# Prevalence and predictors of HIV-syphilis co-infection among HIV-infected pregnant women in China, 2011-2018

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## Abstract

# Background

The co-infection of Human Immunodeficiency Virus (HIV) and syphilis is risky for pregnant women and their expected children. In 2015, the Integrated Prevention of Mother-to-Child Transmission (iPMTCT) programwas established to offer all pregnant women with free screening, counseling, and testing of HIV and syphilis during regular obstetric inspections. To summarize the phase progress of this program, we reported the trends of maternal HIV-syphilis co-infection in China. We tried to socioeconomic factors associated with HIV-syphilis co-infection to inform the stratified control strategy for future work.

# Methods

We obtained the prevalence data of HIV and syphilis over 2011–2018 by reviewing the Sexually Transmitted Infection (STI) monthly update reporting to the central surveillance system. With health status, background characteristics, and health outcomes reported, we collected the case reports from 2,578 HIV-positive pregnant women who accepted the screening at the local clinic. The trends of HIV and syphilis prevalence were examined using the Cochran-Armitage trend test. Logistic regression was applied to detect the features associated with syphilis infection among HIV-positive women and the potential risk factor to neonatal death.

# Results

The prevalence of HIV decreased from 0.076–0.039% among registered pregnant women but increased slightly to 0.054% in 2018. The trend of syphilis prevalence in HIV-infected pregnant women fluctuated slightly around an average of 1.80% ($p = .378$). Multivariate logistic regression indicated finishing education of junior high school or below (aOR: 1.79, 95%CI: 1.31–2.43; $p < .001$), on regular Antiretroviral Therapy (ART) (aOR: 1.89, 95%CI: 1.47–2.45; $p < .001$) and exposed HIV from injective drug use (aOR: 5.49, 95%CI: 3.51–8.61; $p < .001$) are associated with high syphilis infection risk. Syphilis co-infection with HIV (aOR: 2.81, 95%CI: 1.32–5.96; $p < .007$) significantly increases the risk of newborns death.

# Conclusion

Syphilis infection is still very prevalent in HIV-positive pregnant women five years after the implementation of iPMTCT program. Promoting the health education for maternal infection of STIs and increasing the availability of early intervention to link more marginalized women with care service should be the focuses of work in the next stage.

## Background

The co-infection of sexually transmitted infections (STIs) is harmful to pregnant women who live with HIV, as well as the children they are expecting. Particularly, STIs such as human immunodeficiency virus (HIV) [1][2], syphilis [3][4] and hepatitis B virus (HBV) could be passed from mother to children during gestation period [5][6][7][8], the adverse pregnancy outcomes of which include miscarriage, stillbirth, preterm delivery and neonatal death[4][9]. Mother-to-child transmission (MTCT) of STIs are preventable with early intervening approaches. However, without any interventions from gestation, infants who infected congenitally will grow up with pathogens, especially HBV and HIV

[3][4][9], and transmit those to others at some stage of their lives. Infection of HIV and syphilis in infants often occur simultaneously due to the similar pathways of transmission (i.e., from the placenta) [10][11][12][13][14][15]. Maternal co-infection with HIV and syphilis is dangerous. The secondary infection speeds up the progression of HIV-related conditions. The treatment outcomes of HIV-positive pregnant women are usually not ideal either [16][17][18]. The co-infection of HIV and syphilis may compromise the placental barrier and increase the vulnerability of the fetus to both infections [11][16][17][19]. Besides, there is a higher risk of developing early neurological and ophthalmic defects among infants [16].

