THE MATERNAL AND CHILD HEALTH RESEARCH PROGRAM

FINAL REPORT: ASSESSMENT OF SEASONAL AND RACIAL VARIATION IN VITAMIN D DEFICIENCY OF NEWBORNS AND THEIR MOTHERS

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I. Introduction

A. Nature of the research problem

Adequate vitamin D is essential for normal human growth and development; insufficient vitamin D compromises long term health, and increases the risk of chronic disease. In recent years, reports in the medical literature have indicated that vitamin D deficiency in the US is widespread and rising.[1-19] In humans, vitamin D is derived primarily through the effect of solar ultraviolet light B radiation on 7-dehydrocholesterol in skin. Vitamin D can also be obtained from oily fish, eggs, and fortified foods like milk.[20]

Vitamin D deficiency during infancy or childhood can lead to rickets, manifested by growth retardation and bone abnormalities.[13-15,21-24] In adults, the secondary hyperparathyroidism associated with vitamin D deficiency leads to bone loss, osteoporosis, and osteomalacia, [4,6,10,25,26] and to increased risk of fracture and tooth loss. Recent research suggests that vitamin D insufficiency may be associated with a far wider range of illnesses and conditions than has previously been acknowledged. These include an increased incidence of type 1 diabetes mellitus, hypertension, multiple sclerosis, and breast, colon, and prostate cancer.[1,5,6,27-30]

One population particularly at risk of vitamin D deficiency is the maternal child health population: newborns, exclusively breastfed infants, and pregnant and newly delivered mothers. [7-9,13-15,21,22,31-36] Among pregnant women, newborns, and lactating mothers, compromised vitamin D status has far reaching effects for the fetus, the newborn, and the breastfeeding dyad;[8,9,13,15,21,22,32-37]. Consequences include, but are not limited to, rickets, retarded growth, and inadequate bone mineralization.

B. Purpose, scope, and methods of the investigation

The specific aim of this study was to examine vitamin D status in an urban population of mothers and newborns in Boston by measuring vitamin D levels in the immediate postpartum period, and to determine whether there was a correlation between maternal and infant vitamin D status. This was a cross sectional study, where blood was obtained from mothers and their infants within 72 hours of birth, and tested for levels of 25(OH)D, which is considered the best method of measuring vitamin D status.

We controlled for variables assumed to be pertinent to vitamin D status, including Impact of seasonality (hours of sunlight), use of prenatal vitamins, use of sunscreen, milk consumption, clothing habits and other measures of sunlight exposure, and maternal skin color. Skin color was categorized as “white”, “brown” or “black” according to categories derived from the Fitzpatrick skin type matrix.[38]

C. Nature of the findings

We performed analyses on 433 women and 376 newborns. Median maternal 25(OH)D was 24.8 ng/mL [95% CI: 23.2-25.8; range <5-79.2 ng/mL]. Median infant 25(OH)D was 17.2 ng/mL [95% CI 16-18.8; range <5-60.8 ng/mL]. Overall, 36% of mothers and 58%

of infants were vitamin D deficient [25(OH)D <20 ng/mL], and 23% of mothers and 38% of infants were severely deficient [25(OH)D <15 ng/mL].

Significant predictors of maternal deficiency included winter birth [AOR 4.78; 95% CI: 2.39-9.55] and dark skin color [AOR 2.74; 95% CI:1.53-4.88].Significant predictors of infant deficiency included maternal deficiency [AOR 5.28; 95% CI: 2.90-9.62]; winter compared to summer birth [AOR 3.86; 95% CI: 1.74-8.55]; African American race [AOR 3.35; 95% CI: 1.37-8.25] and maternal BMI >35 [AOR 2.78; 95% CI: 1.18-6.55].

In addition, we found that women with severe vitamin D deficiency were more likely to have a cesarean birth. Specifically, 28% of women with serum 25(OH)D <15 ng/mL had a caesarean, compared to only 14% of women with 25(OH)D ≥15 ng/mL (p=0.012). In multivariable logistic regression analysis controlling for race, age, education level, insurance status, and alcohol use, women with 25(OH)D <15 ng/mL were almost 4 times as likely to have a caesarean than women with 25(OH)D ≥15 ng/mL [AOR 3.84; 95% CI: 1.71-8.62].

