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Maternal Vitamin D Deficiency Is Associated with Preterm Birth in HIV-infected Women

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POSTER #798

NICHD International Site Development Initiative NISDI

BACKGROUND

- Several studies in pregnant women have shown an association between low maternal vitamin D and preterm birth (PTB). HIV and antiretroviral therapy (ART) can affect vitamin D status as reflected by 25-hydroxyvitamin D (25OHD) levels. Few studies have assessed the relationship between maternal vitamin D and PTB in HIV-infected pregnant women.

OBJECTIVES

- Assess the association between maternal 25OHD levels and PTB in HIV+ pregnant women.

METHODS

- STUDY POPULATION: Prospective cohort study of maternal-infant dyads in Latin America from the NICHD International Site Development Initiative (NISDI) cohort 2002-2009
- EXCLUSION CRITERIA: HIV-infected infants, pregnancies with multiple gestations or ending in intrauterine fetal demise, stillbirths
- PRIMARY OUTCOME: PTB [spontaneous or non-spontaneous, delivery at < 37 weeks gestational age (GA)]
- EXPOSURE OF INTEREST: Maternal plasma 25-hydroxyvitamin D (25OHD) levels (Abbott Architect® immunoassay) measured on stored samples collected at 12-34 wks GA
- CONFOUNDERS: Maternal age, socio-demographics, anthropometrics, previous PTB, pre-eclampsia/eclampsia, CD4 cell count and HIV RNA level, substance use during pregnancy, and maternal ART
- STATISTICAL ANALYSIS: Characteristics of pregnant women and their infants were compared between groups using Kruskal-Wallis, chi-square, or Fisher's exact tests as appropriate. Logistic regression modeling was used to assess the association between maternal vitamin D status and PTB while adjusting for confounders.

TABLE 1. CHARACTERISTICS OF WOMEN AND INFANTS

	Maternal Vitamin D Status					
Characteristics	Severe deficiency (<10 ng/ml) (n = 13) n (%)	Deficiency (10-20 ng/ml) (n = 224) n (%)	Insufficiency (21-29 ng/ml) (n = 233) n (%)	Sufficiency (≥30 ng/ml) (n = 245) n (%)	Total (n = 715) n (%)	*p* value
MATERNAL						
Age, years						
<20	0 (0.0)	8 (3.6)	12 (5.2)	17 (6.9)	37 (5.2)	0.26
20-29	4 (30.8)	110 (49.1)	121 (51.9)	131 (53.5)	366 (51.2)	
>29	9 (69.2)	106 (47.3)	100 (42.9)	97 (39.6)	312 (43.6)	
Season during vitamin D assessment						
Autumn	2 (15.4)	55 (24.6)	70 (30.0)	96 (39.2)	223 (31.2)	<0.01
Spring	5 (38.5)	70 (31.3)	70 (30.0)	45 (18.4)	190 (26.6)	
Summer	1 (7.7)	25 (11.2)	52 (22.3)	88 (35.9)	166 (23.2)	
Winter	5 (38.5)	74 (33.0)	41 (17.6)	16 (6.5)	136 (19.0)	
Gestational age at vitamin D assessment						
≤22 weeks	3 (23.1)	86 (38.4)	75 (32.2)	73 (29.8)	237 (33.1)	0.21
CD4 count, cells/mm³ at enrollment						
<200	1 (7.7)	34 (15.2)	32 (13.8)	45 (18.4)	112 (15.7)	0.17
200-49	7 (53.8)	123 (54.9)	113 (48.7)	136 (55.7)	379 (53.2)	
≥500	5 (38.5)	67 (29.9)	87 (37.5)	63 (25.8)	222 (31.1)	
HIV RNA level, copies/mL at enrollment						
<1,000	10 (76.9)	108 (48.4)	140 (60.3)	135 (55.6)	393 (55.3)	0.07
1,000-9,999	0 (0.0)	53 (23.8)	41 (17.7)	55 (22.6)	149 (21.0)	
≥10,000	3 (23.1)	62 (27.8)	51 (22.0)	53 (21.8)	169 (23.8)	
ART regimen ≥ 28 days during pregnancy						
2NRTIs or 1NRTI	1 (7.7)	9 (4.0)	16 (6.9)	15 (6.1)	41 (5.7)	<0.01
2NRTIs+1NNRTI	6 (46.2)	39 (17.4)	41 (17.6)	41 (16.7)	127 (17.8)	
2NRTIs+1PI	4 (30.8)	48 (21.4)	55 (23.6)	88 (35.9)	195 (27.3)	
No ARV >=28 days	2 (15.4)	124 (55.4)	115 (49.4)	96 (39.2)	337 (47.1)	
Other	0 (0.0)	4 (1.8)	6 (2.6)	5 (2.0)	15 (2.1)	
Pre-eclampsia/ Eclampsia	2 (15.4)	8 (3.6)	5 (2.1)	7 (2.9)	22 (3.1)	0.12
Prior preterm birth	1 (7.7)	19 (8.5)	21 (9.0)	33 (13.5)	74 (10.3)	0.26
INFANT						
Preterm Birth	56 (22.9)	43 (18.5)	59 (26.3)	8 (61.5)	166 (23.2)	<0.01
LBW (<2500 g)	3 (23.1)	22 (9.8)	32 (13.7)	36 (14.7)	93 (13.0)	0.26
SGA	2 (15.4)	24 (10.7)	32 (13.7)	34 (13.9)	92 (12.9)	0.67

