

Towards the Elimination of Mother to Child Transmission of Syphilis 2015-2020: Practice and Progress in Zhejiang Province, Eastern China

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Abstract

Objectives

To estimate the progress towards elimination of mother-to-child transmission (EMTCT) of syphilis in Zhejiang province.

Methods

Data were obtained from Zhejiang provincial EMTCT network. Childbearing women infected with syphilis during 2015–2020 were recruited from. Joinpoint mode was used to analyze changing trends in syphilis screening, treatment and adverse pregnancy outcomes (APOs), presented as the annual percentage of change (APC). Multivariate logistic regression mode was used to investigate risk factors of APOs.

Results

Of 3,658,266 participants, an average maternal syphilis incidence was 0.38%. From 2015 to 2020, the coverage of syphilis screening in pregnancy (96.31–99.24%; $P < 0.001$) and coverage of antenatal health care (ANC) within 13 gestational weeks were increased (55.27–77.82%; $P = 0.002$). The coverage of maternal syphilis treatment (88.30–98.25%; $P = 0.001$) and adequate treatment were also increased (66.92–83.37%; $P = 0.001$). Over years, the APC was –19.30% (95%CI: -24.33~–13.92, $P = 0.001$) in perinatal death, –26.55% in congenital syphilis (95%CI: -38.75~–11.92, $P = 0.009$) and –14.67% in infant with abnormal signs (95%CI: -23.96~–4.24, $P = 0.019$). In 2020, 11.58% of women had APOs. Women with syphilis infection during pregnancy aged (< 20 years) or (≥ 35 years), multiparous, with pregnancy complications increased (all $P < 0.05$). APOs risk increased in those with higher maternal RPR/TRUST titers, decreased when women had therapy, adequate therapy or early ANC, or aged in 21–34 years (all $P < 0.001$).

Conclusions

Despite steady progress towards the goal of EMTCT in implementing universal screening and treatment, syphilis continuously affects a large number of pregnant women. Increasing vulnerable women, small proportions of inadequately treated and delay in early ANC should be noticed.

Introduction

The estimated worldwide prevalence of maternal syphilis in 2016 was 0.69% (95% confidence interval: 0.57–0.81%).¹ It has been estimated that 20–60% of adverse pregnancy outcomes (APOs) occur in syphilitic women, which would be worse in those unscreened, untreated, or inadequately treated.^{1–4} Maternal syphilis and associated negative impacts on infants are preventable.⁵ In 2007, WHO advocated eliminating mother-to-child transmission of syphilis (EMTCT).⁶ With the improvement of syphilis screening and treatment in pregnant women, several countries such as Thailand and the Republic of Cuba have already achieved the EMTCT goals.^{7–8}

In 2010 the Ministry of Health (MOH) of China made an announcement of a national Plan for Syphilis Control and Prevention (2010–2020) under the call of global EMTCT.⁹ In 2011, Guidelines for Prevention of Mother-to-Child Transmissions of HIV, Syphilis, and Hepatitis B virus (HBV) were integrated and implemented, which set an overall target of achieving 95% syphilis-screening coverage; 90% syphilis-screening coverage during pregnancy; 90% intervention coverage for infected pregnant women and their babies, and an incidence of congenital syphilis under 15 per 100,000 live births by 2020.⁹ In 2017, the Chinese government launched a pilot project of EMTCT. Zhejiang was appointed as one of the three pilot provinces. According to our national surveillance data in 2013 and 2019, approximately half of pregnant women with syphilis were from Eastern China, and only half of them received their first antenatal health care (ANC), syphilis treatment coverage were still under 90%, APOs were steady at 13% 14% over these years.^{11, 12}

The Zhejiang Province, located on the southeast coast of China, has a high gross domestic product (GDP) and large migrant population.^{13, 14} Data from the Chinese Center for Disease Control and Prevention shows that syphilis incidence in Zhejiang Province ranked second in China in 2016.¹⁵ The burden of maternal syphilis is also critical in Zhejiang province, as 2013–2014 data shows that the average incidence was 0.3%.¹⁶ The province has strengthened prevention mother to child transmission of syphilis project since 2015, performing routine maternal syphilis screening, treatment and surveillance at provincial level. Since inception of EMTCT program in 2017, we have taken series of measures to enhance the program towards WHO EMTCT goals, advocating social support, upholding human rights and reviewing MTCT failure cases etc. This study explored changing trends in maternal syphilis screening, treatment, APOs along with related risk factors since 2015. This analysis updated our previous research of 2013–2014.¹⁶ The findings would contribute to significant further guidance on EMTCT of syphilis in a high prevalence setting.

