

Title: Risk Factors for Low Birth Weight and Preterm Delivery in the PROMISE Trial

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Abstract.

Background: Although antiretroviral therapy (ART) in pregnancy can reduce vertical HIV transmission to <1%, it may also increase the risk of low birth weight (< 2500g, LBW) and preterm delivery (<37 weeks, PTD), conditions that confer significant morbidity and mortality to newborns in resource limited settings. In the multi-site PROMISE trial, we previously reported an increased risk of LBW and PTD among women initiating protease inhibitor (PI)-based ART during pregnancy, when compared to ZDV alone. We further describe obstetrical and clinical risk factors for LBW and PTD among study participants.

Methods and Materials: Within the antepartum component of PROMISE, we assessed baseline clinical and obstetrical risk factors associated with LBW and PTD. Risk factors with p-value <0.15 in univariate logistic regression were included in multivariate backward logistic regression models. We also adjusted for treatment arm, gestational age (GA) at entry, and country.

Results: Birth outcomes were available for 3423 HIV-infected women delivering between 4/2011-11/2014 across 14 sites in Africa and Asia. Among the 3333 women delivering at least one live born infant, median maternal age at enrollment was 26 years (IQR 22–30); 661 (20%) were primiparous, and 110 (3.3%) reported at least one prior PTD. Median birth weight was 2900g (IQR 2600–3200); and 558 (17%) infants weighed \leq 2500 g. Median GA at birth was 39 weeks (IQR 38–40); 557 (17%, 95%CI: 16.1%-18.9%) were born prior to 37 weeks. In univariate analyses, clinical factors including maternal age 18-<21 year and entry RNA \geq 20,000 copies were significant for PTD but not LBW; however, maternal age 18-<21 dropped out in the backward logistic model. In the final multivariate models, adjusted for country and GA at entry, obstetrical risk factors for LBW and/or PTD included BMI, multiple gestation, prior PTD, pregnancy or chronic hypertension, IUGR, placental abruption, preterm labor, oligohydramnios, PROM, and antenatal ART were significant risk factors (table).

Conclusion: Besides receipt of antenatal PI-based ART, a number of obstetrical risk factors contributed to LBW and PTD for HIV-infected pregnant women in PROMISE. Along with optimization of ART regimens, public health interventions are needed to address modifiable obstetrical risk factors, including education of pregnant women and clinicians on early warning signs and management of pregnancy-associated complications.

Multivariate Analyses of Obstetrical and Clinical Factors Associated with LBW and PTD					
Low Birth Weight <2500gm	Adjusted Odds Ratio	95% CI	Preterm Delivery <37 wks	Adjusted Odds Ratio	95% CI
Maternal BMI at entry (ref 18-<30)					
<18.5	1.97	0.74-5.22		2.05	0.83-5.04
>=30	0.70	0.53-0.91		0.65	0.49-0.85
Multiple Gestation (ref singleton)	21.96	11.05-43.64		6.47	3.69-11.33
Prior Preterm Delivery (ref parous, no prior PTD)					
Nulliparous	1.22	0.95-1.58		1.13	0.86-1.48
Parous, at least one prior PTD	2.40	1.49-3.86		1.77	1.09-2.88
Hypertension					
Chronic Hypertension	2.31	0.89-5.96		2.63	0.98-7.04
Pregnancy Hypertension	3.38	2.08-5.50		3.54	2.18-5.76
Placental abruption	9.17	1.68-50.06		20.33	3.60-114.81
Oligohydramnios	11.04	3.49-34.90		2.62	0.87-7.90
Intrauterine Growth Restriction (IUGR)	49.09	5.66-425.66		5.61	1.20-26.18
Preterm labor	6.76	3.11-14.68		5.84	2.84-12.00
Premature Rupture of Membranes (PROM)	12.79	5.69-28.77		10.80	4.90-23.80
Treatment allocation (ref ZDV alone)					
3TC/ZDV/L/r	2.60	2.07-3.26		1.76	1.42-2.18
FTC-TDF/L/r	2.10	1.49-2.94		1.70	1.24-2.33

*Adjusted for country and gestational age.