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Surveillance of Maternal Syphilis in China: Pregnancy Outcomes and Determinants of Congenital Syphilis

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Background:

We sought to describe the epidemiological characteristics of pregnant women with syphilis in Beijing, China, and to investigate the determinants of adverse pregnancy outcomes, including congenital syphilis.

Material/Methods:

We used data from laboratory-confirmed syphilis-infected women who delivered between 2013 and 2015 and were registered in China's Information Management System for Prevention of Mother-to-Child Transmission of Syphilis. Sociodemographic, clinical, and prevention predictors of adverse pregnancy outcomes (i.e., congenital syphilis, neonatal death, and neonatal asphyxia) were assessed using multivariable regression analyses.

Results:

Among 807 eligible pregnant women with syphilis in Beijing, the maternal syphilis ratios increased from 1.1 (in 2013) to 1.4 (in 2015) per 1000 live births, while adverse pregnancy outcomes decreased, including congenital syphilis (1.3% to 0.4%), neonatal deaths (1.3% to 0%), and neonatal asphyxia (0.9% to 0%). Both prevention and treatment interventions increased, including antenatal testing (93.5% to 93.9%), any treatment (76.6% to 85.2%), adequate treatment (51.1% to 65.1%), and treatment initiated in the first trimester (30.7% to 42.8%). In the logistic regression analysis, higher maternal rapid plasma reagin antibody titers (aOR=1.1 95%CI=1.0-1.1) and third-trimester syphilis diagnosis (aOR=1.7 95%CI=1.1-2.6) were independent risk factors for adverse pregnancy outcomes. Protective factors included being married (aOR=0.4; 95%CI=0.2-0.6) and adequate prenatal treatment (aOR=0.3; 95%CI=0.1-0.7).

Conclusions:

Integrated strategies for maternal syphilis control were associated with improved outcomes but must be strengthened. Future efforts should include education and outreach for antenatal care for at-risk women, syphilis screening at first antenatal care visit, immediate initiation of treatment, and syphilis screening extended to women presenting with miscarriage or stillbirth.

MeSH Keywords:

China • Health Services • Pregnancy Complications • Syphilis • Syphilis, Congenital

Full-text PDF:

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Background

Treponema pallidum, the causal agent of syphilis, can be transmitted sexually or from mother to child in utero [1]. Untreated syphilis in pregnancy has a high rate of transplacental transmission, with up to 80% risk of adverse pregnancy outcomes (fetal loss or stillbirth) and, in live-born infants, premature birth, low birth weight, congenital syphilis, or neonatal death [2]. The incidence of syphilis declined rapidly with the widespread use of antibiotics in the early 20th century, but has been increasing in the general population since the 1980s both in China and elsewhere in the world. Since the 1990s, the incidence of maternal syphilis also has been increasing in China [3,4].

Since there are many obstacles to developing an effective *T. pallidum* vaccine [5], universal antenatal screening and adequate treatment for both the mother and newborn remain the most effective strategy for prevention of mother-to-child syphilis transmission. In China, the recommendations for syphilis screening in pregnant women include the TPPA (*Treponema pallidum* particle agglutination) test, which should be performed at the first antenatal care visit. If a pregnant woman about to deliver comes to the hospital and no TPPA results are available, a syphilis rapid detection test (results are obtained within 20 min) should be performed.

Beijing City has integrated the screening and treatment of syphilis for pregnancy into the *Integrated Prevention of Mother-to-Child Transmission of HIV, Syphilis, and Hepatitis B Virus* (HBV) *Program* in 2011. Beijing health officials have been releasing policies every year focusing on early screening and diagnosis, standardized treatment, interventions for newborns at risk, and follow-up service implementation since 2013. Using surveillance data for maternal syphilis, we sought to describe the epidemiological characteristics of pregnant women with maternal syphilis and their pregnancy outcomes in Beijing from 2013 to 2015, investigating the determinants of congenital syphilis and adverse pregnancy outcomes and seeking to improve the effectiveness of comprehensive prevention of mother-to-child transmission of syphilis.