Methods

Study design and data source

The retrospective study obtained data from the Zhejiang provincial EMTCT information network, which is a mandatory case reporting system covering all health care institutions and delivery hospitals. In this study, we recruited pregnant women with syphilis who gave live births or stillbirths at 28 gestational weeks or above in 2015–2020. Study size was calculated by simple random sampling formula as follow.

$$n = \frac{Z^2_{\alpha/2} p(1-p)N}{\delta^2(N-1) + Z^2_{\alpha/2} p(1-p)N}$$

P was defined as the overall rate of APOs (20%).

$\delta = 0.05$ (forgives errors), $\alpha = 0.05$ (examination standard).

The minimum study size of maternal syphilis was 246. Therefore, the total number of maternal syphilis at provincial level is powerful enough to identify the APOs in the study.

Introduction of EMTCT

Integrated HIV, syphilis, and HBV screening is free for women during their first ANC in China. Regarding detection of maternal syphilis; syphilis rapid plasma regain (RPR), or toluidine red unheated serum test (TRUST), and Treponema Pallidum Hemagglutination Assay (TPHA) test or Treponema pallidum particle agglutination (TPPA) are used. If possible, laboratory confirmation of *Treponema pallidum* in clinical specimens by dark-field microscopy or reactive treponemal IgM antibody test is performed. Newborns meeting any of the following criteria are diagnosed with congenital syphilis: (1) Positive treponemal test and a value 4-fold higher titer of anontreponemal test than that of his/her mother's before delivery; (2) laboratory confirmation of *T. pallidum* in clinical specimens by dark-field microscopy; (3) reactive treponemal antibody test of IgM. These criteria are consistent with those mentioned in other literatures from China.^{11,12,16,17} Diagnosis of syphilis is done by professional clinicians; penicillin is offered for free as first line treatment and Ceftriaxone is the treatment choice for women who are allergic to Penicillin. Women infected with syphilis are followed up throughout pregnancy and postpartum by medical staff in women's and children's healthcare centers or hospitals at regional level. Infected women are entitled to safe delivery in hospital. Moreover, infants diagnosed with congenital syphilis and infants born to inadequately treated women are also offered free Penicillin treatment. Information on maternal socio-demographic characteristics, ANC service, syphilis screening, syphilis-related treatment, pregnancy outcomes, and birth information are collected through a web-based information system. Quality control is performed at the local level and provincial level medical staff, involving ANC service, laboratory quality, data collection, and associated therapy. Since 2017, we have initiated activities such as universal advocacy for anti-stigma, health education and social support and so on.

Statistics

SPSS 20.0 (IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY; IBM Corp), Stata version 13 (Stata Corp, College Station, TX, United States) and Joinpoint software (Version 4.7.0.0 - February 2019; Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute) were used for statistical analysis. Descriptive estimates, including the number of syphilis screening per 100 pregnant women, the number of syphilis screening during pregnancy per 100 pregnant women, the number of maternal syphilis therapy per 100 syphilis-positive pregnant women, number and percentage by maternal social characteristics, and incidences of APOs, were calculated. The overall incidence of APOs was defined as births with any of the following low birth weight (LBW, birth weight under 2,500g), preterm birth (born before 37 gestational weeks), perinatal death (fetal death \geq 28 gestational weeks or new infant death within 7 days after birth), an infant with abnormal signs and congenital syphilis. Overall treatment indicates treatment during pregnancy or at delivery. Adequate treatment indicated two courses of Penicillin treatment (three injections per course, once a week) during pregnancy. RPR/TRUST results were divided into four groups according to maternal titres before deliver or the third trimester (titres \geq 1:32, titres = 1:16, titres = 1:8 and titres \leq 1:4).

The chi-square test was used to analyze valuables distributions. Joinpoint Regression mode was used for changing trends analysis over the years to calculate annual percentage change and 95% confidence intervals (APC, 95% CI). The risk of APOs was calculated using logistic regression mode with adjusted odds ratio presented together with 95% confidence intervals (OR and 95% CI). All P value under 0.05 were regarded as statistically significant.

