Published in final edited form as:

Int J Gynaecol Obstet. 2013 July ; 122(1): 37–43. doi:10.1016/j.ijgo.2012.12.021.

Trends in the management and outcome of HIV-1-infected women and their infants in the NISDI Perinatal and LILAC cohorts, 2002–2009

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Abstract

Objective—To describe temporal management and outcome trends among HIV-1-infected pregnant women and their infants enrolled in the NISDI Perinatal and LILAC cohorts.

[1]Manuscript presented in part at: XVIII International AIDS Conference; July 18–23, 2010; Vienna, Austria (abstract MOPE0244); and 15th International Workshop on HIV Observational Databases; March 24–26, 2011; Prague, Czech Republic (abstract 15_174). Members of the NISDI Perinatal/LILAC Study Group are listed in Supplementary Material S1.

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Conflict of interest

The authors have no conflicts of interest.

Methods—A prospective cohort of 1548 HIV-1-infected pregnant women and their 1481 singleton live-born infants was analyzed. Participants were enrolled at 24 Latin American and Caribbean sites and followed-up for at least 6 months postpartum. Variables were compared by 2-year enrollment periods from September 27, 2002, to June 30, 2009, using logistic and linear regression modeling.

Results—Antiretroviral (ARV) use during pregnancy remained high (99.0%). ARVs became increasingly used for treatment (P<0.001). Regimens containing 2 nucleoside reverse transcriptase inhibitors plus a protease inhibitor became more common in later years (P<0.001). The proportion of women with viral loads below 1000 copies/mL at hospital discharge after delivery (HD) increased over time (P=0.0031). Median CD4 lymphocyte counts also rose at HD, from 441 cell/mm^3 to 515 cells/mm^3 (P<0.05). Elective cesarean deliveries increased from 30.5% to 42.0% (P=0.018). Most infants received ARV prophylaxis (99.7%). Few infants were breastfed (0.5%) or became infected with HIV-1 (1.2%).

Conclusion—The results indicate that national HIV-1 treatment and transmission prevention policies are effective among patients with healthcare access in the region.

Keywords

Antiretroviral; HIV-1; Latin America; Mother-to-child transmission; Prophylaxis; Treatment

1. Introduction

Strategies that aim to prevent mother-to-child transmission (MTCT) of HIV-1 have been implemented in many regions worldwide, including Latin America and the Caribbean. These interventions include antiretroviral (ARV) prophylaxis, cesarean delivery before onset of labor and rupture of membranes, and total avoidance of breastfeeding [1–3]. International initiatives to ensure access to HIV-1 prevention and treatment programs, such as the US President's Emergency Plan for AIDS Relief and the Global Fund, have improved outcomes for women with HIV-1 and markedly reduced rates of MTCT, especially in low-income settings [4].

In 2002, the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) began funding sites within 4 Latin American and Caribbean countries—Argentina, the Bahamas, Brazil, and Mexico—as part of the NICHD International Site Development Initiative (NISDI) Perinatal cohort study of HIV-1-infected women and their infants [5, 6]. Sites in Jamaica and Peru were funded from 2005, and the NISDI Perinatal cohort completed enrollment in 2007. The following year, HIV-1-infected pregnant women and their HIV-1-exposed infants began enrollment into a revised protocol, the Longitudinal Study in Latin American Countries (LILAC). Sites in Argentina, Brazil, and Peru were funded for enrollment of participants into LILAC, which involved a longer duration of follow-up than that performed in the NISDI Perinatal protocol [6].

The aim of the present study was to describe changes in management and outcomes that occurred over time among HIV-1-infected women and their infants enrolled in the NISDI Perinatal and LILAC cohorts during the period 2002–2009.

2. Materials and methods

Data regarding HIV-1-infected women and their infants enrolled into the NISDI Perinatal or LILAC cohorts between September 27, 2002, and June 30, 2009, were analyzed. The present study was approved by the relevant institutional or ethics review boards at each of the 24 participating clinical sites, which were located in Argentina, the Bahamas, Brazil, Jamaica, Mexico, and Peru. In addition, approval was obtained from the review boards of the sponsoring institution (NICHD, Bethesda, USA) and the center responsible for data management (Westat, Rockville, USA). All participants provided written informed consent.

The enrollment and follow-up of the NISDI Perinatal and LILAC cohorts have been previously described [5, 6]. Briefly, eligible women were enrolled at 8 weeks of pregnancy or later. Participants attended up to 3 prenatal visits, as well as study visits at delivery, at hospital discharge after delivery (HD), at 6–12 weeks after delivery, and at 6 months after delivery. Women enrolled in the LILAC protocol were then assessed every 6 months for up to 5 years after delivery. Infants were enrolled at birth; study visits were at 6–12 weeks and at 6 months of age. Infants enrolled in the LILAC protocol were then assessed at subsequent 6-month intervals for up to 5 years after birth. Infants diagnosed as HIV-1-infected were given the opportunity to enroll in a concurrent NICHD-funded protocol [7]. A medical history and physical examination were performed at each study visit. Laboratory evaluations, including CD4 lymphocyte count, HIV-1 viral load (VL), hematology, and biochemistry, were performed using blood samples collected at all study visits other than the maternal 6-month postpartum assessment.

