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Risk factors associated with preterm delivery and low delivery weight among HIV-exposed neonates in China

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Abstract

Objective—To examine the relationship between combination antiretroviral therapy (cART) and preterm delivery (PTD) or low delivery weight among pregnant Chinese women with HIV.

Methods—The present retrospective cross-sectional medical chart review enrolled pregnant women with HIV who delivered at five tertiary hospitals in China between January 1, 2009, and December 31, 2014. Generalized linear mixed modeling was used to explore PTD (<37 weeks of pregnancy) and low delivery weight (<2500 g) risk factors.

Results—Among 731 mother–neonate pairs, 93 (12.7%) mothers had PTD and 133 (18.2%) neonates had low delivery weight. Use of cART pre-conception or its initiation in the first

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AUTHOR CONTRIBUTIONS

LW contributed to the conception of the study, development of the data collection tool, data cleaning and analysis, writing the manuscript, and revising the manuscript. HZ, WC, JT, and QZ contributed to the design of the study, data collection, data cleaning and analysis, and revising the manuscript. LS contributed to the design of the study, data collection, and revising the manuscript. QF contributed to the conception and design of the study, development of the data collection tool, and revising the manuscript. APK contributed to the conception of the article and revising the manuscript. CS contributed to the development of the data collection tool and revising the manuscript. FZ contributed to the conception and design of the study, the development of the data collection tool, writing the manuscript, and revising the manuscript.

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

trimester was associated with PTD (adjusted odds ratio [aOR] 2.82; *P*=0.002) and low delivery weight (aOR 1.92; *P*=0.026). First-trimester cART initiation was associated with PTD for lopinavir/ritonavir (aOR 2.59; *P*=0.006) and nevirapine (aOR, 2.64; *P*=0.003) regimens compared with later; the same was not true for efavirenz-based cART (*P*=0.197). Low maternal body mass index (≤23.5) before delivery was independently associated with an increased likelihood of low delivery weight (aOR 1.60; *P*=0.038) but not PTD.

Conclusion—Early use of cART was associated with increased likelihood of PTD and low delivery weight. Efavirenz-based cART appeared to be favorable for women with HIV regardless of the timing of cART initiation. Good nutritional status is essential to prevent low delivery weight.

Keywords

Antiretroviral therapy; Highly active; HIV; Low birthweight; Pregnancy; Prematurity

1 | INTRODUCTION

Combination antiretroviral therapy (cART) substantially reduces mother-to- child transmission of HIV-1.[1] Researchers continue to debate whether prenatal use of cART increases the risk of adverse pregnancy outcomes such as preterm delivery (PTD) and/or low delivery weight. European studies have reported that cART is associated with an approximately two-fold increase in risk of PTD.[2–4] By contrast, studies in the USA and Caribbean countries have generally not shown this association.[5–7]

Many of the data on cART have come from high-income countries. [8,9] Neonates with PTD and/or low delivery weight have a higher risk of perinatal morbidity and mortality[10,11] that could have an additional economic and social burden on families and health systems in low-resource countries. Since 2009, studies have provided data from Africa, but the findings have not been consistent.[12–17] Few studies to date have focused on Asian populations.

Since 2010, China has recommended cART for all pregnant women infected with HIV; to our knowledge, however, there have been no investigations of associations between perinatal cART and PTD or low delivery weight in China. By expanding the evidence base to include populations that are more diverse, recommendations can be optimized regarding cART regimens for HIV-infected pregnant mothers in various low-income countries. The aim of the present study was to evaluate the effects of cART by regimen type and timing of treatment initiation on the risk of PTD and low delivery weight among pregnant Chinese women infected with HIV and their neonates.

2 | MATERIALS AND METHODS

The present retrospective cross-sectional study reviewed medical records pertaining to the perinatal period for all women with HIV who delivered a live neonate between January 1, 2009, and December 31, 2014, at any of five tertiary care hospitals in China (Beijing Ditan Hospital; Beijing You'an Hospital; Liuzhou Prefecture Mother and Child Hospital; Guangzhou Prefecture No. 8 People's Hospital; and Zhengzhou Prefecture No. 6 People's

Hospital). Only women with HIV who had singleton live deliveries were included in the study. Mother–neonate pairs with incomplete treatment information in the medical chart and those who received non-standard regimens (referring treatment regimens below) were excluded. The institutional review board of Beijing Ditan Hospital, Capital Medical University (no. IRB00004487), Beijing, China, reviewed and approved the study protocol with granted exemption from informed consent for study participants. The participating hospitals signed an agreement with Beijing Ditan Hospital regarding recognition of the approval by the review board of Beijing Ditan Hospital. Patient names were concealed during the medical chart review process to protect patient privacy.

