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Effects of *in utero* antiretroviral exposure on longitudinal growth of HIV-exposed uninfected infants in Botswana

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Abstract

Background—The impact of *in utero* exposure to highly active antiretroviral therapy (HAART) on longitudinal growth of HIV-uninfected infants is unknown.

Methods—The Mashi and Mma Bana PMTCT intervention trials enrolled HIV-infected pregnant women at four sites in Botswana. Breastfed (BF), HIV-uninfected infants born ≥ 37 weeks were included in this analysis. Weight-for-age (WAZ), length-for-age (LAZ), and weight-for-length (WLZ) z-scores were calculated using WHO Child Growth Standards. Mean z-scores were compared between *in utero* ARV exposure groups using student's t-test, response profiles analysis and general linear mixed effects modeling.

Results—Growth of 619 HAART-exposed and 440 ZDV-exposed, HIV-uninfected infants was evaluated. Mean birth weights (BW) were 3.01 kg for HAART and 3.15 kg for ZDV-exposed infants ($p < .001$), with lower mean birth WAZ, LAZ, and WLZ among HAART-exposed infants (all $p < .001$). HAART-exposed infants had greater improvement in WAZ and WLZ from birth through 2 months ($p = 0.03$, $p < .001$ respectively). WAZ did not differ between groups from 3 through 6 months ($p = 0.26$). LAZ remained lower in HAART-exposed infants but the incidence of wasting or stunting did not differ between exposure groups.

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Conclusions—Lower weights in HAART-exposed uninfected infants at birth were rapidly corrected during the first 6 months of life.

Keywords

Prevention of mother-to-child transmission; HIV; growth

Introduction

Highly active antiretroviral therapy (HAART) during pregnancy and breastfeeding for the prevention of mother-to-child transmission (MTCT) of HIV is a highly efficacious public health intervention.^{1–5} However, both short-term and long-term effects of *in utero* HAART exposure are poorly studied, particularly in the resource limited settings. Some studies report lower birth weights among HAART-exposed infants^{6–8}, while others do not^{9–12}. Only one study has evaluated longitudinal growth of HIV-exposed uninfected infants over time by *in utero* antiretroviral (ARV) exposure, but this study grouped dual maternal therapy with triple therapy and did not evaluate HAART in isolation.¹³ At a time when developing countries are being encouraged by WHO to scale-up use of HAART during pregnancy and breastfeeding^{14,15}, understanding the broader growth implications of *in utero* HAART exposure on HIV-exposed uninfected infants represents an important public health issue.

We investigated growth patterns through six months of life by *in utero* ARV-exposure among breastfed infants enrolled in two clinical trials in Botswana.

Methods

Sources of Data

The Mashi (meaning “milk” in Setswana) and Mma Bana (meaning “mother of the baby” in Setswana) PMTCT studies were conducted at the same four study sites in southern Botswana. Both studies enrolled HIV-1 infected pregnant women regardless of baseline CD4+ cell count. The Botswana Health Research Development Committee and the Harvard School of Public Health Human Subjects Committee approved both studies, and independent Data and Safety Monitoring Boards reviewed study safety and efficacy data approximately every 6 months. Participants in both studies provided written informed consent.

The Mashi Study, described previously,^{16,17} enrolled a total of 1200 HIV-1 infected pregnant women between March 2001 and October 2003. Women received a short course of zidovudine (ZDV) 300 mg twice daily initiated at 34 weeks gestation and continued through labor. Dosing frequency was increased to every 3 hours during labor. By randomized design, half of the women participating in the Mashi study also received a single dose of NVP, as did more than half of infants (all infants received NVP following a design modification 17 months into the study). The feeding intervention randomized half of the mother-infant pairs to six months of exclusive breast feeding with six months of prophylactic ZDV for the infant, versus formula feeding with 4 weeks of prophylactic ZDV to the infant. HAART was offered as part of the Botswana National ARV program midway through the study. A total of 71 women started HAART antenatally in the Mashi Study. Infants born to Mashi study participants who took HAART during pregnancy were included in the HAART exposure group of this infant longitudinal growth analysis.