II. Review of the literature

In 1898, 80% of children under two in a Boston hospital showed physical signs of rickets.[9] With the discovery of 'vitamin' D; the understanding of the role of sunlight on its production, and mass fortification, the disease became relatively rare by the mid 1900s.[39] However according to a 2003 *Lancet* article,[1] "rickets, once thought vanquished, is reappearing". Estimates drawn from the Georgia hospital records (1990-1997) and the National Hospital Discharge Survey (1990-1998) indicate a rate of nine rickets cases per million; 75% of cases appearing in Black children; 20% in White, and 5% in Asian Americans. Data from the Pediatric Research in Office Settings (January 1999-June 2000) indicated 23 to 32 cases per million; all of them in Black children. Among women of childbearing age, a study in Wales found that 50% of 160 non-European pregnant women were highly vitamin D deficient at their first prenatal visit.[40] Our own preliminary data from 2002 demonstrated that in our urban population, from a sample of 49 mother and infant pairs (65% Black; 24.5% White and 20% Hispanic), 66% of infants were severely deficient.

III. Study Design and Methods

A. **Study design:** This was a cross sectional study: blood was collected within 72 hours of birth from mothers and babies, and tested for 25(OH)D levels.

B. Population studied: The study was conducted at an urban Boston teaching hospital with 2,500 births per year, with a primarily low income, African American and Hispanic population. From January 2005 through December 2007, women were screened for eligibility and approached on the maternity service; those who agreed to participate were enrolled within 72 hours of birth.

C. Sample selection: Mother infant pairs were eligible if the mother spoke English, Spanish or French; was White, Black, or Hispanic; was not using illegal drugs, and had no history of parathryoid, renal, or liver disease. Pairs were ineligible if the infant was premature, had a congenital anomaly or was admitted to the Newborn Intensive Care Unit, or if the mother had spent more than half the pregnancy outside the greater Boston area (due to the probability that this would interfere with regional seasonal

norms for sunlight exposure). After signing informed consent, women answered a questionnaire on demographic, lifestyle and behavioral factors; additional data were obtained from the medical record. Prior to discharge from the hospital, a blood sample was obtained by venal puncture from mother and infant.

D Instruments used: Serum 25(OH)D was measured by competitive protein binding as described by Chen et al.[41] The lower limit of detection was 5 ng/mL, and the intra- and inter-assay coefficients of variation 5.0-10% and 10%-15%, respectively. The reference range was 20-100 ng/mL.

E. Statistical techniques employed

We conducted two separate analyses to examine risks for vitamin D deficiency in mothers and infants. The outcome was Vitamin D deficiency, dichotomized as <20 ng/mL versus $\geq$ 20 ng/mL, and examined separately for mothers and newborns. Explanatory variables in the maternal model were maternal socio-demographics (age, educational attainment, marital status, employment status, health insurance, WIC status, place of birth), parity, mode of delivery, hospitalization, bedrest, weight gain during pregnancy, body and mass index (BMI), and skin color (light, brown, dark). For each trimester of pregnancy, we examined prenatal vitamin use, sun exposure (frequency and duration of time spent outside, sun protective factor use), and diet. Explanatory variables in the infant model were season of birth, mother's skin color and 25(OH)D status, maternal socio-demographics, gestational age, birth weight and length, sex, Apgar score, and mother's sun exposure and prenatal vitamin use.

Differences between explanatory variables and the outcome were assessed by chi-square test for categorical variables. In cross-sectional analysis, no first trimester variables regarding sun exposure and vitamin use were associated with maternal or infant vitamin D status in exploratory analysis at $p<0.20$. We additionally used the generalized estimating equations (GEE) extension of generalized linear models to account for the within-subject correlation among the repeated measures, assuming binomial distributions with log link. None of the repeated measure variables were statistically significant in GEE except for vitamin use. Additionally, variables assessing sun exposure had low correlation between first trimester and third trimester ($r<0.27$, all measures), which was expected due to seasonal variation in weather. The correlation between first trimester vitamin use and third trimester vitamin use was 0.31. Therefore, standard logistic regression modeling was used to identify factors associated with maternal and infant vitamin D deficiency.

Variables significant at the $p<0.20$ level in exploratory analysis were examined by univariate logistic regression. Variables significant at the $p<0.20$ level by likelihood ratio testing were entered into a multivariable logistic regression model using forwards stepwise entry. Wald test p-values are presented for the final multivariable model. Data were analyzed using Stata/SE 9.2 for Windows (Stata Corp., College Station, TX).

IV. Detailed Findings

We enrolled 458 mother/infant pairs between Jan 1 2005 and Dec 31, 2007. Of these, 12 pairs were later excluded for the following reasons: 1 spent >7 months of the pregnancy outside of the United States; 2 withdrew consent, and for 9 pairs we failed to obtain either maternal or infant blood samples. In addition, 13 enrolled women and 70 infants were subsequently excluded because of failure to obtain adequate blood. Analyses were thus performed on 433 women and 376 newborns; maternal analyses were performed wherever maternal blood was available (in other words, women were not excluded from maternal analyses because their infant's blood was not available).

