Rapidly Spreading Human Immunodeficiency Virus Epidemic Among Older Males and Associated Factors: A Large-scale Prospective Cohort Study in Rural Southwest China

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Background: Increasing risk of human immunodeficiency virus (HIV) heterosexual transmission can raise the potential for a more diffuse and generalized epidemic. In response to the paucity of data on HIV incidence among heterosexuals in China, we conducted a large-scale, population-based cohort study located in rural southwest China.

Methods: Baseline enrollment for the study was conducted from 2013 to 2014 and follow-up at 12 months was from 2014 to 2015 among adults 20 years or older in 3 rural counties of Southwest China. Study participants were informed of the study by brochures and leaflets distributed in outreach activities. Interviews and blood collection were conducted in private rooms. Blood samples were tested for HIV infection.

Results: The HIV prevalence of the sample was 0.29% (95% confidence interval [CI], 0.27–0.30) (2063 of 722,795) among the total adult population of 1,090,296 potential participants 20 years or older at baseline. Of the 720,732 individuals who tested HIV-negative at baseline, 493,990 (69%) completed the follow-up. Overall HIV incidence was 2.73 (95% CI, 2.38–3.08) per 10,000 person-years (PY) (235 of 860,627 PY). Human immunodeficiency virus incidence was associated with males, older age, less than secondary schooling and not currently being married. Human immunodeficiency virus incidence was 71.28 (95% CI, 35.21–107.35) per 10,000 PY among males aged 50 to 69 years who had less than secondary schooling and were divorced or widowed. Heterosexual sex was the dominant transmission mode for HIV seroconversions (99.0%).

Conclusions: Older heterosexual males were at disproportionate risk of HIV infection. Health authorities in China need to develop and implement innovative interventions suitable for the broader population of older heterosexuals.

Drug abuse reemerged as a problem in China when an open-door policy was adopted in the late 1980s.1–5 The first human immunodeficiency virus (HIV) outbreak among people who inject drugs (PWID) in China was discovered in Yunnan in 1989.6 Thereafter, HIV transmission spread rapidly among PWID residing along the major drug-trafficking routes to other provinces in Southern and Western China.7–12 Since China adopted elements of a free market economy in 1978, commercial sex activities have increased dramatically across the country.13 The proportion of newly reported HIV/acquired immune deficiency syndrome (AIDS) infections through heterosexual sex increased from 39% in 2007 to 66% in 2014, whereas new HIV/AIDS infections attributed to injection drug use decreased from 29% in 2007 to 6% in 2014.14,15 Generally, the HIV epidemic in China has been similar to other Asian countries, starting as a drug-driven epidemic and shifting to one driven predominantly by sexually transmission.16–22 Human immunodeficiency virus incidence attributed to male-male and female-female sex has increased rapidly in China.14–16 Guangxi is the homeland of the Zhuang nationality, has approximately 50 million people, and is a developing area in China. Guangxi is located in Southwest China bordering Vietnam and is...
in close proximity to the “Golden Triangle,” an area between Myanmar, Laos, and Thailand known for the manufacturing of illicit drugs.7–10 Guangxi lies along the eastern drug-trafficking route linking Yunnan (adjacent to the Golden Triangle), Guangdong, and Hong Kong. Guangxi’s initial HIV epidemic was fueled by PWID, who accounted for the majority of reported HIV/AIDS cases in the late 1990s (Supplementary Figure 1a, http://links.lww.com/OLQ/A325).15 In the meantime, the HIV epidemic has shifted to predominantly heterosexual transmission, accounting for less than 10% of new cases in 2000 to over 90% of new cases in 2013 (Supplementary Figure 1a, http://links.lww.com/OLQ/A325).15.15.The demographics of individuals most afflicted by the epidemic have also shifted. In the same time frame, the elder population (≥50 years of age) as a proportion of new HIV cases increased from less than 4% in 2000 to over 40% in 2013 (Supplementary Figure 1b, http://links.lww.com/OLQ/A326).15 In 2013, 10,877 cases of HIV/AIDS were reported in Guangxi.15