The Mma Bana Study enrolled a total of 730 HIV-1 infected pregnant women between July 2006 and May 2008 and has been described in detail previously.¹ A total of 560 women with CD4+ cell counts ≥ 200 cells/mm³ were randomized to receive either abacavir/zidovudine/

lamivudine co-formulated as Trizivir (GlaxoSmithKline) (TZV) twice daily or lopinavir/ritonavir with zidovudine/lamivudine co-formulated as Kaletra (Abbott)/Combivir (GlaxoSmithKline) (KAL/CBV) twice daily. A total of 170 women with CD4+ cell counts < 200 cells/mm³ or with an AIDS-defining illness were enrolled in an observational arm and received nevirapine/zidovudine/lamivudine (NVP/CBV) twice daily (following 2 weeks of 200 mg once-daily nevirapine) in accordance with Botswana National PMTCT Guidelines. During labor, Mma Bana participants took ZDV every three hours, regardless of their assigned treatment arm. Women initiated HAART between 18–34 weeks gestation and continued through scheduled weaning by 6 months postpartum; HAART was continued for maternal health if indicated. Infants received single-dose NVP at birth and ZDV from birth through 4 weeks of age in keeping with the Botswana National PMTCT Guidelines.

Statistical Methods

We performed a retrospective analysis comparing infant growth data during the first six months of life from qualifying infants in the Mashi and Mma Bana studies. We restricted this analysis to singleton infants carried to term (≥ 37 weeks gestational age) who were breast fed. Gestational age was calculated from an algorithm using maternal reported last menstrual period and a second trimester ultrasound. Infants born to mothers who took HAART for less than two weeks prior to delivery were excluded from the analysis. Any infant with a positive HIV-1 DNA PCR result within the first seven months of life was excluded from the analysis.

During evaluations conducted monthly in the first six months of life for both studies, each infant was weighed and his/her length was measured. These data were used to calculate z-scores for an infant's weight-for-age (WAZ), length-for-age (LAZ), and weight-for-length (WLZ) using the 2006 World Health Organization's (WHO) Child Growth Standards.¹⁸ Two key measures of infant growth that correlate with increased infant mortality include wasting and stunting.^{19–21} WHO guidelines define wasting as a weight-for-length z-score of ≥ 2 standard deviations below the norm, and stunting as a length-for-age z-score of ≥ 2 standard deviations below norm.

Statistical analyses were performed using SAS, version 9.2 (SAS Institute, Cary, North Carolina, USA). P-values for statistical tests involving a continuous normally distributed variable were derived from a two-sided Student's t-test, otherwise a Wilcoxon Rank Sum Test was employed. P-values for comparisons of categorical variables were derived from Fisher's Exact or Chi Square testing. A two-side Student's T-test was used to compare mean weight, length, WAZ, LAZ and WLZ at birth for the two exposure groups. Analysis of response profiles was used to evaluate the sequence of mean WAZ, LAZ and WLZ by exposure group over time. Linear mixed effects models were fitted separately for WAZ, WLZ, and LAZ, using a piecewise linear spline with a knot at 2 months. The models included random effects for intercept and both (early and late phase) slope, and an unstructured correlated covariance matrix was assumed for the random effects. Maternal enrollment CD4+ cell count, maternal BMI at one month postpartum as a marker of maternal nutritional status, and site of enrollment were all controlled for in the linear mixed effects model, as these attributes were found to be significant predictors of infant growth (p value < 0.05). In addition, use of the WHO's Child Growth Standards z-scores ensured that infant gender was also controlled for in the linear mixed effects model. All testing used a significance level of 0.05, with two-sided hypothesis testing and no corrections for multiple testing.

RESULTS

Baseline characteristics of comparison groups

Study schema for the Mashi and Mma Bana studies are shown in Figure 1. There were 1,877 live infants born to the 1,930 HIV-infected pregnant women enrolled in the Mashi and Mma Bana studies (Figure 2). Of live born infants, 1,856 were the product of a singleton birth. Two hundred twenty-seven infants were excluded because delivery took place before 37 weeks gestational age [204 (10.9%)] or gestational age was lacking [23 (1.2%)]. Another 517 (27.9%) Mashi study participants were excluded from the current growth analysis, as they were randomized to formula feeding. Additional exclusions included 47 infants with positive HIV-1 DNA PCR results within the first seven months of life [42 (8.7%) in the ZDV exposure group and 5 (0.8%) in the HAART exposure group], and 6 (1.0%) infants born less than 14 days after maternal HAART was initiated. In total, 619 infants with *in utero* HAART exposure and 440 infants with *in utero* ZDV exposure were included in the study.

