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Delivery After 40 Weeks of Gestation in Pregnant Women With Well-Controlled Human Immunodeficiency Virus

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for the NISDI Perinatal/LILAC Protocol

Abstract

Objective—To evaluate if there is increased mother-to-child transmission of human immunodeficiency virus (HIV-1) associated with deliveries ≥40 weeks estimated gestational age (EGA) in pregnancies with maternal HIV-1 viral load ≥1000 copies/mL.

Methods—We performed a secondary analysis of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) International Site Development Initiative (NISDI) Perinatal and Longitudinal Study in Latin American Countries (LILAC) and International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) P1025 cohorts. We included HIV-1-infected pregnant women with recent viral load ≥1000 copies/mL at time of delivery, and compared delivery outcomes between ≥38 and <40 weeks EGA to delivery outcomes ≥40 weeks EGA, the exposure of interest. Our primary outcome of interest was mother-to-child transmission and secondary outcomes included indicators of maternal and neonatal morbidity. We examined the association between EGA and mother-to-child transmission using Poisson distribution.

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For a list of principal investigators, co-principal investigators, study coordinators, coordinating center representatives, and NICHD staff who participated in this study, see Appendix 1 online at <http://links.lww.com/xxx>.

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Associations between EGA and secondary outcomes were examined through bivariate analyses using Pearson chi-square/Fisher's exact test or the nonparametric Mann-Whitney U-test.

Results—Among the 2,250 eligible mother-infant pairs, 8 infants were infected with HIV-1 (overall transmission rate: 0.4% (95% confidence interval [CI]: 0.2–0.7%), 40 weeks EGA: 0.5% (3/621, 95% CI: 0.2–1.4%), <40 weeks EGA: 0.3% (5/1629, 95% CI: 0.1–0.7%)); there was no significant difference in transmission by EGA (rate ratio=1.57, 95% CI: 0.24–8.09, $p=0.77$). There was no difference in maternal viral load between the two groups, nor was there a difference in timing of transmission among neonates born with HIV-1.

Conclusions—In pregnancies with well-controlled maternal HIV-1, the risk of mother-to-child transmission did not differ significantly by EGA at delivery, although we were not powered to demonstrate equivalence of proportions of mother-to-child transmission between EGA groups.

Introduction

The effect of gestational age at delivery on mother-to-child transmission and maternal and neonatal outcomes is unstudied in pregnancies with well-controlled maternal HIV-1.[1,2] There are no formal guidelines on the timing of delivery for these pregnancies; HIV-1 in the absence of a clear standard of care, there is significant variation in clinical practice between institutions and providers, including planned early delivery between 38 and 39 completed weeks, stemming from concern for mother-to-child transmission with advancing gestational age. The risks of induction of labor with an unfavorable cervix include prolonged labor, failed induction and cesarean delivery [3,4]; the risk of serious consequences secondary to these events is heightened for women with HIV-1[5]. Expectant management until late-term is standard of care for uncomplicated HIV-1 negative pregnancies[6,7]; there is no evidence this is contraindicated in pregnancies with well-controlled HIV-1.

To address this gap in knowledge, we completed a secondary analysis of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) International Site Development Initiative (NISDI) Perinatal and Longitudinal Study in Latin American Countries (LILAC) protocols and the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) P1025 cohorts to evaluate mother-to-child transmission and maternal and neonatal outcomes in pregnancies by EGA at delivery. We hypothesized that the proportion of mother-to-child transmission associated with delivery at or after 40 weeks EGA would be equivalent to that of delivery prior to 40 weeks gestation in pregnancies with viral load ≤ 1000 copies/mL and that there would be no increase in maternal or neonatal morbidity or mortality.

Materials and Methods

Using data from the NISDI Perinatal/LILAC and IMPAACT cohorts, which prospectively followed pregnancies of HIV-1 positive mothers and their HIV-1 exposed (or infected) neonates, we performed a secondary analysis of HIV-1 positive pregnancies that delivered on or after 40 weeks EGA compared to pregnancies that delivered prior to 40 weeks.