Maternal eligibility criteria for the present study were enrollment in either the NISDI Perinatal or LILAC protocols with their first on-study pregnancy (data collected during subsequent pregnancies were excluded from the present analysis so that outcomes were assessed for only 1 pregnancy per woman). Inclusion criteria for infants were eligible mother, singleton, live birth, and availability of relevant data. Mode of delivery was categorized as elective cesarean delivery before onset of labor and ruptured membranes, non-elective cesarean delivery after labor and/or after ruptured membranes, or vaginal delivery. Maternal ARV regimens were classified as follows: use of 1–2 nucleoside reverse transcriptase inhibitors (NRTIs); use of 2 NRTIs and 1 non- NRTI; use of 2 NRTIs and 1 protease inhibitor (PI); and use of any other regimen. Use of ARVs during pregnancy was categorized as “treatment” when these agents were used before pregnancy and/or after the 6–12 week visit. By contrast, ARV use during pregnancy was categorized as “prophylaxis” if these agents were started during pregnancy and discontinued by the 6–12 week visit. Clinical disease stage was categorized at each visit according to the Centers for Disease Control and Prevention scheme [8]. In the present study, only maternal and infant variables that were assessed in both protocols up to 6 months after delivery were included in the analysis.

Births that occurred before 37 weeks of pregnancy were considered preterm. Infants weighing less than 2500 g at delivery were categorized as having low birth weight. Diagnosis of infants as HIV-1-infected required any 2 of the following 4 test results: viral particles detected by cell culture; HIV-1 DNA detected by polymerase chain reaction assay;

presence of neutralizable HIV-1 p24 antigen; or a VL of at least 10 000 copies/mL. These test results had to be recorded using separate specimens (i.e. from different blood-sampling events).

Data were analyzed using SAS version 9.1.3 (SAS Institute, Cary, NC, USA). Temporal changes in management and outcomes were assessed by comparing data by period of maternal enrollment. This parameter was broken down into 2-year intervals: 2002– 2003, 2004–2005, 2006–2007, and 2008–2009. Changes over time in categorical measures were analyzed using logistic regression modeling, with 2008–2009 serving as the reference period. Linear regression modeling was used for continuous-scaled measures. The Wald χ^2 test was used to test differences between periods; *P* values below 0.05 were considered statistically significant.

3. Results

Figure 1 shows the derivation of the present study population. Of the 1630 pregnancies enrolled in the NISDI Perinatal or LILAC protocols, 1548 women with first-time, on-study pregnancies were included in the present analysis. The 82 subsequent pregnancies were excluded to avoid potential over-representation bias. A total of 1481 infants were eligible for inclusion in the present study. Follow-up throughout the 6-month period after delivery was completed by 1463 women (94.5%) and 1407 infants (95.0%). The median follow-up duration was 9 months for the women and 6 months for their infants.

During the follow-up period, 7 women and 9 infants died within 6 months of delivery. The causes of the 7 maternal death were AIDS with disseminated cryptococcosis and septicemia; HIV wasting syndrome with electrolyte abnormalities and metabolic acidosis; shock, disseminated tuberculosis, and AIDS; disseminated cancer (vulvar embryonal rhabdomyosarcoma) and AIDS; cardiac arrest related to respiratory failure caused by community-acquired severe pneumonia; septic shock; and severe dyspnea and hypotension, attributed to a pulmonary thromboembolism during the postpartum period. The causes of the 9 infant deaths were perinatal asphyxia and meconium aspiration; necrotizing enterocolitis, sepsis, and septic shock syndrome; bronchoaspiration of gastric contents resulting in respiratory insufficiency; pneumothorax in an extremely low birth weight infant, leading to respiratory failure and cardiopulmonary arrest; sudden death; respiratory distress owing to sepsis and pneumonia; bilateral bronchopneumonia; sepsis; and preterm delivery at 27 weeks, with death occurring within 1 hour of birth.

