

THE PREVALENCE OF SEXUALLY TRANSMITTED AND OTHER LOWER REPRODUCTIVE TRACT INFECTIONS AMONG RURAL WOMEN IN SICHUAN PROVINCE, CHINA

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Abstract. To estimate the prevalence of sexually transmitted infections (STI) and lower reproductive tract infections (RTI) and determine risk factors for STI among rural women in Sichuan Province, China, a cross-sectional, community-based cluster sample of 2,000 rural, married women were interviewed, examined and clinical specimens collected to assess for six STI and two non-sexually transmitted RTI. The overall prevalence of any STI was 10.9% (95% CI 9.5-12.3); of any STI or RTI was 30.8% (95% CI 28.7-32.8). *Chlamydia trachomatis* was detected in 6.4% of women, *Neisseria gonorrhoeae* in 1.7%, *Treponema pallidum* in 0.5%, human papilloma virus in 0.6%, herpes simplex virus type-2 in 2.0%, *Candida albicans* in 8.8%, *Trichomonas vaginalis* in 0.7% and bacterial vaginosis in 15.4%. The reported low risk sexual behavior was corroborated by the prevalence of STI based on laboratory findings. The prevalence of *Chlamydia trachomatis* alone and the combined prevalence rates of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* were high enough (7.9%) to consider interventions for the control of cervical infections. Health promotion messages regarding safe sexual and health care seeking behavior is important. Routine STI surveillance, including prevalence studies, which provide accurate information for decision-making should be continued as an essential component of good STI control.

INTRODUCTION

Sexually transmitted infections are a major cause of disease with an estimated 340 million new cases of curable infections per

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year globally (WHO, 2001). The consequences of STI include neonatal infection, spontaneous miscarriage, postpartum infection, ectopic pregnancy, cervical cancer, infertility and chronic abdominal pain among women (Holmes, 2008). Substantial evidence demonstrates that STI, particularly ulcerative STIs, facilitate the sexual transmission of human immunodeficiency virus (HIV) (Laga *et al*, 1993; Hayes *et al*, 1995; Wald and Link, 2002; WHO, 2006).

In China, syphilis and gonococcal infections were almost eliminated during the 1960s, but since the economic reforms of the

1980s, the number of STI has been gradually increasing and the geographic areas reporting cases has expanded (Shao, 1993). The Chinese government is aware of the situation and is positioned to support prevention and control efforts (Sichuan Provincial Government, 1987; Kuang and Mei, 1990; Lin *et al*, 1990; Wang, 1991). Currently, the data available for China come from limited geographic areas, such as the 16 national sentinel centers. A study by Parish *et al* (2003) in eastern and developed provinces in China estimated the prevalence of chlamydia among women in 2000 at 2.6% and gonorrhea at 0.08%. This study did not include Sichuan Province, since this province did not meet the selection criteria. Other studies conducted among key populations at higher risk in geographically disparate regions found the prevalence of chlamydial infection between 17.0 and 50.8% (Liao *et al*, 1991; Ye *et al*, 1993).

We conducted a systematic study of the prevalence of *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG), *Treponema pallidum*, human papilloma virus (HPV), herpes simplex virus type 2 (HSV2), *Candida albicans* (CA), *Trichomonas vaginalis* (TV) and bacterial vaginosis (BV) infections, and factors associated with cervical infection (NG or CT) among married women of reproductive age living in rural communities in Sichuan Province, China to obtain documented information about the burden and factors associated with sexually transmitted and other lower genital tract infections. The study population residing in this third most populous province of China, where 85% of the total population of 84.3 million live in rural areas, are predominantly in the mid-level economic class.

MATERIALS AND METHODS

This study was conducted between March 2003 and June 2004. Ethical clearance was obtained from both the Sichuan Fam-

ily Planning Research Institute (SFPRI) and the Scientific and Ethical Review Group of the UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human. Before the field work, a provincial level training workshop was held and a pilot survey was carried out.