Material and Methods

Surveillance data for maternal syphilis were obtained from the China's Information Management System of Prevention of Mother-to-Child Transmission of Syphilis in Beijing. This nation-wide surveillance program has been described elsewhere [4]. In Beijing, surveillance is conducted through mandatory case-reporting by all health facilities providing delivery services in all 16 city districts. The hospital birth rate in Beijing approaches 100%, so this surveillance includes nearly all births in Beijing.

The study inclusion criteria for the pregnant women and their children were: (1) syphilis diagnosis during pregnancy or delivery at health facilities; (2) delivery in 2013–2015; and (3) delivery at gestational age of 28 weeks or more. The children first diagnosed in Beijing with syphilis were excluded if the infection status of the mother was unclear, as such women did not deliver in Beijing and did not receive the measures for preventing mother-to-child transmission in Beijing [4,6]. These cases were mostly children born in other cities or provinces and they were excluded because their mothers were not submitted to the Beijing's surveillance program.

In the Beijing surveillance program, diagnosis of maternal syphilis is based on at least 1 of the following criteria: (1) positive results to both rapid plasma reagin test (ortolulized red unheated serum test) and TPPA test; (2) any positive screening test combined with laboratory confirmation of *T. pallidum* in clinical specimens by dark-field microscopy; or (3) reactive treponemal IgM antibody test [1]. Pregnant women who met any of these 3 diagnostic criteria were registered in the health system and followed up through the pregnancy and postpartum periods. Live births to mothers with syphilis were followed up carefully until a syphilis diagnosis was made or excluded. Adverse pregnancy outcomes (APOs) of syphilis were defined as fetal loss or stillbirth and, in live-born infants, premature birth, low birth weight, congenital syphilis, neonatal asphyxia, or neonatal death.

Adequate treatment for maternal syphilis was confirmed only if the women met all the following criteria: 1) penicillin treatment including intramuscular injection of benzathine benzylpenicillin or procaine benzylpenicillin; 2) two completed penicillin courses according to the Chinese Guidelines for Pregnancy Syphilis Treatments (i.e., 2 courses or treatment, 3 injections/course, 1 injection/week) [1]; and 3) more than 2 weeks between the 2 courses of treatment. Infants at risk of congenital syphilis were defined as children born to a mother with syphilis who did not receive adequate treatment or who had positive non-treponemal antibody tests.

In China, the household registration system allows only 1 place of residence, which cannot be changed easily. Therefore, migrants refer to people without full legal residency in a given city (Beijing, in this case) and who have migrated from another city or province, mainly for work or specific health care. Migrants in China often have demographic and health characteristics that are different from local residents' [7–9]. Therefore, comparisons were made between migrants to Beijing and persons with full local legal residency (hukou).

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics 20.0. Categorical variables are presented as numbers and

Table 1. Adverse pregnant outcomes (APO) from 2013-2015 in Beijing, China.

	Total		Stillbirth		Neonatal death				Neonatal asphyxia		Congenital syphilis			APO (excluding premature or low birth weight)					
	n	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% Cl
2013	233	5	2.15	[0.70– 4.94]	3	1.29	[0.27– 3.72]	22	9.82	[6.01– 13.95]	2	0.89	[0.10– 3.07]	3	1.34	[0.27– 3.72]	13	5.63	[3.00– 9.35]
2014	350	4	1.14	[0.31– 2.90]	1	0.29	[0.72– 1.58]	25	7.25	[4.68– 10.36]	3	0.87	[0.18– 2.48]	3	0.87	[0.18– 2.48]	11	3.17	[1.58– 5.55]
2015	2330	5	2.15	[0.70– 4.94]	0	0	[0-1.57]	26	11.40	[7.42– 15.92]	0	0	[0-1.57]	1	0.44	[0.01– 2.37]	6	2.62	[0.95– 5.52]
Total	8160	14	1.72	[0.94– 2.86]	4	0.49	[0.13– 1.25]	73	9.16	[7.08– 11.12]	5	0.63	[0.20 - 1.42]	7	0.88	[0.35– 1.76]	30	3.72	[2.49– 5.21]

percentages. Values for continuous variables are presented as means and standard deviations (SD). Using the χ^2 statistic for categorical variables and the F statistic (analysis of variance) for continuous variables, we calculated the P values. Crude ORs (cOR) and adjusted ORs (aOR) were determined with logistic regression analyses to explore the potential factors associated with adverse pregnancy outcomes. We included all potentially associated factors as per our prior hypotheses, regardless of the P values in the crude analysis. Then, we used a reverse stepwise logistic regression process to decide which factors were suitable for inclusion in the final multivariable model.