Ethics approval and and data availability

The study was performed in accordance with the Declaration of Helsinki and approved by Women's Hospital School of Medicine Zhejiang University ethics committee (No.20180180). The informed consent was not required since the data is secondary and available in Zhejiang provincial EMTCT information network, which has been mentioned as above. Data are available upon reasonable request.

Results

Changes in syphilis screening and incidence in pregnant women

During 2015–2020, the total number of pregnant women was 3,658,266. Of them, 3,655,371 had syphilis screening during pregnancy, and the rest had it at childbirth. The coverage of syphilis screening in pregnant women has remained at a high level and has improved gradually throughout the study period. Particularly, the coverage of syphilis screening in pregnancy increased significantly from 96.31% in 2015 to 99.24% in 2020 (APC = 0.60, 95%CI:0.48 ~ 0.71, $P < 0.001$), and the coverage of ANC in first trimester in women increased from 55.27–77.82% (APC = 6.71, 95%CI:4.17 ~ 9.31, $P = 0.002$). The maternal syphilis incidences were stable over years (APC=2.08, 95%CI:-2.79 ~ 7.19, $P = 0.307$), which was 0.44% in 2020. Totally, 13,829 women were diagnosed with syphilis, giving an average incidence of 0.38%. (Table 1)

Table 1

Changes in coverage of syphilis screening, first antenatal health care visit and incidences of maternal syphilis during 2015–2020.

Year	Number of pregnant women (a)	Number of pregnant women with syphilis screening (b)	Coverage of syphilis screening in pregnant women (b/a, %)	Number of syphilis screening in women during pregnancy (c)	Coverage of maternal syphilis screening during pregnancy (c/a, %)	Number of women with syphilis (d)	Incidence of maternal syphilis (d/b, %)	Number of women with syphilis with ANC in first trimester (e)	Coverage of Women with syphilis with ANC in first trimester (e/d,%)
2015	574,030	573,185	99.85	552,867	96.31	2,231	0.39	1,233	55.27
2016	724,485	723,400	99.85	703,646	97.12	2,520	0.35	1,551	61.55
2017	704,024	704,007	100.00	688,063	97.73	2,647	0.38	1,809	68.34
2018	602,107	601,257	99.86	590,344	98.05	2,240	0.37	1,618	72.23
2019	582,227	582,173	99.99	575,995	98.93	2,135	0.37	1,584	74.19
2020	471,393	471,349	99.99	467,819	99.24	2,056	0.44	1,600	77.82
Total	3,658,266	3,655,371	99.99	3,578,734	97.83	13,829	0.38	9,395	67.94

Changes in the characteristics of women with syphilis

During 2015–2020, the characteristics of women with syphilis significantly differed in some categories. There was an increase in women aged (< 20 years) or (\geq 35 years), with college or above education, multiparous, with pregnancy complications, and those who had relative lower RPR/TRUST serological titers (\leq 1:4). However, the proportion of local residents and women getting married decreased. In 2020, the predominance were those aged \geq 35 years (22.23%), with secondary education (73.78%), multipara (60.55%), with pregnancy complications (19.60%), married (89.98%) and local residents (48.54%). (Table 2)

Table 2
Changes in maternal characteristics with syphilis.

