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## Complications and route of delivery in a large cohort study of HIV-1-infected Women- IMPAACT P1025

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#### Abstract

**Objective**—Investigate complications of cesarean section in a cohort of HIV-infected pregnant women.

**Methods**—IMPAACT P1025 is a prospective cohort study of HIV-1-infected women and infants, enrolled 2002 to 2013, at clinical sites in the United States and Puerto Rico. Demographic, medical, and obstetric data were collected and analyzed including cesareans indications. Delivery route was categorized as elective cesarean (ECS, before labor and <5 minutes before membrane rupture), non-elective cesarean (NECS, all other cesareans) or vaginal delivery. Logistic regression models evaluated associations between delivery route and maternal intrapartum/postpartum morbidities. Composite morbidity of vaginal delivery was compared to ECS and NECS.

**Results**—This study included 2297 women. 99% used antiretroviral medication and 89% were on a combination antiretroviral therapy regimen. 84% had a HIV-1 viral load 400 copies/mL before delivery. 46% (1055) delivered vaginally, 35% (798) by ECS, and 19% (444) by NECS. While interruption of HIV-1 infection was the second most frequent indication for cesarean after repeat cesarean, it decreased as an indication over time. There were no delivery-related maternal mortalities. Overall 19% of women had 1 complication(s) - primarily wound complications (14%) or other infections (11%). Vaginal delivery had the lowest complication rate (13%), followed by ECS (23%), and highest NECS (28%) with an overall p<0.001. HIV-1 mother-to-child transmission rates were low and did not differ by delivery mode group.

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**Conclusions**—HIV interruption as cesarean indicator declined during the study. Morbidity was more common in HIV-infected women delivering by NECS than ECS and lowest with vaginal delivery.

#### Keywords

cesarean section; HIV-1; pregnancy; surgical morbidity

#### Introduction

The US Preventive Health Services Task Force (USPTF) and American College of Gynecologists recommend cesarean delivery before labor and before ruptured membranes for HIV-1-infected pregnant women with elevated or unknown HIV-1 plasma viral loads to prevent mother to child HIV-1 transmission.<sup>1, 2</sup> Despite use of highly effective and better tolerated combination antiretroviral therapy (cART) ( 3 antiretroviral drugs from 2 classes) to prevent transmission and improve the health of the mother, cesarean delivery rates remain high among HIV-infected women in the U.S. Additionally, there are concerns regarding increased rates of maternal morbidity and mortality of cesarean delivery in this patient population.<sup>3–5</sup>

Due to these multiple concerns for the HIV-1 infected mother and fetus, planning a delivery route that optimizes outcomes for both patients can be challenging. Our current knowledge of the maternal morbidities and complications associated with delivery route in the effective combination antiretroviral therapy (cART) era is limited and provides conflicting data regarding risk.<sup>4-10</sup> The Women Infant transmission study in HIV infected women in the US reported increased rates of morbidity from cesarean delivery.<sup>5</sup> A later study from New Orleans suggested morbidity in HIV infected women undergoing cesarean was due to other co-morbidities aside from HIV.9 Likewise, data from a Latin American HIV infected pregnant cohort suggested low rates of morbidity.<sup>7</sup> European data also reports conflicting results regarding morbidity.<sup>4, 8, 10</sup> A 2005 Cochrane Meta-analysis of 6 studies suggested a higher rate of postpartum morbidity in HIV infected women but acknowledged the risk was dropping over time.<sup>6</sup> This reported decline may reflect improved medical care of these HIV positive women resulting in better outcomes similar to their HIV negative peers.<sup>11–13</sup> Differences between these studies may reflect varying definitions of morbidity or other changes in general obstetric practice such as earlier and broader use of prophylactic antibiotics. Updated information regarding cesarean morbidity with widespread use of cART will be valuable for HIV1- infected women and their clinicians considering the risks and benefits of cesarean vs vaginal deliveries when making decisions regarding the mode of delivery.

We therefore aimed to compare maternal intrapartum and postpartum complications by mode of delivery in a large cohort of HIV-infected pregnant women enrolled across the United States and Puerto Rico. Additionally we aimed to describe the primary indications for cesarean by calendar year of delivery.