STIs are hyperendemic and the co-infection of which remains a significant public health concern in many developing countries. The global incidence of STIs is estimated at over 125 million cases yearly [20]. In Asia, syphilis prevalence was around 2.5% among people living with HIV, for instance, 1.6% among HIV infected women in India [21][22]. HIV-syphilis co-infection is very prevalent in the developing countries that are suffering from poverty and under-serviced health care because fewer resources and fundings are pointed to healthcare systems in these places [23]. Sub-Saharan countries such as Rwanda, Tanzania, Ethiopia, Uganda, Zambia, and Nigeria are coming across a greater problem of maternal HIV-syphilis co-infection than any other part of the world [24][25][26]. In Congo, it was reported that the HIV-syphilis co-infection occurred at the rate of 0.73% among pregnant women attending antenatal clinics. The syphilis-infection in HIV-positive pregnant women increased from 6.0–10.8% from 2002 to 2011 in Rwanda [14]. Another few cross-sectional studies in Tanzania indicated a co-infection rate was found at around 0.7–1.4% in pregnant women [13][27][28]. Whereas, it is not a concern in developed countries like the United States - the prevalence of syphilis in women is close to 0.023%, and the co-infection with HIV is already not concentrated in pregnant women [29].

In China, the STIs have also been spreading widely since the last century [2][3][4][30][31]. Given the large population base, China is facing severe challenges of MTCT caused by HIV and syphilis infection [2][3][4][9]. Several previous studies reported the prevalence of HIV or syphilis infection in Chinese pregnant women at 0.05–0.10% (2009 to 2013) [3][9]. In order to curb the epidemics in pregnant women, and to fulfill the international obligation on the elimination of MTCT of HIV and syphilis, from 2001, National Center for women and children's health Chinese Center for Disease Control and Prevention (China CDC) established a series of pilot study sites in health facilities in the high-risk region to explore the optimal intervention strategies. Followed by that, In 2004, the Central Government started to provide financial support to programsites [9]. In 2010, the National Implementation Guidelines on Integrated Prevention of Mother-to-Child Transmission (iPMTCT) of HIV, syphilis, and HBV program initiated to provide comprehensive service to pregnant women [4][9]. Starting from 2015, China government invested 1.4 billion RMB (approximately 206 million USD) in the iPMTCT programon an annyal basis, which increased the expansion of coverage nationally. The local clinics offer all pregnant women with free screening, counseling, and testing of HIV, syphilis, and HBV during regular obstetric inspections to pregnant women and follow-up treatment to their exposed children. China is one of the pioneering countries in the world developed the iPMTCT strategies for HIV, syphilis, and HBV. Based on the National iPMTCT Programme, with national effort experts and the support from the elimination of mother-to-child transmission (EMTCT) programled by the United Nation, we expect to see the EMTCT goal of "getting to zero" are largely achieved in the next decade [3][9][31][32].

We believed, a few years after the iPMTCT programimplementation, it is essential to profile the overall trend of HIV-syphilis co-infection in pregnant women to summarize the phase progression of the early intervention. By identifying the risk factor for co-infection, we may further tailor the program to match the need of pregnant women at different disease stages or from different socioeconomic backgrounds. In this study, we reported the prevalence and trends of maternal HIV-syphilis co-infection among HIV-infected pregnant women in China, as well as socioeconomic factors

associated with HIV-syphilis co-infection. We then further explored the risk factors leading to infant death. This work will direct the obstetrics clinical practitioners and STI program managers to adapt the strategies to deliver the care services to pregnant women better.

## Method

# Data source

The data were extracted from the PMTCT national surveillance system administrated by the National Center for Women and Children's Health, China Center for Disease Control. In collaboration with the United Nations Children's Fund UNICEF, the China first-ever PMTCT pilot on HIV was launched in 2001. From 2003 to 2004, the Central Government expanded the coverage from 8 pilot high-risk counties to 453 counties, cities, and districts all over China [9]. The local health facilities involved in this project include provincial general hospitals, maternal and children's hospitals, and other Antenatal Care (ANC) clinics at covered regions, from all 31 provinces, municipalities, and autonomous regions in China [9]. In 2003, the participating health facilities offered free HIV screening to pregnant women [9]. In 2010, the iPMTCT Programwas included in the National Major Public Health Programme, and the PMTCT preventive services were expanded from single infection to three infections (HIV, syphilis, and hepatitis B). In 2010, China government also incorporated the nationwide syphilis surveillance module into the existing PMTCT case reporting system. Reporting new cases of HIV and syphilis in pregnant women is mandatory for all participating facilities.

