Antiretroviral Regimen and Pregnancy Outcomes of Women Living with HIV in a US Cohort

Charles Kopp

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Committee:

Alison Roxby MD MSc

Jane Hitti MD MPH

Carey Farquhar MD MPH

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Abstract

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Charles Kopp

Chair of the Supervisory Committee:

Alison Roxby MD MSc

Department of Medicine

Women who are pregnant and living with HIV have traditionally been excluded from clinical trials regarding new pharmacotherapy. Immediate initiation of antiretroviral therapy (ART) is recommended for women who are pregnant and living with HIV. Given there is limited data regarding the safety of ART in pregnancy, high-quality research of maternal and fetal outcomes in women who are pregnant and on ART is of paramount importance. Integrase inhibitors (INSTIs) are of particular interest as newer data suggests that these can lead to more rapid viral load reduction. This was a retrospective study of women who are pregnant and living with HIV who received prenatal care at the University of Washington. Groups were determined by the ART class: INSTI, protease inhibitors (PI), and non-nucleoside reverse transcriptase inhibitors (NNRTI). Chi-square and t-tests were used as appropriate for the analysis of baseline characteristics and generalized estimating equations to adjust for the rate of HIV viral suppression between groups. There were a total of 235 mother-infant pairs whose pregnancies progressed beyond 20 weeks. The study demonstrated that women on INSTI regimens were more likely to have a shorter time to viral load suppression than women on NNRTI regimens. Additionally, six congenital anomalies were identified in this cohort, none of which were neural tube defects. There was no perinatal transmission of HIV to any of the infants. This small cohort

of women provides high-quality data regarding the safety and efficacy of INSTI use in resource-rich settings.

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Introduction

Women who are pregnant and living with HIV continue to face limited data on the suitability of different antiretroviral therapy (ART) regimens[1–3]. Current recommendations for persons living with HIV, especially women who are pregnant, are to begin ART as soon as possible regardless of CD4 count or viral load, with regimens incorporating integrase strand inhibitors (INSTIs) as optimal first-line regimens[4–6]. Dolutegravir is an INSTI with a favorable profile, including once-daily dosing, high barrier to drug resistance, low transmitted drug resistance, and high tolerability,[7–11] and is projected to be used by up to 15 million people by the year 2025[12]. Efforts to improve access to INSTIs have been undertaken, including incorporating generic INSTI into first-line regimens worldwide. INSTIs have demonstrated rapid viral load reduction in individuals who are pregnant and have reduced perinatal transmission of HIV, leading to improved outcomes for both mother and baby[13–15].

Despite enthusiasm for INSTI regimens, data remain limited describing safety and outcomes in women who are pregnant using different ART regimens. This paucity of data is especially true in upper- and middle-income countries, where there are fewer women who are pregnant and living with HIV and more diversity of available ART options. Recent studies have shown that dolutegravir and elvitegravir/cobicistat promote a rapid reduction in maternal HIV RNA levels, cross the placental barrier, and are present in cord blood and fetal circulation at the time of delivery, but data around effects in infants remains limited[16–20]. A systematic review of the literature on the risk of low birth weight and preterm birth among women who are pregnant and using ART found only 13 published studies to include[21]. The lack of data can lead to outsized consequences, with a worldwide halt on dolutegravir initiation in pregnancy after preliminary data from Botswana raised concern for increased neural tube defects (NTDs) in infants; however, further analysis revealed a lower NTD prevalence, which was only slightly above the national NTD rate[8,22]. A more extensive country-wide review of ART use in pregnancy included 1427 pregnancies in Brazil and found no significant increase in NTD with dolutegravir use compared to efavirenz use. However, the prevalence of NTD was slightly higher among infants exposed to dolutegravir than among infants born to HIV-uninfected women in Brazil[9]. A study of 808 women in France demonstrated that pregnancies with raltegravir use during conception were more likely to be affected by congenital anomalies than pregnancies with raltegravir initiation later in pregnancy[23].