#### Methods

#### **Study Population**

IMPAACT Protocol 1025 is a prospective cohort study and was designed to "assess maternal and infant safety, and the effectiveness of new and existing interventions prescribed for prevention of mother-to-child transmission (MTCT) of HIV and/or women's health."<sup>14</sup> Beginning in 2002, mothers were enrolled during pregnancy at 14 weeks gestation, 8 weeks beginning in 2007, or postpartum within 2 weeks after delivery. Study participant follow-up continued for at least 6 months after delivery. Institutional review boards approved the protocol at all 56 clinical sites located in the US and Puerto Rico and written informed consent was obtained from women who had enrolled in P1025. The population eligible for this analysis included women (with at least 1 visit at or after 2 weeks postpartum as of February 1, 2013) with singleton or multiple gestation and live birth or IUFD (intrauterine fetal demise) 20 weeks gestation. Only the most recent pregnancy with complete information on mode of delivery and intrapartum and postpartum complications was included in analyses.

#### **Exposure of interest**

Mode of delivery was classified as "elective cesarean" (ECS), "non-elective cesarean" (NECS) or "vaginal". For study purposes, ECS was defined as a scheduled cesarean prior to the onset of labor and prior to ruptured membranes or rupture of membranes 5 minutes prior to delivery. NECS was defined as a cesarean performed after the onset of labor or ruptured membranes 5 minutes prior to delivery. P1025 also collected information of planned mode of delivery.

#### **Outcomes of interest**

During maternal study visits, sites were asked to report laboratory abnormalities and diagnoses that met clinical definitions set in an Appendix of Diagnoses by the IMPAACT network. Maternal medical events were ascertained through review of study visit forms for additional visit diagnoses, laboratory abnormalities and adverse events. Those reported during intrapartum (defined as the time from admission for delivery until delivery) and postpartum periods (defined as the time between delivery and 6 weeks after delivery) were reviewed by 2 obstetricians (E.L, A.S) and classified into 6 different morbidity outcomes: (1) Surgery plus delivery wound complications: including wound infection with erythema/ induration; wound infection with pus; wound separation with blood; wound dehiscence; wound abscess; perineal cellulitis; episiotomy/laceration abscess; and other complications related to episiotomy, cesarean section, laceration or postpartum tubal ligation; (2) Infections: including endomyometritis; bacteremia/sepsis; pyelonephritis; pneumonia; mastitis; breast abscess; and perineal cellulitis (not related to an episiotomy); (3) Thromboembolic events: including septic pelvic thrombophlebitis; ovarian vein thrombophlebitis; pulmonary embolus; and deep vein thrombosis; (4) Gastrointestinal complications: including ileus; antibiotic-associated colitis; and obstruction; (5) Hemorrhagic events: including postpartum hemorrhage with hemodynamic instability; postpartum hemorrhage requiring surgery; and postpartum hemorrhage requiring blood transfusion; (6) Other complications: including febrile morbidity; retained products of

conception; postpartum hemolytic uremic syndrome; vulvovaginal hematoma; congestive heart failure; postpartum depression; and postpartum cardiomyopathy.

Extended hospital stay was defined by the clinical sites. The majority of US insurance carriers and prenatal care providers however use greater than 4 days post-operatively from cesarean delivery and greater than 2 days postpartum from vaginal delivery as the standard.

#### **Covariates of interest**

Maternal demographic and clinical covariates of interest included race, ethnicity, age at delivery, prenatal care, number of prior pregnancies, body mass index close to delivery, smoking and alcohol use during pregnancy, last CD4 count and viral load prior to or at delivery, last CDC classification during pregnancy, and cART use during pregnancy. Diagnoses, abnormal laboratory events and signs/symptoms during pregnancy identified by 2 obstetricians as potential risk factors for the outcomes were also considered covariates of interest.