From 2002 to 2009, HIV-1-infected pregnant women and their infants were enrolled into the NISDI Perinatal/LILAC protocols in Latin America and the Caribbean. These protocols and the cohort have been described in detail previously [8,9]. Briefly, women were enrolled at sites in Argentina, the Bahamas, Brazil, Mexico, Peru, and Jamaica. Pregnant women >8 weeks EGA were eligible for the Perinatal protocol, while those >22 weeks EGA were eligible for the LILAC protocol. Study visits were conducted antepartum (up to 3 visits), at delivery, at hospital discharge after delivery, and 6 months (Perinatal protocol) or every 6 months thereafter until 2 years (LILAC protocol) postpartum. At each study visit, a medical history, physical examination, and laboratory assessments (hematology, flow cytometry, HIV-1 RNA levels, and biochemistries) were performed. The protocols were approved by the ethical review board at each clinical site where participants were enrolled, the Brazilian National Ethics Committee (CONEP), the NICHD Institutional Review Board (IRB), and the data management and statistical center IRB (Westat).

The IMPAACT Protocol 1025 was a prospective cohort study from 2002 to 2013, designed to assess the safety and effectiveness of new and existing interventions for prevention of mother-to-child transmission of HIV-1 and maternal health. Study participants were enrolled either during pregnancy or within two weeks postpartum with follow-up 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. (Further details of the P1025 study design have been described previously)[10,11]. Of note, per standard of care, participants in both cohorts were prescribed antiretroviral therapy during pregnancy, regardless of maternal CD4 count or viral load.

Our primary objective was to determine if there was increased mother-to-child transmission associated with delivery at or after 40 weeks EGA in pregnancies of women living with well-controlled HIV-1. Our secondary objective was to determine if there was increased maternal or neonatal morbidity or mortality associated with delivery at or after 40 weeks EGA in pregnancies of women living with well-controlled HIV-1, specifically maternal post-operative infections, preeclampsia, postpartum endometritis, neonatal low birth weight, transient tachypnea of the newborn, respiratory distress syndrome, and prolonged neonatal intensive care (NICU) admission. For our primary outcome, we included mother-to-child transmission data from both the NISDI Perinatal/LILAC and IMPAACT P1025 cohorts. For our secondary outcome, we included data from the NISDI Perinatal/LILAC cohort alone, as we were unable to merge maternal and neonatal outcome data due to differences in outcome measures used by the two studies. We included women with singleton pregnancies with well-controlled HIV-1 status, who delivered after 38 weeks EGA, with known neonatal HIV-1 status. We excluded stillbirths from the analysis for our primary objective, as neonatal HIV-1 status was not collected on stillborn infants.

We defined a woman's HIV-1 as being well-controlled if her viral load < 1000 copies/mL; we based this definition HIV-1 upon when Zidovudine and cesarean would be indicated for prevention of mother-to-child transmission per the United States (US) perinatal guidelines [2]. We defined pregnancy less than 40 weeks as 38 weeks 0 days, the earliest gestational age some institutions are inducing for well-controlled HIV-1, to 39 weeks 6 days. We

defined pregnancy at or after 40 weeks as at or after 40 weeks and 0 days until 42 weeks and 0 days, based on the current American College of Obstetricians and Gynecologists' guidelines and standard of care for HIV-1 negative pregnancies [6,7]. Study physicians at each site determined neonatal gestational age by Capurro method (a maturation scale based upon 4 physical and 2 neurological exam criteria)[12], obstetrical estimate or Ballard pediatric newborn exam (a maturation scale based on 5 neuromuscular and 5 physical exam criteria)[13], depending on the standard of care for each site. If the physician's determination of EGA at birth was not available, we extrapolated the gestational age at birth using EGA at enrollment. We characterized the timing of mother-to-child transmission as "unknown", "in utero", "intrapartum", and "intrapartum or postnatal". If diagnostic test results were unavailable within 7 days of birth, we characterized the timing as unknown. If test results were available within 7 days of birth, we defined in utero transmission as cases where the infant's first positive test was $\leq$ 7 days of birth (irrespective of any breastfeeding); we defined intrapartum transmission as cases where the infant's first positive test was after 7 days of life and the infant was never breastfed, and intrapartum or postnatal transmission if the first positive test was after 7 days of age and the infant was breastfed. These definitions are consistent with those used by Madger and colleagues [14]. We defined low birth weight as <2500 g and used the standard definition of small for gestational age (SGA) of birth weight less than the 10th percentile for gestational age. Data published by Williams and colleagues were used as the reference population for the 10th percentile birth weight [14].

