months.

Drug Dependence

Among all the subscales, scores on this subscale showed the largest improvement in the first month, improving dramatically from 45.65 to 91.31 in the first month ($F = 1095.39$, $P < 0.05$). The scores remained stable at this level from day 30 to day 90 ($F = 3.44$, $P > 0.05$).

TABLE 2. Quality of Life of 142 Outpatients at Day 1, Day 30, and Day 90

	Day 1 ($\bar{x} \pm s$)	Day 30 ($\bar{x} \pm s$)	Day 90 ($\bar{x} \pm s$)
Quality of life	51.92 ± 10.893	74.83 ± 8.786	75.99 ± 8.635
Physical health	56.17 ± 14.286	74.91 ± 11.220	76.94 ± 12.260
Mental health	52.46 ± 16.134	78.85 ± 13.833	81.33 ± 13.492
Family relationship & social support	57.31 ± 16.172	75.82 ± 15.203	74.82 ± 14.882
Living condition	52.85 ± 10.146	62.45 ± 10.632	63.55 ± 10.346
Drug dependence	45.65 ± 14.893	91.31 ± 9.275	92.92 ± 8.780
Satisfaction with life	47.06 ± 13.335	65.65 ± 13.102	66.50 ± 12.701

Satisfaction With Life

This improved significantly in the first month ($F = 226.34$, $P < 0.05$), and there was only a minor improvement between day 30 and day 90 ($F = 0.86$, $P > 0.05$).

DISCUSSION

Heroin addiction is not only symptomatic of problems in the lives of drug addicts but also can introduce serious problems into the lives of such users. More than 70% of drug addicts in China suffer from physical illnesses including gastritis, bacterial infections, cardiovascular diseases, pulmonary disease, hepatitis, and HIV/AIDS.[17] In our study, physical health of outpatients improved continuously from day 1 to day 90. This indicates that although some outpatients experienced side effects from methadone, their physical health improved greatly due to MMT.

In China, drug addicts, and in particular those who use heroin, have poor mental health, such as low self-esteem and high anxiety, compared with nonaddicts.[18,19] The results of our study showed that MMT continually improved outpatients' mental health from treatment initiation to day 90. This may be because MMT enabled outpatients to feel less stressed after the start of treatment due to being free from the financial burdens of drug addiction and not needing to worry about being arrested or having an overdose. In addition, there is strong stigma toward drug addicts in China, and most outpatients feel ashamed of their addiction to heroin. After treatment initiation, they slowly became independent from heroin addiction, and their self esteem returned as a result.[20] Moreover, the support they received from the MMT doctors and family members may have helped to further improve the mental health of outpatients.

The improved living condition in the first month of MMT might be because most clients receive more financial support from their families compared with before treatment initiation. However, due to most drug addicts lacking suitable employment skills, and combined with the strong discrimination against drug addicts in China, it is extremely difficult for MMT outpatients to gain and maintain meaningful employment. Thus, their living condition score did not improve much. This suggests a need to provide career-training programs in MMT clinics and conduct interventions in communities to reduce stigma against drug addicts.

Addicts usually receive less social support than nonaddicts.[21,22] In our study, outpatients in MMT improved relationships with their families and received more social support from day 1 to day 30; however, this improvement did not continue from day 30 to day 90 and in fact decreased slightly. This might be due to misunderstanding from family members of the effectiveness with which MMT can assist outpatients to detoxify and be rehabilitated; they may have

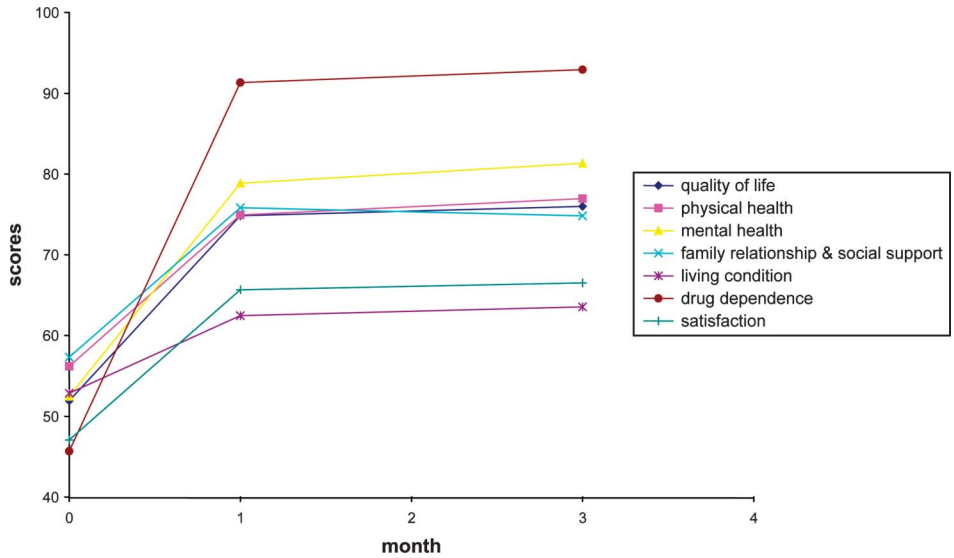

FIGURE 2. Changes of quality of life and subscale scores.