It is important to study the rapid evolution of the HIV epidemic in Guangxi to understand the specific characteristics and factors contributing to these dramatic changes. These research findings will help to explain the epidemic shift and guide targeted interventions for the most vulnerable populations. During the earlier phases of the epidemic, high-risk populations were largely restricted to paid blood donors and PWID. In the current sexually driven epidemic, risk groups are much broader. Population-based incidence rates of HIV infection are still difficult to obtain in both China and elsewhere in the world. In response to this gap in the literature, the aim of this study was to use a large-scale population-based prospective cohort study to evaluate HIV incidence and demographic correlates in 3 rural counties in the Guangxi Zhuang Autonomous Region, a provincial-level region located in southwest China that reports 12% of all new cases of HIV in China.15

METHODS

Study Design and Study Population

Under the support of the National Mega Project on Infectious Disease Prevention and Control, we designed a population-based cohort study in 3 rural counties in Guangxi. The baseline survey was conducted from January 2013 to March 2014 and the follow-up at 12 months among individuals who tested HIV-negative at baseline was conducted from October 2014 to June 2015. Participants were informed of this study by brochures and leaflets distributed in outreach activities. Local health staff were trained to distribute recruitment information to potential participants. Recruitment materials included basic knowledge of HIV, transmission and prevention, counseling and testing, care and national free treatment services. All participants, regardless of HIV diagnosis, were contacted directly by outreach workers and indirectly through word of mouth to invite them to join the study for testing HIV. There was no incentive for study participation. Eligibility criteria included residency in 1 of the 3 counties, 20 years or older, willing to participate, and provision of informed consent. All participants who met the study criteria then received HIV pretest counseling, had blood drawn to test for HIV antibody, and were given HIV testing results and post-testing counseling. Interviews and blood collection were conducted in private rooms at township hospitals and village clinics. All individuals who tested positive for HIV during the study were introduced to the National AIDS Control and Care policy by health staff and then referred to the National Free Antiretroviral Treatment Program. To maintain high follow-up retention rates, outreach workers made telephone calls and/or home visits if a participant missed initial follow-up testing. The study protocol and informed consent form were approved by the institutional review board of the Guangxi Center for Disease Control and Prevention.

Of 1,090,296 potential participants 20 years or older, 722,795 study participants completed the baseline survey. Two thousand sixty-three participants tested positive for HIV during the baseline survey. Of the 720,732 participants who tested HIV-negative at baseline, 493,990 completed the follow-up. Two hundred thirty-five seroconversions were observed during the follow-up. Reasons for participant nonenrollment and lost to follow-up were not documented.

Data Collection

Questionnaire-based interviews were conducted in a private room. Trained health staff conducted the interviews. Each study participant was assigned a unique and confidential identification number for the questionnaire and blood samples. Questionnaire data included age, ethnicity, education, marital status, and occupation. If participant HIV test results were positive, additional questions about transmission route were asked, such as heterosexual sex, male-to-male sex, and drug injection. Questions concerning HIV transmission modes were asked to guide the development of future interventions.

Laboratory Testing

Blood samples were tested for HIV infection. Human immunodeficiency virus antibody was screened in each blood sample by enzyme-linked immunosorbent assay (Diagnostic Kit for Antibody to Human Immunodeficiency Virus, Beijing WANTAI Biological Pharmacy Enterprise Co. Ltd, China; and Gentscreen ULTRA HIV Ag-Ab, Bio-Rad Laboratories, USA), and was confirmed by HIV Western Blot confirmation (MP Diagnostics HIV BLOT2.2, MP Biomedicals Asia Pacific Pte. Ltd).

Statistical Analysis

Questionnaire-based data and biological testing results were recorded, double-entered and compared with SPSS version 17.0 (SPSS, Inc., Chicago, IL). Human immunodeficiency virus prevalence at baseline was calculated as the number of HIV infections/number of participants enrolled. The incidence of HIV was estimated by using the number of seroconversions detected within the follow-up period as the numerator and the cohort’s total number of person-years (PY) exposure to the risk of transmission as the denominator. To identify factors associated with HIV infection and incidence, logistic regression and Cox regression models were used, respectively. Adjusted regression models included the following control variable covariates: age, sex, ethnicity, education, marital status, occupation, and county. Statistical significance was defined as a P less than 0.05 (2-tailed).

Ethics Statement

The study was approved by the institutional review board of the Guangxi Center for Disease Control and Prevention.