# Data extraction

We reviewed the STI monthly update reporting to the central surveillance system to obtain the prevalence data of HIV and syphilis over 2011–2018. Individual case reports of pregnant women who registered due to HIV infection were available from 2011 to 2017 due to the delay of report circulation. In total, 2,578 anonymous pregnant women who diagnosed as HIV positivity were identified through the system. We collected patients' socio-demographic characters (e.g., maternal age, ethnicity, marital status, education level), maternal HIV and syphilis infection details (e.g., time of diagnosis, infection route, HIV antiviral therapy [ART] status), delivery details (delivery location, delivery type, gestation period) and pregnancy outcomes (mother outcome and newborn outcome) for syphilis infection risk analysis. Additionally, 1,693 out of 2,578 pregnant women who reported their pregnancy outcomes (i.e., did not have their children aborted naturally or artificially) were further identified to understand the contributing factors to neonatal death.

# Diagnosis criteria

At ANC, HIV screening was performed with ELISA/rapid tests, and the infection confirmed by Western Blot. The health status survey was distributed while waiting for the results of regular care, in which the pregnant woman was asked to self-report their syphilis infection status. If they confirmed they accepted syphilis tests satisfied with one of the following standards: 1) positive signs in treponemal and nontreponemal tests or 2) clinical specimen laboratory confirmation of Treponema pallidum with dark-field microscopy, they will be marked as HIV-syphilis coinfected individuals. Pregnant women diagnosed as maternal HIV positivity were mandatory to register in the reporting system and would be followed up through their pregnancy and the postpartum period.

# Statistical analysis

We first described the demographic, socioeconomic, and clinical characteristics of the involved pregnant women by HIV infection status and distinguished the characteristics in pregnant women had their children delivered. Statistical

test of t-test, chi-squared test was performed as appropriate to show the variance in features among groups. The trend of HIV infection in pregnant women attending ANC and the trend of syphilis infection in pregnant women and HIV-positive pregnant women attending ANC were showed in plots. The trends of HIV and syphilis prevalence were examined using the Cochran-Armitage trend test. We performed univariate logistic regression to detect the potential risk factors to syphilis infection among HIV-positive women. Eligible independent predictors were fitted into a multivariate logistic regression model, eliminated in backward selection fashion, to obtain the final full model. A two-sided p-value < .05 was set as the statistical significance level in statistical tests and the univariate/ multivariate analyses. Odds ratio (OR) in univariate analysis and adjusted odds ratio (aOR) with 95% confidence interval (95% CI) in multivariate analysis were reported as the model outputs. The same model construction procedures were repeated when analyzing the association with neonatal death risk. The data cleaning and statistical analyses were performed in R 3.5.0 for Mac.

## Results

# The national reporting system links the HIV and syphilis infected pregnant women

From when the China CDC first enabled the integrated nationwide health facility-based case reporting surveillance system in 2010, the number of linked pregnant women increased by 3.4 folds over the last seven years (from 5.5 million in 2010 to 18.3 million in 2016). As the surveillance data indicates over 2011–2016, the prevalence of HIV kept on decreasing from 0.076–0.039% among registered pregnant women at ANC but slightly increased to 0.054% in 2018 (Cochran-Armitage Trend test: p = 0.994; Fig. 1a). However, the increace (0.11–0.24%) of syphilis infection in pregnant women at ANC was outstanding, as shown by statistical test (p < .001, Fig. 1b). The pooled prevalence of syphilis infection over seven years was significantly higher in HIV-infected women than in uninfected women (0.14% vs. 1.80%, chi-squared test: p < .001). The syphilis prevalence in HIV-infected women stablized around the average over these eight years (p = .377, Fig. 1).