#### Statistical Analysis

Descriptive statistics for maternal demographic and clinical characteristics were calculated both overall and by the actual mode of delivery. Maternal morbidity outcomes were summarized by delivery mode. Chi-square tests and Kruskal-Wallis tests were used, as appropriate, to compare characteristics by modes of delivery. The distribution of primary indications for cesarean by year of birth was also summarized.

Associations between mode of delivery and the maternal morbidity outcomes of interest were estimated using logistic regression models. Only the morbidity outcomes with 10% prevalence were evaluated in multivariable analyses. Analysis on a combined outcome defined as "any intrapartum/postpartum morbidity," was also performed. For each morbidity outcome, including "any morbidity", a crude logistic model (including only mode of delivery) was first built; each covariate of interest was then individually added to evaluate whether it was a confounder of the mode of delivery and morbidity association; any covariate changing the effect estimate (Odds Ratio) for the association between mode of delivery and the morbidity outcome by 10% or more was retained as a potential confounder in the final multivariable regression model. In fitting the final multivariable models, a missing indicator was created for covariates with > 5% missing data, covariates with 20% missing data were excluded from multivariable analyses. Based on previous studies of mode of delivery and maternal morbidity, maternal disease severity measures including last CD4 count, viral load, CDC classification during pregnancy, and clinical diagnoses during pregnancy were forced in all final multiple regression models to adjust for potential confounding by indication.<sup>4–6, 9, 10</sup> Odds ratios and 95% confidence intervals were obtained from the final regression models as estimates of the adjusted association between mode of delivery and each maternal morbidity outcome. Statistical significance was defined as twosided p-value < 0.05.

#### Results

As shown in, there were a total of 2980 maternal enrollments in P1025 as of February 1<sup>st</sup>, 2013; 2725 had completed a study visit at or after 2 weeks postpartum, 2719 had live births or IUFD at 20 weeks gestation, and 2540 had complete information on mode of delivery and intrapartum and postpartum complications. After limiting the analytic population to the most recent pregnancy enrolled in P1025, there were a total of 2297 women included in our final study population.

summarizes the distribution of demographic and clinical characteristics by mode of delivery. Forty-six percent of our study population (n = 1055) delivered vaginally; 35% (n = 798) had an ECS; and 19% (n = 444) had a NECS. Hispanic women, women whose last viral load during pregnancy was > 400 copies/mL, and women with BMI 40 kg/m<sup>2</sup> during pregnancy were more likely to deliver by ECS; women with a lower CD4 count during pregnancy were more likely to have a NECS; and women who had a prior birth were more likely to have a vaginal delivery. In this analytic subset of IMPAACT P1025 there were 13 instances of Mother-to-child transmission (MTCT) of HIV. Table 1 shows the distribution of these cases by mode of delivery stratified by last viral load during pregnancy. The small number of cases limited our ability to make statistical inferences about the association between mode of delivery and mother-to-child transmission.

Serious morbidity was considered to be need for extended / or additional care. Women with cesarean section delivery (elective or non-elective) were more likely to have their hospitalization extended, be readmitted to a hospital, or go to an ER/outpatient clinic for postpartum complication evaluation.(Table 1)

Of the 2297 women in the study population, 2219 (97%) had available information on planned mode of delivery. Of the 1361 women who planned a vaginal delivery, 27% delivered by either elective cesarean section (n = 141, 10%) or non-elective cesarean section (n = 222, 16%). Of the 858 women who planned a cesarean section, 632 (74%) delivered as planned (i.e., ECS) and 202 (24%) underwent a cesarean section after the onset of labor or ruptured membranes (i.e., NECS). There were no maternal deaths in this IMPAACT 1025 analysis.

Table 2 summarizes the primary indications for cesarean by year of delivery (2002 to 2013). The most common primary indication for women delivered by cesarean section was a history of a prior cesarean section (33%). Other primary indications included interruption of HIV transmission (26%); a non-reassuring fetal heart rate (9%), arrest disorder (7%), and failed induction (6%). Over time, there was a decreasing trend of having cesarean section delivery for interrupting HIV transmission.