Variable		2015	2016	2017	2018	2019	2020	total	χ^2	P
Maternal age										
< 20 years old	N	82	72	69	50	60	93	426	80.186	<0.001
	%	3.68	2.86	2.61	2.23	2.81	4.52	3.08		
≥ 35 years old	N	343	417	552	438	448	457	2655		
	%	15.37	16.55	20.85	19.55	20.98	22.23	19.20		
Unemployed	N	1134	1288	1372	1107	1115	1043	7059	4.342	0.501
	%	50.83	51.11	51.83	49.42	52.22	50.73	51.04		
Education										
Primary	N	333	346	324	267	325	276	1871	43.626	<0.001
	%	14.93	13.73	12.24	11.92	15.22	13.42	13.53		
College	N	183	259	265	246	239	263	1455		
	%	8.20	10.28	10.01	10.98	11.19	12.79	10.52		
Middle	N	1715	1915	2058	1727	1571	1517	10503		
	%	76.87	75.99	77.75	77.10	73.58	73.78	75.95		
Multipara	N	1170	1438	1587	1322	1285	1245	6802	43.586*	<0.001
	%	52.44	57.06	59.95	59.02	60.19	60.55	57.78		
Marital status	N	2047	2321	2474	2089	1957	1850	12738	24.560	<0.001
	%	91.75	92.10	93.46	93.26	91.66	89.98	92.11		
Local residents	N	1222	1508	1503	1241	1053	998	7525	87.867*	<0.001
	%	54.77	59.84	56.78	55.40	49.32	48.54	54.41		
Pregnancy complications	N	367	407	441	368	372	403	2358	12.262*	0.031
	%	16.45	16.15	16.66	16.43	17.42	19.60	17.05		
Maternal RPR/TRUST Serological titer (≤ 1:4)	N	1803	2129	2225	1926	1852	1763	11698	37.024*	<0.001
	%	80.82	84.48	84.06	85.98	86.74	85.75	84.59		

* P for trend

Changes in syphilis treatment

During 2015 to 2020, we observed a dramatic change in the overall treatment coverage, increasing from 88.30–98.25% (APC = 2.37, 95%CI: 1.63 ~ 3.12, P = 0.001). Also, the coverage of adequate treatment gradually increased from 66.92–83.37% (APC = 4.84, 95%CI: 3.49 ~ 6.21, P = 0.001). It is worth mentioning that the gap between natives and migrants was narrowed (all P < 0.001). (Table 3)

Table 3
Changes in maternal syphilis treatment between women living in Zhejiang or coming from other provinces.

Year	Number of women with syphilis	Overall treatment		Adequate treatment		Zhejiang	Overall treatment		Adequate treatment		Other provinces	Overall treatment		Adequate treatment
		Number	Rate (%)	Number	Rate (%)		Number	Rate (%)	Number	Rate (%)		Number	Rate (%)	Number
2015	2231	1970	88.30	1493	66.92	1222	1107	90.59	892	73.00	1009	863	85.53	601
2016	2520	2261	89.72	1715	68.06	1509	1366	90.52	1084	71.84	1011	895	88.53	631
2017	2647	2467	93.20	1932	72.99	1503	1408	93.68	1124	74.78	1144	1059	92.57	808
2018	2240	2154	96.16	1762	78.66	1241	1194	96.21	995	80.18	999	960	96.10	767
2019	2135	2084	97.61	1702	79.72	1053	1026	97.44	864	82.05	1082	1058	97.78	838
2020	2056	2020	98.25	1714	83.37	997	984	98.70	837	83.95	1059	1036	97.83	877
APC (95%CI)		2.37(1.63, 3.12)		4.84(3.49, 6.21)			1.99(1.33, 2.65)		3.46(1.87, 5.08)			2.88(1.73, 4.04)		6.89(4.63, 9.15)
P		< 0.001		< 0.001			< 0.001		< 0.001			< 0.001		< 0.001

Changes in pregnancy outcomes and risk factors

Over the years, there have been no significant decrease in the overall incidence of APOs (from 11.56% to 10.02%); however the incidences of perinatal death, congenital syphilis and infant with abnormal signs decreased significantly. In 2020, all of the above mentioned incidences decreased to the lowest level, which were 6.14‰, 2.36‰ and 0.57%, respectively. The APC of perinatal death was -19.30% (95%CI:-24.33~-13.92, P = 0.001), and that of congenital syphilis was -26.55% (95%CI:-38.75~-11.92, P = 0.009). The APC of children with abnormal physical signs was -14.67% (95%CI:-23.96 to -4.24, P = 0.019). (Table 4)

Table 4
Changes of APOs incidences by categories during 2015–2020.