While it is clear that pregnant women benefit from ART, it remains challenging to counsel women regarding the comparative risks of different ART regimens. More data around the safety and outcomes of all ART, especially INSTIs, is needed to ensure the medical community provides evidence-based treatment for pregnant women living with HIV. We conducted a cohort study to examine the maternal and infant outcomes with different ART regimens.

Methods

Study design and population

We conducted a retrospective cohort study of pregnancies among women living with HIV and presenting for care at the University of Washington Medical Center (UWMC) in Seattle, WA from 2007-2018. A pregnancy was included in the cohort if the woman received prenatal care at UWMC and delivered at an affiliated hospital. Cohort inclusion began in 2007 to coincide with approval of the first INSTI, raltegravir. Women could contribute more than one pregnancy to the cohort. Mother-infant pairs were excluded if delivered at an outside facility or lost to follow-up with an unknown pregnancy outcome.

Data Collection

Clinical data were abstracted from patient charts and included maternal demographics (age, race, ethnicity), comorbidities (gestation hypertension, gestational diabetes, and co-infections including syphilis and hepatitis B and C.), ART use, laboratory data, birth outcomes, and infant information, including the presence of any congenital malformations. Study data were collected and managed using a secure REDCap electronic database.

ART regimens were categorized into three groups based on the primary agent: INSTI, protease inhibitor (PI), or non-nucleoside reverse transcriptase inhibitor (NNRTI). Two tests determined HIV RNA levels: the Aptima HIV-1 Quant assay (Aptima), which has a lower limit of detection (LLD) of 30 copies/µl; and the Abbott RealTime HIV-1 viral load assay (Abbott), which has a LLD of 40 copies/µl.

Statistical methods

The primary analysis of interest was comparing maternal and pregnancy outcomes among those treated with INSTI regimens to those treated with non-INSTI regimens (specifically, PI or NNRTI regimens). Regimen changes late in pregnancy were not included in the analysis. Outcomes of interest included time to HIV viral suppression, change in CD4 count, and fetal outcomes including preterm, twin births, NICU admission, congenital anomalies, and HIV test outcome. Early adverse events such as spontaneous abortion were not included if there was no exposure to ART at the time of the outcome. Baseline characteristics were compared between ART groups using t-test and chi-square tests as appropriate. Birthweight and gestational age at delivery were analyzed using linear regression and adjusted for advanced maternal age. We utilized generalized estimating equations (GEE) adjusting for baseline HIV RNA levels to compare the rate of HIV viral suppression between the groups and account for women contributing multiple pregnancies. Plasma HIV RNA levels were log-transformed. Statistical analysis was conducted using Stata SE 15.1 (StataCorp, College Station, TX).

Ethics

The study was approved by the University of Washington Institutional Review Board, which gave permission to use medical records from the hospital information system. Individual informed consent was not obtained.

Results

Case selection

A total of 255 pregnancies were identified for primary inclusion in the dataset. Four pregnancies were excluded, two due to having abortions prior to initiating ART, one who was misdiagnosed with HIV, and finally one who declined ART. Among the 251 pregnancies included in the study, there were 185 unique women, with 43 mothers who contributed two pregnancies (18%) and 10 who contributed three or more pregnancies (4%). Among the 251 pregnancies, 91 women (36%) were using an INSTI-based regimen, 116 (48%) were using a PI-based regimen, and 44 (18%) were using an NNRTI-based regimen. There were 234 pregnancies that progressed beyond 20 weeks; 131 of these were unique mother-infant pairs, and the rest were from mothers that contributed multiple pregnancies.

Demographic and health data of mothers in the cohort

Baseline characteristics are outlined in Table 1. The median age of women using INSTI & PI was 32 years, compared to 31 years for NNRTI. Co-infections were rare in the cohort (1.6% with hepatitis B, 7.2% with hepatitis C, and 1.2% with syphilis). Of the 251 pregnancies, 57 occurred in mothers receiving a new diagnosis of HIV at their first prenatal visit (23%). There were a total of 77 mothers naïve to ART, with no significant differences in the proportion of naïve mother-infant pairs between treatment groups (INSTI 32%; PI 28%; NNRTI 34%, p=0.28). A complete listing of ART regimens can be found in Supplemental Table 1.

