

# Seroepidemiology of Syphilis Infection among 2 Million Reproductive-age Women in Rural China: A Population-based, Cross-sectional Study

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## Abstract

**Background:** Quantifying syphilis prevalence is important for planning interventions and advocating for resources on syphilis. However, data on large sample studies regarding the prevalence of syphilis among reproductive-age women in rural China were not available for analysis. The aim of the study was to determine the prevalence, epidemiological characteristics, and related factors of syphilis infection among reproductive-age women in rural China.

**Methods:** Data were obtained from a nationwide, population-based, cross-sectional study under the National Free Preconception Health Examination Project which covered all the 31 provinces in Mainland China. Women intending to get pregnant within the next 6 months were enrolled between January 1, 2010, and December 31, 2012. Sociodemographic, gynecological and obstetric characteristics, and other relevant information were obtained through face-to-face interviews. *Treponema pallidum* particle agglutination assay test was used to detect positive samples of syphilis. Univariate and multivariate logistic regressions were performed to assess the associations between syphilis seropositivity and related factors.

**Results:** The overall seroprevalence of syphilis (SPS) among the 2,044,126 women who received syphilis screening test during 2010–2012 was 0.37% (95% confidence interval [CI]: 0.36–0.37%). The SPS appeared 0.24% (95% CI: 0.23–0.26%) and 0.66% (95% CI: 0.59–0.72%) in women at 21–24 and 40–44 years of age, respectively, showing an increase of SPS, parallel with age, and the difference was significant. SPS was significantly higher in ethnic minorities than that in Han nationality (0.58% vs. 0.35%, respectively, odds ratio [OR] = 1.41, 95% CI: 1.30–1.53) and higher in workers than that in farmers (0.45% vs. 0.36%, respectively, OR = 1.27, 95% CI: 1.14–1.41). Women with primary school or below level had a higher SPS as compared to those with college or above educational level (0.61% vs. 0.32%, respectively, OR = 2.49, 95% CI: 2.14–2.89), and the increase reversely correlated with the levels of education. Women whose spouses were syphilis seropositive had significant greater risk (OR = 48.26, 95% CI: 44.38–52.48) as compared those whose spouses were seronegative. Women who reported having had a history of sexually transmitted infections were more likely to be tested positive for serological syphilis (OR = 27.17, 95% CI: 20.44–36.11) as compared to those without.

**Conclusions:** High SPS is seen among reproductive-age women in rural China that calls for targeted interventions on syphilis prevention and control in this target population, with emphasis on those who are 35 years of age and above, less educated, being minor ethnicity, workers, and living in the western regions of China.

**Key words:** Preconception Care; Reproductive-age Women; Seroprevalence; Syphilis

## INTRODUCTION

Syphilis in pregnancy is under global public health concern, with 950,000 women estimated to have active syphilis in pregnancy in 2012 worldwide, and 96% of those occurred in low- and middle-income countries.<sup>[1]</sup> Untreated syphilis infection is associated with adverse pregnancy outcomes including miscarriage, stillbirth, preterm birth, hydrops,

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and polyhydramnios.<sup>[2]</sup> *Treponema pallidum* (TP) can be transmitted to the fetus, causing growth restriction, low birth weight, and long-term sequelae such as deafness, neurological impairment, and bone deformities of the fetus.<sup>[3,4]</sup> A recent meta-analysis on this issue revealed that 66.5% of the women without effective treatment on syphilis would experience adverse pregnancy outcomes.<sup>[2]</sup> The WHO estimated that maternal syphilis resulted in 36,000 adverse pregnancy outcomes in 2012.<sup>[1]</sup>

China has experienced a dramatic resurgence of syphilis epidemic during the past 20 years, and syphilis is one of the most common infectious diseases in the country.<sup>[5-7]</sup> Number of the reported incidence on syphilis in women increased at a rate of 13.99%/year from 6.52 to 35.77 cases per 100,000 from 2000 to 2013.<sup>[8]</sup> Along with the high prevalence of syphilis in women at reproductive age, congenital syphilis has become a public health problem in China. It was reported that the national incidence of congenital syphilis had increased annually since 2000, reaching 69.9 cases per 100,000 live births in 2013.<sup>[8,9]</sup>