Table 3 presents data on the complications by delivery mode. Overall, 19% of the women had one or more complications after delivery, with the highest incidence for cesarean surgical wound/vaginal delivery laceration/wound complications (14%), followed by infections (11%) and other complications (7%). The frequency of all types of morbidities was highest for women who delivered by NECS, followed by ECS, and lowest for vaginal delivery. The morbidities with 10% frequency, surgical wound/vaginal delivery laceration/

Table 4, shows that after adjusting for the last CD4 count, viral load and CDC classification during pregnancy and clinical diagnoses during pregnancy, ECS and NECS remained significantly associated with higher odds of any maternal morbidity, surgical wound/vaginal delivery laceration/wound complications, and infections, as compared to vaginal delivery.

#### Discussion

In IMPAACT P1025, 19% of participants experienced at least 1 intrapartum or postpartum morbidity. The most common were wound complications and infectious complications. Other cohorts and case series of HIV-1 infected pregnant women have produced mixed results when evaluating delivery morbidity.<sup>4-10, 15-20</sup> The morbidity rate in IMPAACT P1025 population is higher than that reported in a Latin American/Caribbean NICHD International Site Development Initiative (NISDI) cohort of 5% complications overall.<sup>7</sup> The difference cannot be accounted for by viral load suppression variations since IMPAACT P1025 had an 84% rate of viral load 400 copies/mL and the NISDI population had a 70% rate. As in the NISDI cohort, IMPAACT P1025 maternal delivery morbidity was more common in women delivering by NECS than by ECS and lowest with vaginal delivery. A low morbidity rate was also reported in a study of 97 HIV-infected women undergoing cesarean at Emory, from 1992 to 2000 that utilized HIV-uninfected controls.<sup>18</sup> The HIVinfected women at Emory had more minor complications, but no difference in major postoperative morbidity. The Swiss Mother and Child HIV Cohort Study reported in 2006 on postpartum complications in 53 matched HIV-infected and uninfected pairs of women undergoing elective cesarean delivery.<sup>10</sup> Minor complications were 8-fold more frequent in the HIV-infected Swiss women. All HIV-infected Swiss women received cART and >60% had undetectable viral load at delivery.

Older studies of HIV-infected pregnant women in the pre-cART era generally report higher rates of delivery-related morbidity.<sup>3–5</sup> The European HIV in Obstetrics Group found that HIV-infected women were at higher risk of postpartum complications regardless of mode of delivery than uninfected women (29% vs. 19% overall complications).<sup>4</sup> Fifty-two percent of European HIV-infected women delivering by cesarean had complications (complications were 5-fold higher with cesarean vs. vaginal delivery). In 2000, the WITS study of 1200 HIV-1 infected pregnant women reported that both scheduled and non-scheduled cesareans were associated with increased postpartum morbidity, mostly postpartum fever.<sup>5</sup> In 2000, the ACTG 185 team reported on 497 pregnant women, 132 of whom delivered by cesarean from 1993–1997.<sup>19</sup> These women were not on cART and median viral load at delivery was >6000 copies/mL. They found an increased risk of postpartum morbidity such as endometritis and wound infection associated with cesarean delivery. Marcollet et al reported on their experience with 401 HIV-infected women at a single center in Paris from 1989–1999.<sup>20</sup> Similar to P1025, Parisian women delivering by NECS had a higher rate of complications than women delivering by ECS. Women delivering vaginally had the lowest rate of complications. NICHD's Maternal-Fetal Medicine Units Network reported maternal morbidity among 378 HIV-infected and 54,281 uninfected women undergoing cesarean

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delivery from 1999–2002.<sup>17</sup> This study found an increased risk of overall maternal perioperative morbidity among HIV-infected vs -uninfected women. Rates of common complications, including endometritis (12% vs 6%), transfusion (4% vs 2%), sepsis or pneumonia were higher among HIV-infected vs HIV-uninfected women. A 2005 Cochrane review of safety and efficacy of cesarean delivery and HIV compiled the results of several studies between1999–2004.<sup>6</sup> Similar to our findings, the Cochrane review concluded that postpartum morbidity was highest in NECS, followed by ECS and lowest in vaginal delivery. Factors in the Cochrane review associated with risk of postpartum morbidity were advanced HIV disease stage and co-morbid medical conditions.<sup>6</sup> In P1025, the NECS group had a lower rate of HIV viral load detection 400, but also higher rate of depressed CD4 counts <350, suggesting the common finding of a delay in immune reconstitution.<sup>21</sup> It is unclear how this lower CD4 count /immune reconstitution delay affected the NECS cesarean complication rate.