Pregnancy outcomes

Of pregnancies seen in the clinic, 17 women had pregnancies that ended before 20 weeks. These women were included in the demographic and baseline laboratory analyses and pregnancy outcomes but were excluded from the rest of the analyses. Of the 16 spontaneous early pregnancy losses, 5 were using INSTI, 8 using PI, and 3 using NNRTI. One spontaneous abortion was of a fetus with Trisomy 17 anomaly in a woman using NNRTI-based ART (lamivudine/zidovudine & nevirapine) (Table 4). In addition, one woman on an NNRTI regimen (lopinavir/ritonavir & lamivudine/zidovudine) chose to terminate the pregnancy because of serious congenital anomalies identified in the fetus. Finally there was one women on an INSTI regimen (elvitegravir/cobicistat & tenofovir DF/emtricitabine) with an intrauterine fetal demise at 37 weeks with no anomalies discovered on autopsy (Table 5).

Of the 234 pregnancies that continued past 20 weeks of gestation, 131 were a mother's only pregnancy, 39 were from mothers with two pregnancies, 7 were mothers with three pregnancies, and one mother contributed four pregnancies. Comorbidities included 15 mother-infant pairs affected by hypertension (6.4%) and 14 affected by gestational diabetes (6.0%). There were 110 vaginal deliveries and 124 deliveries via cesarean section. Preeclampsia occurred in four pregnancies, with one developing eclampsia and requiring emergent delivery. The mean time between the first prenatal visit and delivery was 163 days (Standard Deviation (SD):64) for women using INSTI, 186 days (SD:62) for those using PI, and 154 days (SD:60) for NNRTI. There were no maternal deaths.

Among 77 ART-naïve women, the mean peak HIV RNA level was significantly different between the ART groups, at 3.29 log copies/mL for INSTI, 2.68 log copies/mL for PI, and 2.09 log copies/mL for NNRTI (p=0.04). When examining change in HIV RNA level over time in ART-naïve women, there was a significantly greater drop in HIV RNA level in the INSTI group compared to the NNRTI group (-0.009 vs -0.002 RNA $\log_{10}$ copies/ml/day, p<0.001) (Figure 1). This difference remained significant after adjusting for baseline HIV viral load in the INSTI compared to NNRTI groups (p<0.01), but not in the INSTI vs PI (p = 0.28). There was no statistically significant difference among the entire cohort in mean CD4 nadir in women naïve to ART between the groups (423 cells/μL for INSTI, 371 cells/μL for PI, and 368 cells/μL for NNRTI, p=0.28).

Neonatal outcomes

There were 7 infants with a congenital anomaly identified; 3 with exposure to InSTI, 1 with exposure to a PI, and 3 with exposure to NNRTI (Table 5). No neural tube defects were noted. There were five pregnancies complicated by oligohydramnios. Due to small sample sizes, statistical comparisons were not performed.

Preterm birth was noted for 29 infants, with no significant differences between cohorts: InSTI with 11 (13%) vs PI with 10 (8%) vs NNRTI with 8 (20%) p = 0.25). Infants delivered to mothers on PI regimens had a lower prevalence of neonatal intensive care unit admission at 6%, compared to infants whose mothers used INSTI and PI regimens at 16% and 20% respectively (p=0.02). This association was not significant after adjusting for maternal age greater or equal to 35 years (p=0.21).

Women using NNRTI regimens had a lower mean gestational age of 37.6 weeks compared to 38.4 weeks for women on INSTI and PI regimens. Infants of mothers using NNRTI regimens had lower mean birth weights compared to other regimens: 2814 grams for NNRTI vs 3134 grams for INSTI vs 3102 grams for PI. These differences were not statistically significant after adjusting for maternal age. There were no documented cases of perinatal transmission of HIV.