In China, syphilis among reproductive-age women in rural areas has not been fully studied, with social inequalities and other gaps in access to health-care service, in particular. Women at reproductive age have not been viewed as under higher risk on syphilis infection. Most studies related to the prevalence of syphilis were focused on urban areas or on those populations at high risk.<sup>[10,11]</sup> Since 2010, the Chinese government has launched National Free Preconception Health Examination Project (NFPHEP), with the aim to provide free health examinations including syphilis screening for rural couples who had planned for pregnancy.<sup>[12]</sup> Using data that were derived from the NFPHEP, we analyzed the results derived from women's syphilis screening programs, from 220 counties in 31 provinces to determine the prevalence, epidemiological characteristics, and related factors of syphilis infection among reproductive-age women in rural China.

## METHODS

### Ethical approval

The study was conducted in accordance with the *Declaration of Helsinki* and was approved by the Institutional Review Board of Chinese Association of Maternal and Child Health Studies (IRB-201001). Informed written consent was obtained from all participants in this study.

### Study design and participants

A nationwide, population-based, cross-sectional study was conducted. Data were obtained from NFPHEP, which was carried out between 2010 and 2012 in 220 pilot counties of 31 provinces in Mainland China. The NFPHEP was conducted by the Chinese National Health and Family Planning Commission and Ministry of Finance since 2010, providing 19 items on free preconception health service involving health education, health examination, risk evaluation, and medical consultation. All rural couples of reproductive age (21–49 years) who planned to be pregnant within the next 6 months had access to these health services and those who had risk factors for

pregnancy were provided with appropriate medical care and referred to specialized hospitals, if necessary.

All participants were interviewed and completed a standardized family health file. Questionnaire and medical examination items were handled by trained local health workers in Centres for Maternal and Child Health Care and Family Planning Service. Data from the family health files and questionnaire were then included in a web-based electronic data collection system and sent to the National Office of the NFPHEP. Detailed design, organization, and implementation of this project are described elsewhere.<sup>[13-15]</sup>

### Procedures

Medical examination and preconception consultations were conducted for all enrolled women at the local county Centres for Maternal and Child Health Care and Family Planning Service. During the physical checkup process, 5 ml of venous blood was obtained from each participant and immediately sent to local laboratories where sera were separated and stored at  $-30^{\circ}\text{C}$  before being tested. All serum specimens were tested in the local laboratories affiliated to medical institutions under qualified quality control mechanisms. *Treponema pallidum* particle agglutination assay (TPPA) was used to detect antibodies specific for TP antigens among women and their spouses. Choices regarding reagent kits used were decided by local county laboratories, all of which were approved by the China Food and Drug Administration. An external quality assessment was performed twice a year as described previously by the National Centre of Clinical Laboratories for Quality Inspection and Detection.<sup>[16]</sup>

A standardized questionnaire was used to collect data on sociodemographic, gynecologic and obstetric characteristics, history of sexually transmitted infections (STIs), and other relevant information through a face-to-face interview by trained local health staff. According to residential address, participants from 31 provinces were divided into three regions: eastern region (including Beijing, Fujian, Guangdong, Hainan, Hebei, Jiangsu, Liaoning, Shandong, Shanghai, Tianjin, and Zhejiang), central region (including Anhui, Heilongjiang, Henan, Hubei, Hunan, Jiangxi, Jilin, and Shanxi), and western region (including Chongqing, Gansu, Guangxi, Guizhou, Inner Mongolia, Ningxia, Qinghai, Shaanxi, Sichuan, Tibet, Yunnan, and Xinjiang).

### Statistical analysis

Proportions were used to describe the sociodemographic characteristics of the participants. Seroprevalence of syphilis (SPS) and its 95% confidence interval (CI) in the total population were calculated, as well as in subpopulations. Uni- and multi-variate logistic regressions were used to identify factors associated with seropositivity of syphilis. All variables examined in the univariate analysis were considered as candidates for the multivariate model. Adjusted odd ratios (aORs) and 95% CI were obtained based on the multivariate logistic regressions. All analyses were done with SPSS version 18.0 (SPSS Inc., Chicago, IL, USA).