Baseline characteristics of mothers and infants included in this analysis are presented in Table 1. Many maternal characteristics, including age, number of pregnancies, marital status, education level, and hemoglobin level at time of enrollment did not differ significantly between groups. Mothers taking HAART during pregnancy had more personal income, even after adjustment for inflation, compared to women who took ZDV during pregnancy and were more likely to have electricity at home. Over 50% of the women in each exposure group reported the current pregnancy to be either their first or second pregnancy.

The maternal enrollment CD4+ counts for women in the ZDV exposure group were higher compared with the HAART group (median 392 cells/mm³ vs. 331 cells/mm³, $p = <0.001$); 24% of infants exposed to HAART *in utero* were born to mothers with enrollment CD4+ counts < 200 cells/mm³, while only 11% of infants exposed to ZDV *in utero* were born to mothers with enrollment CD4+ counts < 200 cells/mm³. Therefore, a stratified analysis of CD4+ cell count was undertaken, based upon maternal enrollment CD4+ cell count either < 200 cells/mm³ or ≥ 200 cells/mm³ (Table 2). Baseline plasma HIV-1 RNA viral load was higher for women in the ZDV exposure group compared to women in the HAART exposure group (median 4.34 log₁₀ copies/ml vs. 4.18 log₁₀ copies/ml, $p = 0.02$).

There were no statistically significant differences in sex or distribution of gestational age of infants between the two groups. Nor was there a difference in the percent of infants born small for gestational age (SGA), defined as a weight of less than 2500 grams for an infant at 37 weeks or greater gestational age. Median duration of *in utero* exposure to HAART (12.1 weeks, range 2.6, 22.3 weeks) was longer than median duration *in utero* exposure to ZDV (5.7 weeks, range 2.0, 10.9 weeks), due to study design differences relative to gestational age at enrollment between the Mma Bana and Mashi studies.

Weight and Length at Birth

Infants exposed *in utero* to HAART had a mean birth weight z-score of -0.64 while the ZDV exposed group had a birth weight z-score of -0.34 (p -value = <0.001) (Table 2). These differences were similar for both male and female subgroups, but mean birth weight z-scores were lower for females. In a stratified analysis of normalized weight for age based on maternal enrollment CD4+ cell count of either < 200 cells/mm³ or ≥ 200 cells/mm³, mean birth weight z-score was lower if maternal CD4+ cell count was < 200 cells/mm³ compared to ≥ 200 cells/mm³ regardless of exposure group (Table 2).

Overall, the birth length z-score was also higher in the ZDV exposed group. However, in stratified analysis based upon maternal enrollment CD4+ count, this difference was only

statistically significant for infants born to mothers with CD4⁺ counts ≥ 200 cells/mm³, where the ZDV group had a mean birth length z-score of 0.08 versus a mean birth length z-score of -0.15 ($p = 0.018$). This same trend was observed in birth weight-for-length z-scores.

Growth over 6 months

Weight-for-Age—Controlling for enrollment site, maternal enrollment CD4⁺ as a binary variable (< 200 cells/mm³ or ≥ 200 cells/mm³), maternal BMI at one month postpartum, and infant gender, using a liner mixed effects model, infants exposed to HAART *in utero* had a lower birth weight z-score, but a more rapid increase in weight-for-age z-score during the first 2 months of life than the ZDV exposed infant group (p -value = 0.03). From three months through six months of life, the two groups experienced similar rates of weight gain for age (p -value = 0.26). (Figure 3)

Length for Age—In adjusted analyses, the mean change in age-adjusted length-for-age z-score differed significantly between the two exposure groups from birth through the 2 months of life (p -value = 0.002) (Figure 3). From the 3rd through 6th month of life, the mean change in the length-for-age z-score for both the HAART and ZDV exposed infants was no longer statistically different (p -value = 0.08). When comparing absolute differences in mean recumbent length at six months of life between exposure groups by gender, mean recumbent length for HAART exposed males was 0.4 cm shorter than ZDV exposed males. The difference in mean recumbent length for females by exposure group at six months of life was 1.0 cm, with HAART exposed female infants, on average having a lower recumbent length.