Discussion

This cohort aggregates 11 years of data to compare maternal and infant outcomes across ART regimens used in pregnancy. Overall, mothers in the cohort had few complications with ART, and results were favorable for maternal viral suppression and infant outcomes. In this relatively small cohort, we observed a significant difference in the slope of HIV viral suppression in mothers naïve to ART, with InSTI resulting in more rapid suppression compared to NNRTI. This supports prior observations that INSTI-based regimens cause rapid viral suppression and are therefore an ideal choice when rapid suppression is desired, such as initiating ART in pregnancy[24].

Data from mother-baby cohorts detailing the full spectrum of outcomes for all trimesters of pregnancy and postpartum remain key to assessing outcomes of maternal ART exposure. The prevalence of congenital anomalies in this cohort was 3.00% (7/234), which is comparable to the baseline US prevalence of 3.30%[25]. This work adds important data about congenital anomalies noted with exposure to ART and INSTIs. While our sample was small, the anomalies that were noted are important as there is little published about newer INSTIs. While there are now extensive data from sub-Saharan African regarding dolutegravir use in pregnancy, data on the possible effects of elvitegravir and raltegravir remain sparse, despite the common use of these regimens. One notable study from the UK and Ireland showed similar prevalence of congenital anomalies but only reported data from 33 pregnancies exposed to elvitegravir[26]. Notably, it adds to the evidence of the safety and efficacy of INSTI use in upper-income countries where folic acid supplementation of food is implemented.

The strengths of this data include that it was collected in a healthcare setting with a high level of care for obstetric patients, including first-trimester confirmation of pregnancy, regular antenatal appointments, and frequent ultrasounds. This provides a robust set of data on the included pregnancies. This approach allowed for the inclusion of first trimester anomalies resulting in miscarriage or pregnancy termination. Other datasets that look only at live births or late pregnancy outcomes are unable to include these types of observations and are biased by not observing early pregnancy losses. Additionally, all data were prospectively entered into the electronic medical record at the time of clinical care, thus reducing the risk of recall bias that can be seen with other retrospective studies. Another strength of the study is that it reports both maternal and infant outcomes, recognizing that the health of the mother is of paramount

importance to any infant outcomes; studies that report only infant outcomes lack this important accompanying data.

The limitations to this study include that HIV management has changed over the 11 years the study was conducted, which included the possibility of women not on ART for years before 2007. Additionally, women were tested for viral loads at varying intervals. This impairs the study's ability to definitively say how quickly women achieved viral load suppression, given it may be weeks or months between tests. In addition, our small cohort size limits our ability to examine relationships between ART and rare congenital anomalies. For many of the observations, data were aggregated into three categories (INSTI, PI, & NNRTI), which could have obscured effects from specific drugs. These issues are common in retrospective studies conducted on women who are pregnant and living with HIV[20]. Some mothers contributed more than one pregnancy, which could bias outcomes based on maternal characteristics. The study was conducted in an urban area of the northwestern United States and only included women who received care and delivered at an academic institution, which limits the generalizability of these results to other populations of pregnant women living with HIV.

Initiating ART in women who are or wish to become pregnant remains critical to preventing perinatal HIV transmission, and any risk from ART therapy is unlikely to outweigh the risk of infant acquisition of HIV[9,20]. In higher-income countries, where HIV is becoming less common among women of childbearing potential, further studies should focus on stratifying risk by specific drug regimens, conducting age-matched cohort studies, and using multicenter data to improve statistical power to detect rare effects on infants. Studies specifically examining ART use in pregnancy are needed to provide adequate counseling, rather than extrapolating outcomes from original ART studies that excluded pregnant women. To best counsel obstetric patients on the risks and benefits of HIV ART in pregnancy requires pregnancy-specific data.