## RESULTS

### Sociodemographic characteristics

From January 1, 2010, to December 31, 2012, a total of 2,120,131 women at reproductive age were enrolled and 2,044,126 (96.42%) received syphilis screening tests. Sociodemographic characteristics of participants were presented in Table 1. Median age of the participants was 27 years (interquartile range, 25–30 years). Among those who were screened for syphilis, 1,831,852 (89.61%) participants were between the age of 21 and 34 years, 1,851,840 (91.22%) were Han nationality, 1,448,767 (71.58%) had an education level of junior high school or below, 1,566,487 (77.90%) were engaged in agricultural activities, and 1,009,711 (49.40%) came from central regions of China.

### Seroprevalence of syphilis among women at reproductive age

A total of 7485 women at reproductive age were tested seropositive for syphilis, with an overall SPS as 0.37% (95% *CI*: 0.36–0.37%). Table 2 summarizes the SPS of syphilis in different subgroups. SPS was 0.24% (95% *CI*: 0.23–0.26%) and 0.66% (95% *CI*: 0.59–0.72%) in women at 21–24 and 40–44 years of age, respectively, showing an increase of SPS, parallel with age, and the difference was significant. The SPS in ethnic minorities (0.58%, 95% *CI*: 0.55–0.62%) appeared significantly higher than that in Han nationality (0.35%, 95% *CI*: 0.34–0.36%). Women with education level of primary school or below had a higher SPS (0.61%, 95%

*CI*: 0.56–0.66%) as compared to those with college or above educational level (0.32%, 95% *CI*: 0.30–0.35%), and the increase of SPS was reversely associated with the levels of education. The SPS was significantly higher among workers (0.45%, 95% *CI*: 0.41–0.48%), compared with farmers (0.36%, 95% *CI*: 0.35–0.37%) or with other occupations (0.35%, 95% *CI*: 0.33–0.38%). The SPS varied dramatically across regions, with the highest in the western (0.42%, 95% *CI*: 0.41–0.44%) and lowest in the central (0.32%, 95% *CI*: 0.31–0.33%) regions.

SPS appeared as 0.45% or above in seven of the 31 provinces (Xinjiang, Guangdong, Guizhou, Hainan, Zhejiang, Sichuan, and Anhui) while eight of those showed SPS lower than 0.15% (Shanxi, Inner Mongolia, Heilongjiang, Jiangxi, Ningxia, Beijing, Tianjin, and Tibet).

### Association between sociodemographic characteristics and syphilis seropositivity among women at reproductive age

Table 2 summarizes the association between sociodemographic characteristics and syphilis seropositivity in both uni- and multi-variate models. Compared to women aged 21–24 years, women aged 25–29, 30–34, 35–39, 40–44, and 45–49 years were significantly more likely to be infected with syphilis, with *ORs* (95% *CI*) as 1.18 (1.10–1.27), 1.62 (1.49–1.76), 2.18 (1.97–2.42), 2.22 (1.94–2.54), and 1.92 (1.43–2.57), respectively. Women who were ethnic minorities appeared 1.41 times more likely to be infected (95% *CI*: 1.30–1.53), as

**Table 1: Sociodemographic characteristics of 2,044,126 reproductive-age women screened for syphilis from 2010 to 2012, *n* (%)**