We determined overall mother-to-child transmission and mother-to-child transmission according to estimated gestational age (≥ 40 weeks, <40 weeks EGA); given the small numbers of transmissions, 95 percent confidence we calculated intervals by Wilson score interval. We used simple descriptive statistics (frequency, proportion, mean, standard deviation, median) to describe characteristics of the study population and bivariate analyses to examine associations between the outcome measures (mother-to-child transmission, maternal or neonatal morbidity or mortality) and the primary exposure (gestational age at delivery) and with the outcomes and the participant characteristics (covariates). Investigation of the association between mother-to-child transmission and EGA was based on Poisson distribution. Investigation of associations between the outcomes and primary exposure measure and outcomes with categorical covariates were based on the Fisher's exact test. Examination of associations of the outcome measures with continuous-scaled characteristics, employed the Student's T-test and nonparametric Mann-Whitney U test. All analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC).

Results

Among 1630 pregnancies enrolled in the NISDI Perinatal and LILAC protocols, we excluded 711 for lack of viral suppression at the time of delivery, multiple gestation, delivery prior to 38 weeks, and insufficient data to determine neonatal HIV-1 status (see Figure 1). For the primary analysis, an additional 3 pregnancies were excluded secondary to term stillbirth, for an analysis population of 916; 613/916 (67%) delivered at less 40 weeks versus 303/916 (33%) at 40 weeks or more (see Figure 1). The IMPAACT P1025 cohort enrolled 3,029 pregnancies, of which 1,334 were singleton live birth pregnancies after 38

weeks EGA, with maternal viral load 1000 copies/mL within 7 days of delivery; 1016/1334 (76.2%) delivered at less 40 weeks versus 318/1334 (23.8%) at 40 weeks or more (see Figure 2). The combined NISDI and P1025 populations resulted in an analysis population of 2,250 mother-infant pairs.

Among the 2,250 eligible pregnant mothers in the combined NISDI Perinatal/LILAC and P1025 cohorts, 8 delivered infants infected with HIV-1, for an overall transmission rate of 0.4% (95% Confidence interval [CI]: 0.2–0.7%) (see Table 1). There was no significant difference in transmission by EGA at delivery; there was a 0.5% (95% CI: 0.2–1.4%) transmission rate (3 transmissions) among 621 women who delivered at 40 weeks, compared to a 0.3% (95% CI: 0.1–0.7%) transmission rate (5 transmissions) among 1629 women who delivered at <40 weeks (rate ratio=1.57, 95% CI: 0.24–8.1, $p=0.77$). The distribution of cases of mother-to-child transmission in the NISDI cohort according to EGA is presented in Table 2; the gestational age at delivery of the infected infants were distributed proportionately by gestational age week: two infected infants were delivered at 38 weeks EGA, two at 39 weeks, one at 40 weeks, and one at 41 weeks. Of note, approximately 5% of infants had a status of either “indeterminate” or, in a very few cases, “presumed uninfected” — however, there was no difference in the distribution of these cases by EGA group. Mean maternal viral load at delivery was not significantly higher in mothers with mother-to-child transmission compared to mothers of uninfected infants (170.8 copies/mL vs. 151.6, $p=0.76$).