Results

Characteristics of the population

We identified 807 pregnant women with laboratory-confirmed syphilis who delivered in Beijing from 2013 to 2015. The infection rate in pregnant women increased from 1.1 in 2013 to 1.4 per 1000 live births in 2015.

The average age of pregnant women with syphilis was 30.1 years old (interquartile range: 26–34). The rate of pregnancies at >35 years of age increased from 16.5% in 2013 to 26.2% in 2015, coincident with China's relaxation of its >30-year policy of only 1 child per family (with some exceptions) to a new universal 2-child per family policy. Most women had middle school to university education (84.9%). Migrants without Beijing *hukou* accounted for 67.5% of maternal syphilis cases, while unmarried (i.e., single, cohabitating, divorced, or widowed) women accounted for 12.0%.

Adverse pregnant outcomes (APOs)

The incidence of most types of APOs (12.0% overall) decreased from 2013 to 2015 (Table 1). The incidence of premature

birth/low birth weight increased from 9.8% in 2013 to 11.4% in 2015 (Table 1). Congenital syphilis decreased from 1.3% in 2013 to 0.4% in 2015; neonatal death decreased from 1.3% in 2013 to 0% in 2015; and neonatal asphyxia decreased from 0.9% in 2013 to 0% in 2015. The incidence of stillbirth decreased in 2014 but returned to the 2013 level in 2015.

Comprehensive prevention for mother-to-child transmission

From 2013 to 2015, both preventive and treatment interventions increased over time, including antenatal testing (slightly, from 93.5% to 93.9%), any treatment (76.6% to 85.2%), adequate treatment (51.1% to 65.1%), and treatment initiated in the first trimester (30.7% to 42.8%). Over the 3 years, the initiation time of antenatal care became earlier in pregnancy, from 17.2 gestational weeks in 2013 to 14.9 in 2015, as did the time of the first treatment course, from 18.8 to 17.1 weeks. The time gap between the first antenatal care visit and first treatment course narrowed from 7.1 weeks in 2013 to 6.0 weeks in 2015 period. The treatment rate for exposed infants increased from 53.9% to 79.5%.

Possible determinants associated with congenital syphilis and adverse pregnancy outcomes

In the bivariate analyses of the sociodemographic characteristics, only unmarried status was significantly associated with more APOs. The incidence of APOs was almost the same in the migrant population as in local residents (Table 2). In the analysis of intervention of mother-to-child transmission, the treatment rate was not found statistically different between different residence statuses, but the rates of adequate treatment and treatment initiated in the first trimester were higher in local residents than in the migrant population (Table 3).

Table 2. Sociodemographic characteristics associated with adverse outcomes in pregnant women with syphilis in Beijing, 2013-2015 (n=807).

	Women with APOs	%	All women	Odds ratio		confidence Iterval
Ethnicity						
Han	91	12.3%	743	1.0*	0.9	1.1
Minority****	6	9.4%	64			
Total	97	12.0%	807			
Marital status						
Unmarried	15	37.5%	40	3.5*	2.2	5.5
Married****	82	10.7%	767			
Total	97	12.0%	807			
Resident						
Local	37	14.1%	262	1.3*	0.9	1.9
Migration****	60	11.0%	545			
Total	97	12.0%	807			
Adverse pregnancy history						
Yes	13	12.3%	106	1.0*	0.6	1.9
No****	84	12.0%	701			
Total	97	12.0%	807			
Education						P=0.90
Primary school and illiteracy	24	3.3%	25			
Junior middle	178	25.1%	208			
Senior middle	212	29.9%	236			
College and above	217	30.5%	248			
Unknown	79	11.1%	90			
Total	710	100.0%	807			
	Max	Minimum	Mean	SD N	Nedian	P value
Gravidity						
APOs	1	6	2.6	1.3	2	0.80**
Non-APOs	1	11	2.6	1.4	2	
Parity						1.00**
APOs	0	4	0.9	0.8	1	
Non-APOs	0	3	0.8	0.7	1	
Children						1.00**
APOs	0	4	0.8	0.8	1	
Non-APOs	0	4	0.7	0.7	1	
	Mean	SD		N		
Age						
APOs	30.1	5.2		97		0.50***
Non-APOs	30.1	6.0		710		

^{*} Chi-Square test; ** Wilcoxon test P value; *** t test; **** reference category. APOs – adverse pregnancy outcomes (any); N – number; SD – standard deviation.