Characteristics	2010–2012	2010	2011	2012
Age				
21–24 years	493,046 (24.12)	41,870 (12.85)	187,289 (21.07)	263,887 (31.82)
25–29 years	935,037 (45.74)	156,737 (48.10)	410,667 (46.20)	367,633 (44.33)
30–34 years	403,769 (19.75)	83,236 (25.54)	186,571 (20.99)	133,962 (16.15)
35–39 years	142,488 (6.97)	29,384 (9.02)	69,025 (7.76)	44,079 (5.32)
40–44 years	58,899 (2.88)	12,294 (3.77)	29,548 (3.32)	17,057 (2.06)
45–49 years	10,887 (0.53)	2358 (0.72)	5838 (0.66)	2691 (0.32)
Ethnicity*				
Han	1,851,840 (91.22)	302,922 (93.10)	802,573 (90.71)	746,345 (91.01)
Minority	178,349 (8.78)	22,460 (6.90)	82,179 (9.29)	73,710 (8.99)
Education†				
Primary school or below	102,344 (5.06)	19,037 (5.87)	48,276 (5.48)	35,031 (4.28)
Junior high school	1,346,423 (66.52)	227,816 (70.22)	597,436 (67.77)	521,171 (63.70)
Senior high school	359,226 (17.75)	53,358 (16.45)	147,155 (16.69)	158,713 (19.40)
College or above	216,085 (10.68)	24,235 (7.47)	88,635 (10.05)	103,215 (12.62)
Occupation‡				
Farmer	1,566,487 (77.90)	259,678 (80.57)	690,704 (78.96)	616,105 (75.70)
Workers	166,695 (8.29)	27,215 (8.44)	65,417 (7.48)	74,063 (9.10)
Others	277,702 (13.81)	35,417 (10.99)	118,627 (13.56)	123,658 (15.19)
Region				
Eastern	473,434 (23.16)	75,784 (23.26)	206,426 (23.22)	191,224 (23.06)
Central	1,009,711 (49.40)	150,832 (46.28)	450,910 (50.72)	407,969 (49.19)
Western	560,981 (27.44)	99,263 (30.46)	132,602 (26.05)	230,116 (27.75)
Total	2,044,126 (100)	325,897 (100)	888,938 (100)	8,293,098 (100)

\*13,937 (0.68) missing values in ethnicity; †20,048 (0.98) missing values in education; ‡33,242 (1.63) missing values in occupation.

**Table 2: Association between sociodemographic characteristics and syphilis seropositivity among women at reproductive age**

Characteristics	Number of screened women	Number of syphilis seropositivity	Percentage of syphilis seropositivity (95% CI)	cOR (95% CI)	aOR (95% CI)
Age					
21–24 years	493,046	1204	0.24 (0.23–0.26)	1.00	1.00
25–29 years	935,037	3050	0.33 (0.31–0.34)	1.34 (1.25–1.43)	1.18 (1.10–1.27)
30–34 years	403,769	1889	0.47 (0.45–0.49)	1.92 (1.79–2.06)	1.62 (1.49–1.76)
35–39 years	142,488	896	0.63 (0.59–0.67)	2.59 (2.37–2.82)	2.18 (1.97–2.42)
40–44 years	58,899	386	0.66 (0.59–0.72)	2.69 (2.40–3.02)	2.22 (1.94–2.54)
45–49 years	10,887	60	0.55 (0.41–0.69)	2.26 (1.75–2.94)	1.92 (1.43–2.57)
Ethnicity					
Han	1,851,840	6418	0.35 (0.34–0.36)	1.00	1.00
Minority	178,349	1036	0.58 (0.55–0.62)	1.68 (1.57–1.79)	1.41 (1.30–1.53)
Education					
College or above	216,085	701	0.32 (0.30–0.35)	1.00	1.00
Senior high school	359,226	1349	0.38 (0.36–0.40)	0.53 (1.16–1.27)	1.59 (1.40–1.81)
Junior high school	1,346,423	4746	0.35 (0.34–0.36)	1.09 (1.01–1.17)	1.85 (1.63–2.09)
Primary school or below	102,344	627	0.61 (0.56–0.66)	1.89 (1.70–2.11)	2.49 (2.14–2.89)
Occupation					
Farmers	1,566,487	5639	0.36 (0.35–0.37)	1.00	1.00
Workers	166,695	742	0.45 (0.41–0.48)	1.24 (1.15–1.34)	1.27 (1.14–1.41)
Others	277,702	985	0.35 (0.33–0.38)	0.99 (0.92–1.05)	1.35 (1.24–1.48)
Region					
Eastern	647,651	2454	0.38 (0.36–0.39)	1.00	1.00
Central	835,494	2650	0.32 (0.31–0.33)	0.84 (0.79–0.88)	1.40 (1.30–1.50)
Western	560,981	2381	0.42 (0.41–0.44)	1.12 (1.06–1.19)	1.53 (1.42–1.65)
Cigarette smoking					
No	2,010,388	6417	0.32 (0.31–0.33)	1.00	1.00
Yes	9522	103	1.08 (0.87–1.29)	3.42 (2.81–4.15)	2.12 (1.70–2.65)
Alcohol drinking					
No	1,949,819	6203	0.32 (0.31–0.33)	1.00	1.00
Yes	67,739	317	0.47 (0.42–0.52)	1.47 (1.32–1.65)	1.30 (1.14–1.48)
Total	2,044,126	7485	0.37 (0.36–0.37)		