hoped MMT could solve all problems caused by heroin addiction. Family members may lose heart if the outpatient relapses into drug use or conducts property crime. This suggests the need to provide consulting services for family members, because family is of central importance in Chinese culture, and most support for outpatients come from their families as social support services of this nature for drug users are not widely available in China.

Although the provision of comprehensive services using MMT clinics as a platform for delivery needs require expanding, improving, and scaling up, the quality of life of outpatients receiving treatment in the existing MMT clinics improved significantly. This result is consistent with studies in western countries.[23–25]

It is well know that retention rates are a potential problem for MMT programs, and many studies have investigated this issue.[26–29] In our study, 9 participants dropped out by the end of the first month, and the retention rate at day 90 was 82.6%. These results were similar with another study in China, which showed the average retention rate was 93.5% at day 30 and 81.5% at day 90.[30]

Due to good relationships between outpatients and doctors in the MMT clinics, only 4 qualified potential participants refused to participate in our study. Thus, the results of our study are reliable to reflect upon quality of life changes in literate outpatients in MMT clinics. In our study, all participants were required to administer the questionnaire themselves; therefore, illiterate drug addicts were excluded. Illiterate MMT clinic outpatients still need to be studied as their quality of life may be different to that of literate MMT clinic outpatients; the latter of whom may have greater employment opportunities.

CONCLUSIONS

MMT is helpful in improving the quality of life of outpatients in MMT clinics and should be expanded further in China.

ACKNOWLEDGMENTS

Thanks go to the staff at Xi'an CDC and the Directors of the 5 MMT Clinics in Xi'an for their help with this study. The authors would also like to thank Naomi Juniper and Adrian Liau for their assistance in editing the article.

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Reliability and Validity of the Chinese Version of the Addiction Severity Index

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Objective: The addiction severity index (ASI) is one of the most commonly used assessment devices used in the field of substance abuse. There is no research on the Chinese version of the newest scale in China so far. The study is to validate a Chinese adaptation of the fifth version of the ASI instrument.

Method: The Chinese version of the ASI was translated and revised based on the fifth English version. Psychometric properties of the ASI were tested through face-to-face interviews. Five hundred and twenty-six patients who had been in the methadone maintenance treatment clinic in Xi'an City, Shanxi Province, for more than 3 months were interviewed by 3 trained interviewers. About 83% of the 526 interviewees were male. Analysis of internal consistency, reliability measures including test-retest and inter-rater correlation, and criterion validity were conducted.

Results: Across 7 domains of the Chinese version of the ASI, Cronbach α coefficients ranged from 0.44 to 0.79, test-retest correlation coefficients ranged from 0.68 to 0.84, inter-rater correlations ranged from 0.74 to 0.98, and the criterion validity was 0.5.

Conclusions: The Chinese version of the ASI has acceptable reliability and validity in a sample of drug-dependent patients.

Key Words: addiction severity index, reliability, validity

(*J Acquir Immune Defic Syndr* 2010;53:S121–S125)

INTRODUCTION

The Addiction Severity Index (ASI) is one of the most widely used semistructured interviews in the field of substance abuse,[1] having been translated into more than 13 languages.[2–6] It has been used for more than 26 years to explore the problems of addiction patients and to measure illness outcomes and treatment effectiveness in 7 different areas. In recent years, the ASI has been increasingly used for special subgroups of drug users such as homeless persons,[7] pregnant and postpartum women,[2] and adolescents.[8]

Methadone maintenance treatment (MMT) has been considered one of the best practices in the treatment for opiate dependence.[9] In addition to decreasing the use of drugs, MMT can also decrease both drug-related crimes and the transmission of diseases such as HIV. The first MMT program in China began in 2004 to prevent HIV transmission through drug use. However, there are many problems associated with MMT clinics programs, including their management and evaluation. It is therefore particularly important to study the Chinese version of the ASI to assess the effectiveness of MMT programs.