The sample was based on a three-stage cluster design with probability proportional to size (PPS). Three counties were randomly selected among the 99 Han ethnicity counties; one township was randomly selected from each of the three counties; two villages were randomly selected from each township. All households in the six selected villages were visited to establish the population of married women of reproductive age. Women were informed of the objectives of the study. Participants in the study included women of Han ethnicity, aged 20-49 years who were ever married. The minimum age of consent was set at 20 years since this is in accordance with Chinese marriage law. All women who met the admission criteria and consented to take part in the survey were included as study participants. Each woman received a booking card with the time of the local health clinic visit.

Interviews and clinical examinations were conducted at the township health clinic. The study procedures were explained in detail to the woman who were assured confidentiality, then the women gave written informed consent to participate. Interviews were conducted by study doctors trained by the research team. Clinical examination by a gynecologist consisted of an external and bimanual gynecological examination, speculum examination and the collection of vaginal, endocervical and blood specimens for microbiological tests. Each woman was allocated a unique identification number and the laboratory staff were blinded to clinical findings.

Laboratory examinations provided the basis for the estimated rates of infection. Bacterial vaginosis was diagnosed when three of the following four criteria were noted: 1) characteristic homogeneous, white, adherent discharge; 2) vaginal fluid pH >4.5; 3) release of amine odor with potassium hydroxide (KOH); and 4) $\geq 20\%$ of epithelial cells were characteristic "clue" cells. The number of polymorphonuclear leukocytes (PMN) present was graded as <10 (0), 10-19 (+), 20-29 (++), or ≥ 30 (+++) per high-power field.

Specimens for microbiological examination were collected during vaginal speculum examination. After the ectocervix was cleared of secretions, two sterile Dacron-coated swabs were placed in the cervical canal and rotated to collect endocervical secretions and cells for the culture of NG and antigen detection of CT. Swabs for NG were inoculated directly onto chocolate-blood-agar selective medium plate with polymyxin B and vancomycin and immediately placed in a candle-extinction jar. Cervical swabs for antigen detection of CT were placed in a tube containing extraction buffer. The specimen for HPV polymerase chain reaction (PCR) testing was collected from the ectocervix and placed in 1 ml of Roche transport medium. The final sample was collected with a cotton-tipped swab from the upper lateral vaginal sidewalls and tested for pH (Shanghai Guowang Chemical Reagent, Shanghai, China), then placed into a test tube containing approximately 0.5 ml of bacteriostatic normal saline solution.

After removal of the speculum, a bimanual examination was carried out to assess tenderness of the fornices and excitation of the cervix. Suspected pelvic inflammatory disease (SPID) was clinically diagnosed when a woman experienced pelvic or lower abdominal pain and cervical motion,

uterine or adnexal tenderness were present. After gynecological examinations, 5 ml venous blood was drawn by an experienced laboratory technician from each subject for syphilis and HSV-2 antibody testing.

All samples for HPV PCR testing, serological testing and CT antigen testing were kept at 4°C and transported daily to the laboratory of SFPRI, where the serum was separated and stored at -70°C. The plates for the NG culture were transported to the laboratory of SFPRI, incubated at 35-37°C, and inspected after 24 and 48 hours. Simple, field-based tests were conducted at the township-level health clinic for TV, CA, and BV using wet-mount microscopy and biochemical tests (KOH test and vaginal pH).

The preparation from the vaginal swabs was immediately examined microscopically (at 400x) for motile trichomonads, yeast and "clue" cells, and semi-quantitative assessment of PMNs. A drop of vaginal fluid was placed on a glass slide, combined with a drop of 10% KOH, and evaluated for the release of amine odor.

NG isolates were identified on the basis of typical colonial morphology, oxidase reaction, Gram stain result and sugar fermentation test. Specimens for CT examination were processed within the week with the Clearview Chlamydia Test kit (Clearview Chlamydia; Unipath, UK).