# Pregnant women characteristics and factors associated with HIV-syphilis co-infection

We have a sample cohort of 2,578 registered women to identify the risk factors of syphilis co-infection in HIV-infected pregnant women. Among these pregnant women, 21% (542/ 2,578) were younger than 25, 48.2% (1,079/ 2,578) were Han ethic, and 23.4% (603/ 2,578) received education of senior high school or above. There were 13.1% (337/ 2,578) women also tested positive for syphilis infection, and only 57.1% (1,473/ 2,578) of them reported they are on the regular ART treatment plan. The ART adoption level was much higher in HIV-syphilis co-infected women (67,4%, chi-squared test p < 0.001) than in HIV sole infected women. The level of performing risk behaviors was also significantly higher in co-infected women (t-test p < 0.001 ).

Multivariate logistic regression indicated minority women (aOR: 0.57, 95%CI: 0.45–0.72; p < .001) were less likely to detect with syphilis positivity during their pregnancy compared to Han women. Only finishing education of junior high school or below (aOR: 1.79, 95%CI: 1.31–2.43; p < .001) is associated with high syphilis infection risk. After adjustment, we found women were on regular ART (aOR: 1.89, 95%CI: 1.47–2.45; p < .001), exposed HIV from injective drug use (aOR: 5.49, 95%CI: 3.51–8.61; p < .001) or their occupations (aOR: 1.87, 95%CI: 1.40–2.50; p < .001) experiencing a higher risk of HIV-syphilis co-infection. However, a long time carrying HIV (aOR: 0.79, 95%CI: 0.74–0.85; p < .001) seemed to decrease syphilis infection risk in pregnant women.

# Maternal and children outcomes

Among 2.578 HIV-infected pregnant women, 1,693 had delivered and had reported the outcomes for themselves and the newborns. Forty death cases and three death cases were observed in newborns and mothers. Shortened gestation than the normal period (aOR: 0.68, 95%CI: 0.61–0.75; p < .001) is strongly associated with neonatal death. Maternal ART (aOR: 0.37, 95%CI: 0.18–0.75; p < .006) is a protective factor. But syphilis co-infection with HIV (aOR: 2.81, 95%CI: 1.32–5.96; p < .007) significantly increases the risk of newborns death.

## Discussion

This was the first study that reported the prevalence of HIV-syphilis co-infection and analyzed the factors associated to infection based on national surveillance data in China. We observed a downward trend in HIV prevalence from 2011 to 2016 in pregnant women at ANC with a slight increase in 2018. The syphilis prevalence in pregnant women at ANC increased, but the syphilis infection in HIV-infected pregnant women almost remain unchanged over 2011–2018. HIV-infected pregnant women of Han ethnicity, with lower education level and exposing HIV from injective drug use or their occupations, had a higher chance of acquisiting syphilis. Even though the gestation period is the crucial determinant, evidence showed that syphilis infection was associated with neonatal death.

In 2016, the World Health Assembly endorsed three linked World Health Organization global health sector strategies on HIV, STIs, and hepatitis. These three strategies call for the elimination of mother-to-child-transmission of HIV by 2020 and syphilis and hepatitis B by 2030 [33]. Integrated testing and intervention play a crucial role in this act. Effective screening is an essential tache to control and prevent co-infection from transmitting from mother to child. In China, once co-infected pregnant women were discerned, the dual HIV and syphilis intervention with antiretroviral therapy and benzathine penicillin injections will be offered to control maternal progression and to reduce the risk of neonatal infection and avoid infant death. The coverage of HIV and syphilis testing among pregnant women should be high enough to reach the goal of elimination. China plays a pioneering role in leading this task that the iPMTCT started to offer HIV testing and syphilis testing to 97.3%, and 96.4% of all pregnant women attending the antenatal care in 2013 (13.07 million) [9]. The findings of this study also provided some insights to adjust the program to meet the need of more pregnant women, for instance, attached much attention to pregnant women who are marginalized (i.e., do not have a higher educational level or from minority ethnic groups).