RESULTS

General Characteristics of Study Population

Of 1,090,296 potential participants 20 years or older, 66.3% (722,795 of 1,090,296) participated in the population-based cohort study. Of 722,795 study participants who completed the baseline survey, participants older than 50 years represented 36.0%. The percentage of males was 48.9%. Participants (62.1% and 36.3%) were ethnically Han and Zhuang, respectively. The
percentage of participants with no schooling, primary schooling or secondary schooling or above was 5.7%, 33.5% and 60.8%, respectively. Participants, 86.4%, 9.9% and 3.7%, were currently married, single, and divorced/widowed, respectively. The occupation for most participants (89.2%) was agricultural farming.

HIV Infection Rates at Baseline

The HIV infection prevalence was 0.29% (95% confidence interval [CI], 0.27–0.30) (2063 of 722,795) among all study participants (group aged ≥20 years) at baseline. Table 1 presents the factors (age, sex, ethnicity, education, marital status, occupation, and county) associated with HIV infection at baseline. Factors significantly associated with HIV infection in the final multivariable logistic model was aged 50 to 59 years (adjusted odds ratio [AOR], 1.32; 95% CI, 1.15–1.52), aged 60 to 69 years (AOR, 1.44; 95% CI, 1.24–1.68), male (AOR, 2.68; 95% CI, 2.43–2.96), primary school education attainment (AOR, 1.43; 95% CI, 1.29–1.58), married (AOR, 0.29; 95% CI, 0.20–0.39), divorced/widowed (AOR, 6.23; 95% CI, 5.46–7.11), county A (AOR, 0.2; 95% CI, 0.18–0.23), and county C (AOR, 0.21; 95% CI, 0.19–0.24). Supplemental Table 1, http://links.lww.com/OLQ/A327 presents HIV prevalence by sex and age groups.

HIV Incidence

Of the 720,732 study participants who tested HIV-negative at baseline, 493,990 (69%) completed the follow-up. The median duration of follow-up was 1.7 years (Q1–Q3, 1.4–1.8 years) among those who returned for follow-up. Baseline demographics between individuals followed up and lost to follow-up were generally comparable, though individuals lost to follow-up were slightly younger, had higher educational attainment, and were less likely to be from county “A” (Table 2).

Table 3 presents the factors associated with HIV incidence in the follow-up study. Overall HIV incidence was 2.73 (95% CI, 2.38–3.08) per 10,000 PY (235 of 860,627 PY). The bivariate analysis using the Cox regression model indicated that HIV incidence was associated with age, sex, education, and marital status. After adjustments in the final Cox regression model, age 40 to 49 years (Adjusted hazard ratio, 1.74; 95% CI, 1.04–2.92), age 50 to 59 years (AHR, 1.96; 95% CI, 1.15–3.33), age 60 to 69 years (AHR, 3.47; 95% CI, 2.07–5.82), male (AHR, 4.41; 95% CI, 3.22–6.05), no schooling (AHR, 2.36; 95% CI, 1.34–4.13), primary school (AHR, 2.35; 95% CI, 1.69–3.28), single (AHR, 5.98; 95% CI, 3.81–9.40), and divorced/widowed (AHR, 5.19; 95% CI, 3.56–7.57) were significantly associated with HIV incidence. Human immunodeficiency virus infection incidence was 7.47 (95% CI, 5.97–8.98), 8.51 (95% CI, 7.04–9.98), and 35.61 (95% CI, 22.65–48.58) per 10,000 PY among males aged 50 to 69 years, males with less than secondary schooling, and males divorced or widowed, respectively. Human immunodeficiency virus incidence was 71.28 (95% CI, 35.21–107.35) per 10,000 years among males aged 50 to 69 years who had less than secondary schooling and were divorced or widowed. Supplemental Table 2, http://links.lww.com/OLQ/A328 presents HIV incidence by sex and age group.

Of 235 individuals who had HIV seroconversions during the follow-up period, heterosexual sex was the identified mode of transmission for 99.0% of cases, followed by male-to-male sex (1.0%). Among males who seroconverted, 79% had sex with female sex workers and 18% had sex with casual sexual partners,
but not sex workers. Among females who seroconverted, 62% and 37% were infected through their spouse or steady sexual partners, and casual sexual partners, respectively.

**DISCUSSION**

Our study indicated that the HIV prevalence was 0.29% and HIV incidence was 2.73 per 10,000 PY among adults of the general population in a population-based, large-scale prospective cohort study. The major mode of HIV transmission was heterosexual sex. Findings from this population-based study suggest that HIV is spreading rapidly among older heterosexual adults in rural southwest China. From an international perspective, the HIV incidence rate among individuals aged 50 to 69 years in this study was 10 times greater than that of their counterparts in the United States. Our study results show that HIV incidence was comparable among the 3 counties, thus supporting the observation that the HIV epidemic which began as a drug-driven epidemic has shifted to one driven predominantly by sexual contact. These new changes pose greater challenges than ever before in China's AIDS control efforts.