Sera were tested for syphilis using the Rapid Plasma Reagin test (RPR test; Shanghai Shiye Kehua Biological Technology, China) without titration, followed by the *Treponema pallidum* Haemagglutination Assay test (TPHA test; Fujirebio, Japan). A positive TPHA and RPR test result was interpreted as recent or untreated syphilis. Sera were tested for HSV-2 using an enzyme-linked immunosorbent assay (Huamei Biological Technology, China) which detects IgG antibodies to HSV-2 glycoprotein G.

Cervical swabs for HPV PCR testing were processed (PCR test, Huamei Biological Technology, China) using a "hot start" step that was used to reduce non-specific amplification. The PCR targets a 206 base-pair segment in the open reading frame. The resulting PCR products were electrophoresed through 2% agarose gel, stained, and photographed under ultraviolet light.

All study participants were informed of the results of the physical examination, educated and counseled appropriately. All women with signs of acute infection at the time of the visit were offered free treatment. All the results of the laboratory tests were posted to the participant in a letter with instructions to follow up, if needed, and offered care for the partner if the test was positive.

Data analysis

All analyses were conducted with SPSS 11.0 (SPSS, Chicago, USA), except for logistic regression analysis which was conducted in Stata 8.0 (Stata Corp. College Station, TX, USA) which allows adjusting for survey design by taking into account the sampling weights and clustering. Associations between categorical variables were assessed using chi-square or Fisher's exact tests (when appropriate). Logistic regression was used to calculate the adjusted odds ratios (AOR), 95% confidence intervals and *p*-values for cervical infection. The likelihood ratio test in Stata was used to select the final set of significant variables ($p \leq 0.05$) to be retained in the final multivariate regression model. Logistic regression was not used for rare events such as TV, syphilis, HPV and HSV2.

RESULTS

A total of 2,308 married women of reproductive age were identified in the 6 villages, of whom 90.9% (2,099) came to the health center of the township. Among the

9.1% (209) who did not come, the main reason was absence from their home. Among the women who did come to the health center, 4.7% (99) refused to participate in the study. The final sample included 2,000 women.

The mean age of the studied population was 34.3 years (Table 1), 10% were in the youngest age group (20-24 years). Nearly all the women (95%) had some schooling. Few respondents (2.9%) had left home for more than 2 weeks during the last six months. The mean age of the subjects' husbands was 36.6 years. Most (99%) had attended some school. One-fifth of husbands had left home for more than 2 weeks during the last 6 months. Nearly all subjects and their husbands had been married only once. The subjects had a mean age at first marriage of 21.6 years. Most women (99%) were currently married.

Use of modern contraception was common with the majority of women having ever used an intrauterine device (IUD) (84.5%), followed by condoms (34.0%), withdrawal (16.6%) and oral contraceptives (13.5%). Most women (70%) reported the main contraceptive method used in the last three months was an IUD and about 10% used condoms. The subjects' mean age at first sexual intercourse was 20.9 years old (Table 2). Half the respondents had their first sexual intercourse with their husband after marriage and almost half with their fiancé or boyfriend before marriage. Few respondents (7%) had two sexual partners in their lifetime. Rarely (0.6%) did respondents indicate they had more than one sexual partner in the last 6 months. Only 0.1% had new sexual partners and 0.2% had ever exchanged sex for money in the last 6 months (data not shown).

Two-thirds (66.0%) of women expressed that they currently had abnormal gynecological symptoms including genital itching,

Table 1

Selected socio-demographic characteristics of study respondents and their spouses (percentage and number), Sichuan Province China, 2003-2004.