Table 3. Residency status associated with intervention services for syphilis in pregnant women, Beijing, 2013–2015.

	Local residents	Proportion	Migrants**	Proportion	Total	Odds ratio	95% con inter		
Treatment									
Yes	217	82.8%	431	79.4%	648	1.0*	1.0	1.1	
No	45	17.2%	112	20.6%	157				
Total	262	100%	543	100%	805				
Adequate trea	tment								
Yes	173	66.0%	307	56.3%	480	1.2*	1.0	1.3	
No	89	34.0%	238	43.7%	327				
Total	262	100%	545	100%	807				
Treatment sta	Treatment starting from first trimester								
Yes	103	48.8%	167	39.7%	270	1.2*	1.0	1.3	
No	108	51.2%	254	60.3%	362				
Total	211	100%	421	100%	632				

^{*} Chi-Square test; ** reference category. Adequate treatment for maternal syphilis was confirmed only if the women met all the following criteria: 1) penicillin treatment including intramuscular injection of benzathine benzylpenicillin or procaine benzylpenicillin; 2) two completed penicillin courses according to the Chinese Guidelines for Pregnancy Syphilis Treatments (i.e. two courses or treatment, three injections/course, one injection/week)¹; and 3) more than two weeks between the two courses of treatment.

Table 4. Clinical characteristics associated with adverse pregnancy outcomes in Beijing women with syphilis, 2013–2015.

	Total N	APOs	Proportion	P value
Maternal syphilis clinical stage				
Latent syphilis	721	77	10.7%	0.001*
Primary syphilis	22	6	27.3%	
Secondary syphilis	5	2	40.0%	
Tertiary syphilis	2	0	0%	
Unknown	57	12	21.1%	
Total	807	97	12.0%	
	Total N	Mean	SD	P value
Naternal antibody titer				
APOs	86	22.6	45.1	0.03**
Non-APOs	605	13.9	34.2	

^{*} Wilcoxon test P value; ** t test. APOs – adverse pregnancy outcomes (any); N – number; SD – standard deviation.

Among the clinical characteristics of maternal syphilis, the clinical stage of syphilis and the maternal plasma regain antibody titer were positively associated with the frequency of APO (P=0.001). The higher the stage or titer, the higher was the likelihood of APO (P=0.034; Table 4).

In the analysis of integrated intervention to prevent mother-tochild transmission, lower APOs were seen among those women who received treatment, got adequate treatment, were diagnosed in the antenatal period, had earlier first antenatal care visits, and had shorter time gaps between first antenatal care

Table 5. Comprehensive interventions and adverse pregnancy outcomes (APOs) in pregnant Beijing women with syphilis, 2013–2015.

	APOs N	Proportion	Total N	Odds ratio		confidence nterval
Treatment						
Yes	58	9.0%	648	0.4*	0.3	0.5
No****	39	24.8%	157			
Total	97	12.1%	805			
Adequate treatment						
Yes	33	6.9%	480	0.4*	0.2	0.5
No****	64	19.6%	327			
Total	97	12.0%	807			
Period of diagnosis						
Prenatal	79	10.5%	755			P<0.0001*
Delivery	7	35.0%	20			
Postnatal	11	50.0%	22			
Others	0	0.0%	10			
Total	97	100.0%	807			
		Mean	SD	N		P value
nitiation time of antenatal care						
APOs		17.4	10.0	96		<0.0001***
Non-APOs		14.9	8.1	703		
Time gap between first antenatal car	e and treatme	nt				
APOs		8.2	9.2	46		<0.0001***
Non-APOs		6.2	7.3	402		

^{*} Chi-Square test; ** Wilcoxon test P value; *** t test; **** reference category. APOs – adverse pregnancy outcomes (any); N – number; SD – standard deviation.

Table 6. Stepwise backward logistic regression of associated factors of APO for syphilis infected women.