In China, two standard cART regimens are available for pregnant women with HIV: a non-nucleoside reverse transcriptase inhibitor (NRTI)-based regimen with nevirapine (NVP) or efavirenz (EFV); or a protease inhibitor-based regimen with lopinavir boosted by ritonavir (LPV/r; Kaletra, AbbVie, Chicago, IL, USA) plus two background NRTIs. Patients were given one of these two regimens at the discretion of treating physicians on the basis of patient medical history, stage of HIV disease, and previous history of ART use, tolerance or resistance, as well as drug availability at the site.

Maternal demographic characteristics, timing of maternal HIV diagnosis and cART initiation, maternal obstetric history, prenatal course, results of clinical laboratory testing, neonate gender, delivery weight, delivery mode, delivery date, and pregnancy duration at delivery, were extracted from patient medical records.

Pregnancy dating was based on the pregnancy duration recorded in the medical charts. Maternal $CD4^+$ T-cell count at delivery was recorded and categorized into three groups (<350 cells/mm^3, 350–500 cells/mm^3, >500 cells/mm^3). Maternal body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters) before delivery was calculated and divided into three quantiles (<25%, 25%–75%, ≥75%). Anemia was defined as a hemoglobin level of less than 100 g/L before delivery. Maternal hypertension and gestational diabetes were based on diagnosis recorded in the medical charts. The main outcome measures were PTD (<37 weeks of pregnancy) and low delivery weight (<2500 g).

The study patients were divided into three groups based on the timing of cART initiation: no cART (patients who had HIV and were pregnant who received a single dose of NVP [sd-NVP] or no treatment before delivery); early cART (women who initiated cART before pregnancy or during the first trimester of pregnancy); and late cART (women initiating cART during the second or third trimester of pregnancy).

SAS version 9.3 (SAS Institute, Cary, NC, USA) was used for data analysis. Continuous variables were expressed as mean ± SD or median (interquartile range [IQR]). Categoric variables were expressed as numbers with percentages. The χ^2 test was used to compare demographic and clinical characteristics between treatment groups. Generalized linear mixed modeling, accounting for possible site level clustering, was used to conduct univariate and multivariate analysis to explore risk factors for PTD and low delivery weight. The variables considered in the multivariate logistic regression model were based on possible associations in previous studies and a threshold of $P \leq 0.10$ in the univariate analysis. A

subgroup analysis restricted to women with prenatal cART exposure was also conducted to explore the effect of maternal cART regimen type and timing of treatment initiation on PTD and low delivery weight. The results were reported as odds ratios (ORs) and adjusted ORs (aORs) with 95% Wald confidence intervals (CIs). $P \leq 0.05$ was considered to be statistically significant.

3 | RESULTS

During the 5-year study period, there were 748 singleton deliveries in the five study hospitals among 709 women who had HIV and were pregnant. Thirty-nine women had a second delivery during the study period. Seventeen women were excluded owing to incomplete maternal ART information (n=11), stillbirth (n=3), and maternal ART with three NRTIs (n=3); consequently, 731 mother–neonate pairs were included in the final analysis (Fig. 1).

Overall, 559 (76.5%) mothers had cART exposure during pregnancy, and 172 (23.5%) did not. In the latter group, 12 (7.0%) received sd-NVP and 160 (93.0%) did not receive any treatment before delivery. Among the women exposed to cART during pregnancy, the numbers of women treated with a regimen containing EFV, NVP, or LPV/r were 104 (18.6%), 190 (34.0%), and 265 (47.4%), respectively (Fig. 1).

In total, 10 neonates experienced vertical transmission of HIV; viral load was detected in nine neonates at delivery, and in one neonate during the follow-up period. The overall transmission rate was 1.4% (10 of 731 neonates).