Weight for Length—In adjusted analyses using a linear mixed effects model, the HAART exposed group had a more rapid increase in weight-for-length z-score during the first 2 months of life compared to the ZDV exposed group (p -value < 0.0001), such that the mean for this group was higher than the mean score of the ZDV exposed group at two months of life (Figure 3). From the 3rd through the 6th months of life, the mean weight-for-length z-score in the HAART exposed group declined, reflecting a more rapid increase in length-for-age than weight-for-age. Over the same period, the ZDV exposed group had a modest increase in mean weight-for-length z-score. These distinctively different growth patterns by exposure group from the 3rd through the 6th month of life were statistically different ($p = 0.04$).

Wasting and stunting—There was no significant difference in the proportion of infants between exposure groups meeting criteria for wasting (≤ 2 standard deviations below norm for weight for length z-score) or stunting (≤ 2 standard deviations below norm for length for age z-score) at six months of life. Wasting was present in 6.02% of the ZDV exposed infants and 6.09% of the HAART exposed infants ($p = 0.96$) at 6 months of life. Stunting was present in 4.76% of the ZDV exposed group and 4.70% of the HAART exposed infants ($p = 0.96$) at 6 months of life.

DISCUSSION

This is the first study to compare early growth of infants over time following *in utero* HAART or ZDV exposure. At birth, infants exposed to HAART *in utero* had significantly lower weight, length, and weight-for-length normalized scores compared to those exposed to ZDV *in utero*. However, weight differences were not apparent by 3 months of age and the incidence of wasting (defined as weight-for-length falling more than 2 standard deviations below norm) did not differ significantly between the two groups at six months of life.

It is reassuring that mean infant weights in the HAART exposed group improved rapidly over the first three months of life, with the two exposure groups experiencing an overlapping mean normalized weight pattern from three months through six months of life. In an exploratory analysis, the normalized longitudinal growth pattern was similar for infants in the HAART exposure group, regardless of the maternal regimen. However, the lower mean birth weight for HAART exposed HIV-uninfected infants represents a potential for higher rates of early infant mortality and/or morbidity. Survival rates for low birth weight infants remains a challenge in many resource limited settings, including those where HAART is now becoming increasingly available for maternal treatment and for PMTCT. In the Mashi Study, as well as a cohort from the Zambia Exclusive Breastfeeding Study, low birth weight was associated with increased infant mortality.^{22,23} A study from Tanzania that evaluated risk factors for infant mortality among HIV-exposed infants observed that lower birth weight, but not transmission of HIV, was associated with higher mortality in the first 28 days of life; for infants who remained HIV-negative, lower birth weight continued to be associated with a higher risk of mortality after the first month of life and through the first year of life.²⁴ Therefore, infants exposed to maternal HAART may benefit from programs to optimize growth in the first several months of life in an effort to mitigate morbidity and mortality.

While HAART exposed infants were observed to have shorter normalized length-for-age throughout the first six months of life, their mean normalized weight-for-length was more age appropriate by the second month of life than the ZDV exposed cohort and there was no statistically significant difference between exposure groups in the proportion of infants with growth stunting according to WHO guidelines. Of note, we are unable to identify a biologically plausible explanation for short mean length-for-age z-score among HAART exposed infants, and this presents an opportunity for further research. The clinical significance of lower normalized length-for-age for HAART-exposed infants at 6 months of life is uncertain and should be interpreted with caution. However, as Mma Bana infants continue to be followed beyond 6 months of life, the pattern in normalized mean length can be re-evaluated and correlated with morbidity and/or mortality outcomes.

Maternal HAART provided a possible advantage to infants in terms of normalized weight-for-length, in comparison to infants exposed to *in utero* ZDV and ongoing ZDV prophylaxis during breastfeeding. Overall, the cohort of infants exposed to HAART *in utero* were observed to have normalized weight for length that approached or exceeded norms from two months of life through six months of life, while the ZDV exposure group had lower normalized weight-for-length over this same period. In resource limited settings where infants are at higher risk of infant morbidity and mortality from diarrheal disease and respiratory illnesses, infants with weight-for-length z-scores which are near normal may have a survival advantage. This hypothesis is consistent with reports of lower mortality among infants whose mothers received HAART in Malawi.²⁵ However, further studies are required to confirm whether better weight for length correlates with infant survival and whether it mediates any observed benefit from maternal HAART.