Factors	В	P	Adjusted odds ratio	95% confidence interval		
Period of diagnosis	.550	.011	1.7	1.1	2.6	
Maternal titer of nontreponemal antibodies	.006	.036	1.1	1.0	1.1	
Adequate treatment	-1.243	.006	0.3	0.1	0.7	
Marriage status	-1.039	.000	0.4	0.2	0.6	

B – coefficients obtained from the logistic regression and indicate the magnitude of the changes of the dependent variable due to the change of the independent variables.

and treatment. We found that no mother who initiated the treatment course in the first trimester had either a perinatal death or a congenital syphilis case (Table 5).

In the multivariable regression analysis, higher maternal plasma reagin antibody titer (aOR=1.1, 95%CI=1.0-1.1) and late syphilis diagnosis (aOR=1.7, 95%CI=1.1-2.6) were risk

factors for adverse pregnancy outcomes. Protective factors included being married (aOR=0.4; 95%CI=0.2-0.6) and adequate prenatal treatment (aOR=0.3; 95%CI=0.1-0.7; Table 6).

Discussion

From the second gestational week, *T. pallidum* can infect the fetus through the placenta and cause miscarriage. From gestational week 16, the pathogen spreads to different organs of the fetus and directly damages both the placenta and umbilical cord (microvascular proliferation and inflammation) [1]. Both pathogenic pathways compromise fetal growth and viability and can lead to stillbirth or premature birth [2]. Congenital syphilis itself is by no means the only adverse pregnancy outcome from maternal syphilis; perinatal death is also more common. All pregnant women with miscarriage, stillbirth, or neonatal death should receive syphilis screening and adequate treatments for syphilis-positive cases to protect the women and their subsequent pregnancies.

We found that the rate of syphilis infection increased from 2013 to 2015. Higher-risk pregnant women should be contacted for targeted education, including migrants and unmarried women. China has a unique Household Registration System (hukou) that confers legal status for Chinese citizens in just 1 venue. Therefore, migrants refer to people not having full legal residency in a given city (Beijing, in this case) and who have migrated from another city or province, mainly for work or to receive specific health care. Other studies in China have shown that treatment services provided for pregnant migrant women with syphilis were inferior to care provided for local residents and that APOs were also more likely to occur [10]. The present study shows that the rates of adequate treatment and early initiation of treatment were significantly lower among migrant mothers, confirming the importance of enhancing outreach and care for the migrant population.

Significantly more adverse pregnancy outcomes were seen among mothers with syphilis. In the 2013-2015 period, the perinatal deaths represented 0.4% of all pregnancies in Beijing, which was lower than the 2.2% of perinatal deaths noted in our study among women with syphilis. Our findings indicate that all frequencies of APOs decreased from 2013 to 2015, even in the face of higher syphilis cases, except for premature birth/ low birth weight. The frequencies of APOs in the present study were lower than those observed nationally, perhaps reflecting the relative prosperity of Beijing. Indeed, the frequency of congenital syphilis was 0.9% during the study period, compared with 3.48% among treated mothers from Shenzen Province [11]. This discrepancy could be due to differences in the implementation of the surveillance programs. In addition, we believe that a plausible reason for the obviously increased frequencies of premature birth/low birth weight in 2015 is the increased average age of pregnancy due to the previous one-child family planning policy in China that changed to a two-child policy in the 2014-2015 period [12].

Our study found that, independent of the socioeconomic characteristics and clinical severity index, fewer APOs were noted among women who had early initiation of antenatal care, antenatal syphilis diagnosis, and adequate syphilis treatment, as suggested by another Chinese study [11]. Initiation of treatment in the first trimester could decrease APO risk further. No mother was found to have initiated the treatment course in the first trimester when perinatal death or congenital syphilis occurred.

Adequate treatment was associated with elimination of congenital syphilis and perinatal mortality [13,14]. Early diagnosis and early definitive penicillin treatment are the most crucial components of syphilis management during pregnancy. Penicillin is effective for all clinical stages of syphilis, including latent syphilis and syphilis in stages I to III. No cases of penicillin-resistance maternal syphilis have been reported so far [15-17]. In China, the recommendation is 2 courses of penicillin treatment [1], but 1 course of treatment before gestational week 28 has been suggested to be effective [11]. For pregnant women with penicillin allergies, the US Centers for Disease Control and Prevention recommend penicillin desensitization followed by penicillin treatment [5], while in the UK, ceftriaxone is recommended in penicillin allergy cases [10]. In China's Integrated Program of Prevention for Mother-to-Child Transmission (iPMTCT) of human immunodeficiency virus (HIV), syphilis, and hepatitis B virus (HBV), ceftriaxone is recommended as second-line treatment for maternal syphilis [4].