Among the groups no significant differences were recorded in terms of maternal age, ethnicity, primiparous status, BMI before delivery, delivery mode, and gestational diabetes (Table 1). More women in the late cART group had a lower education level (illiterate or primary school only) (P=0.022). Fewer women with no cART exposure had a prepartum $CD4^+$ T-cell count of over 500 cells/mm^3 compared with women in the early cART and late cART groups (P=0.009). Women in the early treatment group had a lower proportion of anemia at delivery (compared with those in the non-cART and late cART groups (P=0.008). Prepartum maternal hypertension was uncommon and affected more women in the early cART group, compared with the non-cART and late cART groups (P=0.039). The distribution of neonate gender was similar in three treatment groups (P=0.166). The proportion of patients who received early cART increased between 2009 and 2014 (P<0.001). For women who received perinatal cART only, a greater proportion in the early cART group received NVP-based cART compared with those in the late cART group, who tended to receive LPV/r-based cART (P<0.001) (Table 1).

The median (IQR) pregnancy duration at delivery was 38 weeks (37–38 weeks). The overall incidence of PTD was 93/731 (12.7%); 14/172 (8.1%) in the no cART group, 54/263 (20.5%) in the early cART group, and 25/296 (8.4%) in the late cART group (P<0.001). The median delivery weight was 2900 g (2600–3200 g). The overall incidence of low delivery weight was 133/731 (18.2%); 21/172 (12.2%) in the no cART group, 62/263 (23.6%) in the early cART group, and 50/296 (16.9%) in the late cART group (P=0.008).

In the univariate analysis (Table 2), the early cART group had a nearly three-fold higher likelihood of PTD and a two-fold higher likelihood of low delivery weight compared with the no cART group. No such effects were observed in the late cART group compared with the no cART group. Low maternal BMI (≤23.5) was associated with increased likelihood of low delivery compared with a BMI of 23.6–27.2. Female neonates exhibited a higher likelihood of low delivery weight compared with males (Table 2).

In the multivariate analysis (Table 2), the effect of early treatment remained significant with nearly three-fold higher odds of PTD and nearly two-fold higher odds of low delivery weight compared with the no-cART group. Similar results to the univariate analysis were also observed for low delivery weight among women with low BMI before delivery and female neonates. High maternal BMI (≥27.2) before delivery was associated with lower odds of low delivery weight compared with a BMI of 23.6–27.2 (Table 2).

In the subgroup analysis (Table 3), early cART was associated with a higher likelihood of PTD compared with initiation of cART in the second or third trimester. A similar trend—higher likelihood among those in the early-cART group compared with the late-cART group–was demonstrated among women receiving cART with LPV/r and cART with, but this was not the case for patients who received the EFV-based regimen. By contrast, neither regimen nor timing of cART initiation had a significant effect on the odds of low delivery weight (Table 3).

4 | DISCUSSION

In the present study, the overall incidences of PTD and low delivery weight were 12.7% and 18.2%, respectively. These rates are higher than the national averages reported as 7.0% for PTD[18] and 2.3% for low delivery weight.[19]

The present study reported on the association of prenatal cART with PTD and/or low delivery weight in a Chinese population. As compared with no perinatal cART, perinatal exposure to cART was associated with an increase in both PTD and low delivery weight. These findings are similar to most studies from European[2–4,9] and African[13,15,17,20] countries, but conflict with those from the USA and the Caribbean.[5–9] The effect was stronger among women who initiated cART before the pregnancy or in the first trimester. Only a few studies have evaluated the risk of adverse pregnancy outcomes associated with initiation of treatment earlier in pregnancy.[21] A meta-analysis of 14 studies in high-income countries[8] concluded that women starting cART pre-conception or in the first trimester had 1.71-fold higher odds of PTD as compared with those who initiated treatment in the second or third trimester. Subsequent to that meta-analysis, four more studies and two meta-analyses[3,7,12,16,22,23] examined this issue. The conclusions of the studies were similar, reporting a higher risk of PTD and sometimes low delivery weight when cART was initiated before as compared with after conception.

In the subgroup analysis, LPV/r- or NVP-based cART starting pre-pregnancy or in the first trimester was associated with a higher likelihood of PTD compared with initiating therapy later, but not low delivery weight. This analysis took into account the joint effects of cART

regimen and the timing of treatment initiation on pregnancy outcomes. Although not consistent, similar findings have been previously reported. In a large USA-based surveillance cohort including 1869 mother–neonate pairs with HIV, premature delivery was significantly higher among mothers using protease inhibitor-based cART in the first trimester with an aOR of 1.55 (95% CI, 1.16–2.07; P=0.003),[7] which is similar to the magnitude of odds obtained in the present study. There are limited and inconsistent reports on the association of prenatal NVP use and adverse pregnancy outcomes.[12,15,17] Those studies have varied in study design, population, and reference group, making a direct comparison with the present findings difficult. Further studies are needed to clarify any such associations.