Median maternal 25(OH)D was 24.8 ng/mL (95% CI: 23.2-25.8 ng/mL; range <5-79.2 ng/mL). Median infant 25(OH)D was17.2 ng/ml [95% CI:16-18.8; range <5–60.8 ng/mL). Using the currently applied standard of 20 ng/mL as deficient,[42] 35.8% of mothers and 58.0% of infants were vitamin D deficient. Using 25(OH)D <15 ng/mL as a marker of severe deficiency, 23.1% of mothers and 38% of infants were severely vitamin D deficient.

A. Maternal vitamin D status

Variables associated with maternal vitamin D status in chi square analysis included season of birth, skin color, bedrest in pregnancy, use of vitamins in the third trimester, drinking milk, and sun exposure. These findings are described in Table 1 below:

Table 1: Factors significantly associated with maternal 25(OH)D status

Variable	>20 ng/ml (N=278) N (%)	<20 ng/ml (N=155) N (%)	P value
Season of birth			*<0.001*
Summer	91 (81.3)	21 (18.7)	
Fall	66 (62.9)	39 (37.1)	
Winter	45 (45.5)	54 (54.4)	
Spring	76 (65.0)	41 (35.0)	
Skin color			*<0.001*
Light	107 (76.4)	33 (23.6)	
Medium	92 (63.0)	54 (37.0)	
Dark	79 (53.7)	68 (46.3)	
Maternal race/ethnicity			*0.001*
Black	87 (53.0)	77 (47.0)	
White	35 (76.1)	11 (23.9)	
Hispanic	156 (70.0)	67 (30.0)	
Place of birth			*0.001*
Non US born	196 (70.0)	84 (30.0)	
US born	82 (53.6)	71 (46.4)	
Education			*0.008*
<High school	129 (72.1)	50 (27.9)	
High school graduate/GED	82 (61.7)	51 (38.3)	
>High school	66 (55.0)	54 (45.0)	
Bedrest in pregnancy			*0.004*
No	257 (66.2)	131 (33.8)	

Yes	19 (44.2)	24 (55.8)	
Body Mass Index			*0.014*
<35	252 (66.3)	128 (33.7)	
35+	26 (49.1)	27 (50.9)	
Prenatal vitamin use 3rd trimester			*0.008*
No	29 (49.2)	30 (50.8)	
Yes	246 (66.8)	122 (33.2)	
Frequency of prenatal vitamins 3rd trimester			*0.001*
Never, <1day/wk	34 (50.7)	33 (49.3)	
1-4days/wk	20 (48.8)	21 (51.2)	
5+ days/wk	221 (69.3)	98 (30.7)	
Ever drink milk during pregnancy			*0.004*
No	27 (47.4)	30 (52.6)	
Yes	250 (66.8)	124 (33.2)	
Employment status during pregnancy			*0.034*
No/Part-time	204 (67.1)	100 (32.9)	
Full-time	71 (56.3)	55 (46.7)	
Ave time out 3rd trimester			*0.041*
<1 hr	139 (59.9)	93 (40.1)	
1+ hr	128 (69.6)	56 (30.4)	
Average time spent outside during 2nd or 3rd trimester[1]			*0.031*
< 1 hr/day	118 (59.3)	81 (40.7)	
1+ hr/day	150 (69.4)	66 (30.6)	
Frequency of exposing arms or legs during 3rd trimester[2]			*<0.001*
0-4 days/wk	128 (56.1)	100 (43.9)	
5-7 days/wk	149 (73.4)	54 (26.6)	
Smoking status			*0.008*
Never/Prior to pregnancy	256 (66.3)	130 (33.7)	
During pregnancy	22 (46.8)	25 (53.2)	

[1] The average amount of time spent outside daily was highly correlated between 2nd and 3rd trimester (0.76), and so they were combined into a single variable.

[1] Frequency of exposing arms and legs during 1st and 2nd trimester differed significantly by mother's 25(OH)D status. However, the direction of association were clearly confounded by season (i.e., results were not in keeping with the pattern seen in the 3rd trimester of decreasing prevalence of vitamin D deficiency with increasing time spent outside.

In multivariable logistic regression, the strongest predictor of maternal vitamin D deficiency was giving birth in winter, compared to summer [AOR 4.78; 95% CI: 2.39 - 9.55]. Other statistically significant risk factors for maternal deficiency were dark skin color [AOR 2.74; 95% CI:1.53-4.88]; fall birth [AOR 2.73; 95% CI:1.41-5.32]; and US maternal birthplace [AOR 2.03; 95% CI:1.25-3.30]. Frequent vitamin use in the third trimester, drinking milk in pregnancy, and spending at least one hour per day outside during the 2nd or 3rd trimesters were protective against vitamin D deficiency.