Findings of this study should be considered in the context of protocol differences, which represent the major limitation of this study. First, Mashi ZDV exposed infants received prophylactic ZDV throughout the period of breastfeeding up to six months of life, whereas Mma Bana infants only received 4 weeks of ZDV. While the reported differences at birth by exposure group were not impacted by this issue, if ZDV prophylaxis during breastfeeding affected infant growth it would represent a confounder with respect to longitudinal results. Second, mean duration of *in utero* ARV exposure differed significantly between the groups as a result of each study's enrollment protocol, and the potential impact of different exposure durations could not be evaluated. However, no differences were observed when we

included or excluded HAART-exposed infants from the Mashi cohort, and we found no trend for lower z-scores among infants with longer HAART exposure in the Mma Bana cohort (data not shown). Third, it is possible that if lower weight infants died during the period of the study at a higher rate than larger infants, then observed mean weight gain within either group could be a function of informative censoring by death. However, only 13 (2.1%) infants in the HAART exposure group and 12 (2.7%) infants in the ZDV exposure group died during the first six months of life.

Finally, while the Mashi and Mma Bana studies were conducted at the same four sites in Botswana, the Mashi study took place before the Mma Bana study and temporal differences (including limited HAART availability and lower inflation-adjusted income in the Mashi Study period) may have influenced study findings. Of note, there were no policy changes calling for nutritional, vitamin or mineral supplementation between these studies and the fact that both cohorts of infants were exclusively breastfed controlled for difference in the infants' nutritional status. We controlled for baseline CD4+ cell count differences in the linear mixed effects model, and by stratifying infant growth outcomes by maternal enrollment CD4+ cell counts as a binary variable, either < 200 cells/mm³ or ≥ 200 cells/mm³ (Table 2). Although maternal plasma HIV-1 RNA level also differed by exposure groups, it was neither a significant predictor nor an effect modifier of growth outcomes.

In summary, HIV-uninfected infants exposed *in utero* to HAART had lower birth weight than comparable infants exposed to short-course ZDV, but subsequent weight gain was rapid and approached the norm for age and sex by 3 months of life. HAART-exposure was associated with lower mean infant length throughout the first six months of life. While statistically significant, the lower mean length coupled with weight gain resulted in more age and sex appropriate normalized weight-for-length for HAART exposed infants. Higher weight-for-age z-scores have been noted to have a survival benefit.²¹ This analysis is the first to provide reassurance that lower birth weight associated with *in utero* HAART exposure does not persist during early infancy. It also highlights the importance of early and routinely scheduled health care for HAART exposed HIV-uninfected infants.

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Figure 1. Mashi and Mma Bana Mother-Infant Pair Antiretroviral Exposures for Breast Fed Infants

¹ Beginning in Oct 2002, HAART became available through the national program. Women enrolled in the Mashi Study with CD4+ counts < 200 cells/mm³ were offered HAART.

² In Aug 2002, as a result of efficacy data from a trial in Thailand, the peripartum intervention was revised to eliminate infant placebo and provide open label nevirapine to all infants to be given as a single dose within 72 hours of birth.

³ Infants in the ZDV exposure group remained on oral prophylactic ZDV up to a maximum of six months throughout the period of breast feeding.

sdNVP = single dose nevirapine, ZDV = zidovudine, BF= breast feeding, 3TC = lamivudine, rtv = ritonavir

Figure 2.
Study Eligibility

Figure 3.
Response profile analysis modeling for mean infant z-scores by ARV exposure status