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Table 1: Baseline characteristics of women who are pregnant and living with HIV on ART and receiving prenatal care at UWMC from 2007-2018

		Overall cohort N = 251 Median (IQR) or N(%)	INSTI N=91 Median (IQR) or N(%)	PI N=116 Median (IQR) or N(%)	NNRTI N=44 Median (IQR) or N(%)
Race	Asian	13 (5)	6 (7)	7 (6)	0
	African American	132 (53)	56 (62)	47 (41)	29 (66)
	Native American	6 (2)	1 (1)	5 (4)	0
	White	44 (18)	18 (20)	20 (17)	6 (14)
	Other	25 (10)	3 (3)	17 (15)	5 (11)
	Multiracial	31 (12)	7 (8)	20 (17)	4 (9)
Ethnicity	Hispanic	21 (8)	6 (7)	10 (9)	5 (11)
Median age (years)		32 (28-36)	32 (28-36)	32 (28-36)	31 (29-36)
Maternal coinfections	Hepatitis B	4 (2)	1 (1)	3 (3)	0
	Hepatitis C	18 (7)	8 (9)	7 (6)	3 (7)
	Syphilis	3 (1)	0	1 (1)	2 (5)

Abbreviations: ART (Anti-retroviral therapy) INSTI (Integrase inhibitor), PI (Protease inhibitor), NNRTI (Non-nucleoside reverse transcriptase inhibitor), SD (Standard deviation), IQR (Inter-quartile range)
Missing values: Hepatitis B (20), Hepatitis C (28), Syphilis (89)
Women can appear in this table more than once to account for additional pregnancies during the study period.

Table 2: Maternal laboratory values and pregnancy outcomes of women living with HIV using antiretroviral therapy and receiving prenatal care at UWMC from 2007-2018

	Overall cohort N = 251 Mean (SD)	INSTI N=91 Mean (SD)	PI N=116 Mean (SD)	NNRTI N=44 Mean (SD)
Creatinine (mg/dL)	0.566 (±0.1)	0.541 (±0.1)*	0.588 (±0.1)	0.578 (±0.2)
ALT (IU/L)	22.1 (±30.5)	20.2 (±18.5)	22.2 (±19.9)	25.6 (±58.7)
Hemoglobin (g/dL)	11.9 (±1.2)	11.8 (±1.3)	12.0 (±1.1)	12.0 (±1.0)
Baseline CD4 for ART Naïve (cells/mm^3)	390 (±197)	423 (±213)	371 (±168)	368 (±230)
Baseline HIV RNA level (log_{10} copies/ml)	2.89 (±1.3)	3.29 (±1.1)**	2.68 (±1.5)	2.09 (±1.1)
Pregnancy outcomes of mother-baby pairs	Overall cohort N = 251 Mean (SD) or N (%)	INSTI N=91 Mean (SD) or N(%)	PI N=116 Mean (SD) or N(%)	NNRTI N=44 Mean (SD) or N(%)
Length of care (days)^	172 (±63)	163 (±64)	186 (±62)	154 (±60)
New diagnosis of HIV	57 (23)	19 (21)	25 (22)	13 (30)
Prior pregnancy resulting in delivery	159 (63)	55 (60)	76 (66)	28 (64)
Spontaneous abortion	16 (6)	5 (5)	8 (7)	3 (7)

Abbreviations: ART (Anti-retroviral therapy) INSTI (Integrase inhibitor), PI (Protease inhibitor), NNRTI (Non-nucleoside reverse transcriptase inhibitor), SD (Standard deviation)

Missing values: Length of care (2), New diagnosis (11), ART Naïve (13), Prior pregnancy (11)

^ N = 234 as this did not include mothers with spontaneous or elective abortions

*INSTI significantly lower than PI $p<0.05$

**INSTI significantly higher than NNRTI and PI $p<0.01$

Table 3: Neonatal outcomes for mother-baby pairs affected by HIV on ART and receiving prenatal care at UWMC from 2007-2018 with pregnancy duration longer than 20 weeks