[1] The average amount of time spent outside daily was highly correlated between 2nd and 3rd trimester (0.76), and so they were combined into a single variable.

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TABLE 2. Results of Univariate and Multivariable Logistic Regression for Risks for Maternal 25(OH)D Deficiency at Term

Variable	Crude OR	AOR (95% CI) N=410
Skin color		
Light	referent	referent
Medium	1.90 (1.14-3.18)	2.46 (1.36-4.42)
Dark	2.79 (1.68-4.63)	2.74 (1.53-4.88)
Season of birth		
Summer	referent	referent
Fall	2.56 (1.38-4.75)	2.73 (1.41-5.32)
Winter	5.20 (2.80-9.64)	4.78 (2.39-9.55)
Spring	2.34 (1.27-4.29)	1.87 (0.96-3.65)
Place of birth		
Non US born	referent	referent
US born	2.02 (1.34-3.04)	2.03 (1.25-3.30)
Prenatal vitamins/ 3rd trimester		
No vitamin use/<1 per week	referent	referent
1-4 days/week	1.08 (0.50-2.35)	0.79 (0.32-1.91)
5 or more days/week	0.46 (0.27-0.78)	0.37 (0.20-0.69)
Ever drink milk		
No	referent	referent
Yes	0.45 (0.25-0.78)	0.45 (0.24-0.87)
Time spent outside/2nd & 3rd Trimester		
<1 hr/day 2nd & 3rd T	referent	referent
≥1 hr/day 2nd or 3rd T	0.64 (0.43-0.96)	0.55 (0.34-0.87)

AOR = Adjusted Odds Ratio. All parameter estimates are adjusted for other covariates presented
CI = Confidence Interval for estimate
Variables entered from univariate analysis that were not statistically significant in multivariate analysis: maternal race (correlated with skin color, r=0.66), bed rest during pregnancy, smoking during pregnancy, educational attainment, BMI, employment status.

B. Maternal vitamin D status and cesarean birth: An unexpected finding

During preliminary data analysis, we noticed that women who gave birth by cesarean appeared to have low vitamin D status. Using data from the first two years of the study, and excluding women who had already had a previous cesarean, because of the strong correlation between primary and subsequent cesareans, we analyzed data on 253 women to determine whether any correlation existed between vitamin D status, and risk of cesarean delivery.

We assessed the statistical significance of differences in maternal factors associated with cesarean delivery using Pearson's Chi-Square test. Multivariate logistic regression analysis tested all variables with p-values <0.25 in univariate analysis. Backward selection techniques were used to derive the final model, which maintained variables with p-values $\leq$ 0.05. Statistical analyses were conducted using Stata/SE 9.2 for Windows (Stata Corp., College Station, TX).

Of the 253 women, 43 (17%) had a primary cesarean section. Reasons for cesarean included: failure to progress (17/43); non-reassuring fetal tracing (11/43); malpresentation (6/43); and 3 each of cephalopelvic disproportion, variable fetal heart rate, and other. We found that 28% of women with serum 25(OH)D <15 ng/mL had a primary cesarean section, compared to only 14% of women with 25(OH)D ≥15 ng/mL (p=0.012; unadjusted odds ratio = 2.43;[95% CI:1.20-4.92]). In addition, women who had cesareans had a lower median 25(OH)D level than women who delivered vaginally (18.0 ng/mL vs 25 ng/mL, p=0.007). Compared to women who had vaginal births, women who had cesareans were also significantly more likely to be Caucasian/non Hispanic than Black and/or Hispanic [p=0.006; OR=3.81; 95% CI: 1.47-9.86], to be US born [p=0.023; OR=2.14; 95% CI: 1.10 – 4.16], and to have used alcohol in pregnancy [p=0.039; OR=2.92; 95% CI: 1.02-8.38].

In multivariable logistic regression analysis controlling for race, age, education level, insurance status, maternal birthplace, and alcohol use, women with 25(OH)D < 15 ng/mL were almost four times as likely to have a primary cesarean section as women without deficiency [AOR 3.84; 95% CI: 1.71- 8.62].

C. Infant vitamin D status

In chi square analyses, variables associated with infant vitamin D status at birth included the mother's vitamin D status, skin color, use of prenatal vitamins, and clothing habits.