Year	Number of birth	Overall APOs		LBW/preterm birth		Perinatal death		Congenital syphilis		Abnormal sign	
		n	%	n	%	n	‰	n	‰	n	%
2015	2246	259	11.53	251	11.18	42	18.70	18	8.01	28	1.25
2016	2539	288	11.34	261	10.28	36	14.18	23	9.06	37	1.46
2017	2689	282	10.49	251	9.33	29	10.78	15	5.58	33	1.23
2018	2273	258	11.35	243	10.69	25	11.00	7	3.08	21	0.92
2019	2196	246	11.20	241	10.97	16	7.29	5	2.28	18	0.82
2020	2116	245	11.58	205	9.69	13	6.14	5	2.36	12	0.57
APC(95% CI)		0.16(-2.57, 2.97)		-1.00(-6.02, 4.28)		-19.30(-24.33, -13.92)		-26.55(-38.75, -11.92)		-14.67(-23.96, -4.24)	
P		0.877		0.618		0.001		0.009		0.019	

The risk of APOs for untreated or incompletely treated, below 20 years and above 34 years, late in ANC or unmarried decreased when compared with those who were treated or adequately treated, aged between 21 and 34 years, had early ANC. It was worth noting that risk of APOs increased with increasing maternal RPR/TRUST titers.(Table 5, Fig. 1)

Table 5
Predictors for adverse pregnancy outcomes by multiple logistic mode

Variable	B	Wald	P	OR _{adj} , 95% CI
Treatment	-0.35	15.33	< 0.001	0.71(0.59 ~ 0.84)
Complete-treatment	-0.50	60.98	< 0.001	0.61(0.54 ~ 0.69)
Maternal age		22.26	< 0.001	
≥ 35years old				
< 20 years old	-0.08	0.42	0.516	0.92(0.73 ~ 1.18)
21-34 years old	-0.29	20.06	< 0.001	0.75(0.66 ~ 0.85)
Education		3.81	0.149	
College				
Middle	0.22	3.76	0.052	1.24(1.00 ~ 1.55)
Primary or under primary	0.13	1.84	0.175	1.14(0.95 ~ 1.37)
Multipara	-0.05	0.777	0.378	0.95(0.86 ~ 1.06)
Adverse pregnancy history	0.11	2.69	0.101	1.11(0.98 ~ 1.26)
RPR/TRUST		101.33	< 0.001	
≤ 1:4				
≥ 1:32	0.83	81.68	< 0.001	2.30(1.92 ~ 2.75)
1:16	0.58	28.77	< 0.001	1.78(1.44 ~ 2.19)
1:8	0.19	3.58	0.058	1.21(0.99 ~ 1.48)
First ANC				
Third trimester		18.91	< 0.001	
First trimester	-0.33	16.79	< 0.001	0.72(0.61 ~ 0.84)
Second trimester	-0.35	15.70	< 0.001	0.70(0.59 ~ 0.84)
Married	-0.12	6.58	0.010	0.89(0.81 ~ 0.97)
Employment	0.04	0.21	0.648	1.04(0.88 ~ 1.23)

Discussion

This study indicates improvement in syphilis screening and treatment in pregnant women, especially the narrowed gap between local residents and migrants. In 2020, vast majority of pregnant women were screened for syphilis in their ANC, over 95% maternal syphilis received therapy, congenital syphilis (CS) incidence was at a low level, meeting the global goals of EMTCT⁴. Between 2012 and 2016, and coverage of syphilis testing increased from 59–66%, and treatment increased from 74–78% all over the world¹. At Chinese national level, treatment coverage reached 89.52% in 2019, and remarkable achievements on EMTCT of syphilis have also been reported at regional level at home and abroad^{11, 17–21}. Findings in our study reflected persistent progress towards EMTCT over the past years as a pilot area. EMTCT program were enhanced and financed by both Chinese and Zhejiang local government, promoting accessibility and equality of services. EMTCT has been integrated with current basic ANC services for women in Zhejiang, an increase in coverage of early ANC as well as sustainable provision of Penicillin also contributed to the improvement.

Maternal syphilis incidence has remained at high level throughout the study period in Zhejiang. In 2020, it reached 0.44%, which is higher than the Netherlands (0.06–0.08%), lower than Africa (2.7%), Latin American (1.1%) and Beijing(China) (1.4‰), however similar to Shanghai (0.20–0.38%)(China).^{19, 21–28} The epidemic of maternal syphilis in this study is slightly expanded compared to the previous study of Zhejiang in 2013–2014.¹⁶ As the global maternal syphilis remained stable in most area, the growth of syphilis in pregnant women in Zhejiang should be given serious consideration.¹ On the one hand, it should be possible due to changes in sexual network structure and increase in screening. On the other hand, growth in multipara with syphilis would also result in increase of maternal syphilis prevalence.