Findings of methodological studies showed that test-retest reliability of the ASI was quite good. Butler et al[10] found Pearson correlations ranging from 0.62 to 0.95. The inter-rater reliability was also high.[1] Studies reported that internal consistency measured by Cronbach α coefficient ranged from 0.62 for the legal area category to 0.93 for the medical area category.[2,11–13] Studies conducted among drug users confirmed good validity of the ASI. Hendriks et al[4] found that the correlation between psychiatric subscale of ASI and Symptom Checklist-90 (SCL-90) was 0.54.

The purpose of this study was to test the reliability and the validity of the Chinese version in a sample of MMT patients.

METHODS

Setting and Participants

The study was conducted in 5 MMT clinics in Xi'an city, Shanxi Province. All participants had been in MMT for more than 3 months when the study began. Exclusion criteria included severe mental or physical deterioration. This study was approved by the institute review board (IRB) of the National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and Prevention, and informed consent was given by all patients.

Instrument

The ASI assesses the severity of addiction and need for treatment in 7 areas, each reflecting a separate problem area of drug/alcohol abuse: (1) medical status; (2) employment and social support; (3) drug use; (4) alcohol use; (5) legal status; (6) family and social relationships; and (7) psychiatric status. The Chinese version of the ASI was based on items from the fifth English version.[14] It was translated by 2 independent

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Supported by the China Multidisciplinary AIDS Prevention Training Program with NIH Research Grant #U2RTW006917 and U2RTW006918, funded by the US National Institutes of Health, the Fogarty International Center, the National Institute of Drug Abuse, and the National Institute of Mental Health (China ICOHRTA, with Principal Investigator Z. Wu).

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TABLE 1. Demographic Characteristics of the Study Population

Variable	Statistic	n
Age	37.84 ± 6.04	526
Gender		
Male	83.3%	438
Female	16.7%	88
Occupation		
Owner	5.9%	31
Service	1.1%	6
Unemployed	82.1%	432
Staff	1.5%	8
Worker	6.7%	35
Farmer	2.3%	12
Other	0.4%	2
Education		
Primary school or lower	7.6%	40
Junior middle school	51.7%	272
Senior middle school	36.7%	193
College or higher	4.0%	21
Marital status		
Single	34.8%	183
Married	54.6%	287
Divorced/widowed	10.7%	56

translators specializing in different areas of research and revised by editors specializing in addiction research. The result was then translated back into the original language and compared with the English version by native English-speaking editors. In the interest of international comparability, only the necessary, minimal changes were made to the original questionnaire. The changes made were mainly based on unique Chinese linguistic and sociocultural factors such as wording or expression style, criminal categories, and compliance with legal regulations, etc. Compared with the original scale, 2 items in the "legal status" area was deleted and 2 other items in the "employment and social support" area were replaced by 2 new items. One separate section was added for clinical purpose, which addressed HIV risk factors, such as needle sharing and unprotected sex. Reliability and validity of this section was not evaluated because it did not interfere with the ASI composite scores (CSs) scoring. Item numbering remained similar to the ASI (5th English version).

TABLE 2. Cronbach's α Coefficient (n = 526)

ASI Scale	α
Medical	0.73
Employment	0.63
Alcohol	0.68
Drug	0.67
Legal	0.44
Family/social	0.79
Psychiatric	0.73

TABLE 3. Test-Retest: Spearman ρ Correlations of CSs (n = 51)

ASI Scale	CSs (ρ)
Medical	0.84*
Employment	0.75*
Alcohol	0.75*
Drug	0.70*
Legal	0.72*
Family/social	0.80*
Psychiatric	0.68*

*$P < 0.01$.

Procedures and Analysis

Three interviewers (1 researcher and 2 doctors) participated in the study. Each of the 2 doctors involved had several years of psychiatric clinic experience. All of the interviewers completed a 1-day training program that reviewed the ASI manual, through discussions and practice sessions.

During the face-to-face interview, patient and interviewer rated the level of severity using separate rating scales for each of the 7 ASI areas. The patient uses a scale of 0–4 to rate (1) how serious he/she thinks the problem is, and (2) how important he/she considers it is to receive treatment or counseling. The interviewer uses a 9-point scale for each area to rate the patient's requirement for further treatment. This assessment relies on the patient's symptoms at that time and the patient's own subjective evaluation. The interviewer has to decide how much additional treatment the patient needs in each of the areas.