CI: Confidence interval; cOR: Crude odds ratio; aOR: Adjusted odds ratio.

compared to the Han people. When comparing the education level of college or above, groups with the education levels of primary school or below, junior high school, and high school were more likely to be infected with syphilis, with ORs (95% CI) as 2.49 (2.14–2.89), 1.85 (1.63–2.09), and 1.59 (1.40–1.81), respectively. When compared with farmers, workers were more likely to be infected with syphilis (OR = 1.27, 95% CI: 1.14–1.41). Cigarette-smoking women had higher chance to be infected than the nonsmokers (OR = 2.12, 95% CI: 1.70–2.65) and alcohol-taking women were 1.30 times more likely to be infected than those who did not (95% CI: 1.14–1.48).

### Associations between gynecological and obstetric characteristics, syphilis seropositivity status of the spouses, and syphilis seropositivity among women at reproductive age

Table 3 summarizes the associations between gynecological and obstetric characteristics, syphilis seropositivity status of the spouses, and syphilis seropositivity among

women. Women with pregnant experience had greater risk of syphilis infection compared to those without the experience (OR = 1.23, 95% CI: 1.15–1.31). Women who never used condoms showed 1.27 times greater risk of syphilis infection than women who ever used condoms (95% CI: 1.19–1.35). Women who reported having histories of gynecological diseases or STIs were more likely to be tested positive for serological syphilis, compared to those without the history (OR = 1.44, 95% CI: 1.29–1.61, OR = 27.17, 95% CI: 20.44–36.11, respectively). Women whose spouses were syphilis seropositive were under significantly greater risk on syphilis seropositivity (OR = 48.26, 95% CI: 44.38–52.48) as compared to those whose spouses were negative.

## DISCUSSION

Since the prevalence of syphilis has risen in the 1990s, the Chinese government had made great efforts in developing strategies related to the prevention of vertical transmission on syphilis.<sup>[9,17]</sup> However, studies on syphilis among

**Table 3: Associations between gynecological and obstetric characteristics, syphilis seropositivity status of the spouses, and syphilis seropositivity among women at reproductive age**

Characteristics	Number of screened women	Number of syphilis seropositivity	Percentage of syphilis seropositivity (95% CI)	cOR (95% CI)	aOR (95% CI)
Previous pregnancy					
No	1,072,584	2707	0.25 (0.24–0.26)	1.00	1.00
Yes	954,170	3848	0.40 (0.39–0.42)	1.60 (1.52–1.68)	1.23 (1.15–1.31)
Ever used condoms					
Yes	641,486	2186	0.34 (0.33–0.36)	1.00	1.00
No	1,374,775	4333	0.32 (0.31–0.32)	0.93 (0.88–0.97)	1.27 (1.19–1.35)
History of gynecological diseases					
No	1,949,213	6129	0.31 (0.31–0.32)	1.00	1.00
Yes	72,601	406	0.56 (0.50–0.61)	1.78 (1.61–1.97)	1.44 (1.29–1.61)
History of STIs					
No	2,022,766	6465	0.32 (0.31–0.33)	1.00	1.00
Yes	695	76	10.94 (8.62–13.26)	38.29 (30.14–48.65)	27.17 (20.44–36.11)
Syphilis seropositivity of spouses					
Negative	1,907,452	5996	0.31 (0.31–0.32)	1.00	1.00
Positive	7039	1046	14.86 (14.03–15.69)	55.35 (51.59–59.39)	48.26 (44.38–52.48)
Total	2,044,126	7485	0.37 (0.36–0.37)		

CI: Confidence interval; cOR: Crude odds ratio; aOR: Adjusted odds ratio; STIs: Sexually transmitted infections.

reproductive-age women in rural areas have rarely been conducted due to the scarcity of STIs clinics and limited diagnostic capacities.<sup>[18,19]</sup> We conducted a study with large samples on syphilis seroepidemiology to better understand the syphilis situation among reproductive-age women in rural China.