Many women with HIV of childbearing age will face early exposure to cART, owing to either becoming pregnant while being treated with cART or starting cART immediately when found to be pregnant under the “test and treat” strategy. Efforts should be made to optimize cART regimens, not only to reduce mother-to-child transmission but also to minimize adverse pregnancy outcomes. The findings of the present study suggest that EFV-based cART is preferable to other regimens for treatments that are started earlier in pregnancy.

Low maternal BMI (≤23.5) before delivery was independently associated with low delivery weight in the present study. Although different thresholds of BMI have been used to define underweight, the present findings are in line with most studies.[16,24] They are also consistent with findings among women without HIV infection.[25] A study in the Côte d’Ivoire of 326 HIV-infected pregnant women (46% receiving cART in pregnancy) found that low BMI (<25) at delivery increased the risk of low delivery weight by a factor of 2.43 (95% CI, 1.20–4.91; P=0.013).[14] A secondary data analysis of the HPTN024 trial of 2294 pregnant women with HIV who received monotherapy for prevention of mother-to-child transmission[24] showed that a BMI lower than 21.8 at delivery was associated with both PTD (OR, 1.82; 95% CI, 1.34–2.46) and low delivery weight (OR, 2.09; 95% CI, 1.41–3.08). The present study did not find an association between low BMI before delivery and PTD.

The present study had some limitations. First, it was a retrospective observational study; owing to the nature of the study design, the associations of cART with PTD and low delivery weight could be explored, but causality could not be inferred. Second, unmeasured bias could have been introduced in the earlier initiation of ART or in the choice of ART regimen, leading to confounding by indication. Finally, some factors that have been previously reported to affect PTD, such as maternal illicit drug use, preterm delivery history, and maternal HIV viral load at delivery, were not examined because the data were unavailable or were not documented uniformly in the medical charts.

In conclusion, as compared with no prenatal cART, cART in pregnancy was found to be associated with both PTD and low delivery weight; however, this effect was present only among women who initiated cART before pregnancy or in the first trimester of pregnancy. For women who recevied prenatal cART, those who received LPV/r- and NVP-based cART and started the treatment before conception or in the first trimester had a higher likelihood of PTD, but not low delivery weight. Malnutrition with low maternal BMI before delivery was

found to be an independent risk factor for low delivery weight. Even though the benefits of cART for pregnant women with HIV in decreasing mother-to-child transmission of HIV are well documented, the present findings suggest that EFV-based regimens could be favorable to avoid PTD or low delivery weight, at least in the Chinese population, and particularly if exposure occurs before pregnancy or in the first trimester of pregnancy. Improving the nutritional status of women with HIV who are pregnant could also help to reduce the risk of low delivery weight.

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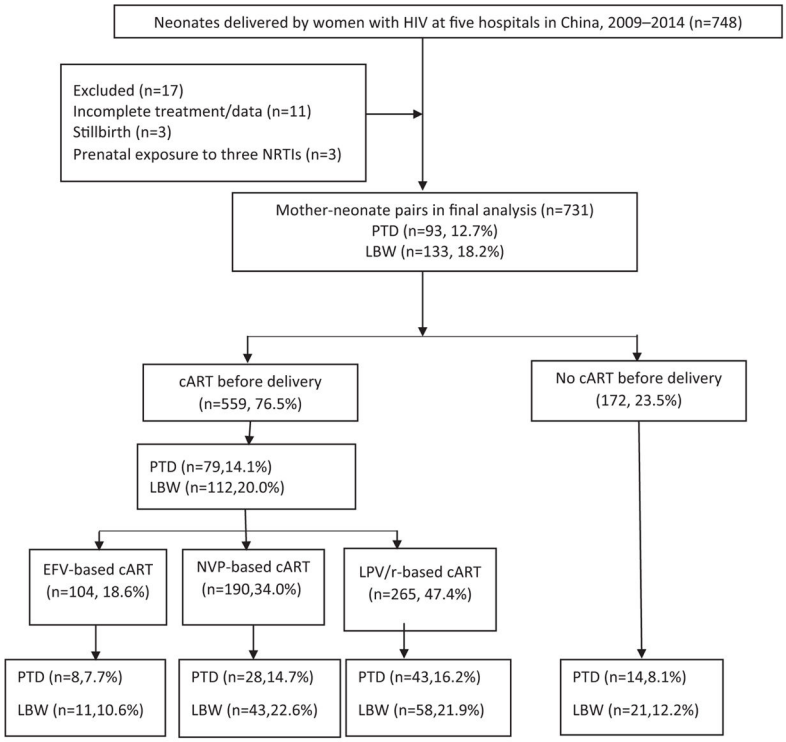

FIGURE 1.