Our cohort study also found that HIV infection was much higher among older heterosexual males, especially among those with low education and who were not currently married. These results underscore the fact that many older people over 50 years of age are still sexually active. Older adults, especially older men without a spouse or steady sex partner may seek sex with female commercial sex workers or casual partners. The reason for older men engaging in unprotected sex may be related to poor education about safer sex practices and underestimating their risk of contracting HIV. Another reason may be that older men might be more likely to use male erectile dysfunction medications that improve sexual function. By prolonging intercourse, erectile dysfunction medications may allow more bodily fluids to transfer, and thus increase the possibility of HIV sexual transmission. These drugs labeled as aphrodisiacs may be produced illegally by underground workshops and sold without regulation. Older males with lower levels of education and inconsistent

**TABLE 2.** Baseline Demographics Between Individuals Followed Up and Lost to Follow-up Among Participants Who Tested HIV-Negative at Baseline (Adults Aged ≥20 Years) in Guangxi, China

| Factor                  | Total   | Lost to Follow-up | Followed up | χ²  | P       |
|-------------------------|---------|-------------------|-------------|-----|---------|
| Total                   | 720,732 | 226742            | 493990      |     |         |
| Age, y                  |         |                   |             |     |         |
| 30–39                   | 142951  | 51143             | 91808       | 22647.2 | <0.001 |
| 20–29                   | 155139  | 68406             | 86733       | 9     |
| 40–49                   | 163311  | 46850             | 116461      | 18    |
| 50–59                   | 113032  | 25557             | 87475       | 24    |
| 60–69                   | 83507   | 16764             | 66743       | 14    |
| ≥70                     | 62792   | 18022             | 44770       |       |
| Sex                     |         |                   |             | 588.3 | <0.001 |
| Female                  | 368972  | 111299            | 257673      | 52    |
| Male                    | 351760  | 115443            | 236317      | 48    |
| Ethnicity               |         |                   |             | 1854.9 | <0.001 |
| Zhuang                  | 261822  | 78816             | 183006      | 37    |
| Han                     | 448010  | 142555            | 305455      | 62    |
| Other                   | 10900   | 5371              | 5529        | 1     |
| Education               |         |                   |             | 10381.6 | <0.001 |
| Secondary school or above | 438540 | 156007            | 282533      | 57    |
| No schooling            | 40722   | 13663             | 27059       | 5     |
| Primary school          | 241740  | 57072             | 184398      | 37    |
| Marital status          |         |                   |             | 11518.3 | <0.001 |
| Current married         | 622972  | 184699            | 438273      | 89    |
| Single                  | 71616   | 35122             | 36494       | 7     |
| Divorced/widowed        | 26144   | 6921              | 19223       | 4     |
| Farmer                  |         |                   |             | 3468.8 | <0.001 |
| No                      | 77795   | 31679             | 46116       | 9     |
| Yes                     | 642937  | 195063            | 447874      | 91    |
| County                  |         |                   |             | 22275.9 | <0.001 |
| A                       | 152074  | 24085             | 127989      | 26    |
| B                       | 341189  | 117911            | 223278      | 45    |
| C                       | 227469  | 84746             | 142723      | 29    |
condom use with females reported that aphrodisiacs helped sexual performance. Our previous study found scientific evidence that aphrodisiac usage was associated with higher HIV prevalence among older males, especially older male clients of low-priced female sex workers. Unfortunately, health promotion staff are often face difficulties implementing HIV interventions with female sex workers because most low-priced female sex workers are often face difficulties implementing HIV interventions with socially undesirable behaviors such as injection drug use or MSM behaviors. This was corroborated by the fact that no HIV seroconversions were found to be attributable to injection drug use. To our knowledge, this is the first large-scale population-based prospective follow-up cohort study in China to evaluate HIV incidence among the general population. Study results provide compelling evidence that current HIV prevention interventions are urgently needed for this population. Health authorities in China need to develop and implement innovative interventions suitable for the broader population of older heterosexuals.

