Growth Differences in Infants Born to Perinatally vs. Non-Perinatally HIV-infected Women

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BACKGROUND

Limited information has been published on neonatal outcomes of infants born to PHIV pregnant women . In contrast to non-perinatally HIV-infected (NPHIV) pregnant women, PHIV women have been observed to have poorer immunologic status in pregnancy, lower rates of viral suppression at delivery, and higher rates of low birth weight (LBW) (<2500 g) and small-for-gestational age (SGA) outcomes in their infants.

OBJECTIVES

To evaluate growth differences between offspring of PHIV and NPHIV women during the first year of life.

METHODS

Design: Retrospective cohort study of HIV-infected pregnant women who received care and delivered a live born at two urban tertiary centers [Mount Sinai Hospital (MSH) and Johns Hopkins University Hospital (JHU)] from January 2004- March 2012.
Exclusion criteria: HIV-infected infants, twin gestations, deceased infants, those not followed at MSH or JHU.
Primary Outcome: Weight-for-age (WAZ), length-for-age (LAZ), and weight-for-length (WLZ) z-scores, calculated based on World Health Organization (WHO) child growth standards.
Exposure of Interest: Maternal mode of HIV acquisition
Predictor Variables: Maternal age, pre-pregnancy body mass index (BMI), race, substance use in pregnancy, infant birth weight (BW), infant gestational age (GA), CD4 cell count and nadirs, HIV RNA level s and combination antiretroviral therapy (cART) in pregnancy.
Statistical analysis: Loess plots were fit to compare infant WAZ, LAZ, and WLZ over time between groups. Mixed effects models were used to assess the association between maternal mode of HIV acquisition and each of the three primary growth outcomes. Models included random effects for intercept, slope, and the mother (to account for repeat pregnancies) with an unstructured covariance matrix.

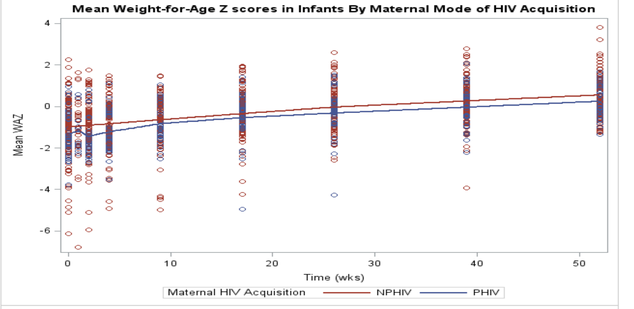
TABLE 1. CHARACTERISTICS OF WOMEN AT FIRST PREGNANCY AND INFANTS

PREGNANT WOMEN					
	PHIV (n=25)		NPHIV (n=99)		p value
Age of Mother, years (Median) (IQR)	20 (18-22)		26 (21-30)		<0.001
Race, No. (%)					0.055
White	1	(4.0)	6	(6.1)	
African American	20	(80.0)	78	(78.8)	
Hispanic	4	(16.0)	13	(13.1)	
Other	0	(0.0)	2	(2.0)	
Gravida (Median) (IQR)	1 (1-2)		3 (2-5)		<0.001
Any Substance Abuse During Pregnancy, No. (%)	4	(16.0)	22	(22.2)	0.495
Heroin/Cocaine	0	(0.0)	4	(4.1)	0.582
Marijuana	3	(12.0)	16	(16.2)	0.762
Alcohol	0	(0.0)	1	(1.0)	>0.999
Tobacco	4	(16.0)	18	(18.2)	>0.999
Maternal Height, cm (Median) (IQR)	155 (152.5-158.5)		160 (155-165)		0.009
Maternal Pre-Pregnancy BMI, kg/m² (Median) (IQR)	24.1 (22.0-28.3)		27.9 (23.5-32.2)		0.039
Nadir CD4+ cells during pregnancy, cells/mm³, No. (%)					0.004
<50 cells/mm³	5	(20.0)	2	(2.0)	
50-200 cells/mm³	4	(16.0)	11	(11.1)	
201-350 cells/mm³	5	(20.0)	24	(24.2)	
>350 cells/mm³	11	(44.0)	62	(62.7)	
HIV RNA level <400 copies/mL at delivery, No. (%)	17	(68.0)	86	(86.9)	0.036
On Second-line cART *, No. (%)	6	(24.0)	4	(4.0)	0.005
Hepatitis B co-infection, No. (%)	0	(0.0)	3	(3.1)	>0.999
Hepatitis C co-infection, No. (%)	2	(8)	5	(5.1)	0.629
INFANTS					
	Born to PHIV Women (n=32)		Born to NPHIV Women (n=120)		p value
GA at Birth, weeks (Median) (IQR)	38 (36-38)		38 (37-39)		0.402
GA at first prenatal visit, weeks (Median) (IQR)	10 (8-16)		12 (9-18)		0.306
Female Gender, No. (%)	9	(28.1)	60	(50.0)	0.030
Race, No. (%)					0.764
White	1	(3.1)	8	(6.7)	
African American	27	(84.4)	95	(79.2)	
Hispanic	4	(12.5)	15	(12.5)	
Other	0	(0.0)	2	(1.7)	
APGAR score at 5 minutes (Median) (IQR)	9 (9-9)		9 (9-9)		0.092
Preterm (<37 weeks GA), No. (%)	8 (25)		26 (21.7)		0.688
SGA at Birth, No. (%)	9 (28)		24 (20)		0.322
Birth Weight, g (Median) (IQR)	2607 (2380-3021)		2910 (2571-3269)		0.040
Birth Length, cm (Median) (IQR)	46 (45.7-48.8)		48 (46.0-50.8)		0.225
Birth Head Circumference, cm (Median) (IQR)	33.5 (32.5-34.0)		33.0 (31.0-34.5)		0.799
Birth WAZ (Median) (IQR)	-1.61 (-2.13, -0.53)		-0.81 (-1.57, -0.11)		0.032
Birth LAZ (Median) (IQR)	-1.87 (-2.20, -0.28)		-0.62 (-1.69, 0.48)		0.131
Birth WFLZ (Median) (IQR)	-1.00 (-1.78, -0.27)		-0.46 (-1.15, 0.46)		0.183
Birth HCAZ (Median) (IQR)	-0.74 (-1.54, -0.32)		-0.74 (-2.43, 0.10)		0.98