Similar but adapted dual infection intervening approaches with linked screening, treatment, and consulting should be proposed in other underdeveloped countries with a high burden of HIV infection. In China, the observed prevalence of syphilis in HIV-positive pregnant women ranged from 1.17 ~ 1.57% without apparent alternation over time. A similar trend of epidemics was found in Asia; the prevalence of syphilis was found at 1.6% in HIV infected women in India [21], at 3.6% in a female sex worker in Karnataka, India [22]. Even though the observed prevalence of syphilis in HIV-positive pregnant women was much lower than those reported by Sub-Sahara countries such as Rwanda, Tanzania, Ethiopia, Uganda and Zambia [13][14][27][28], extra attention should be given to those are experiencing HIV-syphilis co-infection, as it was associated with poorer maternal outcomes and higher risk of MTCT of both HIV and Syphilis [34][35].

Local health practitioners should attach close attention to pregnant women from deprived socioeconomic status and offer the screening service as early as possible. We noticed that lower education level was associated with high syphilis infection. This is consistent with a nationwide multicenter study of HIV-positive females in Israel [36]. Our study also agreed with an Indian study that female injective drug users potentially have a higher risk of HIV and syphilis confection than women acquiring HIV from other routes [21]. Other than the demographic and

socioeconomic risk factors, besides, the timing of detection plays a crucial role in controlling the development of adopted syphilis infection [37]. Syphilis and HIV infections in pregnancy are essential causes of adverse birth outcomes, including neonatal death and vertical transmission [38]. Latent and primary syphilis infection is more manageable compared to those progress to secondary infection phase. Prompt and efficient treatment of maternal infection is critical in preventing maternal transmission to the fetus and for treating fetal infection [39]. Globally in 2008, in a middle case scenario, untreated maternal syphilis resulted in approximately 304,091 fetal or perinatal deaths and 216,814 syphilis-infected infants at risk for early death [40]. HIV, on the other hand, leads to more unwonted clinical symptom and treatment outcome of syphilis by favoring escape of the Treponema from the host immune response [41][42]. The local practitioners at health facilities should favor pregnant women to accept screening as early as possible (e.g., during first or second trimesters) to reduce the adverse outcomes for mothers and children at large. However, in practice, we found that co-infection was more likely to be diagnosed during or after delivery. Delayed or absence of antenatal care of syphilis is unfavorably common among those with co-infection. Stigma and discrimination toward people living with HIV are very widely seen in conventional areas in China. Pregnant women with HIV infection may concern about being discriminated against when attending antenatal care, which may reduce their motivation to seek service promptly when feeling ill. Linking the marginalized population with preventive care should be one of the focuses of work in the next stage.

## Strengths And Limitations

Leveraging on a nationwide integrated surveillance and reporting system, our study, for the first time, attained the data on HIV-syphilis coinfected pregnant women, which allowed us to describe and analyze the epidemics of syphilis-HIV co-infection in China. This study provided good references to filter out the at-risk pregnant women and further inform the intervening policy to eliminate the epidemic in the future.

We had a prevalence trend of one more year to report than individual cases. We estimated the epidemic trend from China’s integrated surveillance information system based on automatically generated monthly reports; whereas, the individual case report submission lagged behind the monthly reports, which also requires extra time for data entry and data cleansing for analytical purposes. Moreover, this passive surveillance system might be biased by low or differential incidence reporting due to under-detection, misclassification, and under-reporting at selected facilities. Secondly, partial individual cases were stilla under close follow-up; therefore, we were ignorant about the longterm outcomes of HIV-syphilis co-infection for children.

## Conclusion

Syphilis infection is still very prevalent in HIV-positive pregnant women five years after the implementation of iPMTCT program. Promoting the health education for maternal infection of STIs and increasing the availability of early intervention to link more marginalized women with care service should be the focuses of work in the next stage.