Older heterosexual males were at disproportionate risk of HIV infection in southwestern China, especially older heterosexual males who were single, divorced or widowed. Targeted interventions are urgently needed for this population. Health authorities in China need to develop and implement innovative interventions suitable for addressing HIV transmission among the older, general population.

**TABLE 3. HIV Incidence of Study Participants in a Follow-Up Study (Adults Aged ≥20 Years) in Guangxi China**

| Factor          | No. Seroconversions | PYs | Incidence Rate (10,000 PYs) | HR (95% CI) | P     | AHR* (95% CI) | P   |
|-----------------|---------------------|-----|----------------------------|-------------|-------|---------------|-----|
| Total           | 235                 | 860,627.0 | 2.73                       |             |       |               |     |
| Age, y          |                     |     |                            |             |       |               |     |
| 30–39           | 22                  | 159,501.5 | 1.38                       |             |       |               |     |
| 20–29           | 5                   | 151,613.0 | 0.33                       | 0.24 (0.09–0.64) | 0.004 | 0.12 (0.05–0.34) | <0.001 |
| 40–49           | 48                  | 202,827.2 | 2.37                       | 1.71 (1.03–2.84) | 0.037 | 1.74 (1.04–2.92) | 0.034 |
| 50–59           | 46                  | 152,058.4 | 3.03                       | 2.18 (1.31–3.63) | 0.003 | 1.96 (1.15–3.33) | 0.014 |
| ≥60–69          | 81                  | 117,616.3 | 6.89                       | 5.03 (3.14–8.05) | <0.001 | 3.47 (2.07–5.82) | <0.001 |
| ≥70             | 33                  | 77,010.5  | 4.29                       | 3.08 (1.79–5.28) | <0.001 | 1.45 (0.79–2.68) | 0.232 |
| Sex             |                     |     |                            |             |       |               |     |
| Female          | 55                  | 447,076.9 | 1.23                       |             |       |               |     |
| Male            | 180                 | 413,550.1 | 4.35                       | 3.56 (2.63–4.81) | <0.001 | 4.41 (3.22–6.05) | <0.001 |
| Ethnicity       |                     |     |                            |             |       |               |     |
| Zhuang          | 89                  | 322,375.6 | 2.76                       |             |       |               |     |
| Han             | 145                 | 528,864.5 | 2.74                       | 0.99 (0.76–1.29) | 0.934 | 1.23 (0.93–1.64) | 0.143 |
| Other           | 1                   | 9386.9   | 1.07                       | 0.37 (0.05–2.68) | 0.328 | 0.52 (0.07–3.76) | 0.519 |
| Education       |                     |     |                            |             |       |               |     |
| Secondary school or above | 62 | 492,534.0 | 1.26                       |             |       |               |     |
| No schooling    | 22                  | 47,145.5  | 4.67                       | 3.69 (2.27–6.7) | <0.001 | 2.36 (1.34–4.13) | 0.003 |
| Primary school  | 151                 | 320,947.5 | 4.7                        | 3.71 (2.76–4.98) | <0.001 | 2.35 (1.69–3.28) | <0.001 |
| Marital status  |                     |     |                            |             |       |               |     |
| Current married | 168                 | 762,620.4 | 2.2                        |             |       |               |     |
| Single          | 27                  | 64,746.0  | 4.17                       | 1.92 (1.28–2.88) | 0.002 | 5.98 (3.81–9.40) | <0.001 |
| Divorced/widowed| 40                  | 33,260.6  | 12.03                      | 5.42 (3.84–7.66) | <0.001 | 5.19 (3.56–7.57) | <0.001 |
| Farmer          |                     |     |                            |             |       |               |     |
| No              | 16                  | 80,652.1  | 1.98                       |             |       |               |     |
| Yes             | 219                 | 779,974.9 | 2.81                       | 1.42 (0.86–2.36) | 0.175 | 1.24 (0.73–2.1) | 0.432 |
| County          |                     |     |                            |             |       |               |     |
| A               | 67                  | 213,674.6 | 3.14                       |             |       |               |     |
| B               | 83                  | 384,131.2 | 2.16                       | 0.73 (0.53–1.01) | 0.057 | 0.72 (0.52–1.02) | 0.062 |
| C               | 85                  | 262,821.2 | 3.23                       | 1.14 (0.83–1.57) | 0.433 | 1.36 (0.98–1.88) | 0.065 |

*Covariates of the adjusted model included: age, sex, ethnicity, education, marital status, farmer and county.*
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