The maternal characteristics are presented in Table 1. Enrollment by country varied substantially throughout the study period ($P<0.001$); clinical sites in the Bahamas, Jamaica, Mexico, and Peru did not enroll participants during the years when they were not funded to participate in the NISDI Perinatal protocol. Maternal age at delivery, years of education, and gainful employment outside the home differed over time in the logistic model ($P=0.0083$, $P<0.001$, and $P<0.001$, respectively). The diagnosis of HIV-1 infection during pregnancy also differed ($P=0.0026$), with appreciably more women diagnosed during pregnancy in the period 2002–2003 than in 2008–2009 ($P=0.0012$). Substance abuse differed significantly between enrollment periods ($P=0.0134$). In particular, alcohol use during pregnancy differed

significantly, with women enrolled in 2008–2009 more likely to use alcohol than women enrolled in the earlier years ($P<0.001$). Differences were observed over time in clinical disease stage at enrollment, first CD4 lymphocyte count during pregnancy, and first VL measurement during pregnancy. Fewer women with class B and C disease enrolled in 2004–2005 and 2006– 2007 than in 2008–2009 ($P=0.0087$). Fewer women had a first CD4 lymphocyte count during pregnancy of 500 cells/mm^3 or higher in 2002–2003 and 2004–2005 than in 2008–2009 ($P=0.002$). Finally, fewer women had a plasma VL below 1000 copies/mL in 2002–2003 and 2004–2005 than in 2008–2009 ($P<0.001$). Similar changes were observed at HD and at the 6–12 weeks postpartum visit for the CD4 lymphocyte count and the plasma VL ($P<0.005$ for all comparisons).

The median first CD4 lymphocyte count during pregnancy was higher among women enrolled in later time periods than among those enrolled earlier. The values (expressed as cell/mm^3) were 396.5 (2002–2003); 385.0 (2004–2005); 444.0 (2006–2007); and 450.5 (2008–2009). The overall value was 407.0 cells/mm^3 ($P>0.001$). A similar trend was observed for the median CD4 lymphocyte count at HD. The values (expressed as cells/mm^3) were 441.0 (2002–2003); 446.0 (2004–2005); 475.0 (2006–2007); and 515.0 (2008–2009). The overall value was 463.5 cells/mm^3 ($P=0.0439$). Finally, the median CD4 lymphocyte count at the 6–12 week postpartum visit was also higher among women enrolled in the later time periods. The values (expressed as cell/mm^3) were 470.5 (2002–2003); 451.5 (2004–2005); 495.0 (2006–2007); and 556.0 (2008–2009). The overall value was 484.0 cell/mm^3 ($P<0.001$). By contrast, differences in the median last CD4 lymphocyte count before delivery by year of enrollment were not statistically significant ($P=0.19$).

Most of the women (99.0%) used ARVs during pregnancy; the rate of ARV use did not vary by period of enrollment ($P=0.93$). The most complex ARV regimen used for 28 days or more during pregnancy and during the third trimester of pregnancy varied by enrollment period ($P=0.0029$ and $P=0.002$, respectively); more women used a PI-based 3-drug regimen in the later periods of enrollment than in the earlier periods. The median duration of ARV use during pregnancy was 149 days for women enrolled in 2008–2009, which was significantly longer than the median duration for 2002–2003 (130.5 days), 2004–2005 (130 days), and 2006–2007 (130.5 days; $P<0.005$). Fewer women used ARVs for treatment during pregnancy in the earlier time periods than in 2008–2009 ($P<0.001$). Although elective cesarean delivery became more frequent over time ($P=0.018$), mode of delivery differed significantly only between 2002–2003 and 2008– 2009 ($P=0.0024$).

The infant characteristics are presented in Table 2. No statistically significant changes in preterm birth or low birth weight were observed ($P>0.2$). In all, 99.8% of infants received ARV prophylaxis within 7 days of birth for each enrollment period, preventing a model from being fit to the data for this outcome. Zidovudine (ZDV) alone was the predominant infant ARV prophylaxis regimen (97.2%). However, other ARV regimens— especially ZDV with nevirapine (NVP)—were used more often among the infants of mothers enrolled in 2006–2007 than in 2008–2009 ($P<0.001$). Breastfeeding was reported rarely, although a slight increase was observed over time: from 0.0% (2002– 2003 and 2004–2005) to 0.8% (2006–2007) and 1.4% (2008–2009). Of the 7 infants who were breastfed, 1 became HIV-infected, 1 had indeterminate HIV-1 test results, and 5 were HIV-uninfected at 6 months of age. The

rate of MTCT of HIV-1 did not vary significantly over time. The overall MTCT rate was 1.16% (95% CI, 0.66%–1.87%; P=0.53). All 16 HIV-infected infants received ARV prophylaxis within 7 days of birth; 93.8% of these infants received ZDV alone.

4. Discussion

The present study population came from 24 sites located throughout Latin America and the Caribbean. Caution should be used when generalizing the current findings to Latin America as a whole, as the study population was heavily weighted by Brazil, many of the study sites were referral hospitals, and sites and countries were added and removed throughout the study period. This latter point could have biased some of the observed trends. Nevertheless, as similar national treatment guidelines were followed by all of the sites, it seemed important to include every participant in the present analysis so as to provide the most representative view possible for the region. Other study requirements, such as the need for all sites to have formula feeding options available, might have further affected the representative nature of the participants. Despite these issues, the findings of the present study provide insight into general trends that may be occurring within the region among HIV-infected women and their infants with access to healthcare.