In our IMPAACT P1025 study population, repeat cesarean was the most common indication for cesarean, similar to a 2013 French study.<sup>16</sup> Though we found HIV interruption as the second most common indication while the French study had obstetric indications followed by HIV interruption.<sup>16</sup> IMPAACT P1025 did not record indications for the first cesarean so it is possible the first was done for HIV interruption leading up to a repeat cesarean. In the 1990s, during early use of non-suppressive antiretroviral therapy in pregnancy, a US cohort reported increasing cesarean section rates.<sup>3</sup> In the IMPAACT 1025 cohort, the decreasing trend of HIV-interruption as an indication for cesarean over time parallels the development of more effective and better tolerated combination antiretroviral regimens in pregnancy leading to improved HIV-1 viral load suppression.<sup>11–13</sup>

Mother-to-child transmission rates were low in IMPAACT 1025, therefore we are unable to draw clinical conclusions regarding impact of route of delivery. There were no direct obstetric maternal deaths in this IMPAACT 1025 analysis. This differs from a report from the Maternal Fetal Medicine Network units of HIV-1 infected women delivering from 1999–2002 where 3 maternal deaths were noted.<sup>17</sup>

A limitation of our study is the women were cared for at centers of expertise in HIV and obstetric care so may have experienced more optimal care and lower complication rates than many HIV-infected pregnant women. Our results may not be generalizable to other populations. Additionally, the IMPAACT P1025 database relied on medical diagnoses, adverse events and concomitant medications forms completed by the sites so events may be underreported. IMPAACT P1025 also allowed women to enroll postpartum which may have led to selection of participants into the study by experience of morbidity. However, only 17% of subjects were enrolled in the postpartum period. Another limitation is we limited our evaluation of morbidity to a single gestation. Since, frequently, a cesarean delivery leads to repeat cesareans morbidity may occur in a future pregnancy that is not accounted for in a single gestation study.<sup>22</sup>

Per USPTF guidelines, most obstetricians recommend cesarean delivery to HIV-1 infected patients who have a viral load > 1,000 copies/mL to prevent mother-to-child transmission. For an individual patient, many factors may influence the final choice of mode of delivery

including perceived safety of the surgery. This report suggests that rates of cesarean for the indication of interruption of HIV infection are declining. Vaginal delivery provides the least maternal morbidity, followed by elective and non-elective cesarean. Rates of cesarean morbidity are lower in IMPAACT 1025 than in reports prior to use of combined antiretroviral therapy.

#### **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

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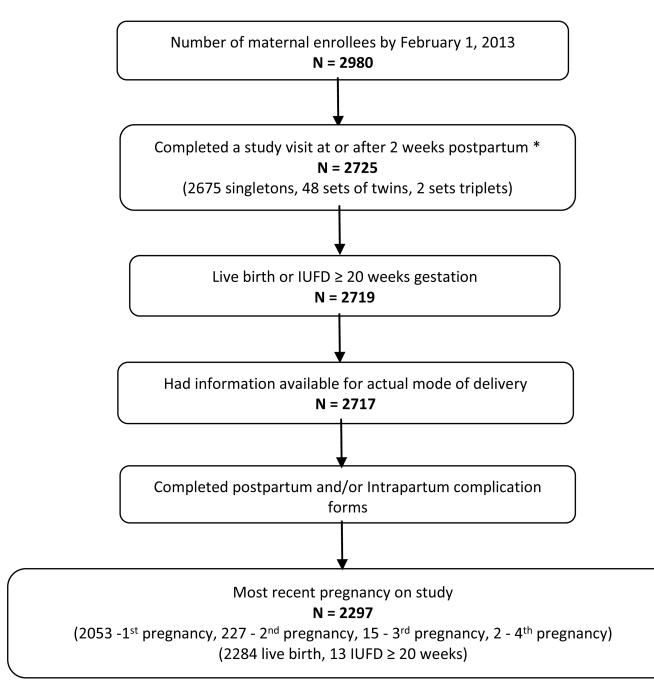


Figure 1.

