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Birth Weight and Preterm Delivery Outcomes of Perinatally vs. non-Perinatally HIV-infected Pregnant Women in the U.S.: Results from the PHACS SMARTT study and IMPAACT P1025 Protocol

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BACKGROUND

The success of antiretroviral therapy (ART) has resulted in perinatally HIV-infected (PHIV) youth reaching reproductive age. Pregnancy outcomes of PHIV women compared to women acquiring HIV non-perinatally (nPHIV) are poorly defined.

OBJECTIVE

To assess whether maternal perinatal infection is associated with adverse birth weight and preterm delivery outcomes.

METHODS

Design: We compared birth weight (BW) and preterm delivery (PTD) outcomes of PHIV versus nPHIV pregnant women enrolled in the PHACS Surveillance Monitoring for ART Toxicities Study (SMARTT) or IMPAACT P1025 protocol.

Inclusion Criteria:
► HIV-infected pregnant women ages 13-30 years old
► Singleton live borns
► Available birth weight, gestational age, maternal mode of HIV acquisition information

Exclusion Criteria:
►HIV-infected infants

Primary Outcome:
Birth Weight (BW) measured in the following manners:
►BW *z* scores (BWZ)
►Small for Gestational Age (SGA)
►Low Birth Weight (LBW) < 2500g
►PTD (<37 weeks GA)

Predictor Variables:
Maternal PHIV status was identified by self-report, medical record review, or HIV infection documented within 5 years of birth.

Statistical analysis:
BW *z*-scores (BWZ) and small-for-gestational-age (SGA) were calculated using U.S. standards. Mixed effects models were applied to assess the association of maternal PHIV status with infant BWZ. Log binomial models using generalized estimating equations were fit for PTD and SGA outcomes.

TABLE 1. CHARACTERISTICS OF HIV-INFECTED PREGNANT WOMEN AND INFANTS

Characteristic	PHIV	NPHIV	Total	P-Value
WOMEN AT FIRST PREGNANCY	(n=235)	(n=2035)	(n=2270)	
Age, years	21 (19, 23)	25 (22, 28)	25 (22, 28)	<0.01
Race				
White/Other	91 (39%)	535 (26%)	626 (28%)	<0.01
Black	129 (55%)	1,360 (67%)	1,489 (66%)	
Unknown/ Declined	15 (6%)	140 (7%)	155 (7%)	
Hispanic Ethnicity	85 (36%)	545 (27%)	630 (28%)	<0.01
Year of Delivery				
1996-2005	16 (7%)	670 (33%)	686 (30%)	<0.01
2006-2009	80 (34%)	717 (35%)	797 (35%)	
2010-2013	138 (59%)	647 (32%)	785 (35%)	
BMI, kg/m²				
<18.5	15 (6%)	54 (3%)	69 (3%)	<0.01
18.5-24.9	86 (37%)	485 (24%)	571 (25%)	
25.0-29.9	35 (15%)	333 (16%)	368 (16%)	
30-34.9	21 (9%)	217 (11%)	238 (10%)	
35-39.9	8 (3%)	132 (6%)	140 (6%)	
≥40	11 (5%)	172 (8%)	183 (8%)	
Tobacco Use in Pregnancy	32 (14%)	397 (20%)	429 (19%)	0.01
CD4 at enrollment, cells/mm³				
<200	44 (19%)	228 (11%)	272 (12%)	0.01
200-500	107 (46%)	943 (46%)	1,050 (46%)	
>500	81 (34%)	774 (38%)	855 (38%)	
HIV RNA level at delivery, copies/mL				
≤400	164 (70%)	1,572 (77%)	1,736 (76%)	<0.01
>400-1000	12 (5%)	86 (4%)	98 (4%)	
>1000-10000	34 (14%)	158 (8%)	192 (8%)	
>10000	20 (9%)	105 (5%)	125 (6%)	
ART during pregnancy				
≥3 classes	54 (23%)	50 (2%)	104 (5%)	<0.01
INSTI-based	3 (1%)	18 (1%)	21 (1%)	
PI-based	159 (68%)	1,422 (70%)	1,581 (70%)	
NNRTI-based	3 (1%)	158 (8%)	161 (7%)	
NRTI-based	11 (5%)	233 (11%)	244 (11%)	
Non-combination ART regimen	2 (1%)	82 (4%)	84 (4%)	
No ARVs/Unknown	3 (1%)	72 (4%)	75 (4%)	
INFANTS	**PHIV (n=270)**	**NPHIV (n=2422)**	**TOTAL (n=2692)**	**P-Value**
Preterm Delivery (<37 weeks)	388 (16%)	41 (15%)	429 (16%)	0.67
Small for Gestational Age	265 (11%)	32 (12%)	297 (11%)	0.73
Low Birth Weight (<2500 g)	350 (14%)	48 (18%)	398 (15%)	0.19
Birth Weight Z score	-0.38 (-0.85, 0.18)	-0.38 (-0.96, 0.03)	-0.38 (-0.86, 0.15)	0.06

ART=antiretroviral therapy; ARVs=antiretrovirals; BMI=Body Mass Index; INSTI=Integrase Strand Transfer Inhibitor; NNRTI=Non-Nucleoside Reverse Transcriptase Inhibitor; NRTI=Nucleoside Reverse Transcriptase Inhibitor

TABLE 2. UNADJUSTED AND ADJUSTED MODELS FOR LBW, SGA, AND PRETERM DELIVERY COMPARING PHIV VS. NPHIV

LBW		SGA		Preterm Delivery	
RR (95% CI)	***p* value**	**RR (95% CI)**	***p* value**	**RR (95% CI)**	***p* value**
Unadjusted:					
1.22 (0.92,1.62)	0.17	1.06 (0.76,1.49)	0.72	0.94 (0.70,1.27)	0.69
Adjusted:*					
1.19 (0.88,1.61)	0.25	1.03 (0.71,1.49)	0.86	0.90 (0.65,1.25)	0.53

TABLE 3. MIXED MODEL FOR MEAN BIRTH WEIGHT Z SCORE COMPARING PHIV VS. NPHIV

Unadjusted Difference		Adjusted* Difference	
Mean (95% CI)	*p* value	Mean (95% CI)	*p* value
-0.11 (-0.22,-0.01)	0.03	-0.13 (-0.24, -0.01)	0.03

** All models adjusted for age, race/ethnicity, pre-pregnancy BMI, tobacco use, substance use, CD4, and maternal ART.*

RESULTS

- **From 1998-2013, 2,270 HIV-infected pregnant women delivered 2,692 newborns (270 born to PHIV and 2,422 to nPHIV women). Compared to nPHIV women, PHIV women were younger (mean age 21 vs. 25 years, *p*<0.01**
- **After adjustment, BWZ was 0.13 lower in infants of PHIV vs. nPHIV women (adjusted mean: -0.46 vs. -0.33, *p*=0.03).**
- **Black race, tobacco and substance use in pregnancy, and maternal pre-pregnancy BMI <18.5 kg/m² were also significantly associated with lower infant BWZ.**
- **No associations between maternal PHIV status and PTD or SGA were observed.**

CONCLUSIONS

- **Infants of PHIV versus nPHIV women may be at greater risk for lower BW, although the absolute difference was small.**
- **Future studies are warranted to understand mechanisms by which the intrauterine environment of PHIV women may affect fetal growth.**

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