The results of the present study suggest that the proportion of women receiving ARVs during pregnancy was high. Although the rates of ARV use did not change substantially over time, a shift was observed in the types of regimens being used during pregnancy. A greater proportion of women enrolled in the later years received 2 NRTIs and 1 PI, while a smaller proportion received 2 NRTIs plus 1 non-NRTI. This observation might be a consequence of women with advanced disease enrolling toward the end of the study period.

The increased proportion of women with advanced CDC clinical classification observed in 2008–2009 is probably caused by enrollment from a different group of research sites. The observed increase in alcohol consumption during pregnancy in 2008–2009 may reflect changes in the composition of the study population, or changes in the way the question about substance use was asked in the LILAC protocol. Nonetheless, the possibility that this observation may have been the result of a real effect cannot be ruled out.

Over time, more women had elevated CD4 lymphocyte counts and lowered VLs both before and after delivery, possibly reflecting a shift in ARV access or clinical management. These findings might also indicate changes in the composition of the study population, which had a greater proportion of women with advanced disease in the later years and, therefore, a high proportion of women remaining in treatment for a prolonged period of time.

Most of the women (99.0%) used ARVs during pregnancy and 99.7% of the infants received ARVs within 7 days of birth, a finding that did not vary by year of enrollment. The infants mostly received ZDV alone, although a greater proportion received NVP plus ZDV in 2006–2007 than in the other years. This high rate of coverage is consistent with national policies and recommendations for ARV prophylaxis of HIV-1-exposed infants in Latin America and the Caribbean. Current HIV-1 prophylaxis policies in Peru and Argentina [9, 10] indicate that all women who are newly diagnosed with HIV-1 during pregnancy should receive ZDV,

lamivudine (3TC), and lopinavir plus ritonavir after week 14 of pregnancy. Women with CD4 lymphocyte counts below 250 cells/mm^3 should receive AZT, 3TC, and NVP combination therapy. Infants born to HIV-1-infected women in Peru [9] should receive 1–6 weeks of ZDV prophylaxis, starting within the first 24 hours after delivery, while Argentinean infants should receive prophylaxis that may include ZDV, 3TC, and NVP [10]. Brazilian guidelines have similar recommendations for combination ARV prophylaxis among HIV-1-infected women after week 14 of pregnancy [11].

No differences were observed over time in infant HIV-1 infection status, with fewer than 2.0% of infants infected during any time period. A very low proportion of the infants received any breast milk. All reports of breast milk exposure occurred in the later years of the present study, which probably reflects increased opportunities for ascertainment of infant feeding information in the LILAC protocol. The low rates of breastfeeding observed in the present study are consistent with national guidelines, which recommend that HIV-1-infected women do not breastfeed their infants. Additionally, these low rates were expected given the added NISDI site selection criterion, which dictates that sites must advise against breastfeeding and have infant formula available.

In conclusion, the results of the present study suggest that national HIV-1 treatment and prevention policies are being successfully implemented among HIV-1-infected women and their infants with access to healthcare and that the resulting rates of MTCT of HIV-1 are extremely low.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Synopsis: Management and outcome trends indicate that national policies for HIV-1 treatment and prevention are effective among pregnant Latin American women with access to healthcare.