## Abbreviations

ANC - Antenatal Care

aOR - adjusted Odds Ratio

ART - Antiretroviral Therapy

China CDC - Chinese Center for Disease Control and Prevention

CI - Confidence Interval

EMTCT - Elimination of Mother-to-Child Transmission

HBV - Hepatitis B Virus

HIV - Human Immunodeficiency Virus

iPMTCT - Integrated Prevention of Mother-to-Child Transmission

MTCT - Mother-to-Child Transmission

OR - Odds Ratio

PMTCT - Prevention of Mother-to-Child Transmission

STI - Sexually Transmitted Infection

# Declarations

*Ethics approval and consent to participate*

The ethical approval of this study was obtained from the ethical review committee of the National Center for Women and Children's Health, Chinese Center for Disease Control and Prevention on 7th Feb 2018. (No. FY2018-03). Written consent was obtained from all participant at the time of recruiting.

*Consent for publication*

Not applicable, since the individual cases were preprocessed to deidentified records before we obtaining the data.

*Availability of data and materials*

Please contact the corresponding author Ms. Ai-ling Wang at (ailing@chinawch.org.cn) to access the data.

*Competing interests*

All the authors declared they have no competing interests to report.

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*Authors' contributions*

QW and AW identified the research topic and designed the research study. XW administered the database and was in charge of data cleaning and conducted partial analyses. XM did partial of the analytical work and drafted the manuscript with QW, AW. YQ, LD facilitated XW with data entry and data cleaning. LN, XC and XJ participated in the

study design and provided critical ideas to frame the study. All authors read and approved the manuscript for submission.

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# Tables

Table 1. Characteristics associated with maternal syphilis infection among HIV-positive pregnant women in China

| Factors | All (n = 2578) n (%) | Co-infection (n = 337) n (%) | OR (95%CI) | aOR (95%CI) |
|---|---|---|---|---|
| **Socio-demographic characteristics** | | | | |
| Maternal age | | | | |
| *<25* | 542 (21.0) | 82 (24.3) | *ref* | |
| *25~29* | 757 (29.4) | 112 (33.2) | 0.97 (0.77, 1.23) | |
| *30~34* | 732 (28.4) | 81 (24.0) | **0.70 (0.50, 0.97) *** | |
| *≥35* | 547 (21.2) | 62 (18.4) | 0.72 (0.50, 1.02) | |
| Ethnic group | | | | |
| *Han* | 1,079 (48.2) | 182 (54.0) | *ref* | *ref* |
| *Minority* | 1,499 (51.8) | 155 (46.0) | **0.57 (0.45, 0.72) *** ** | **0.71 (0.56, 0.91) *** ** |
| Education | | | | |
| *Senior high and above* | 603 (23.4) | 52 (15.4) | *ref* | *ref* |
| *Junior high and below* | 1,975 (76.6) | 285 (84.6) | **1.79 (1.31, 2.43) *** ** | **1.78 (1.29, 2.46) *** ** |
| Marital status | | | | |
| *Married/ Cohabiting* | 2,292 (88.9) | 301 (89.3) | *ref* | |
| *Single/ Divorced/ Widow* | 286 (11.1) | 36 (10.7) | 0.95 (0.66, 1.38) | |
| Gravidity | | | | |
| *0-1* | 724 (28.1) | 86 (25.5) | *ref* | |
| *2* | 785 (30.4) | 121 (35.9) | **1.35 (1.00, 1.82) *** | |
| *≥3* | 1,069 (42.5) | 130 (28.6) | 1.03 (0.77, 1.37) | |
| Parity | | | | |
| *0-1* | 1,965 (76.2) | 256 (76.0) | *ref* | |
| *2* | 452 (17.5) | 69 (20.5) | 1.20 (0.90, 1.60) | |
| *≥3* | 161 (6.2) | 12 (3.6) | **0.54 (0.29, 0.98) *** | |
| **Disease characteristics** | | | | |
| Year since infection *Mean±SD* | 2.09±2.51 | 1.16±2.03 | **0.80 (0.76, 0.86) *** ** | **0.79 (0.74, 0.85) *** ** |
| Infection route | | | | |
| *Sex transmission* | 1,856 (72.0) | 169 (50.1) | *ref* | |
| *Injective drug use* | 125 (4.8) | 42 (12.5) | **5.05 (3.37, 7.56) *** ** | **5.49 (3.51, 8.61) *** ** |
| *Occupational exposure* | 570 (22.1) | 120 (35.6) | **2.66 (2.06, 3.44) *** ** | **1.87 (1.40, 2.50) *** ** |
| *Blood transmission/ MTCT/ Others* | 27 (1.0) | 6 (1.8) | **2.85 (1.14, 7.16) *** | 2.49 (0.95, 6.51) |
| Number of risky behaviors[1] *Mean±SD* | 0.51±0.69 | 0.73±0.68 | **1.60 (1.37, 1.86) *** ** | 1.21 (0.99, 1.47) |
| On ART | | | | |
| *No* | 1,105 (42.9) | 110 (32.6) | *ref* | ref |
| *Yes* | 1473 (57.1) | 227 (67.4) | **1.65 (1.29, 2.10) *** ** | **1.89 (1.47, 2.45) *** ** |