	Overall cohort N = 234 Mean (SD) or N (%)	INSTI (N=85) Mean (SD) or N (%)	PI (N=108) Mean (SD) or N (%)	NNRTI (N=41) Mean (SD) or N (%)
Mean gestational age (weeks)	38.2 (±2.3)	38.4 (±2.8)	38.4 (±1.6)	37.6 (±3.0)
Mean birthweight (grams)	3062 (±689)	3134 (±802)	3102 (±549)	2814 (±728)*
Preterm	29 (12)	11 (13)	10 (9)	8 (20)
Twin births	4 (2)	2 (2)	1 (1)	1 (2)
NICU admission	27 (12)	13 (15)	6 (6)	8 (20)
Congenital anomalies	6 (3)	3 (4)	1 (1)	3 (7)
Infant HIV Test outcome	0	0	0	0

Abbreviations: NICU (Neonatal Intensive Care Unit), INSTI, (Integrase inhibitor), PI (Protease inhibitor), NNRTI (Non-nucleoside reverse transcriptase inhibitor), SD (Standard deviation)

Missing values: Gestational age (5), Birthweight (5), Preterm (5), Twin births (5), NICU admission (5), Congenital anomalies (7)
*NNRTI significantly lower than INSTI and PI $p<0.05$ & $p<0.05$

Table 4: Antiretroviral therapy regimens of women receiving prenatal care from 2007-2018 and with spontaneous abortion, termination, and intrauterine fetal demise

Spontaneous abortion				
	Mother ID	ART		Abnormalities
	1	Raltegravir	Tenofovir DF/emtricitabine	Unknown
	2	Raltegravir	Tenofovir DF/emtricitabine	Unknown
	3	Elvitegravir/cobicistat	Tenofovir DF/emtricitabine	Unknown
	4	Dolutegravir	Tenofovir DF/emtricitabine	Unknown
	5	Dolutegravir	Tenofovir DF/emtricitabine	Unknown
	6	Lopinavir/ritonavir	Tenofovir DF/emtricitabine	Unknown
	7	Atazanavir/ritonavir	Tenofovir DF/emtricitabine	Unknown
	8	Atazanavir/ritonavir	Tenofovir DF/emtricitabine	Unknown
	9	Atazanavir/ritonavir	Tenofovir DF/emtricitabine	Unknown
	10	Lopinavir/ritonavir	Tenofovir DF/emtricitabine	Unknown
	11	Lopinavir/ritonavir	Tenofovir DF/emtricitabine	Unknown
	12	Lopinavir/ritonavir	Abacavir/lamivudine	Unknown
	13	Nelfinavir	Lamivudine/stavudine	Unknown
	14	Nevirapine	Tenofovir DF/emtricitabine	Unknown
	15	Nevirapine	Lamivudine/zidovudine	Unknown
	16	Nevirapine	Lamivudine/zidovudine	Trisomy 17
Elective termination				
	Mother ID	ART		Abnormalities
	17	Lopinavir/ritonavir	Lamivudine/zidovudine	Cystic Hygroma, aneuploidy
Intrauterine Fetal Demise				
	Mother ID	ART	Other ART	Abnormalities
	18	Elvitegravir/cobicistat	Tenofovir DF/emtricitabine	None seen at autopsy

Abbreviations: UWMC (University of Washington Medical Center), ART (antiretroviral therapy)

Table 5: Congenital anomalies of fetuses and infants exposed to HIV and receiving antenatal care at UWMC from 2007-2018 (N = 7)

	Congenital Anomaly	Gestational Age (Weeks)	Antiretroviral therapy regimen	Other ART
Integrase Inhibitor				
Event 1	Hypothyroidism, Chordee	27.6	Elvitegravir /cobicistat	Tenofovir DF/emtricitabine
Event 2	Hypospadias	26.6	Raltegravir	Tenofovir DF/emtricitabine
Event 3	Cystic hygroma, aneuploidy	TOP	Raltegravir	Tenofovir DF/emtricitabine
Protease Inhibitor				
Event 4	Fetal heterotaxy	31.4	Lopinavir /ritonavir	Lamivudine /zidovudine
Non-nucleoside reverse transcriptase inhibitor				
Event 5	Cranial nerve III palsy	34.1	Efavirenz	Tenofovir DF/emtricitabine
Event 6	Cryptorchidism	36.1	Zidovudine	Tenofovir DF/emtricitabine
Event 7	Trisomy 17	SAB	Nevirapine	Tenofovir DF/emtricitabine