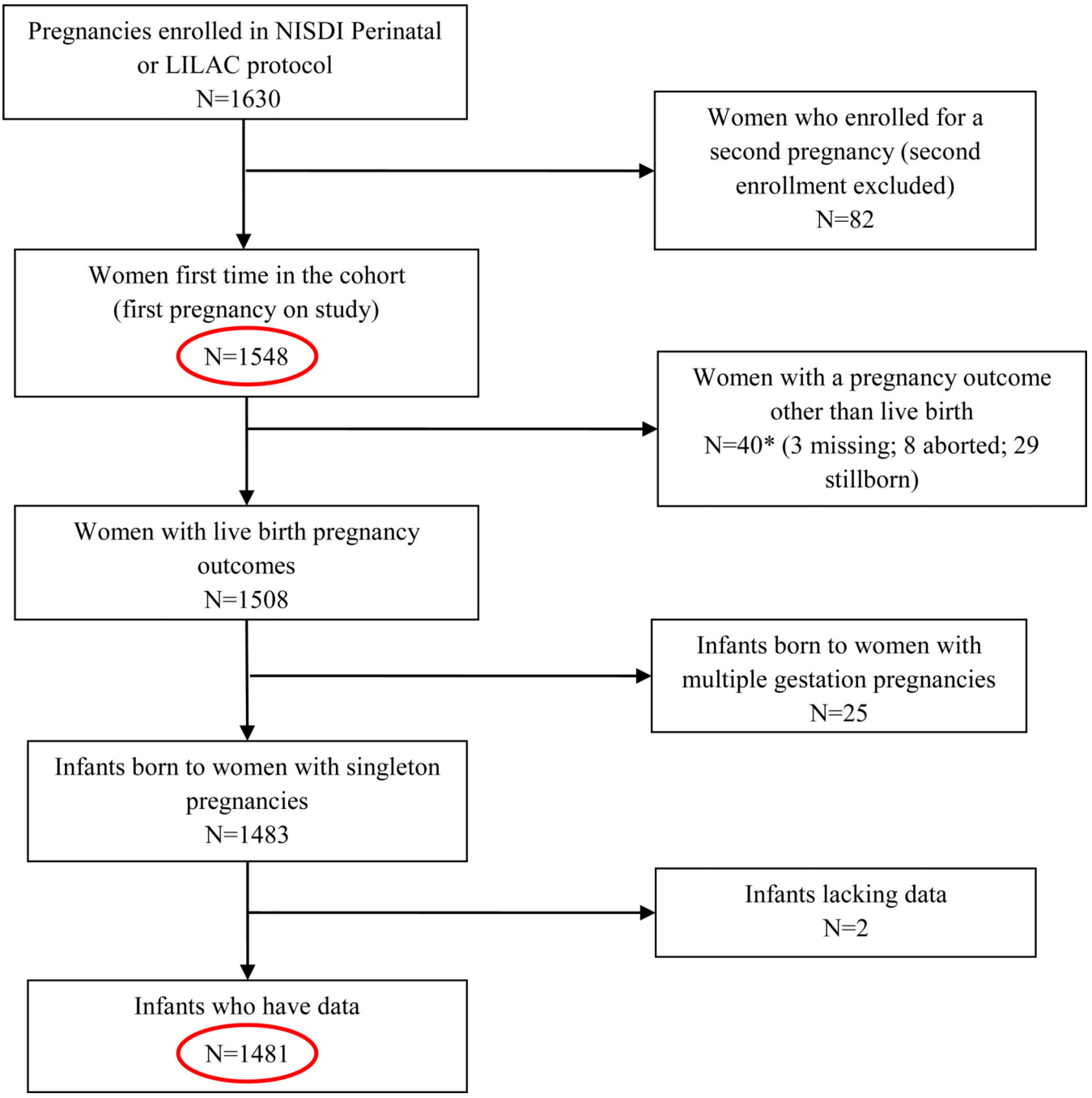

Figure 1.

Derivation of the study population. Abbreviations: LILAC, Longitudinal Study in Latin American Countries; NISDI, Eunice Kennedy Shriver National Institute of Child Health and Human Development International Site Development Initiative. Circled numbers indicate the final populations of mothers and infants included in the present analysis. * Includes 3 participants with missing information.

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Table 1

Maternal characteristics by calendar period of study enrollment (n=1548) [a]

Variable	2002–2003 (n=534)	2004–2005 (n=391)	2006–2007 (n=249)	2008–2009 (n=374)	*P* value [b]
Country where enrolled					
Argentina	121 (22.7)	160 (40.9)	79 (31.7)	27 (7.2)	<0.001
The Bahamas	30 (5.6)	13 (3.3)	0 (0.0)	0 (0.0)	
Brazil	366 (68.5)	200 (51.2)	98 (39.4)	303 (81.0)	
Jamaica	0 (0.0)	0 (0.0)	37 (14.9)	0 (0.0)	
Mexico	17 (3.2)	18 (4.6)	8 (3.2)	0 (0.0)	
Peru	0 (0.0)	0 (0.0)	27 (10.8)	44 (11.8)	
P value for pairwise period comparisons	<0.001	<0.001	0.0223	Reference	
Maternal age at delivery, y					
<20	34 (6.4)	20 (5.1)	15 (6.1)	20 (5.3)	0.0083
20–29	313 (58.6)	198 (50.6)	135 (54.9)	184 (49.2)	
>29	187 (35.0)	173 (44.2)	96 (39.0)	170 (45.5)	
Missing [c]	0	0	3	0	
P value for pairwise period comparisons	0.0024	0.70	0.13	Reference	
Maternal education, y					
0–6	208 (39.0)	116 (29.7)	52 (20.9)	108 (28.9)	<0.001
7–12	306 (57.3)	258 (66.0)	174 (69.9)	243 (65.0)	
>12	20 (3.7)	17 (4.3)	23 (9.2)	23 (6.1)	
P value for pairwise period comparisons	<0.001	0.56	0.0114	Reference	
Employed outside of the home					
Yes	117 (21.9)	84 (21.5)	65 (26.1)	137 (36.6)	<0.001
No	417 (78.1)	307 (78.5)	184 (73.9)	237 (63.4)	
P value for pairwise period comparisons	<0.001	<0.001	0.0062	Reference	
First tested positive for HIV					
Before pregnancy	269 (53.3)	241 (63.4)	143 (57.7)	234 (64.3)	0.0026
During pregnancy	236 (46.7)	139 (36.6)	105 (42.3)	130 (35.7)	
Missing [c]	29	11	1	10	