Note. [1] Risky behavior include multiple sex partners, commercial sexual behaviors, injective drug use, selling blood, blood transfusion and tattooing and ear piercing.

OR: unadjusted odds ratios; aOR: adjusted odds ratios. Statistical significance level: **p<.05***, **p<0.01****, **p<.001*****.

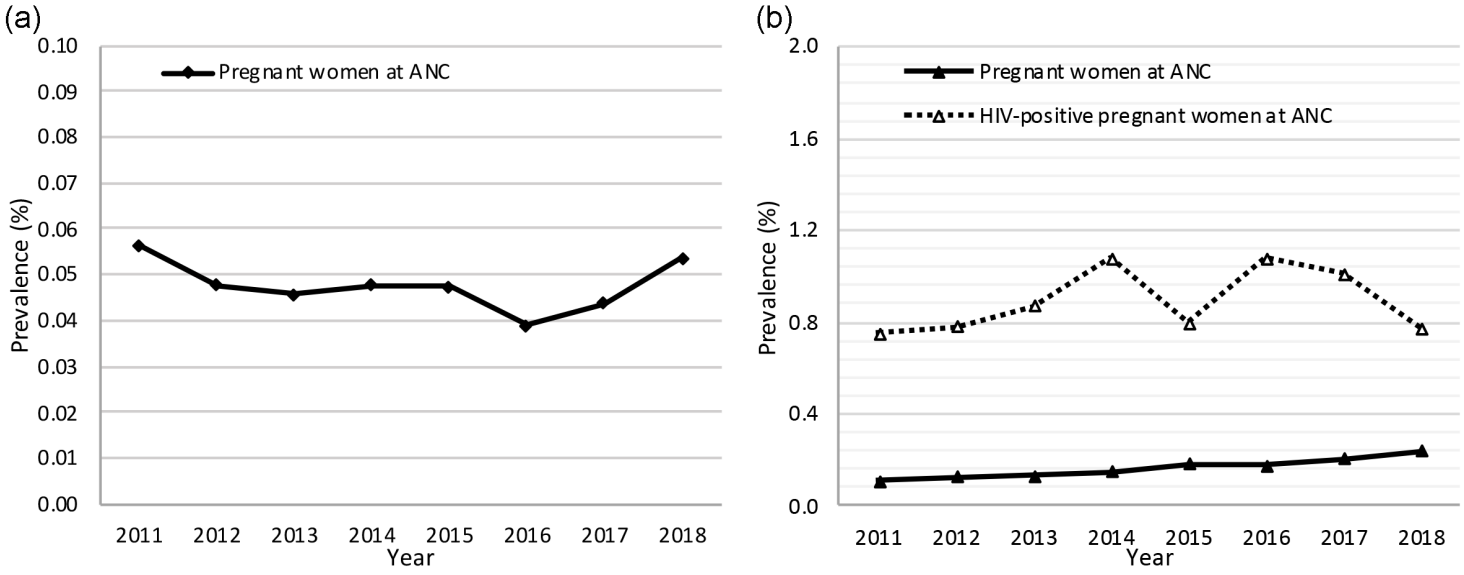
Table 2. Maternal risk factors of infant death in HIV-positive pregnant women