Initiating antenatal care in the first trimester enables timely antenatal diagnosis and treatment of syphilis. Studies consistently show that the earlier the prenatal care starts, the lower the risk of APOs [14]. It was estimated that a 1-week delay in the initiation of antenatal care could raise the risk of congenital syphilis by approximately 10% [18]. We found that most (59.7%) pregnant women with syphilis initiated their antenatal care in the first trimester, and 42.8% started the treatment from first trimester, which is higher than the national level [4]. Nevertheless, we still found an unacceptable and large proportion (57.2%) of women who had not been detected and/or were treated at an early stage of pregnancy. Importantly, taken together, only 65% of the women had been treated adequately, highlighting the need to improve the implementation of the Chinese guidelines.

A logistical obstacle to treating women is that treatment may not be offered at the same institution where the screening test is done. In Beijing, the Integrated Prevention of Mother-to-Child Transmission of Syphilis Program is based on a referral system. The institution providing delivery services also provides syphilis screening services, but the confirmed positive mother is only treated at an institution with an infectious disease department, fearing that an obstetrics/gynecology

department cannot manage a Jarisch-Herxheimer reaction. Referral for syphilis treatment is restricted to only 2 major hospitals specializing in infectious diseases and obstetrics in Beijing. Hence, some diagnosed women never consult at the referral hospital or they arrive too late.

The WHO certified that Thailand had eliminated mother-tochild transmission of HIV and syphilis on June 7, 2016, and several countries announced achievement of their own elimination targets later that year. China set an elimination goal in 2016, and the national capital, Beijing, seeks to take a lead in China to achieve elimination of mother-to-child transmission of HIV and syphilis. Far more pregnant women have syphilis than HIV infection, and the risk of transplacental infection of the fetus is 20% to 80% according to different clinical stages of syphilis, which is much higher compared with the 20% motherto-child transmission rate for HIV [2]. All intervention metrics have improved in the recent years after Beijing released its 2013 policy guidelines focusing on early screening and diagnosis, standardized treatment, intervention for newborns at risk, and follow-up service implementation. Still, there are many quality control and logistical obstacles to overcome in order to optimize maternal syphilis management.

Strengths of our study include its real-world research focus, inclusion of APOs, coverage of all elements of the continuum of care, and evidence for the effectiveness of prevention of mother-to-child syphilis transmission in Beijing. A total of 807 pregnant women with syphilis delivered over the 3-year study period, and all the cases were confirmed by positive treponemal and non-treponemal laboratory tests. Most studies have looked only at neonatal congenital syphilis, but we were able to include congenital syphilis cases diagnosed any time up to 21 months of age.

Limitations of the present study include the lack of generalizability. Indeed, Beijing represents a best-case scenario with a high level of technology, management, executive ability, and other optimized aspects of health care services in China. Second, the data were obtained from China's Information Management System for Prevention of Mother-to-Child Transmission of Syphilis in Beijing, which is a passive surveillance system.

References:

- The Chinese medical association branch of obstetrics and gynaecology infectious diseases group. Expert Consensus on Pregnancy with Syphilis Diagnosis and Treatment. Chin J Obstet Gynecol, 2012; 47: 158–60
- Gomez GB, Kamb ML, Newman LM et al: Untreated maternal syphilis and adverse outcomes of pregnancy: A systematic review and meta-analysis. Bull World Health Organ, 2013; 91(3): 217–26
- 3. Wang AL, Qiao YP, Wang LH et al: Integrated prevention of mother-to-child transmission for human immunodeficiency virus, syphilis and hepatitis B virus in China. Bull World Health Organ, 2015; 93(1): 52–56