Variable	2002–2003 (n=534)	2004–2005 (n=391)	2006–2007 (n=249)	2008–2009 (n=374)	*P* value [b]
P value for pairwise period comparisons	0.0012	0.81	0.10	Reference	
Substance use during pregnancy					
Yes	151 (28.3)	122 (31.2)	70 (28.1)	141 (37.8)	0.0134
No	383 (71.7)	269 (68.8)	179 (71.9)	232 (62.2)	
Missing [c]	0	0	0	1	
P value for pairwise period comparisons	0.0026	0.06	0.0127	Reference	
Substances used during pregnancy					
Tobacco	124 (23.2)	95 (24.3)	65 (26.1)	99 (26.5)	<0.001
Cocaine	13 (2.4)	17 (4.3)	2 (0.8)	12 (3.2)	
Marijuana	12 (2.2)	9 (2.3)	5 (2.0)	13 (3.5)	
Alcohol	53 (9.9)	33 (8.4)	23 (9.2)	84 (22.5)	
Missing [c]	0	0	0	1	
P value for pairwise period comparisons	<0.001	<0.001	<0.001	Reference	
CDC clinical class at enrollment					
A	449 (84.1)	347 (88.7)	226 (90.8)	309 (82.6)	0.0087
B	36 (6.7)	15 (3.8)	11 (4.4)	31 (8.3)	
C	49 (9.2)	29 (7.4)	12 (4.8)	34 (9.1)	
P value for pairwise period comparisons	0.60	0.0215	0.0053	Reference	
First CD4 lymphocyte count during pregnancy, cells/mm ^{3}					
<200	73 (13.9)	60 (15.4)	32 (13.1)	51 (13.6)	0.0020
200–499	280 (53.4)	215 (55.3)	120 (49.2)	159 (42.5)	
≥500	171 (32.6)	114 (29.3)	92 (37.7)	164 (43.9)	
Missing [c]	10	2	5	0	
P value for pairwise period comparisons	0.0049	<0.001	0.23	Reference	
First viral load measurement during pregnancy, copies/mL					
<1000	272 (51.7)	217 (55.9)	164 (66.4)	243 (65.1)	<0.001
1000–9999	124 (23.6)	78 (20.1)	42 (17.0)	70 (18.8)	
≥10 000	130 (24.7)	93 (24.0)	41 (16.6)	60 (16.1)	
Missing [c]	8	3	2	1	

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Variable	2002–2003 (n=534)	2004–2005 (n=391)	2006–2007 (n=249)	2008–2009 (n=374)	*P* value [b]
P value for pairwise period comparisons	<0.001	0.0040	0.83	Reference	
Use of ARVs during pregnancy					0.93
Yes	530 (99.3)	387 (99.0)	246 (98.8)	370 (98.9)	
No	4 (0.7)	4 (1.0)	3 (1.2)	4 (1.1)	
Most complex ARV regimen used during pregnancy for ≥ 28 days					
No ARVs ≥28 days	25 (4.7)	13 (3.4)	14 (5.7)	13 (3.5)	0.0029
1–2 NRTIs	72 (13.6)	42 (10.9)	5 (2.0)	8 (2.2)	
2 NRTIs + 1 NNRTI	184 (34.7)	130 (33.6)	57 (23.2)	52 (14.1)	
2 NRTIs + 1 PI	243 (45.8)	195 (50.4)	165 (67.1)	283 (76.5)	
Other	6 (1.1)	7 (1.8)	5 (2.0)	14 (3.8)	
No ARVs [c]	4	4	3	4	
P value for pairwise period comparisons	0.0014	<0.001	0.0846	Reference	
Most complex ARV regimen used for ≥ 28 days during third trimester of pregnancy					
No ARVs ≥28 days	29 (5.5)	21 (5.4)	17 (6.9)	16 (4.3)	<0.001
1–2 NRTIs	73 (13.8)	43 (11.1)	5 (2.0)	15 (4.1)	
2 NRTIs + 1 NNRTI	188 (35.5)	126 (32.6)	54 (22.0)	48 (13.0)	
2 NRTIs + 1 PI	233 (44.0)	187 (48.3)	164 (66.7)	270 (73.0)	
Other	7 (1.3)	10 (2.6)	6 (2.4)	21 (5.7)	
No ARVs	4	4	3	4	
P value for pairwise period comparisons	<0.001	<0.001	0.0321	Reference	
Reason for ARV use during pregnancy					
Prophylaxis	293 (56.1)	177 (48.4)	131 (56.7)	137 (38.2)	<0.001
Treatment	229 (43.9)	189 (51.6)	100 (43.3)	222 (61.8)	
Unknown [c]	8	21	15	11	
No ARVs [c]	4	4	3	4	
P value for pairwise period comparisons	<0.001	0.0057	<0.001	Reference	
Last CD4 lymphocyte count before delivery, cells/mm^3					
<200	60 (11.5)	54 (13.9)	28 (11.5)	40 (10.7)	0.06
200–499	252 (48.1)	188 (48.3)	112 (45.9)	158 (42.2)	
≥500	212 (40.5)	147 (37.8)	104 (42.6)	176 (47.1)	