Both groups had a median maternal age at delivery of 28 years ($p=0.35$; Table 3). There was no difference in viral load 400 (the lower limit of detectable during the study period) between the two groups (574/613, 93.6% vs. 285/303, 94.1%, $p=0.80$). Median maternal viral load was lower among those delivering at 40 weeks (90.5 vs. 200 copies/mL, $p=0.045$). We found no difference in antepartum, intrapartum or postpartum pregnancy outcomes, other than a higher proportion of deliveries 40 weeks had meconium-stained fluid (19.0% vs. 11.4%, $p=0.002$) and slightly shorter length of postpartum hospital stay (3.04 vs. 3.3 days, $p=0.047$; Table 3). The difference in postpartum length of stay was not statistically significant among women who delivered vaginally. Mode of delivery was significantly associated with gestational age ($p<0.001$); vaginal birth was more common in pregnancies 40 weeks (58.2% vs. 36.7%), while a higher proportion of deliveries <40 weeks were via elective cesarean (45.2% vs. 25.2%). The most common indications cited for elective cesarean were prevention of mother-to-child transmission and repeat cesarean. Prevention of HIV-1 was more frequently cited in the 40 weeks group (53.2 vs. 44.2%), while repeat cesarean was a more common indication in the <40 weeks group, likely secondary to scheduled cesarean. For non-elective cesarean, the most common indication was prevention of mother-to-child transmission in both pregnancies 40 weeks and <40 weeks EGA (21.6 and 32.4%), followed by prolonged rupture of membranes (17.6 and 15.3%) and repeat cesarean (5.9 and 12.6%). There was no significant difference in the proportion of cesarean with an indication of failed induction between the EGA groups, even when stratified by elective and non-elective cesarean. Of note, there were no cases reported of postpartum preeclampsia, eclampsia, intrapartum hemorrhage, uterine rupture/dehiscence, cord prolapse, vulvar/vaginal hematoma, internal organ abscess, septic pelvic thrombophlebitis, deep vein thrombosis, pulmonary embolism, pneumonia, pneumocystis

carinii pneumonia, sepsis, postpartum surgical procedures, meningitis, or maternal death in the analysis population (data not shown).

The method for determining neonatal gestational age was significantly associated with EGA ($p=0.009$); a higher proportion of infants born ≥ 40 weeks had EGA at delivery determined by the Capurro method (81.8% vs. 75.0%) and a lower proportion had EGA determined by pediatric newborn exam (Ballard; 5.6% vs. 11.9%). A lower proportion of infants born ≥ 40 weeks EGA were low birth weight (4.0% vs. 8.2%, $p=0.017$), however there was no difference in SGA between the two groups (Table 4). Zidovudine was the most common neonatal antiretroviral prophylaxis in both groups, although use of another prophylaxis regimen was more common among infants ≥ 40 weeks EGA (5.0% vs. 1.6%, $p=0.009$). Overall, 21 neonates were placed on Nevirapine plus Zidovudine, three on Nevirapine, Zidovudine, and Lamivudine, and 1 neonate with perinatally acquired HIV-1 was started on Lamivudine, Zidovudine, and Nelfinavir. There was no difference in receipt of breast milk between the two EGA groups. A lower proportion of infants born ≥ 40 weeks EGA had anemia during their first 6 months of life (4.9% vs. 8.6%, $p=0.009$); neonatal anemia at 6 weeks or 6 months after birth was not associated with low birth weight ($p=0.37$ and $p=0.44$, respectively). Despite increased meconium stained amniotic fluid in pregnancies ≥ 40 weeks, there was no increase in meconium aspiration syndrome. We did not find a significant difference in transient tachypnea of the newborn, respiratory distress syndrome, prolonged NICU admission or other neonatal morbidity (data not shown).

Discussion

In this secondary analysis, we observed no increase in mother-to-child transmission with delivery at or after 40 weeks EGA in pregnant women with well-controlled HIV-1. We were not powered to demonstrate equivalence; however, even beyond determining equivalence, given the transmission rates observed of 0.4%, we estimate we would need a sample size of 32,394 to discern a difference using a binomial distribution and a sample size of 42,740 using Poisson distribution. It is, unfortunately, not likely feasible to amass a sufficiently large prospective cohort to be powered appropriately to study such a rare outcome. In the absence of spontaneous labor or earlier indication for delivery, uncomplicated HIV-1 negative pregnancies are managed expectantly until late-term induction at 41 or 42 weeks of gestation[6,7]. Expectant management until 41 weeks EGA has been associated with lower rates of perinatal death, infant morbidity, such as meconium aspiration syndrome, and cesarean delivery[6]. In the absence of other data, our data suggests that the timing of delivery for well-controlled HIV-1 positive pregnancies should not differ from HIV-1 negative pregnancies. Further, in pregnant women with an unfavorable cervix, induction of labor carries an increased risk of prolonged labor, failed induction, and cesarean [3,4]. This is of even greater clinical concern in HIV-1 positive women, given their elevated risk of post-cesarean morbidity and mortality, namely infection, prolonged hospitalization, and ICU admission [5]. Of note, our analysis did not show an increase in cesarean secondary to failed induction, however this may have been skewed by the high proportion of elective cesarean deliveries. Given that there are no formal guidelines and that the institutional practice of routine early delivery between 38 to 40 weeks in well-controlled HIV-1 positive pregnancies is not evidence-based, although not statistically conclusive, our data do not show increased