Characteristic	Total (N=2000) % (No.)
Age in years, mean (SD)	34.3 (7.5)
Age group	
20-24	10.1 (202)
25-29	19.0 (379)
30-34	26.4 (528)
35-39	19.7 (394)
40-44	11.6 (231)
45-49	13.3 (266)
Educational level	
No education	3.7 (73)
Primary	38.4 (768)
Junior high school	44.3 (886)
Senior high school or above	13.7 (273)
Age of current husband in years, mean (SD)	36.6 (7.8)
Educational level of spouse	
No education	1.4 (28)
Primary	28.1 (557)
Junior high school	52.3 (1,038)
Senior high school or above	18.2 (361)
Mobility of spouse (left home for >2 weeks at least once in last 6 months)	
No, never went out	80.8 (1,604)
Yes, went out with wife	2.6 (51)
Yes, went out but never with wife	16.6 (329)

SD, standard deviation

abnormal vaginal discharge, genital ulcers/sores, lower abdominal pain, dysuria or abdominal pain with intercourse (data not shown). Very few women (1.0%) reported having genital ulcers/sores. Approximately 15% of respondents reported dysuria or pain with sexual intercourse. Suspected pelvic inflammatory disease was diagnosed in 1.0% of respondents. Visual evidence of

Table 2

Selected reproductive and sexual health behaviors of study participants and their spouses (percentage and number), Sichuan Province China, 2003-2004.

Characteristic	Total (N=2000) % (No.)
Age at first marriage, mean (SD)	21.6 (1.8)
Number of pregnancies	
0	1.2 (24)
1	27.9 (557)
2	32.7 (653)
≥3	38.3 (866)
Contraceptive methods ever used ^a	
None	2.2 (43)
Oral contraceptive	13.5 (270)
Implant and/or injectable	3.6 (71)
IUD	84.5 (1,690)
Condom	34.0 (680)
Withdrawal	16.6 (331)
Safe period and other	8.1 (161)
Main contraceptive methods used in last three months	
None	9.6 (191)
Oral contraceptive	1.6 (32)
Implant	1.9 (38)
IUD	65.9 (1,318)
Condom	10.2 (204)
Withdrawal	6.1 (122)
Safe period with other	4.8 (95)
Condom use in last three months	
Always	5.9 (118)
Sometimes	7.2 (143)
Never	87.0 (1,739)
Ever used condom in last one month	
Yes	10.9 (217)
No	89.2 (1,783)
Age (years) at first sexual intercourse, mean (SD)	20.9 (2.0)
Number of lifetime sexual partners	
1	92.4 (1,847)
2	7.0 (139)
≥3	0.7 (14)

^aMore than one method is possible; SD, standard deviation; IUD, intrauterine device

Table 3
Prevalence of STI/RTIs among study participants (n=2,000) by age group, Sichuan Province
China, 2003-2004.

RTI/STI	Age groups							Total (N=2000)	95%CI
	20-24	25-29	30-34	35-39	40-44	45-49			
	(n=202) %(No.)	(n=379) %(No.)	(n=528) %(No.)	(n=394) %(No.)	(n=231) %(No.)	(n=266) %(No.)	%(No.)		
Bacterial vaginosis	14.9 (30)	11.6 (44)	13.4 (71)	15.5 (61)	23.8 (55) ^a	17.7 (47)	15.4 (308)	13.8-17.1	
<i>T. vaginalis</i>	0.0 (0)	0.0 (0)	0.8 (4)	1.0 (4)	1.7 (4)	0.8 (2)	0.7 (14)	0.4-1.2	
<i>C. albicans</i>	8.4 (17)	6.6 (25)	9.7 (51)	9.9 (39)	9.1 (21)	8.6 (23)	8.8 (176)	7.6-10.1	
<i>N. gonorrhoeae</i>	2.0 (4)	2.1 (8)	1.1 (6)	1.0 (4)	1.3 (3)	3.0 (8)	1.7 (33)	1.1-2.3	
Syphilis	0.0 (0)	0.5 (2)	0.6 (3)	0.5 (2)	0.9 (2)	0.0 (0)	0.5 (9)	0.2-0.9	
HSV2	4.5 (9)	1.1 (4)	2.3 (12)	1.3 (5)	1.3 (3)	2.3 (6)	2.0 (39)	1.4-2.7	
<i>C. trachomatis</i>	5.9 (12)	5.8 (22)	5.1 (27)	8.6 (34)	7.4 (17)	5.6 (15)	6.4 (127)	5.3-7.5	
Human papilloma virus	0.5 (1)	0.3 (1)	0.4 (2)	1.3 (5)	1.3 (3)	0.0 (0)	0.6 (12)	0.3-1.0	
NG/CT	7.9 (16)	7.7 (29)	6.3 (33)	9.6 (38)	8.7 (20)	8.3 (22)	7.9 (158)	6.8-9.2	
Any STI ^b	11.4 (23)	9.5 (36)	10.0 (53)	11.9 (47)	13.0 (30)	10.5 (28)	10.9 (217)	9.5-12.3	
Any RTI/STI ^c	29.7 (60)	24.3 (92)	29.7 (157)	32.7 (129)	38.1 (88)*	33.5 (89)	30.8 (615)	28.7-32.8	