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Variable	2002–2003 (n=534)	2004–2005 (n=391)	2006–2007 (n=249)	2008–2009 (n=374)	*P* value [b]
Missing [c]	10	2	5	0	
Last viral load measurement before delivery, copies/mL					
<1000	396 (75.3)	308 (79.4)	199 (80.6)	282 (75.6)	0.27
1000–9999	80 (15.2)	49 (12.6)	25 (10.1)	52 (13.9)	
≥10 000	50 (9.5)	31 (8.0)	23 (9.3)	39 (10.5)	
Missing [c]	8	3	2	1	
Mode of delivery					
Vaginal	230 (43.6)	146 (38.3)	91 (38.1)	138 (36.9)	0.0180
Elective cesarean delivery	163 (30.9)	125 (32.8)	92 (38.5)	157 (42.0)	
Non-elective cesarean delivery	134 (25.4)	110 (28.9)	56 (23.4)	79 (21.1)	
Unknown [c]	7	10	10	0	
P value for pairwise period comparisons	0.0024	0.09	0.51	Reference	
Pregnancy outcome					
Abortion	5 (0.9)	3 (0.8)	0 (0.0)	0 (0.0)	0.99
Still birth	13 (2.4)	8 (2.0)	3 (1.2)	5 (1.3)	
Live birth	516 (96.6)	380 (97.2)	243 (98.8)	369 (98.7)	
Missing [c]	0	0	3	0	
Singleton or multiple birth					
Singleton	508 (95.1)	372 (95.1)	238 (96.7)	365 (97.6)	0.69
Multiple	8 (1.5)	8 (2.0)	5 (2.0)	4 (1.1)	
No live birth	18 (3.4)	11 (2.8)	3 (1.2)	5 (1.3)	
Missing [c]	0	0	3	0	
CDC clinical class at HD					
A	448 (83.9)	345 (88.2)	224 (90.0)	308 (82.4)	0.0193
B	37 (6.9)	16 (4.1)	12 (4.8)	32 (8.6)	
C	49 (9.2)	30 (7.7)	13 (5.2)	34 (9.1)	
P value for pairwise period comparisons	0.59	0.0298	0.0101	Reference	
CD4 lymphocyte count at HD, cells/mm^3					
<200	50 (10.3)	46 (13.0)	19 (9.0)	32 (9.2)	0.0047

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Variable	2002–2003 (n=534)	2004–2005 (n=391)	2006–2007 (n=249)	2008–2009 (n=374)	*P* value [b]
200–499	231 (47.6)	161 (45.6)	92 (43.6)	130 (37.5)	
≥500	204 (42.1)	146 (41.4)	100 (47.4)	185 (53.3)	
Missing [c]	49	38	38	27	
P value for pairwise period comparisons	0.0035	0.0011	0.24	Reference	
Viral load at HD, copies/mL					
<1000	383 (78.3)	303 (85.4)	189 (86.3)	304 (86.6)	0.0031
1000–9999	63 (12.9)	33 (9.3)	16 (8.5)	30 (8.5)	
≥10 000	43 (8.8)	19 (5.4)	14 (6.4)	17 (4.8)	
Missing [c]	45	36	30	23	
P value for pairwise period comparisons	0.0021	0.63	0.86	Reference	
Maternal CDC clinical class at 6–12 week postpartum visit					
A	447 (83.7)	344 (88.0)	222 (89.2)	307 (82.1)	0.0312
B	38 (7.1)	17 (4.3)	13 (5.2)	32 (8.6)	
C	49 (9.2)	30 (7.7)	14 (5.6)	35 (9.4)	
P value for pairwise period comparisons	0.56	0.0296	0.0176	Reference	
CD4 lymphocyte count at 6–12 week postpartum visit, cells/mm^3					
<200	40 (7.7)	39 (10.6)	18 (8.0)	20 (5.5)	<0.001
200–499	256 (49.0)	174 (47.3)	97 (43.1)	131 (35.9)	
≥500	226 (43.3)	155 (42.1)	110 (48.9)	214 (58.6)	
Missing [c]	12	23	24	9	
P value for pairwise period comparisons	<0.001	<0.001	0.0166	Reference	
Viral load at 6–12 week postpartum visit, copies/mL					
<1000	220 (42.1)	173 (47.4)	99 (43.2)	197 (54.0)	0.0034
1000–9999	126 (24.1)	80 (21.9)	56 (24.5)	77 (21.1)	
≥10 000	177 (33.8)	112 (30.7)	74 (32.3)	91 (24.9)	
Missing [c]	11	26	20	9	
P value for pairwise period comparisons	<0.001	0.0508	0.0106	Reference	
CDC clinical class at 6-month postpartum visit					
A	445 (83.3)	343 (87.7)	219 (88.0)	304 (81.3)	0.0385