risk with expectant management. Following the US perinatal guidelines recommendations for maternal antiretroviral therapy and monitoring of maternal viral load at 34 to 36 weeks EGA[2], our data suggests that pregnancies with viral load ≤ 1000 can be safely managed as per obstetrical indications. The US perinatal guidelines do not recommend monitoring further viral load counts prior to delivery [2], although presumably significant or prolonged changes in maternal antiretroviral adherence should be taken into clinical consideration in further monitoring viral load and delivery planning. The authors acknowledge in some cases early delivery may well be indicated for planned, controlled delivery and that every woman's situation is unique and should be managed on a case-by-case basis. During this study period, it is likely that providers took into account the amount of time needed to prepare and infuse Zidovudine, which was standard of care, as well as other logistic issues such as travel time to the hospital.

There were no differences in maternal antepartum, intrapartum or postpartum morbidity. Women delivering <40 weeks had a slightly longer average postpartum length of hospital stay, although the difference of 0.3 days is not likely clinically significant, and was not statistically significant among women who delivered vaginally. Vaginal birth was more common among pregnancies ≥ 40 weeks, likely secondary to both riper cervixes at more advanced gestational ages and the higher proportion of elective cesarean delivery <40 weeks, many of which were likely scheduled repeat or otherwise planned cesareans. Prevention of mother-to-child transmission was one of the most common indications for cesarean, however given that all pregnancies included had a maternal viral load ≤ 1000 copies/mL at delivery it is unclear if the cesarean was for maternal or provider concern for prevention of mother-to-child transmission above and beyond the guidelines or a mis-categorization of indication. [16]

We found a higher proportion of infants <40 weeks were low birth weight, however this may be secondary to earlier EGA rather than greater growth restriction, as there was no difference in the proportion of SGA neonates. We were also unable to determine if these neonates were delivered earlier secondary to concern for fetal growth restriction. Lastly, this could also potentially be due to greater error in estimation of gestational age at delivery with the Capurro method vs. the Ballard newborn exam, given differences in the distribution of measures of EGA between the groups. Given that maternal viral load ≤ 1000 copies/mL, Zidovudine was the clinically indicated and most common neonatal antiretroviral prophylaxis. Use of another prophylaxis regimen was more common among infants ≥ 40 weeks, although it is unclear if this was given secondary to an unknown viral load at the time of delivery, concern for maternal adherence, or concern for prevention of mother-to-child transmission above and beyond the guidelines. We also found a higher proportion of infants born <40 weeks had anemia during their first 6 months of life. Although anemia was not associated with a low birth weight, it is uncertain if anemia was related to another maternal or fetal indication for early delivery or other risk factors for earlier delivery.

The analysis' strengths include its broad generalizability and the provision of data where previously we were dependent upon expert opinion. The NISDI Perinatal and LILAC had sites in Argentina, the Bahamas, Brazil, Mexico, Peru, and Jamaica and the IMPAACT P1025 cohort was spread across the United States. The analysis involves both resource-rich

and resource-poor countries, although study sites were generally located at large research hospitals in urban areas. The results, although not statistically conclusive, provide data based on the largest, relevant studies to date.

As this was a secondary analysis of two completed prospective cohort studies, our analysis was limited by its retrospective design; for example, we could not determine if the low birth weight in the <40 weeks EGA group was secondary to indicated delivery for fetal growth restriction. Likewise, it is difficult to interpret the cesarean indication of prevention of mother-to-child transmission in a population with maternal viral load 1000 copies/mL. Secondly, this analysis was underpowered to demonstrate equivalence due to the very low incidence of mother-to-child transmission among pregnancies with maternal viral load 1000 copies/mL -- to be sufficiently powered to demonstrate equivalence would require more than double the frequency of mother-to-child transmission or a 20-fold increase in sample size.

