

# Receipt of PI-containing HAART During Pregnancy and Adverse Outcomes (Low Birth Weight, Preterm Birth) Among HIV-1-Infected Women in Latin America and the Caribbean: The NICHD International Site Development Initiative (NISDI) Perinatal Study



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## ORIGINAL ABSTRACT

**Background:** There have been conflicting reports, primarily from the United States and Europe, regarding maternal receipt of ART during pregnancy and adverse outcomes among their infants (low birth weight and preterm birth). We tested the hypothesis that receipt of HAART, including a protease inhibitor (PI), during pregnancy was associated with an increased risk of low birth weight (< 2500 g) and preterm birth (< 37 completed weeks of gestation) among infants of HIV-1-infected women in Latin America and the Caribbean.

**Methods:** We analyzed data from a prospective cohort study of HIV-1-infected women and their infants in Argentina, the Bahamas, Brazil, and Mexico (NISDI Perinatal Study) which began enrollment in September 2002. The study population consisted of women enrolled as of June 1, 2004, with data regarding receipt of ART during pregnancy and who delivered a live-born, singleton infant with known birth weight and gestational age. Maternal ART regimens were categorized according to the most complex regimen received during pregnancy: group 1 (zidovudine (ZDV) or 2 nucleoside reverse transcriptase inhibitors (NRTIs)), group 2 (2 NRTI + 1 PI), group 3 (2 NRTI + 1 NNRTI), group 4 (other). Covariates associated with low birth weight and preterm birth (evaluated using Fisher's exact test for categorical items, t-test for continuous variables) with p < 0.25 were included in multivariate logistic regression analyses.

**Results:** 711 women were enrolled in the cohort, and 569 subjects met the inclusion criteria. The following analyses were restricted to 516 subjects whose ART regimen was categorized in 1 of 3 groups. Incidence of low birth weight: group 1 (6 of 72; 8.3%), group 2 (37 of 233; 15.9%); group 3 (18 of 211; 8.5%). Women in group 2 were (adjusted OR = 1.9; 95% CI 0.7 to 4.8; p = 0.18), but those in group 3 were not (adjusted OR = 0.7, 95% CI 0.2 to 2.0, more likely to have low birth weight infants (group 1: reference). Incidence of preterm birth: group 1 (5 of 72; 6.9%), group 2 (28 of 232; 11.2%); group 3 (13 of 211; 6.2%). Women in group 2 were (adjusted OR = 1.5, 95% CI 0.5 to 4.1; p = 0.45), but those in group 3 were not (adjusted OR = 0.6; 95% CI 0.2 to 2.0, more likely to have infants with preterm birth (group 1: reference).

**Conclusions:** Among HIV-1-infected women in Latin America and the Caribbean, receipt of a regimen of 2 NRTI and 1 PI during pregnancy is associated with a non-statistically significant increase in risk of low birth weight and preterm birth compared with regimens containing only 1 or 2 NRTI.

## BACKGROUND / OBJECTIVES

Maternal receipt of antiretrovirals (ARVs) during pregnancy may be associated with adverse outcomes among their infants [low birth weight (LBW) and preterm birth (PB)].<sup>(1-8)</sup>

**Objectives:** To test the hypothesis that receipt of highly active antiretroviral therapy (HAART) including a protease inhibitor (PI) during pregnancy was associated with an increased risk of LBW (< 2500 grams) and PB (< 37 completed weeks of gestation) among infants of HIV-1-infected women in Latin America and the Caribbean.

## METHODS

Data from the NISDI Perinatal Protocol were analyzed (a multicenter, prospective cohort study with clinical sites in Argentina, the Bahamas, Brazil, and Mexico)

### Inclusion criteria:

- > Women enrolled in the NISDI Perinatal Protocol as of October 22, 2004
- > Delivery of a live born, singleton infant before October 22, 2004
- > Available data regarding primary variables (maternal ARV regimen during pregnancy, infant birth weight, infant gestational age).

**Statistical analysis:** Bivariate associations of each categorical predictor or risk factor (maternal receipt of antiretroviral drugs during pregnancy, maternal clinical HIV disease classification, mode of delivery, maternal hypertension, maternal use of alcohol, tobacco, marijuana, or cocaine/crack during pregnancy) with each outcome (low birth weight and preterm birth) were evaluated using Fisher's exact test. Continuous variables (maternal CD4+ at enrollment and at hospital discharge; log (base 10) RNA at enrollment and at hospital discharge) between outcome classes were compared using t-tests. Only those predictors or risk factors marginally associated with outcome (at the 25% significance level) were considered candidates for the multivariable logistic modeling. In the multivariable logistic regressions, we applied both stepwise and backward elimination strategies to exclude non-significant predictors or risk factors (5% significance level) in order to determine whether both selection procedures arrive at a concurring parsimonious model. Finally, we forced in the maternal antiretroviral drug use during pregnancy variable in both models to evaluate the trend effect in maternal antiretroviral drug use during pregnancy on each outcome variable.