This study showed that SPS among reproductive-age women remained high in rural China. The overall SPS appeared as 0.37% (95% CI: 0.36–0.37%), similar to the previous reported prevalence among pregnant women in rural Guangdong province (0.39%, 106/27,150), but higher than those reported in Shanghai (0.27%, 1471/535,537), Guangzhou (0.26%, 164/64,253), and lower than those in Shenzhen (0.50%, 2208/477,656).<sup>[20–23]</sup> It was postulated that the differences were caused by factors such as access to screening and treatment, related risk, disease prevalence, demographic characteristics of the participants, and the time of the survey. The results on SPS of this study were consistent with what had been discovered among rural couples attending compulsory premarital examination in three provinces (0.33–0.56%),<sup>[24]</sup> and comparable to the prevalence rates reported among voluntary blood donors in the country (0.27–0.47%).<sup>[25–27]</sup> Compared to the similar studies in other countries, the SPS in the study appeared lower than some studies conducted among pregnant women in sub-Saharan African countries,<sup>[28–30]</sup> but higher than those women at low risk, in some high-income countries, such as the U.S. and the UK.<sup>[31,32]</sup>

We noticed that older age was associated with SPS in this study. These results were consistent with other similar studies conducted at home or abroad.<sup>[23,33]</sup> Since the syphilis testing methods we applied were not able to distinguish the historical

or current infections, cumulative effect did exist.<sup>[33]</sup> However, it was not clear whether these results reflected an increased sexual risk in this population. In this study, we also found the association between lower educational background and higher SPS which was similar to the findings from other reports published at home.<sup>[22,23]</sup> Data from previous studies revealed that people with low educational level might be less aware of the risk of STIs, and also have limited access to treatment and preventive measures.<sup>[32,34]</sup> In comparison to women engaging in agricultural farming, women who were workers appeared having increased risk on syphilis infection, which might be explained as most of them were migrant workers, and previous studies had shown that migrant women workers were at higher risk of being infected with syphilis compared to the general population ( $OR = 2.5$ , 95% CI: 1.5–4.4).<sup>[18,35]</sup>

We observed a positive association between the history of previous pregnancy and SPS in this study. A possible explanation was that women who intending to get pregnant would use condoms less frequently, ending with the increase of risks on syphilis infection.<sup>[33]</sup> Women who reported never using a condom were more likely to be infected of syphilis in this study. Women who reported previous infection of STIs would have higher risks becoming syphilis seropositive. This was also likely caused by both cumulative effect and the high-risk sexual behavior of the related participants. In addition, syphilis seropositivity status of the spouses was a strong independent influencing factor on the syphilis seropositivity of women, reflecting the “spouse role” in fueling the STI prevalence. Intervention programs targeting the spouses of the seropositive syphilis women, including health education, syphilis monitoring, and follow-up management, should not be neglected.

This study might be the largest serological epidemiology on syphilis infection of its kind, with high response rates among reproductive-age women in rural China. Large sample size of this study enabled us to calculate the SPS by subpopulations, sociodemographically and geographically. However, limitations of this study would include: (1) confirmatory test of TPPA was performed in this study, which was unable to differentiate the historical infection from the current syphilis infection, causing the SPS to be overestimated, to some degree. (2) Recall bias might exist as data regarding histories on previous pregnancy, gynecological diseases, or STIs were all self-reported. (3) Only the operational data were used, but with no records on sexual behaviors.

In conclusion, the SPS appeared high among reproductive-age women in rural China, especially in those who were 35 years of age or above, with lower education level, being ethnic minority groups, being workers, and living in western regions. Through our findings, we incidentally sensed the relative high SPS in women under low risk, which called for the promotion of targeted intervention programs not only covering women under higher risks as said above, but also those under low risk as well in China.

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### Conflicts of interest

There are no conflicts of interest.

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