Our analysis included 2,250 women and infants pairs and showed no significant difference between proportions of mother-to-child transmission in the two EGA groups. In the NISDI perinatal/LILAC cohort, there were no differences in maternal outcomes by EGA group, and better neonatal outcomes in the group that delivered at or after 40 weeks EGA. Larger studies are needed to conclusively demonstrate no increased mother-to-child transmission or adverse maternal or neonatal outcomes with delivery at or after 40 weeks EGA, given the rarity of mother-to-child transmission and the very large sample size of well-controlled pregnancies needed this is likely not feasible. These results should at least provide equipoise and reassurance from the largest relevant studies to date, to add evidence to the current practice and care of well-controlled pregnant women living with HIV-1.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Source:

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Figure 1.

Study population derivation. NISDI Perinatal and LILAC, NICHD [*Eunice Kennedy Shriver* National Institute of Child Health and Human Development] International Site Development Initiative Perinatal and Longitudinal Study in Latin American Countries; HIV, human immunodeficiency virus.

Figure 2. Study population derivation. IMPAACT P1025, International Maternal Pediatric Adolescent AIDS Clinical Trials; AIDS, acquired immune deficiency syndrome; HIV, human immunodeficiency virus.

Table 1

Maternal to Child Transmission of HIV by Gestational Age at Delivery (≥ 40 weeks vs. <40 weeks), among the **NISDI and P1025 populations** (N=2250)

	Gestational Age at Delivery			
	40 weeks N=621	<40 weeks N=1629	Overall N=2250	
Final Infant HIV Infection Status	N (%) 95% CI	N (%) 95% CI	N (%) 95% CI*	P-value*
Infected	3 (0.5) 0.2–1.4	5 (0.3) 0.1–0.7	8 (0.4) 0.2–0.8	0.77

* From Poisson distribution

Abbreviations: HIV=Human Immunodeficiency Virus, NISDI=NICHD International Site Development Initiative,

Table 2Timing of Maternal to Child Transmission of HIV among the **NISDI population** (N=916)

Timing of infant HIV transmission	EGA		
	40 weeks	<40 weeks	Total
In Utero	2	1	3
Intrapartum	0	2	2
Intrapartum or postnatal	0	1	1
Total	2	4	6

Abbreviations: HIV=Human Immunodeficiency Virus, EGA=Estimated Gestational Age

Table 3

Maternal Characteristics and Outcomes by Gestational Age at Delivery

Characteristic [*]	Gestational Age		Overall (N = 919)	P-value [†]
	40 wk (N = 306)	<40 wk (N = 613)		
Maternal age at delivery (years):				
Mean±SD	28.6±5.8	28.2±5.9	28.3±5.8	0.35‡
Median	28.0	28.0	28.0	
HIV viral load at time of delivery (copies/mL):				
Mean±SD	143.2±158.4	156.7±155.1	152.2±156.3	0.045‡
Median	90.5	200.0	200.0	
Mode of delivery, n (%)				
ECS	77 (25.2)	276 (45.2)	353 (38.5)	<.0001
NECS	51 (16.7)	111 (18.2)	162 (17.7)	
Vaginal	178 (58.2)	224 (36.7)	402 (43.8)	
Unknown	0	2	2	
<i>Antepartum complications</i>				
Abruption (pre-delivery), n (%):				
	0 (0.0)	1 (0.2)	1 (0.1)	1.00‡
Breech position, n (%):				
	7 (2.3)	17 (2.8)	24 (2.6)	0.66
Oligohydramnios or polyhydramnios, n (%):				
	1 (0.3)	6 (1.0)	7 (0.8)	0.43‡
Preeclampsia, n (%):				
	5 (1.6)	5 (0.8)	10 (1.1)	0.31‡
Gestational hypertension, n (%):				
	8 (2.6)	19 (3.1)	27 (2.9)	0.68
Fetal Growth Restriction, n (%):				
	1 (0.3)	5 (0.8)	6 (0.7)	0.67‡
Cholestasis, n (%):				
	0 (0.0)	1 (0.2)	1 (0.1)	1.00‡
<i>Intrapartum complications</i>				
Maternal fever, n (%):				
	2 (0.7)	0 (0.0)	2 (0.2)	0.11‡
Chorioamnionitis, n (%):				
	1 (0.3)	2 (0.3)	3 (0.3)	1.00‡
Meconium-stained fluid, n (%):				
	58 (19.0)	70 (11.4)	128 (13.9)	0.0019
Abruption intrapartum, n (%):				
	0 (0.0)	2 (0.3)	2 (0.2)	1.00‡
<i>Maternal Postpartum complications</i>				
Postpartum Length of stay (days):				
Mean±SD	3.0±1.6	3.3±2.3	3.2±2.1	0.047
Median	3.0	3.0	3.0	