^aDifferences across age groups are significant at $p < 0.05$

^bAny STI here includes *C. trachomatis*, *N. gonorrhoeae*, syphilis, human papilloma virus, herpes simplex virus type 2 and *T. vaginalis*

^cAny RTI/STI includes *C. trachomatis*, *N. gonorrhoeae*, syphilis, human papilloma virus, herpes simplex virus type 2, *T. vaginalis*, bacterial vaginosis and *C. albicans*

STI, sexually transmitted infection; RTI, reproductive tract infection; HSV2, herpes simplex virus type 2; NG, *N. gonorrhoeae*; CT, *C. trachomatis*; CI, confidence interval

acute cervicitis on clinical examination was defined in this study as mucopurulent cervical discharge and/or cervical contact bleeding or friability (Centers for Disease Control and Prevention, 2006) as determined by the examining gynecologist and was identified among 26.3% of study participants with mucopurulent cervical discharge observed in 14.4% of women.

The overall and age-specific prevalences of the eight STI and non-sexually transmitted RTI in the study population are shown in Table 3. Overall, 10.9% (217) of participants had a STI and 30.8% (615) had either an RTI or STI. One point seven percent (33)

of participants were infected with NG and 6.4% (127) with CT; 7.9% (158) of women were diagnosed with either NG or CT and 0.1% (2) were co-infected. Fifteen point four percent (308) were diagnosed with BV and 8.8% (176) with CA. TV, syphilis, and HPV infections were uncommon. Both TPHA and RPR tests were positive in 9 participants indicating active syphilis. Overall, 2.0% (39) of women had HSV-2 infection with the highest prevalence (4.5%) among the 20-24 year old group ($p > 0.05$).

Logistic regression assessment identified an association between the presence of NG or CT and selected risk factors:

Table 4
Adjusted odds ratios(AOR) from logistic regression of the likelihood of having cervical infection (NG or CT).

Risk factor	AOR	95% CI	p-value
Educational level of spouse			
No education	2.60	1.46 - 4.63	0.001
Primary	0.91	0.53 -1.57	0.740
Junior high school	1.03	0.98 -1.08	0.209
Senior high school or above (reference)	-		
Condom use frequency in last three months			
Always(reference)	-		
Sometimes	0.72	1.05 -2.82	0.031
Never	4.59	3.59 -5.86	0.028

NG, *N. gonorrhoeae*; CT, *C. trachomatis*; CI, confidence interval

subject's spouse with no education or occasional condom use in the previous three months (Table 4).

DISCUSSION

Among rural, female study participants in Sichuan Province, China, cervical infections were the most common STI (7.9%). Chlamydia is one of the most common STI globally with reported prevalence rates among asymptomatic or pregnant women ranging from 3-13% (WHO, 2001). The magnitude of STI, particularly *N. gonorrhoeae* and *C. trachomatis*, in this low risk group was higher than anticipated in comparison to other recent studies in China and Asia (Thongkrajai *et al*, 1999; Parish *et al*, 2003; Thammalangsy *et al*, 2006). In general, women's reported sexual behaviors were low risk for sexually transmitted infections. As HSV-2 is a good indicator of sexual behavior, the relatively low rate (2%) in this study corroborates the claims of low risk behavior. Factors associated with increased risk of cervical infection included no or limited condom use and a spouse without education, while risks for any STI included age at initial sexual intercourse and total num-

ber of spouse's marriages (data not shown).