| Factors | All [1] (n = 1,693) n (%) | Infant death (n = 40) n (%) | OR (95%CI) | aOR (95%CI) |
|---|---|---|---|---|
| **Socio-demographic characteristics** | | | | |
| Maternal age | | | | |
| *<25* | 374 (22.1) | 6 (15.0) | *ref* | |
| *25~29* | 541 (31.9) | 11 (27.5) | 1.27 (0.47, 3.46) | |
| *30~34* | 478 (28.2) | 16 (40.0) | 2.14 (0.83, 5.52) | |
| *≥35* | 300 (17.7) | 17 (17.5) | 1.47 (0.49, 4.41) | |
| Education | | | | |
| *Senior high and above* | 412 (24.3) | 4 (10.0) | *ref* | |
| *Junior high and below* | 1281 (75.7) | 36 (90.0) | **2.94 (1.04, 8.31) *** | |
| Marital status | | | | |
| *Married/ Cohabiting* | 1549 (91.5) | 33 (82.5) | *ref* | |
| *Single/ Divorced/ Widow* | 144 (8.5) | 7 (17.5) | **2.37 (1.03, 5.46) *** | |
| Gravidity | | | | |
| *0-1* | 404 (23.8) | 6 (15.0) | *ref* | |
| *2* | 553 (32.5) | 10 (25.0) | 1.22 (0.44, 3.39) | |
| *≥3* | 752 (43.6) | 24 (60.0) | 2.19 (0.89, 5.39) | |
| Delivery location | | | | |
| *City delivery institution* | 978 (57.8) | 26 (65.0) | *ref* | |
| *Township delivery institution* | 689 (40.7) | 14 (35.0) | 0.76 (0.39, 1.46) | |
| *Home delivery/ Others* | 26 (1.5) | - | - | |
| Delivery type | | | | |
| *Spontaneous delivery* | 868 (51.3) | 23 (57.5) | *ref* | *ref* |
| *Elective caesarean section* | 424 (25.0) | 1 (2.5) | **0.09 (0.01, 0.64) *** | 0.14 (0.02, 1.10) |
| *Emergency caesarean section* | 401 (23.7) | 16 (40.0) | 1.53 (0.80, 2.92) | 1.61 (0.19, 10.67) |
| Delivery week *Mean (SD)* | 38.24 (2.13) | 35.16 (3.93) | **0.68 (0.62, 0.75) ***** | **0.68 (0.61, 0.75) ***** |
| **Disease characteristics** | | | | |
| Year since infection *Mean (SD)* | 2.07 (2.52) | 1.78 (2.08) | 0.95 (0.83, 1.09) | |
| Syphilis infection | | | | |
| *No* | 1358 (80.2) | 25 (62.5) | *ref* | *ref* |
| *Yes* | 335 (19.8) | 15 (37.5) | **2.51 (1.31, 4.81) **** | **2.81 (1.32, 5.96) **** |
| On ART | | | | |
| *No* | 280 (16.5) | 17 (42.5) | *ref* | ref |
| *Yes* | 1413 (83.5) | 23 (57.5) | **0.25 (0.13, 0.48) ***** | **0.37 (0.18, 0.75) **** |

Note. [1] All pregnant women who had their infants outcome reported.

OR: unadjusted odds ratios; aOR: adjusted odds ratios. Statistical significance level: **p<.05***, **p<0.01****, **p<.001*****.

# Figures




## Figure 1

Prevalence of (a) HIV and (b) syphilis in pregnant women at ANC. Note: ANC: Antenatal Care. Cochran-Armitage Time trend test was performed for HIV prevalence ($p=0.994$) and syphilis prevalence ($p<0.01$) in pregnant women attending ANC, and syphilis prevalence in HIV-positive pregnant women ($p=0.377$).