Our study might be biased by underdetection, misclassification, and underreporting, since data collection on maternal syphilis relies on health facility reporting. This is mitigated somewhat by the surveillance quality control performed annually to maximize data accuracy. Third, the failure to follow up may result in an undercount of syphilis cases. Pregnant women with syphilis infection were more likely to be migratory, unmarried, and of low educational background, leading to frequent job, residence, and phone number changes. The infected women also had poor knowledge of STD prevention for themselves and their babies, inhibiting successful follow-up of the women and their babies. We included all neonatal congenital syphilis cases, whether diagnosed proximately to the pregnancy or at a later date via cross-checking with the Infectious Diseases Surveillance Reporting System (IDSRS) in China. IDSRS is a mandatory reporting system for all infectious diseases, with substantial punishment for failure to report; still, some cases were probably missed.

Conclusions

In summary, our study revealed that even with all these confirmed effective prevention methods and a high level of health care service provision, there is still a service gap. Syphilis continues to affect a large number of pregnant women in Beijing and China. Universal maternal syphilis screening and comprehensive intervention strategies have been implemented for several years, yet there are still many women who had not been detected or treated in time. Integrated strategies for maternal syphilis control need to be further strengthened in the following aspects: education for women at high risk, screening in the first antenatal care visit, immediate initiation of appropriate 2-course antibiotic treatment at a convenient local health facility as soon as diagnosis is made, and syphilis screening for all pregnant women, including those with miscarriage or stillbirth. Only then will syphilis elimination be a realistic goal.

Conflicts of interest

None.

- Dou L, Wang X, Wang F et al: Epidemic profile of maternal syphilis in China in 2013. Biomed Res Int, 2016; 2016: 9194805
- 5. Cameron CE, Lukehart SA: Current status of syphilis vaccine development: Need, challenges, prospects. Vaccine, 2014; 32(14): 1602–9
- Dou L, Wang A, Wang X: The treatment of pregnancy with syphilis and its influence factors of adverse pregnancy outcomes. Chin J Obstet Gynecol, 2016; 51: 538–41
- Tobe RG, Xu L, Song P, Huang Y: The rural-to-urban migrant population in China: Gloomy prospects for tuberculosis control. Biosci Trends, 2011; 5(6): 226–30

- 8. Wang Z, Wang L, Jing J, Hu C: Prevalence of mental disorders in migrants compared with original residents and local residents in Ningxia, China. BMC Psychiatry, 2016; 16(1): 366
- 9. Gong P, Liang S, Carlton EJ et al: Urbanisation and health in China. Lancet, 2012; 379(9818): 843–52
- 10. Zhu L, Qin M, Du L et al: Maternal and congenital syphilis in Shanghai, China, 2002 to 2006. Int J Infect Dis, 2010; 14(Suppl. 3): e45–48
- 11. Hong FC, Wu XB, Yang F et al: Risk of congenital syphilis (CS) following treatment of maternal syphilis: Results of a CS control program in China. Clin Infect Dis, 2017; 65(4): 588–94
- Zhang X, Liu K, Liu F: [Analysis of the impact of "selective two-child policy" on high risk pregnancy in Beijing.] China's Maternity and Child Care, 2015; 30: 4100–2 [in Chinese]
- Tucker JD, Cohen MS: China's syphilis epidemic: Epidemiology, proximate determinants of spread, and control responses. Curr Opin Infect Dis, 2011; 24(1): 50–55

- 14. Qin JB, Feng TJ, Yang TB et al: Synthesized prevention and control of one decade for mother-to-child transmission of syphilis and determinants associated with congenital syphilis and adverse pregnancy outcomes in Shenzhen, South China. Eur J Clin Microbiol Infect Dis, 2014; 33(12): 2183–98
- 15. Douglas JM Jr.: Penicillin treatment of syphilis: Clearing away the shadow on the land. JAMA, 2009; 301(7): 769–71
- Workowski KA, Bolan GA, Centers for Disease Control and Prevention: Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep, 2015; 64(RR-03): 1–137
- Kingston M, French P, Goh B et al: UK national guidelines on the management of syphilis 2008. Int J STD AIDS, 2008; 19(11): 729–40
- 18. Liu JB, Hong FC, Pan P et al: A risk model for congenital syphilis in infants born to mothers with syphilis treated in gestation: A prospective cohort study. Sex Transm Infect, 2010; 86(4): 292–96