Limitations of the study include, the study sample had a lower proportion of women in the 20-24 year age group compared to the general population which reflects the study eligibility criteria. The diagnostic methods used for *C. trachomatis* were not the most sensitive and thus may have led to an under estimate of the real magnitude. In limited evaluations of both routine care seeking and higher risk populations with prevalence rates of 10-25% (Ferris and Martin, 1992; Woolley and Pumphrey, 1997; Lauderdale *et al*, 1999; Yin *et al*, 2006), Clearview Chlamydia tests have sensitivities of 50-85% compared with culture and nucleic acid amplification tests, which yield specificities of 98% and positive predictive values of 70-100%.

The findings from this study can be used to guide STI control in Sichuan Province, which could contribute to improved reproductive health outcomes and HIV prevention. As there is evidence in China of increasing STI rates and given the location of Sichuan on a drug trafficking route with its associated social and health risks, an opportunity exists for the preven-

tion of STIs, including HIV, through the control of STIs (Ruan *et al*, 2004, 2005; Qian *et al*, 2005). Health promotion messages for safe sexual and health care seeking behaviors should be clear and accurate including correct condom use and risks of infection related to the number, concurrency and timing of partnerships. Education and communication interventions should reach men as well as women in these rural communities. Access to user-friendly, quality care should contribute to maintaining a low burden of STIs.

Given the frequent use of modern contraceptives, the family planning visit provides an opportunity for STI prevention and care including giving appropriate information, education and provision of condoms. Many cervical infections are asymptomatic. Given the infection rate identified in this study and the common use of the IUD, further research is needed regarding health outcomes in the presence of a cervical infection at the time of IUD insertion. Available data suggest a slightly increased risk of PID in the presence of a cervical infection (Shelton, 2001). Currently at the county- or township-level hospital clinic in Sichuan Province, women are commonly prescribed an antibacterial, such as norfloxacin, and an herbal solution, such as "*jie er yin*", for preventive treatment and pudendum cleansing for several days after IUD insertion. Norfloxacin has poor bactericidal activity against CT and NG and should be replaced by single-dose regimens that are effective against these conditions (depending on antimicrobial sensitivity assessments). Screening policies and standards of clinical care should be further clarified for the management of women who choose an IUD as their family planning method and for symptomatic individuals. A cost effectiveness study taking into consideration the accuracy, cost and time required for various diagnostic

tests should be conducted to evaluate the usefulness of point of care diagnostic tests for cervical and vaginal infections or presumptive treatment. One study suggests the use of moderate sensitivity point of care tests, particularly where women may not return or treatment would be delayed, would result in faster treatment, more STIs averted, and potentially reduced adverse consequences (Vickerman *et al*, 2003). The control of chlamydia could have direct and indirect individual and public health impacts including the prevention of ectopic pregnancy, infertility and its psychosocial consequences and the cost of using assisted reproductive therapies (Zhu and Huang, 2001; Fang and Ye, 2003; Liu, 2003).

Routine national surveillance data did not identify Sichuan as a higher than average STI prevalence area, yet the prevalence of chlamydia and gonorrhoeae among women in this low risk, rural population was higher than a survey in eastern and developed provinces (2.6% and 0.08%, respectively) (Parish *et al*, 2003). While routine case reporting can allow trends to be noted, underreporting of cases is a major problem and does not reflect the burden of asymptomatic infections. Population based microbiological studies could provide a more accurate estimate (WHO, 2002) and be considered an essential complementary component of good STI surveillance that enhances the epidemiological understanding of STI and the making of evidence-based decisions. Once interventions have been implemented, a follow-up study should be conducted to determine if interventions have been successful in maintaining low STI rates and reducing chlamydia rates.

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