The data were assessed according to international practice.[15] CSs were calculated for all 7 areas.[16] The inter-rater reliability, test-retest reliability, and internal consistency among the reliability indicators were examined. Inter-rater reliability was established involving 1 primary interviewer questioning the patient and the other 2 observing and scoring independently in 80 separate interviews. The stability of the measures over time was evaluated by comparing CSs between the first and second interviews with a time interval of 7 days. Correlations were calculated between interviewers' severity ratings (ISRs) and CSs, between CSs across different areas, and between "critical items" constituting the different areas and the CSs within sections.

TABLE 4. Inter-Rater Reliability: α Coefficient of CSs and Interviewers' Severity Ratings (n = 80)

ASI Scale	CSs (α)	ISRs (α)
Medical	0.98	0.94
Employment	0.97*	0.91
Alcohol	0.94	0.85
Drug	0.88	0.82
Legal	0.87	0.74
Family/social	0.94	0.89
Psychiatric	0.93	0.88

TABLE 5. Spearman ρ Correlations Between Severity Ratings and CSs (n = 526)

ASI Scale	Correlation Coefficients
Medical	0.73*
Employment	0.67*
Alcohol	0.92*
Drug	0.86*
Legal	0.98*
Family/social	0.94*
Psychiatric	0.71*

*$P < 0.001$.

The data were analyzed using SPSS for Windows 13.0. Internal consistency was calculated by Cronbach α test, with a value of 0.6 and higher considered as acceptable.[2] Spearman correlation test was used to calculate reliability coefficients and validity of similar scales. The significance level (*P* value) was set at 0.05.

RESULTS

Demographic Characteristics

Five hundred and thirty-one patients were randomly chosen and approached while waiting for their methadone dose. Five interviews were abandoned because of incomplete information. Demographic comparisons between the final sample (n = 526) and 331 admissions preceding the study were statistically nonsignificant.

The sample comprised 438 males and 88 females. The average age was 37.8 years (age range: 21–53; SD = 6.0). A majority of the drug users participating in the investigation (59.3%) had finished junior middle school, whereas 4% had a college-level education or higher. Most were unemployed (82.1%; n = 432). Fifty-eight patients (11%) reported abusing alcohol in their lifetime, whereas only thirty-six (6.8%) had alcohol problems during the 30 days before the interview (Table 1).

Internal Consistency

The reliability of the subscales covering the ASI problem areas in our sample was considered acceptable except for the legal subscale (Cronbach α = 0.44). The value of the other 6 domains ranged from 0.63 to 0.79 (Table 2). The legal domain failed to demonstrate good internal consistency in this sample of patients.

Test-Retest Reliability

The CSs before and after a week's interval were highly correlated. Spearman ρ correlations for the test-retest were high (0.68–0.84; Table 3). There was no significant difference between the 2 interviews, indicating that the Chinese version of the ASI was stable.

Inter-Rater Reliability

All severity ratings and CSs had good correlations ranging from 0.74 to 0.98 (Table 4). Overall, the CSs had higher coefficient (mean = 0.93) than the severity ratings (mean = 0.86).

Relationship Between ISRs and CSs

Table 5 showed the correlation between the ISRs and the CSs. In most areas, the correlation was high, ranging from 0.67 to 0.98.

Relationship Between CSs

To demonstrate that different ASI domains reflected distinct problem areas with minimal overlaps, correlations between domains were evaluated (Table 6). The correlation coefficient was quite low.

Relationship Between Items and CSs

Several items were chosen in each of the 7 domains as indicators of problem severity and the correlations between these items and the CSs were presented in Table 7. In most cases, items were significantly correlated with the CSs. The only correlation not of statistical significance was that between prescribed medication for any psychological/emotional problem in last 30 days and the psychiatric score.

Criterion Validity of the CSs

Table 7 presented the correlation between the CSs and the criterion measurement. The correlation of the psychiatric score with *SCL-90* was 0.5, the correlation of the family/social score with the "Family Adaptability and Cohesion Evaluation Scale II-Chinese Version" was 0.45.

TABLE 6. Correlation Coefficients Among CSs (n = 526)

ASI Scale	Medical	Employment	Alcohol	Drug	Legal	Family/social	Psychiatric
Medical	1.0000	—	—	—	—	—	—
Employment	0.0772	1.0000	—	—	—	—	—
Alcohol	0.0461	0.0141	1.0000	—	—	—	—
Drug	0.1896†	0.0377	0.0120	1.0000	—	—	—
Legal	0.0241	0.0500	0.0696	0.1647†	1.0000	—	—
Family/social	0.0925*	−0.0661	0.0281	0.0829	0.0255	1.0000	—
Psychiatric	0.2273†	0.0568	0.1030*	0.1919†	0.1496†	0.1836†	1.0000

*$P < 0.05$.
†$P < 0.01$.