Flow chart of study population. Abbreviations: cART, combination antiretroviral therapy; EFV, efavirenz; LBW, low birthweight; LPV/r, lopinavir/ritonavir; NPV, nevirapine; NRTIs, nucleoside reverse transcriptase inhibitors; PTD, preterm delivery.

TABLE 1

Demographic and clinical characteristics.[a]

Characteristic	No cART[b] (n=172)	Early cART[c] (n=263)	Late cART[d] (n=296)	*P* value
Maternal age at delivery				
>35 y	23 (13.4)	35 (13.3)	31 (10.5)	0.510
≤35 y	149 (86.6)	228 (86.7)	265 (89.5)	
Maternal education level				
Illiterate/primary school	74 (43.0)	103 (39.2)	157 (53.1)	0.022
Middle school	64 (37.2)	103 (39.2)	91 (30.7)	
Secondary school or higher	34 (19.8)	57 (21.7)	48 (16.2)	
Maternal employment[e]				
Unemployed	143 (88.3)	192 (76.5)	216 (76.9)	0.006
Employed	19 (11.7)	59 (23.5)	65 (23.1)	
Maternal ethnicity				
Han	122 (70.9)	188 (71.5)	224 (75.7)	0.415
Minority	50 (29.1)	75 (28.5)	72 (24.3)	
Primiparous[f]				
No	37 (21.8)	66 (25.1)	49 (16.7)	0.048
Yes	133 (78.2)	197 (74.9)	245 (83.3)	
Stage of maternal HIV diagnosis				
Before conception or in 1st trimester	76 (44.2)	263 (100)	87 (29.4)	<0.001
2nd trimester	18 (10.5)	0 (0)	155 (52.4)	
3rd trimester	78(45.3)	0 (0)	54 (18.2)	
Maternal cART regimen				
No cART	172 (100)	0 (0)	0 (0)	
EFV-based cART	0 (0)	23 (8.7)	81 (27.4)	<0.001
NVP-based cART	0 (0)	133 (50.6)	57 (19.2)	
LPV/r-based cART	0 (0)	107 (40.7)	158 (53.4)	
Prepartum maternal $CD4^+$ T-cell count, cells/mm^3				
<350	53 (30.8)	51 (19.4)	79 (26.7)	0.009
350–500	94 (54.7)	158 (60.1)	146 (49.3)	
>500	25 (14.5)	54 (20.5)	71 (24.0)	
Maternal BMI before delivery				
≤23.56	33 (19.2)	66 (25.1)	86 (29.1)	0.075
23.57–27.20	85 (49.4)	126 (47.9)	146 (49.3)	
≥27.21	54 (31.4)	71 (27.0)	64 (21.6)	
Maternal anemia (Hg <100 g/L at delivery)[g]				
Yes	58 (34.3)	57 (21.8)	92 (31.4)	0.008
No	111 (65.7)	204 (78.2)	201 (68.6)	