None of the mothers had gestational diabetes or gestational hypertension

Abbreviations: UWMC (University of Washington Medical Center), ART (Antiretroviral therapy), CN III (Cranial nerve III), TOP (Termination of pregnancy), SAB (Spontaneous abortion)

Supplemental Table 1: Regimens for women who received prenatal care at UWMC from 2007-2018

Integrase Inhibitor based regimens (N=91)			
INSTI N (%)	Other ART		
Raltegravir N=55			
51 (56)	Tenofovir DF/emtricitabine		
1 (1)	Darunavir/ritonavir	Etravirine	
1 (1)	Tenofovir DF/emtricitabine	Atazanavir	Ritonavir
1 (1)	Lamivudine	Zidovudine	
1 (1)	Tenofovir DF/emtricitabine	Zidovudine	
Elvitegravir/cobicistat N=25			
25 (27)	Tenofovir DF/emtricitabine		
Dolutegravir N=11			
7 (8)	Tenofovir DF/emtricitabine		
2 (2)	Tenofovir DF/emtricitabine	Rilpivirine	
1 (1)	Lamivudine	Abacavir	
1 (1)	Lamivudine	Rilpivirine	Abacavir
Protease Inhibitor based regimens (N=116)			
PI N (%)	Other ART		
Atazanavir N=83			
66 (57)	Ritonavir	Tenofovir DF/emtricitabine	
4 (3)	Ritonavir	Abacavir	Lamivudine
3 (3)	Ritonavir	Abacavir	Tenofovir
3 (3)	Ritonavir	Lamivudine	Zidovudine
2 (2)	Ritonavir	Tenofovir DF/emtricitabine	Zidovudine
2 (2)	Ritonavir	Efavirenz	Emtricitabine
1 (1)	Ritonavir	Lamivudine	Tenofovir
1 (1)	Ritonavir	Tenofovir DF/emtricitabine	Raltegravir
1 (1)	Tenofovir DF/emtricitabine		
Ritonavir/Lopinavir N=22			
12 (10)	Tenofovir DF/emtricitabine		
9 (8)	Lamivudine	Zidovudine	
1 (1)	Abacavir	Lamivudine	
Ritonavir/Darunavir N=8			
7 (6)	Tenofovir DF/emtricitabine		
1 (1)	Raltegravir	Etravine	
Nelfinavir N=3			
1 (1)	Tenofovir DF/emtricitabine		
1 (1)	Lamivudine	Zidovudine	
1 (1)	Lamivudine	Stavudine	
Non-nucleoside reverse transcriptase inhibitor based regimens (N=44)			
NNRTI N (%)	Other ART		
Zidovudine N=21			
5 (12)	Monotherapy		
10 (24)	Tenofovir DF/emtricitabine		
5 (12)	Nevirapine	Lamivudine	
1 (2)	Tenofovir DF/emtricitabine	Lamivudine	
Efavirenz N=9			
1 (2)	Monotherapy		
7 (17)	Tenofovir DF/emtricitabine		
1 (2)	Tenofovir DF/emtricitabine	Lamivudine	
Nevirapine N=3			
3 (7)	Tenofovir DF/emtricitabine		
Rilpivirine N=11			
11 (27)	Tenofovir DF/emtricitabine		

Abrieviations: UWMC (University of Washington Medical Center), DF (disoproxil fumarate), INSTI (Integrase inhibitor), PI (protease inhibitor), NNRTI (non-nucleoside reverse transcriptase inhibitor)

Figure 1: Perinatal HIV RNA levels over time, for women not using antiretroviral therapy prior to pregnancy.