Early ANC is critical for timely intervention and adequate treatment. During 2015 to 2020, ANC in first trimester increased by 6.71% annually. Consequently, the most increase was found to be adequate therapy among women, rising by 4.84% per year, and 6.89% increase in migrants. The findings prove the effective because we gave case reviews on those women delayed early ANC, inadequate treatment or vertical transmission since 2017. Barriers to access early ANC or effective EMTCT services were comparable to other studies, such as poor awareness of ANC in pregnant women, limited EMTCT knowledge in healthcare

providers, vulnerabilities in laboratory facilities as reported elsewhere.^{22,24–25} One step of screening and treatment package should be strengthened for improvement of follow up as widely suggested.^{23–24}

We evaluated the characteristics of women with syphilis in order to develop target interventions. The proportion of women with advanced age (≥ 35 years) increased greatly, exceeding 20%. The rapid development of social-economy, work and lifestyle pressure, might force women to put off giving birth, particularly since the new birth policy changes in China.^{29–30} Similarly, reports indicated that women with syphilis infection were more likely to be illiterate, migrants and multiparous at regional and national level.^{11,17} Furthermore, a rise in pregnancy complications proportion in women with syphilis might be the consequence of increasing number of women with advanced age and higher parity. This point highlighted the need for the potential improved risk management for APOs.

The average incidence of APOs at our national level was 13.82% in 2016–2019, reflecting fetal loss or stillbirth, as well as abnormal infant parameters. In Guangzhou, this figure was 27.3% during 2011–2018, including ectopic pregnancy, spontaneous abortion, stillbirth, prematurity or LBW, a live infant birth weight of less than the 10th percentile by gestational age and sex, infant death and CS.³¹ Therefore, differences in inclusion and exclusion criteria in different studies while comparing the overall occurrences of APOs should be given consideration. Exclusion of early fetal loss in our study resulted in decreased incidence of APOs for this reason the incidence of APOs might be underestimated. LBW/preterm birth was the most common subtypes of APOs, which was shown in previous studies.^{4,11,31} No significant decline in LBW/preterm birth was possible for the composite negative effect from increasing maternal age and pregnancy complications. The obvious reduction of APOs categories were predominantly in CS, abnormal signs and perinatal death. Our hypothesis indicates increasing coverage and effectiveness of testing, early ANC, and treatment. Women with treatment, especially adequate treatment, early ANC and appropriate maternal age were less likely to experience APOs. APOs risk increased with maternal RPR/TRUST titers, which was significantly severe among women with a titer of $\geq 1:32$ at delivery or third trimester. The above evidences have been widely reported, and persisting low nontreponemal titers ($< 1:8$) is frequently suggested.^{2–5,11,31}

This study has several limitations. Firstly, we focused on selected APOs. Missing information on early fetal loss and abortion could lead to some selection bias to the comprehensive understanding of APOs associated with syphilis. Secondly, some risk factors, such as the mother's stage of syphilis infection, gestational age at syphilis status, mode of delivery, sexual partner's infection status and congenital birth defects, were not considered.^{5,11,26} Lastly, Zhejiang is a province with rapid economic growth and with qualified healthcare system. The lessons from Zhejiang's experiences need to be considered cautiously by other less developed regions.

Conclusions

This study included a substantial number of pregnant women, thus providing a powerful and effective detection of maternal syphilis and associated APOs. In summary, expanding the coverage of syphilis screening, early ANC, and adequate treatment will be the most effective way to improve pregnancy outcomes and promote the health condition of infants born to maternal syphilis, even in a high endemic region.

Declarations

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Contributors

WH and ZXH conceived the analysis. WH, YX, ZXH designed the study and drafted the manuscript. YX, LD, Muhuza Marie Parfaite Uwimana participated in data collection and statistics analysis. ZXH is responsible for the project. All authors contributed to data interpretation, revision and approval of the final manuscript.

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Data availability statement

Data are available upon reasonable request. The Study group will review proposals. Please contact Corresponding author, Dr Xiaohui Zhang (zjfb_amy@zju.edu.cn).