Characteristic	No cART[b] (n=172)	Early cART[c] (n=263)	Late cART[d] (n=296)	*P* value
Prepartum maternal hypertension				
Yes	3 (1.7)	11 (4.2)	3 (1.0)	0.039
No	169 (98.3)	252 (95.8)	293 (99.0)	
Maternal gestational diabetes				
Yes	7 (4.1)	13 (4.9)	7 (2.4)	0.260
No	165 (95.9)	250 (95.1)	289 (97.6)	
Delivery hospital				
Ditan Hospital	10 (5.8)	5 (1.9)	20 (6.8)	<0.001
You'an Hospital	13 (7.6)	23 (8.7)	25 (8.4)	
Zhengzhou No. 6 Hospital	46 (26.7)	49 (18.6)	16 (5.4)	
Guangzhou No. 8 Hospital	40 (23.3)	70 (26.6)	120 (40.5)	
Liuzhou MCH Hospital	63 (36.6)	116 (44.1)	115 (38.9)	
Delivery mode				
Vaginal delivery	30 (17.4)	36 (13.7)	36 (12.2)	0.280
Cesarean	142 (82.6)	227 (86.3)	260 (87.8)	
Neonate gender				
Male	81 (47.1)	144 (54.8)	165 (55.7)	0.166
Female	91 (52.9)	119 (45.2)	131 (44.3)	
Delivery year				
2009	32 (18.6)	10 (3.8)	46 (15.5)	<0.001
2010	15 (8.7)	26 (9.9)	59 (19.9)	
2011	19 (11.0)	31 (11.8)	49 (16.6)	
2012	39 (22.7)	59 (22.4)	43 (14.5)	
2013	38 (22.1)	53 (20.2)	47 (15.9)	
2014	29 (16.9)	84 (31.9)	52 (17.6)	

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); cART, combination antiretroviral therapy; EFV, efavirenz; Hg, hemoglobin; LPV/r, lopinavir/ritonavir; MCH, Maternal and Child Health; NPV, nevirapine.

[a] Values are given as number (percentage) unless indicated otherwise.

[b] Women who received a single dose of NPV before delivery or no treatment before delivery.

[c] Women who received cART before pregnancy or during the first trimester of pregnancy.

[d] Women who initiated cART in the second or third trimester of pregnancy.

[e] Data were available for 162 (no cART), 251 (early cART) and 281 (late cART) women.

[f] Data were available for 170 (no cART), 263 (early cART), and 294 (late cART) women.

[g] Data were available for 169 (no cART), 261 (early cART), and 293 (late cART) women.

TABLE 2

Risk factors for adverse pregnancy outcomes.

	Preterm delivery				Low delivery weight			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
Factor	**OR (95% CI)**	***P* value**	**aOR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**	**aOR (95% CI)**	***P* value**
Maternal age at delivery								
<35 y	1.0		1.0		1.0			
≥35 y	1.20 (0.64–2.27)	0.570	1.02 (0.51–2.06)	0.951	1.39 (0.81–2.40)	0.230	1.40 (0.77–2.57)	0.273
Prenatal treatment								
No cART[a]	1.0		1.0		1.0		1.0	
Early cART[b]	2.92 (1.56–5.44)	<0.001	2.82 (1.47–5.44)	0.002	2.12 (1.23–3.65)	0.007	1.92 (1.08–3.41)	0.026
Late cART[c]	1.04 (0.53–2.06)	0.908	1.05 (0.52–2.11)	0.898	1.31 (0.75–2.29)	0.338	1.33 (0.75–2.38)	0.333
Prepartum maternal CD4 + T-cell count, cells/mm^3								
>500	1.0		1.0		1.0		1.0	
350–500	1.06 (0.60–1.86)	0.841	1.10 (0.61–1.99)	0.746	0.95 (0.56–1.63)	0.865	0.98 (0.57–1.69)	0.954
<350	0.89 (0.46–1.73)	0.740	1.04 (0.52–2.09)	0.915	0.91 (0.52–1.61)	0.746	1.04 (0.57–1.90)	0.889
Maternal BMI before delivery								
23.6–27.2	1.0		1.0		1.0		1.0	
≤23.5	1.61 (0.98–2.66)	0.062	1.58 (0.93–2.68)	0.089	1.56 (1.02–2.37)	0.040	1.60 (1.03–2.49)	0.038
≥27.2	0.91 (0.52–1.61)	0.750	0.86 (0.48–1.54)	0.601	0.43 (0.25–0.76)	0.004	0.42 (0.24–0.76)	0.004
Maternal anemia at delivery (Hg <100 g/L)								
No	1.0		1.0		1.0		1.0	