Table 1

Maternal and Infant Characteristics

Maternal Characteristics	ZDV (n=440)	HAART (n=619)	p-value
Median age (years) [IQR]	26.7 [23.5–31.5]	27.5 [23.7–31.8]	0.14 [*]
Gravida Including Current Pregnancy (#, %)			0.13 [†]
1	109 (24.8%)	130 (21.9%)	
2	134 (30.5%)	197 (33.3%)	
3	78 (17.8%)	133 (22.5%)	
4 or more	118 (26.9%)	132 (22.3%)	
Screening Labs			
Median HIV-1 RNA (log ₁₀ copies/ml) [IQR]	4.34 [3.77–4.82]	4.18 [3.51–4.85]	0.02 [*]
Median CD4+ count (cells/μl) [IQR]	392 [273–521]	331 [206–463]	<0.0001 [*]
Median hemoglobin (g/dl) [IQR]	10.7 [10.0 – 11.6]	10.7 [9.9 – 11.5]	0.28 [*]
Enrollment Site (#,%)			<0.0001 [†]
Molepolole (Village)	126 (28.6%)	168 (27.1%)	
Mochudi (Village)	109 (24.8%)	117 (18.9%)	
Lobatse (Town)	104 (23.6%)	117 (18.9%)	
Gaborone (City)	101 (23.0%)	217 (35.1%)	
Marital Status (#, %)			0.89 [†]
Single	352 (80.4%)	500 (80.8%)	
Married/Cohabiting	81 (18.5%)	113 (18.2%)	
Widowed	3 (0.7%)	2 (0.3%)	
Divorced	1 (0.2%)	3 (0.5%)	
Other	1 (0.2%)	1 (0.2%)	
Education (#, %)			0.13 [†]
None or Primary	119 (27.1%)	138 (22.3%)	
Secondary	305 (69.6%)	453 (73.2%)	
University	14 (3.2%)	28 (4.5%)	
Employment (#, %)			0.0002 [‡]
Housewife	28 (6.4%)	19 (3.1%)	
Salaried – Government	27 (6.2%)	37 (6.0%)	
Salaried -Private	88 (20.1%)	100 (16.2%)	
Paid Domestic Worker	13 (3.0%)	52 (8.2%)	
Self Employed	14 (3.2%)	38 (6.1%)	
Student	5 (1.1%)	7 (1.1%)	
Unemployed	263 (60.0%)	362 (58.5%)	
Other	NA	5 (0.8%)	

Maternal Characteristics	ZDV (n=440)	HAART (n=619)	p-value
Income (#, %)[*]			<0.0001 [†]
None	275 (62.8%)	296 (47.9%)	
\$1 to \$100/month	79 (18.0%)	187 (20.3%)	
Greater than \$100/month	84(19.2%)	135 (21.8%)	
Electricity in home (#, %)			<0.0001 [†]
Yes	93 (21.2%)	215 (34.7%)	
Infant Characteristics	ZDV Exposed (n= 440)	HAART Exposed (n= 619)	p-value
Gender (#, %)			0.17 [‡]
Female	205 (46.6%)	316 (51.0%)	
Gestational Age at Birth (Weeks) (#, %)			0.72 [‡]
37 weeks	36 (8.2%)	56 (9.0%)	
38 weeks	65 (14.8%)	102 (16.5%)	
39 weeks	107 (24.3%)	160 (25.9%)	
40 weeks	112 (25.5%)	153 (24.7%)	
>40 weeks	120 (27.2%)	148 (23.9%)	
Low Birth Weight			0.08 [‡]
< 2500 grams	26 (5.9%)	55 (8.9%)	

* p-value from Wilcoxon Rank Sums test;

[†] p-value from a Fisher's Exact test;

[‡] p-value from a Chi-Square test;

^{*} Adjusted for inflation using 2001 as the base year per Botswana Central Statistics Office and using a Pula to US dollar conversion ratio of 0.22360 in effect on 1-Jan-2001.

Table 2

Infant Birth Measurements by Maternal Enrollment CD4+

	All Infants		Infants born to mothers with CD4+ ≥200 cells/μl*		Infants born to mothers with CD4+ < 200 cells/μl*	
	ZDV (n=440)	HAART (n=619)	p-value	ZDV (n=378)	HAART (n=469)	p-value
Maternal Median HIV-1 RNA (log10 copies/ml) [IQR]	4.34 [3.77–4.82]	4.18 [3.51–4.85]	0.02 [†]	4.28 [3.67–4.74]	4.03 [3.30–4.64]	<0.001 [‡]
Maternal Median CD4 count (cells/μl) [IQR]	392 [273–521]	331 [206–463]	<0.0001 [‡]	416 [316–547]	381 [293–511]	0.01 [‡]
Infant Mean Birth weight (kg)	3.15	3.01	<0.001 [‡]	3.18	3.03	<0.001 [‡]
Infant Mean Length (cm)	49.6	49.2	0.002 [‡]	50.0	49.2	0.007 [‡]
Infant Mean Birth WAZ score	−0.34	−0.64	<0.001 [‡]	−0.30	−0.60	<0.001 [‡]
Infant Mean Birth LAZ score	0.05	−0.18	0.009 [‡]	0.08	−0.15	0.018 [‡]
Infant Mean Birth WLZ score	−0.56	−0.92	0.001 [‡]	−0.53	−0.94	<0.001 [‡]

* CD4+ at enrollment missing for 15 women in the ZDV group and 3 women in the HAART group;

[†] p-value from Wilcoxon Rank Sum test;

[‡] p-value from student's t-test.