Ethics approval and consent to participants

The study was performed in accordance with the Declaration of Helsinki and approved by Women's Hospital School of Medicine Zhejiang University ethics committee (No.20180180). The informed consent was not required since the data is secondary and available in Zhejiang provincial EMTCT information network, which has been mentioned as above. All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors have no conflict of interest to declare.

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Figures

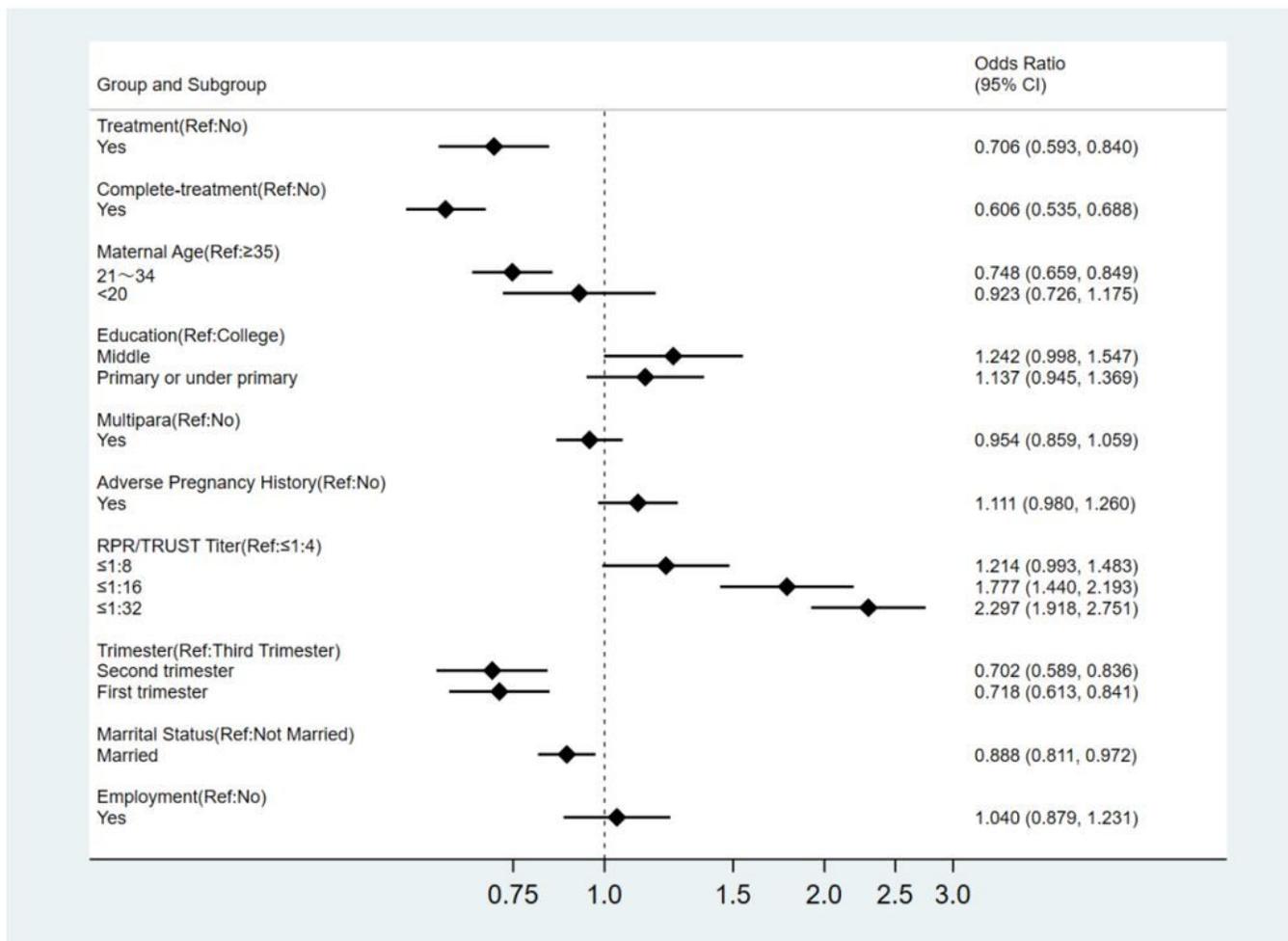


Figure 1

Predictors for adverse pregnancy outcomes by multiple logistic model