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	Preterm delivery				Low delivery weight			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
Factor	**OR (95% CI)**	***P* value**	**aOR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**	**aOR (95% CI)**	***P* value**
Yes	1.31 (0.82–2.10)	0.251	1.45 (0.88–2.39)	0.147	1.12 (0.77–1.73)	0.612	1.03 (0.65–1.63)	0.887
Maternal gestational diabetes								
No	1.0		1.0		1.0		1.0	
Yes	1.59 (0.59–4.32)	0.361	1.36 (0.48–3.89)	0.566	1.79 (0.76—4.21)	0.179	1.64 (0.66–4.06)	0.287
Neonate gender								
Male	1.0		1.0		1.0		1.0	
Female	1.14 (0.74–1.76)	0.561	1.14 (0.72–1.79)	0.577	1.63 (1.11–2.38)	0.012	1.71 (1.15–2.54)	0.008
Delivery year								
2009	1.0		1.0		1.0		1.0	
2010	0.87 (0.33–2.30)	0.776	0.74 (0.27–2.04)	0.559	1.15 (0.49–2.69)	0.745	1.03 (0.42–2.50)	0.955
2011	0.77 (0.28–2.10)	0.611	0.61 (0.22–1.71)	0.342	1.90 (0.86–4.22)	0.114	1.62 (0.70–3.73)	0.258
2012	1.37 (0.59–3.18)	0.467	1.01 (0.42–2.44)	0.980	1.73 (0.81–3.73)	0.159	1.46 (0.66–3.25)	0.351
2013	1.23 (0.52–2.91)	0.632	0.89 (0.36–2.19)	0.801	1.64 (0.74–3.58)	0.217	1.26 (0.56–2.85)	0.574
2014	2.03 (0.92–4.49)	0.080	1.27 (0.54–2.98)	0.583	2.50 (1.19–5.25)	0.015	1.77 (0.81–3.89)	0.154

Abbreviations: aOR, adjusted odds ratio; BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); cART, combination antiretroviral therapy; CI, confidence interval; Hg, hemoglobin; OR, odds ratio.

[a]Women who received a single dose of NPV before delivery or no treatment before delivery.

[b]Women who received cART before pregnancy or during the first trimester of pregnancy.

[c]Women who initiated cART in the second or third trimester of pregnancy.

TABLE 3

Effect of regimen and timing of cART initiation on preterm delivery and low delivery weight.

	Univariate analysis		Multivariate analysis	
Outcome	**OR (95% CI)**	***P* value**	**Adjusted OR (95% CI)[a]**	***P* value**
Preterm delivery (<37 wk)				
cART at conception/1st trimester vs 2nd/3rd trimester	2.80 (1.69–4.66)	<0.001	2.75 (1.55–4.90)	<0.001
cART with LPV/r vs cART with EFV	2.40 (1.07–5.37)	0.033	1.78 (0.68–4.60)	0.237
cART with NVP vs cART with EFV	2.07 (0.91–4.78)	0.079	1.24 (0.50–3.07)	0.644
cART with LPV/r at conception/1st trimester vs 2nd/3rd trimester	3.13 (1.70–5.79)	<0.001	2.59 (1.32–5.08)	0.006
cART with NVP at conception/1st trimester vs 2nd/3rd trimester	2.63 (1.46–4.77)	0.001	2.64 (1.39–5.01)	0.003
cART with EFV at conception/1st trimester vs 2nd/3rd trimester	2.28 (0.72–7.25)	0.162	2.21 (0.66–7.35)	0.197
Low delivery weight (<2500 g)				
cART at conception/1st trimester vs 2nd/3rd trimester	1.55 (1.02–2.36)	0.040	1.19 (0.73–1.95)	0.479
cART with LPV/r vs cART with EFV	2.37 (1.19–4.73)	0.015	1.39 (0.62–3.14)	0.426
cART with NVP vs cART with EFV	2.47 (1.21–5.04)	0.013	1.84 (0.84–4.01)	0.126
cART with LPV/r at conception/1st trimester vs none in 1st trimester[b]	1.53 (0.88–2.64)	0.130	1.12 (0.62–2.04)	0.711
cART with NVP at conception/1st trimester vs none in 1st trimester[b]	1.73 (1.05–2.85)	0.031	1.70 (0.99–2.92)	0.055
cART with EFV at conception/1st trimester vs none in 1st trimester[b]	0.76 (0.22–2.68)	0.672	0.76 (0.20–2.80)	0.674

Abbreviations: cART, combination antiretroviral therapy; cART, combination antiretroviral therapy; CI, confidence interval; EFV, efavirenz; LPV/r, lopinavir/ritonavir; NPV, nevirapine; OR, odds ratio.

[a]Adjusted for maternal age, maternal CD4 + T-cell count at delivery, maternal body mass index before delivery, maternal morbidities (anemia and diabetes) during pregnancy, neonate sex, and delivery year.

[b]Women who initiated cART in the second or third trimester of pregnancy.