Study Population Derivation

\* To allow subjects to complete the first postpartum visit at 6 weeks ( $\pm$  4 weeks).

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## Table 1

Mode of Delivery
Characteristics by
Maternal Background
Distribution of N

				Mode of Delivery		
Characteristics		Total (N=2297)	Vaginal (N=1055)	Elective cesarean section (N=798)	Non elective cesarean section (N=444)	P-Value*
Maternal age at delivery years	< 35	1,894 (82%)	865 (82%)	(%78) (84%)	360 (81%)	0.41
	35	403(18%)	190 (18%)	129 (16%))	84 (19%)	
Race/Ethnicity	Hispanic	721 32%)	297 (28%)	288 (37%)	136 (31%)	< 0.001
	White Non- Hispanic	210 (9%)	103 (10%)	77 (10%)	30 (7%)	
	Black Non- Hispanic	1,300 (57%)	617 (59%)	416 (53%)	267 (60%)	
	Other	48 (2%)	30 (3%)	8 (1%)	10 (2%)	
	Unknown	18	8	6	1	
HIV Characteristics						
Last maternal CD4 (cells/mm <sup>3</sup> ) during pregnancy	< 200	227 (10%)	79 (8%)	83 (11%)	65 (15%)	< 0.001
	200 - 349	419 (19%)	192 (19%)	140 (18%)	87 (20%)	
	350	1,590 (71%)	761 (74%)	551 (71%)	278 (65%)	
	Unknown	61	23	24	14	
Last viral load during pregnancy(copies/mL)	>400	370 (16%)	72 (7%)	207 (27%)	91 (21%)	< 0.001
	400	1,874 (84%)	966 (93%)	568 (73%)	340 (79%)	
	Unknown	53	17	23	13	
Most intensive maternal ARV regimen during pregnancy	PI- containing HAART	1,856 (81%)	844 (80%)	652 (82%)	360 (82%)	0.26
	NNRTI- containing HAART	161 (7%)	87 (8%)	47 (6%)	27 (6%)	
	Other HAART	25 (1%)	8 (1%)	10 (1%)	7 (2%)	

Characteristics Non- 23   HAART 23   HAART 23   No ARV 23   No ARV 23   Unknown 1,5   Dostetrical and other medical characteristics 65   Trimester of first 1,5   prenatal visit 3rd Trimester   Stating (delivery 1   Darity (delivery 1   Alt 1   Alt 1   Parity (delivery 1   Alt 1   Alt 1	RT RV Wn					
No AR No AR No AR No AR Unkno 3rd Tri 7rimes 3rd Tri 0 pre care Care Care Care Care Care Care Care C	ZT ZV SWn	Total (N=2297)	Vaginal (N=1055)	Elective cesarean section (N=798)	Non elective cesarean section (N=444)	P-Value*
No AR   Unknov   Unknov   1st Trit   1st Trit   1st Trit   2nd   Trimes   3rd Tri   No preve   care   Unknov   1   1	SV awn	230 (10%)	108 (10%)	76 (10%)	46 (10%)	
Unknoo other medical ch lst Trii lst Trii 2nd 3rd Tri Trimes 3rd Tri No pre care Unknoo 1	um	12 (1%)	4 (0%)	7 (1%)	1 (0%)	
other medical ch 1st Trii 2nd 2nd 2nd 0rimes no pre- care Unknov - - - - - - - - - - - - -		13	4	9	3	
	naracteris	tics				
	1st Trimester	1,513 (66%)	684 (65%)	526 (66%)	303 (68%)	0.68
	ster	670 (29%)	317 (30%)	230 (29%)	123 (28%)	
	3rd Trimester	97 (4%)	43 (4%)	38 (5%)	16 (4%)	
	enatal	16(1%)	10 (1%)	4 (1%)	2 (0%)	
	um	1	1	0	0	
V		1,676 (73%)	795 (75%)	592 (74%)	289 (65%)	< 0.001
		621 (27%)	260 (25%)	206 (26%)	155 (35%)	
Last maternal BMI 40 during pregnancy kg/m <sup>2</sup>		257 (15%)	90 (11%)	117 (19%)	50 (14%)	< 0.001
<40		1,491 (85%)	712 (89%)	484 (81%)	295 (86%)	
Unknown	um	549	253	197	66	
Cigarettes use during Yes pregnancy		363 (22%)	157 (21%)	136 (25%)	70 (22%)	0.12
No		1,254 (78%)	605 (79%)	400 (75%)	249 (78%)	
Unknown	nwu	680	293	262	125	
Alcohol use during Yes pregnancy		569 (28%)	270 (29%)	199 (29%)	100 (25%)	0.30
No		1,452 (72%)	655 (71%)	498 (71%)	299 (75%)	
Unknown	uwu	276	130	101	45	
Duration of follow-up Mean (SD) (weeks)	(SD)	32.80 (16.67)	32.62 (16.75)	33.76 (16.41)	31.50 (16.91)	0.05