Variable	2002–2003 (n=534)	2004–2005 (n=391)	2006–2007 (n=249)	2008–2009 (n=374)	*P* value [b]
B	38 (7.1)	18 (4.6)	14 (5.6)	34 (9.1)	
C	51 (9.6)	30 (7.7)	16 (6.4)	36 (9.6)	
P value for pairwise period comparisons	0.47	0.0190	0.0301	Reference	
Death within 6 months of delivery					
Yes	3 (0.6)	1 (0.3)	2 (0.8)	1 (0.3)	0.71
No	529 (99.4)	389 (99.7)	241 (99.2)	372 (99.7)	
Unknown or lost to follow-up [c]	2	1	6	1	

Abbreviations: ARV, antiretroviral, CDC, Centers for Disease Control and Prevention; HD, hospital discharge after delivery; NRTI, nucleoside reverse-transcriptase inhibitor; NNRTI, non-nucleoside reverse-transcriptase inhibitor; PI, protease inhibitor.

[a] Values are given as number or number (percentage), unless otherwise stated.

[b] Obtained by logistic or linear regression modeling. *P* values for pairwise period comparisons were not performed when the overall period *P* value was above 0.05.

[c] Not incorporated into the *P* value calculations.

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Table 2

Infant characteristics by maternal calendar period of study enrollment (n=1481) [a]

Variable	2002–2003 (n=508)	2004–2005 (n=370)	2006–2007 (n=238)	2008–2009 (n=365)	*P* value [b]
Preterm birth					
Yes	51 (10.0)	31 (8.4)	18 (7.7)	44 (12.1)	0.25
No	457 (90.0)	338 (91.6)	217 (92.3)	321 (87.9)	
Missing [c]	0	1	3	0	
Low birth weight					
Yes	65 (12.8)	51 (13.8)	35 (14.9)	59 (16.2)	0.55
No	443 (87.2)	318 (86.2)	200 (85.1)	306 (83.8)	
Missing [c]	0	1	3	0	
Sex					
Male	252 (49.6)	196 (53.1)	121 (51.3)	190 (52.1)	0.76
Female	256 (50.4)	173 (46.9)	115 (48.7)	175 (47.9)	
Missing [c]	0	1	2	0	
Received ARVs within 7 days of birth					
Yes	508 (100.0)	369 (99.7)	236 (99.2)	364 (99.7)	NA [d]
No	0 (0.0)	1 (0.3)	2 (0.8)	1 (0.3)	
ARV regimen received within 7 days of birth					
Zidovudine	506 (99.6)	367 (99.5)	200 (84.7)	360 (98.9)	<0.001
Other	2 (0.4)	2 (0.5)	36 (15.3)	4 (1.1)	
No ARVs c	0	1	2	1	
P value for pairwise period comparisons	0.23	0.41	<0.001	Reference	
Received breast milk					
Yes	0 (0.0)	0 (0.0)	2 (0.8)	5 (1.4)	NA [d]
No	508 (100.0)	370 (100.0)	236 (99.2)	360 (98.6)	
HIV-1 infection status of the infant					
Infected	5 (1.0)	2 (0.6)	4 (1.9)	5 (1.4)	0.53
Uninfected	482 (99.0)	336 (99.4)	202 (98.1)	346 (98.6)	

Variable	2002–2003 (n=508)	2004–2005 (n=370)	2006–2007 (n=238)	2008–2009 (n=365)	*P* value [b]
Indeterminate or pending evaluation c	17	24	27	12	
Missing [c]	4	8	5	2	
Death within 6 months of birth					
Yes	2 (0.4)	3 (0.8)	1 (0.4)	3 (0.8)	0.80
No	504 (99.6)	366 (99.2)	233 (98.6)	357 (99.2)	
Unknown or lost to follow-up [c]	2	1	4	5	

Abbreviations: ARV, antiretroviral; NA, not available.

[a] Values are given as number or number (percentage), unless otherwise stated.

[b] Obtained by logistic or linear regression modeling. *P* values for pairwise period comparisons were not performed when the overall period *P* value was above 0.05 or when the overall models were not fit to the data.

[c] Not incorporated into the *P* value calculations.

[d] Models were not fit to the data.

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