TABLE 7. Correlation Coefficients Between Items and CSs

Items	Correlation Coefficients
Medical status (n = 526)	
Days experienced medical problems (last 30 days)	0.86*
Troubled by medical problems (last 30 days)	0.69*
Treatment importance for the medical problems	0.73*
Employment/social support (n = 526)	
If vehicle available when going out	−0.14†
If the vehicle convenient when going out	−0.32*
Days paid for work (last 30 days)	−0.77*
Money received from employment (last 30 days)	−0.91*
Drugs (n = 526)	
Heroin use (last 30 days)	0.27*
Days experienced drug problems (last 30 days)	0.63*
Troubled by drug problems (last 30 days)	0.67*
Treatment importance for drug problems	0.57*
Alcohol (n = 526)	
Alcohol consumption: moderate use (last 30 days)	0.99*
Alcohol consumption: intoxication (last 30 days)	0.50*
Days experienced alcohol problems (last 30 days)	0.46*
Troubled by alcohol problems (last 30 days)	0.25*
Treatment importance for alcohol problems	0.22*
Money spent for alcohol (last 30 days)	0.94*
Legal (n = 526)	
Severity of present legal problems	0.88*
days engaged in illegal activities for profit (last 30 days)	0.39*
Money received from illegal activities (last 30 days)	0.66*
Family/social relationships (n = 526)	
Satisfied with marital status	0.87*
Troubled by family problems (last 30 days)	0.51*
Treatment importance or counseling needs for these family problem	0.54*
Days experienced serious conflicts with your family (last 30 days)	0.34*
Psychiatric (n = 526)	
Experienced serious depression (last 30 days)	0.66*
Experienced serious anxiety or tension (last 30 days)	0.47*
Experienced hallucinations (last 30 days)	0.22*
Experienced trouble understanding, concentrating or remembering (last 30 days)	0.59*
Experienced trouble controlling violent behavior (last 30 days)	0.34*
Experienced serious thought of suicide (last 30 days)	0.39*
Attempted suicide (last 30 days)	0.14†
Prescribed medication for any psychological/emotional problem (last 30 days)	0.08
Days experienced psychological or emotional problems (last 30 days)	0.95*
Troubled by these psychological or emotional problems (last 30 days)	0.72*
Treatment importance for these psychological problems	0.53*
SCL-90 (n = 47)	0.5*
Family Adaptability and Cohesion Evaluation Scale II-Chinese Version (n = 44)	0.45*

*$P < 0.001$.
†$P < 0.01$.

DISCUSSION

The findings with the Chinese version of the ASI were consistent with many other studies.[4,14,17] However, the internal consistency was moderate to weak for the "legal" domain. This was likely because of the modification to the original items in this area in terms of Chinese sociocultural background and drug-related criminal categories. Two of the 5 critical items used to calculate the CSs were abandoned (whether presently awaiting charges, trial, or sentencing and importance of counseling or referral for legal problems). For the other 6 domains of the ASI, the Cronbach α coefficient was acceptable and similar to results found in the literature.[18–20]

The test-retest reliability[10,21] and inter-rater reliability also corresponded to the values found in other studies.[1,22] The CSs coefficient being higher than the ISRs coefficient was also consistent (Gerevich et al[4]). Greater agreement among the CSs would be expected because these scores were based on mathematical formulas and did not take into account the interviewer's subjective interpretation. Criterion validity of the CSs was acceptable. The correlation between CSs and SCL-90 in the study was similar to findings of Hendriks et al.[4]

Correlations between domains of the ASI were generally low. The result indicated a relative independence between domains. This independence has been found in other studies.[12,23] CSs and items within the same domain were significantly correlated, confirming the validity of the ASI original scale construct.

One limitation in this study involves the alcohol domain. Ninety-three percent of the interviewees have not experienced alcohol problems in the last 30 days because the patients were prohibited from drinking alcohol during treatment in MMT clinic. This may have led to an underestimation of the alcohol problems of the patients, which would also have an effect on the evaluation of the reliability and validity of the scale.

Overall, this Chinese version of the ASI seemed to have acceptable reliability and validity. The scale was demonstrated to be a valid instrument for Chinese drug-dependent patients and can be used widely in addiction research areas such as assessing addiction of patients in methadone maintenance patients and assessing effectiveness of the treatment.

ACKNOWLEDGMENTS

Authors thank Ying Wang and Rui Zhang for their contribution to the interviewing work; thank Wei Jia, Quncai Zhang, Hong Yan, and Liangliang Li for their organizational work; thank Jianhua Li for his comments and suggestions; and thank Adrian Liau for editing the article.

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