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			F	Mode of Delivery		
Characteristics		Total (N=2297)	Vaginal (N=1055)	Elective cesarean section (N=798)	Non elective cesarean section (N=444)	P-Value*
Last viral load during pregnancy (copies/mL)	Infant HIV infection status					
> 400	Infected	7 (0.3%)	2 (0.2%)	3 (0.4%)	2 (0.5%)	
	Uninfected	332 (15%)	62 (6%)	187 (23%)	83 (19%)	
	Indeterminate	31 (1%)	8 (0.8%)	17 (2%)	6 (1%)	
400	Infected	5 (0.2%)	4 (0.4%)	1 (0.1%)	0 (%0) 0	
	Uninfected	1782 (78%)	912 (86%)	541 (68%)	329 (74%)	
	Indeterminate	87 (4%)	50 (5%)	26 (3%)	11 (2%)	
Unknown	Infected	1 (0.04%)	0 (0%)	0(0%)	1 (0.2%)	
	Uninfected	48 (2%)	15 (1%)	22 (3%)	11 (2%)	
	Indeterminate	4 (0.2%)	2 (0.2%)	1 (0.1%)	1 (0.2%)	

cART was defined as regimen containing 3 or more antiretroviral drugs from at least 2 classes.

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Delivery Outcome and Distribution of Maternal Intrapartum/Postpartum Morbidities

			M	Mode of Delivery	'n	
Characteristics		Total (N=2297)	Vaginal (N=1055)	Elective cesarean section (N=798)	Non elective cesarean section (N=444)	P-Value*
Planned /actual mode of delivery	Vaginal	1,361 (61%)	(%86) 866	141 (18%)	222 (52%)	< 0.001
	Cesarean section	858 (39%)	24 (2%)	632 (82%)	202 (48%)	
	Unknown	78	33	25	20	
Any intrapartum/postpartum complications	Yes	442 (19%)	138 (13%)	180 (23%)	124 (28%)	< 0.001
	No	1,855 (81%)	917 (87%)	618 (77%)	320 (72%)	
Surgery plus delivery wound complications	Yes	327 (14%)	81 (8%)	145 (18%)	101 (23%)	< 0.001
	No	1,970 (86%)	974 (92%)	653 (82%)	343 (77%)	
Infections	Yes	250 (11%)	76 (7%)	98 (12%)	76 (17%)	< 0.001
	No	2,047 (89%)	979 (93%)	700 (88%)	368 (83%)	
Other complications	Yes	168 (7%)	57 (5%)	60 (8%)	51 (11%)	< 0.001
	No	2,129 (93%)	998 (95%)	738 (92%)	393 (89%)	
Hemorrhagic events	Yes	71 (3%)	23 (2%)	24 (3%)	24 (5%)	0.004
	No	2,226 (97%)	1,032 (98%)	774 (97%)	420 (95%)	
Gastrointestinal complications	Yes	14 (1%)	2 (0%)	9 (1%)	3 (1%)	0.04
	No	2,283 (99%)	1,053 (100%)	789 (99%)	441 (99%)	
Thromboembolic events	Yes	8 (0%)	2 (0%)	4 (1%)	2 (0%)	0.49
	No	2,289 (100%)	1,053 (100%)	794 (99%)	442 (100%)	
Clinical diagnoses during pregnancy potentially associated with ANY	Yes	1,440 (63%)	658 (62%)	498 (62%)	284 (64%)	0.83