ART=combination antiretroviral therapy; LBW=Low Birth Weight; SGA=Small for gestational age

TABLE 2. LOGISTIC REGRESSION RESULTS FOR THE RELATIONSHIP BETWEEN MATERNAL VITAMIN D AND PRETERM BIRTH

Effect	Unadjusted Odds Ratio	Unadjusted 95% CI	Adjusted Odds Ratio	Adjusted 95% CI
Maternal Vitamin D Status				
Severe Deficiency (<10 ng/mL)	5.4	1.7 – 17.2	4.7	1.3 – 16.8
Deficiency (10-20 ng/mL)	1.2	0.8 – 1.8	1.3	0.8 – 2.1
Insufficiency (21-29 ng/mL)	0.9	0.5 – 1.2	0.8	0.5 – 1.3
Sufficiency (≥ 30 ng/mL)	Ref	---	Ref	---
Maternal Age, years				
<20	0.9	0.4 – 2.1	0.9	0.4 – 2.2
20-29	Ref	---	Ref	---
>29	1.1	0.8 – 1.5	1.0	0.7 – 1.5
Maternal BMI (GA-adjusted), kg/m²				
Underweight (<19.8)	1.7	1.0 – 2.7	1.8	1.1 – 3.0
Normal (19.8-26.0)	Ref	---	Ref	---
Overweight (26.1-28.9)	1.1	0.6 – 1.8	1.0	0.6 – 1.9
Obese (≥29)	1.3	0.7 – 2.2	1.0	0.6 – 1.9
Substance Use in Pregnancy	1.0	0.7 – 1.5	1.1	0.7 – 1.7
Pre-eclampsia/ Eclampsia	6.2	2.6 – 15.1	5.8	2.3 – 14.7
Prior Preterm Birth	2.5	1.5 – 4.2	2.7	1.6 – 4.6
CD4 cell count,* cells/mm³				
<200	0.9	0.5 – 1.6	0.9	0.5 – 1.7
200 – 499	1.1	0.7 – 1.6	0.9	0.6 – 1.5
≥500	Ref	---	Ref	---
HIV RNA level,* copies/mL				
<1,000	Ref	---	Ref	---
1,000 – 9,999	1.1	0.7 – 1.7	1.1	0.7 – 1.8
≥ 10,000	1.0	0.7 – 1.6	1.1	0.7 – 1.9
ART Regimen *				
2 NRTIs (dual) or 1 NRTI (mono)	1.5	0.7 – 3.1	1.5	0.7 – 3.4
2 NRTIs + 1 NNRTI	1.1	0.7 – 1.8	1.1	0.6 – 1.9
2 NRTIs + 1 PI	1.3	0.9 – 2.0	1.2	0.7 – 1.9
Other	0.6	0.1 – 2.6	0.6	0.1 – 3.0
No ARV	Ref	---	Ref	---

ART=Antiretroviral Therapy; BMI=Body Mass Index; CI=Confidence Interval; GA=Gestational Age; NRTI=Nucleoside Reverse Transcriptase Inhibitor; NNRTI=Non-Nucleoside reverse Transcriptase; Inhibitor; PI=Protease Inhibitor

* At enrollment

RESULTS

- Overall, 23.2% (166/715) of pregnancies resulted in PTB [median GA of PTBs=36 wks (Interquartile Range: 34-36)].
- In multivariate analysis, severe vitamin D deficiency was associated with PTB [adjusted Odds Ratio (aOR)=4.7, 95% Confidence Interval (CI): 1.3-16.8)].
- In stratified analyses, these results remained the same amongst women with vitamin D testing at ≤22 wks GA (aOR=2.7, 95%CI: 1.1-6.7) and those with vitamin D testing at >22 wks GA (aOR=7.0, 95%CI: 1.6-30.9).

CONCLUSIONS

HIV-infected pregnant women with severe vitamin D deficiency may be at risk for PTB. Further studies may be warranted to determine if vitamin D supplementation in HIV-infected women may impact risk of PTB.

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This work was supported by the National Institutes of Health [*Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Contract # N01-HD-3-3345 (2002-2007) and NICHD Contract #HHSN267200800001C (NICHD Control #: N01-HD-8-0001) (2007-2012)] and by Abbott® Laboratories. JJ is supported by NICHD K23HD070760.