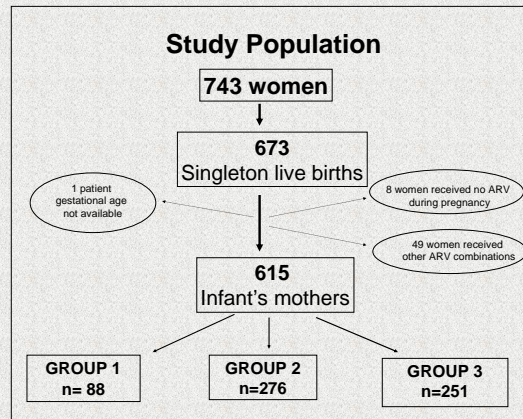
The maternal ARV regimens were grouped as follows:

- 1) Group 1: ZDV or 2 NRTIs
- 2) Group 2: 2 NRTIs and 1 PI
- 3) Group 3: 2 NRTIs and 1 NNRTI

Mode of delivery was categorized as follows:

- 1) Vaginal delivery
- 2) Cesarean section before labor and before ruptured membranes (ECS)
- 3) Cesarean section after labor and/or after ruptured membranes (NECS)

## RESULTS



### Results (Maternal ARV Regimen and Infant LBW)

Maternal ARV Regimen	Infant LBW: Yes N (%)	Infant LBW: No N (%)	TOTAL
GROUP 1	9 (10.2)	79 (89.8)	88
GROUP 2	46 (16.7)	230 (83.3)	276
GROUP 3	21 (8.4)	230 (91.6)	251
TOTAL	76 (12.4)	539 (87.6)	615

### Results (Maternal ARV Regimen and Preterm Birth (PB))

Maternal ARV Regimen	Infant PB: Yes N (%)	Infant PB: No N (%)	TOTAL
GROUP 1	7 (7.9)	81 (92.0)	88
GROUP 2	29 (10.5)	247 (89.5)	276
GROUP 3	14 (5.6)	237 (94.4)	251
TOTAL	50 (8.1)	565 (91.9)	615

### Adjusted Odds Ratios: Maternal ARV Regimen and LBW

Predictor or Risk Factor	Adjusted Odds Ratio	95 % CI	
<b>Maternal ARV regimen</b>			
Group 1 (9/88=10.2%)	1.0		
Group 2 (46/276=16.7%)	1.7	0.8	3.7
Group 3 (21/251=8.4%)	0.7	0.3	1.6
<b>Hypertensive diagnoses</b>			
Eclampsia/pre-eclampsia (7/10=70.0%)	28.4	6.7	119.9
Chronic hypertension (6/30=20.0%)	2.5	0.95	6.5
Pregnancy induced hypertension (4/16=25.0%)	5.0	1.5	17.3
No hypertension (59/559=10.6%)	1.0		
<b>Tobacco used during this pregnancy</b>			
Yes (25/141=17.7%)	2.0	1.2	3.5
No (51/474=10.8%)	1.0		

### Adjusted Odds Ratios: Maternal ARV Regimen and PB (612 patients)\*

Predictor or Risk Factor	Adjusted Odds Ratio	95 % CI	
<b>Maternal ARV regimen</b>			
Group 1 (7/88=7.9%)	1.0		
Group 2 (29/276=10.5%)	1.3	0.5	3.1
Group 3 (14/251=5.6)	0.6	0.2	1.5
<b>Mode of Delivery</b>			
ECS (25/224=11.2%)	2.4	1.1	5.3
NECS (15/120=12.5%)	3.7	1.6	8.7
Vaginal (10/268=3.7%)	1.0		
<b>Hypertensive diagnoses</b>			
Eclampsia/pre-eclampsia (6/10=60%)	20.0	4.9	80.9
Chronic hypertension (5/30=16.7%)	3.1	1.1	9.0
Pregnancy induced hypertension (1/16=6.3%)	1.3	0.2	10.5
No hypertension (38/559=6.8%)	1.0		

\* (3 patients without known mode of delivery)

## CONCLUSIONS

Among HIV-1-infected women in Latin America and the Caribbean, receipt of a regimen of 2 NRTIs and 1 PI during pregnancy is associated with a non-statistically significant increase in risk of LBW and PB compared to regimens containing only 1-2 NRTIs. The regimen of 2 NRTIs and 1 NNRTI was not associated with an increased risk of LBW or PB.

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