No
Yes
No 1,758 (77%)
Yes 1,145 (50%)
No 1,152 (50%)
Yes
No 2,216 (96%)
Yes
No 2,188 (95%)

# P-Value\* 160 (36%) 106 (24%) 338 (76%) 233 (52%) 211 (48%) 18 (4%) 426 (96%) 31 (7%) Non elective cesarean section (N=444)

< 0.001

< 0.001

0.25

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0.75

## Table 3

3 Vaar Intervale	J LCAL HILLIVALS
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			Birth	Birth Years	
Primary Indication for Cesarean Delivery	Total (N=1242)	2002–2004 (N=177)	2005-2007 (N=370)	2008–2010 (N=436)	2011–2012 (N=259)
Repeat	409 (33%)	46 (26%)	99(27%)	146 (33%)	118 (46%)
Interruption of HIV Infection	328 (26%)	84 (47%)	105 (28%)	95 (22%)	44 (17%)
Non-reassuring fetal heart rate (FHR)	109 (9%)	8 (4%)	43(12%)	40(9%)	18 (7%)
Arrest disorder	86 (7%)	8 (4%)	21 (6%)	31 (7%)	26 (10%)
Failed induction	72 (6%)	8 (4%)	20 (5%)	30 (7%)	14 (5%)
Malpresentation	60 (5%)	6 (3%)	14 (4%)	27 (6%)	13 (5%)
Subject desire	55 (4%)	4 (2%)	24 (6%)	23 (5%)	6 (2%)
HTN/preeclampsia/eclampsia	29 (2%)	2 (1%)	13 (4%)	9 (2%)	5 (2%)
Other*	73 (6%)	12 (7%)	21 (6%)	28 (6%)	11 (4%)
-					

\* Other- Maternal medical/surgical indication (n=12), Prolonged rupture of membranes (n=12), Fetal risk for stillbirth (n=11), Multiple gestation (n=9), Macrosomia (n=6), Fetal anomaly(n=2), Placenta abruption (n=2), Cord prolapse(n=1), unknown (n=3)

#### Table 4

Associations between Mode of Delivery and Intrapartum/Postpartum Morbidities

Maternal Intrapartum/ Postpartum Morbidity	Mode of Delivery (vs. Vaginal)	Unadjusted OR (95% CI)	Adjusted OR <sup>*</sup> (95% CI)	P- value **
Any intrapartum/postpartum	Elective cesarean section	1.94 (1.52,2.47)	1.82 (1.40,2.36)	< 0.001
complications	Non elective cesarean section	2.57 (1.96,3.39)	2.47 (1.85,3.28)	< 0.001
Surgery plus delivery wound	Elective cesarean section	2.67 (2.00,3.58)	2.43 (1.79,3.30)	< 0.001
complications	Non elective cesarean section	3.54 (2.58,4.87)	3.37 (2.43,4.68)	< 0.001
Infrations	Elective cesarean section	1.80 (1.32,2.48)	1.68 (1.21,2.36)	0.002
Infections	Non elective cesarean section	2.66 (1.89,3.74)	2.55 (1.78,3.63)	< 0.001

OR: Odds Ratio of presence of a specific maternal intrapartum/postpartum morbidity between women who delivered by a specific route vs. vaginally.

\* Model adjusted for last maternal CD4, viral load, CDC classification during pregnancy, and clinical diagnoses during pregnancy potentially associated with the specific morbidity.

\*\* P-value from adjusted analyses.