Characteristic [*]	Gestational Age		Overall (N = 919)	P-value [†]
	40 wk (N = 306)	<40 wk (N = 613)		
Maternal Postpartum complications - up to 6 weeks				
Pregnancy induced hypertension, n (%):	1 (0.3)	0 (0.0)	1 (0.1)	0.33‡
Endometritis, n (%):	5 (1.6)	6 (1.0)	11 (1.2)	0.52‡
Wound complications (infection, seroma, hematoma, dehiscence), n (%):	6 (2.0)	13 (2.1)	19 (2.1)	0.87
Postpartum Hemorrhage, n (%):	1 (0.3)	0 (0.0)	1 (0.1)	0.33‡
Fever, n (%):	9 (2.9)	9 (1.5)	18 (2.0)	0.13
Mastitis, n (%):	0 (0.0)	1 (0.2)	1 (0.1)	1.00‡
Postpartum Depression, n (%):	0 (0.0)	2 (0.3)	2 (0.2)	1.00‡
Anemia, n (%):	5 (1.6)	14 (2.3)	19 (2.1)	0.51
Hospital readmission, n (%):	6 (2.0)	7 (1.1)	13 (1.4)	0.38‡
Maternal Diagnoses: any time during pregnancy to 6 months postpartum				
Pyelonephritis, n (%):	5 (1.6)	4 (0.7)	9 (1.0)	0.17‡

* Missing are not included in percentage calculations. All percentages shown are column percentages.

[†] Categorical characteristics: P-values are from Pearson chi-square test; If the data are sparse in one or more cells the Fisher's exact test is used, denoted by an asterisk (*). Continuous characteristics: The p-values are from the Student's T-test or nonparametric Mann-Whitney U test [denoted by an asterisk (*)].

Abbreviations: wk=week, SD=standard deviation, mL=milliliter, HIV=Human Immunodeficiency Virus, EGA=Estimated Gestational Age, ECS=Cesarean section before labor and before ruptured membranes; NECS= Cesarean section after labor and/or ruptured membranes.

Table 4

Neonatal Outcomes by Gestational Age at Delivery

Characteristic, n (%) [*]	40 wk (N = 303)	<40 wk (N = 613)	Overall (N = 916)	P-value [†]
<i>Neonatal Morbidities/Outcomes of interest</i>				
Small for gestational age:	30 (9.9)	69 (11.3)	99 (10.8)	0.53
Low birth weight (<2500g):	12 (4.0)	50 (8.2)	62 (6.8)	0.017
Neonatal HIV prophylaxis:				
Other	15 (5.0)	10 (1.6)	25 (2.7)	0.0037
ZDV	288 (95.0)	603 (98.4)	891 (97.3)	
Anemia- up to 6 weeks:	3 (1.0)	16 (2.6)	19 (2.1)	0.11
Anemia- up to 6 months:	12 (4.0)	53 (8.6)	65 (7.1)	0.009
<i>Infant Diagnoses: Any time from birth to 6 months of age</i>				
Sepsis:	3 (1.0)	4 (0.7)	7 (0.8)	0.69‡
Meningitis:	2 (0.7)	1 (0.2)	3 (0.3)	0.26‡

^{*} Missing are not included in percentage calculations. All percentages shown are column percentages.

[†] P-values are from Pearson chi-square test. If the data are sparse in one or more cells the Fisher's exact test is used, denoted by an asterisk (*).

Abbreviations: wk=week, g=grams, HIV=Human Immunodeficiency Virus, ZDV=zidovudine.