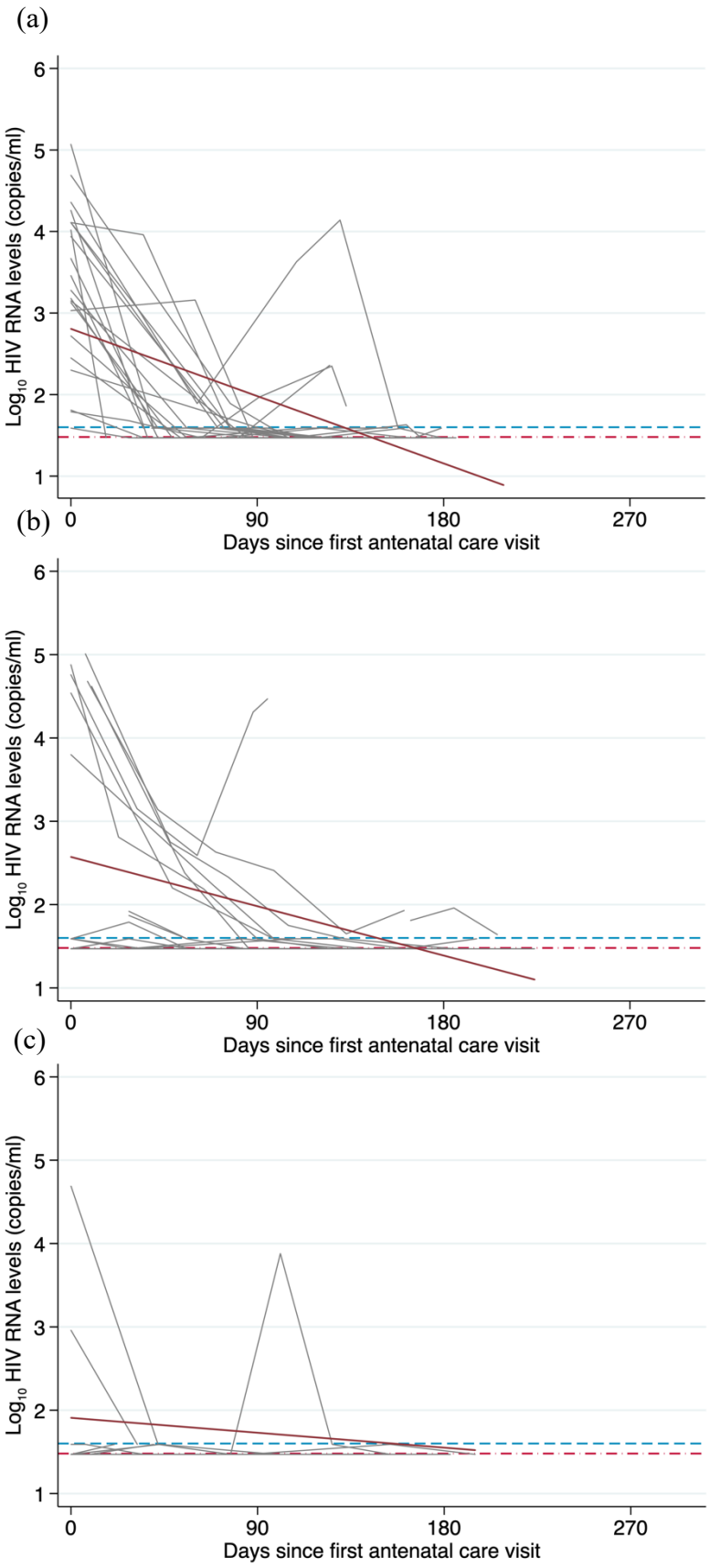

Figure 1: Maternal HIV RNA levels were collected at first prenatal visit and then subsequently throughout pregnancy at follow-up appointments with their primary care provider or obstetrician. These values were log-transformed and RNA values for each pregnancy were plotted on a connected scatterplot to observe changes in HIV RNA levels during pregnancy. Red line indicates the fitted slope. The dash-dot red line and the blue dashed line across the bottom of the graph indicate the lower limits of detection for the HIV viral load assays at 1.48 and 1.60 copies per milliliter respectively. Panel A, N = 29 women using integrase inhibitors; Panel B, N = 33 women using protease inhibitors; Panel C, N = 15 women using NNRTI.