P-values from Wilcoxon test for continuous variables and Chi-square or Fisher's exact for categorical variables.
PHIV=Perinatally HIV-infected, NPHIV=Non-Perinatally HIV-infected, IQR=Interquartile Range, cART=Combination Antiretroviral Therapy, GA=Gestational Age, IQR=Interquartile Range, WAZ=Weight-for-age z score, LAZ=Length-for-age z score, WFLZ=Weight-for-length z score, HCAZ=Head Circumference-for-age z score

*Second-line cART includes: Enfuvirtide, Etravirine, Darunavir, and Raltegravir

FIGURE. MEAN WAZ AND LAZ IN INFANTS BY MATERNAL MODE OF HIV ACQUISITION



RESULTS

- **Overall, by 12 months, 9.2% (14/152) of infants remained underweight (WAZ ≤ -2), and 13.2% (20/152) remained short statured (LAZ ≤ -2).**
- **Infants of PHIV women exhibited lower mean WAZ and LAZ throughout the first year of life.**
- **After adjusting for maternal and infant confounders, the relationship between PHIV & LAZ persisted (β=-0.54, *p*=0.026).**
- **SGA for each birth anthropometric parameter [BL, BW, and BW/BL] was associated with decreased LAZ (β=-0.48, *p*=0.007), WAZ (β=-0.99, *p*<0.001) and WLZ (β=-0.36, *p*=0.027) respectively.**
- **A delivery HIV RNA level <400 copies/mL was associated with increased WAZ & WLZ (β=0.43, *p*=0.015; β=0.38, *p*=0.021).**

TABLE 2. MIXED EFFECTS MODELS OF MATERNAL/INFANT FACTORS ASSOCIATED WITH Z-SCORES OF WEIGHT, LENGTH AND WEIGHT-FOR-LENGTH IN HIV-EXPOSED UNINFECTED INFANTS

	Weight		Length		Weight-for-Length	
	Coefficient	p value	Coefficient	p value	Coefficient	p value
Maternal HIV Acquisition						
PHIV	-0.29	0.137	-0.54	0.026	0.09	0.597
NPHIV	0		0		0	
Age of mother, per year	-0.02	0.090	-0.01	0.611	-0.01	0.391
Pre-pregnancy BMI of mother	0.00	0.913	0.00	0.678	0.00	0.622
Nadir CD4 cells in pregnancy						
≤ 200 cells/mm³	0.16	0.42	0.44	0.085	-0.29	0.114
> 200 cells/mm³	0		0		0	
HIV RNA level at delivery						
< 400 copies/mL	0.43	0.015	0.17	0.443	0.38	0.021
≥ 400 copies/mL	0		0		0	
Second line ART use in pregnancy						
Not on second line ART	0.03	0.912	0.24	0.483	-0.31	0.216
On second line ART	0		0		0	
Infant SGA for BW			---	---	----	----
SGA for BW	-0.99	<0.001				
Not SGA for BW	0					
Infant SGA for BL	---	---			----	----
SGA for BL			-0.48	0.007		
Not SGA for BL			0			
Infant SGA for BW and BL	---	---	---	---		
SGA for BW and BL					-0.36	0.027
Not SGA for BW and BL					0	

CONCLUSIONS

- **Infants of PHIV women may be at increased risk for poor growth in the first year of life.**
- **Careful monitoring of these infants is essential. Further studies aimed at understanding both intrauterine and external environmental factors in PHIV women are warranted.**

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