Table 3: Factors significantly associated with infant 25(OH)D status

Variable	>20 ng/mL (N=158) N (%)	<20 ng/mL (N=218) N (%)	P value
Maternal 25(OH)D			*0.000*
>20	129 (56.1)	101 (43.9)	
<20	24 (18.0)	109 (82.0)	
Season of birth			*0.000*
Summer	54 (55.7)	43 (44.3)	
Fall	38 (42.7)	51 (57.3)	
Winter	18 (20.5)	70 (79.5)	
Spring	48 (47.1)	54 (52.9)	
Maternal race/ethnicity[3]			*0.002*
Black	46 (32.6)	95 (67.4)	
White	25 (62.5)	15 (37.5)	
Hispanic	87 (44.6)	108 (55.4)	
Maternal skin color			*0.023*
Light	64 (51.6)	60 (48.4)	
Medium	51 (39.5)	78 (60.5)	
Dark	43 (35.0)	80 (65.0)	
Frequency of prenatal vitamins 1st trimester			*0.002*
< 5 days/week	35 (29.7)	83 (70.3)	
5+ days/wk	119 (48.0)	129 (52.0)	

[3] Maternal race and skin color were highly correlated (0.76). Therefore, only one of these variables was entered in multivariate regression. Maternal race/ethnicity was chosen as it explained a greater amount of variance than did skin color.

Frequency prenatal vitamins 2nd trimester			*0.001*
< 5 days/week	21 (25.0)	63 (75.0)	
5+ days/wk	136 (47.7)	149 (52.3)	
Frequency of prenatal vitamins 3rd trimester			*0.000*
< 5 days/week	23 (25.0)	69 (75.0)	
5+ days/wk	134 (48.2)	144 (51.8)	
Frequency of prenatal vitamin use[4]			*<0.001*
<5 days/week in > 1 trimester	20 (23.8)	64 (76.2)	
5+ days/week in at least 2nd & 3rd trimester	129 (48.9)	135 (51.1)	
Ever drink milk			*0.011*
No	13 (25.5)	38 (74.5)	
Yes	144 (44.4)	180 (55.6)	
Exposed arms or legs/3rd trimester			*<0.001*
0-4 days/wk	66 (33.5)	131 (66.5)	
5-7 days/wk	91 (51.4)	86 (48.6)	
Maternal BMI			0.001
<35	148 (45.3)	179 (54.7)	
35+	10 (20.4)	39 (79.6)	

Following multivariable logistic regression, risk factors for infant vitamin D deficiency that remained statistically significant included maternal 25(OH)D <20 ng/mL; [AOR 5.28; 95% CI: 2.90-9.62]; winter birth [AOR 3.86; 95% CI:1.74-8.55); African American race [AOR 3.35; 95% CI 1.37-8.25] and maternal BMI >35 [AOR 2.78; 95% CI:1.18-6.55]. Using prenatal vitamins 5 or more days a week during at least the 2nd and 3rd trimesters (compared to using prenatal vitamins less than 5 days a week in more than 2 trimesters) was strongly protective of vitamin D deficiency in the infant [AOR=0.30; 95% CI:0.16-0.56].

TABLE 4. Results of Univariate and Multivariate Logistic regression for Risks for Infant 25(OH)D Deficiency at Term

Variable	**Crude OR**	**AOR (95% CI)**
Maternal 25(OH)D		
≥ 20 ng/mL	referent	referent
<20 ng/mL	5.80 (3.47-9.69)	5.28 (2.90-9.62)
Race/ethnicity		
White	referent	referent
Hispanic	2.07 (1.03-4.16)	2.47 (1.05-5.80)
Black	3.44 (1.66-7.15)	3.36 (1.37-8.25)
Season of birth		
Summer	referent	referent
Fall	1.69 (0.94-3.01)	1.66 (0.82-3.34)
Winter	4.88 (2.54-9.40)	3.86 (1.74-8.55)
Spring	1.41 (0.81-2.47)	1.14 (0.58-2.21)
Frequency of Prenatal vitamin use		
< 5 days per week in more than one trimester	referent	referent

[4] Frequency of vitamin use in the 1st trimester was correlated with 2nd trimester (0.51) and 3rd trimester (0.38), and 2nd trimester vitamin use was correlated with 3rd trimester use (0.76). Therefore, a composite variable was created to summarize use over all trimesters.

5+ days per week during at least 2nd and 3rd trimester	0.33 (0.19-0.57)	0.30 (0.16-0.56)
BMI		
<35	referent	referent
≥35	3.22 (1.56-6.68)	2.78 (1.18-6.55)

AOR = Adjusted Odds Ratio. All parameter estimates are adjusted for other covariates presented
CI = Confidence Interval for estimate
Variables entered from univariate analysis that were not statistically significant in multivariate analysis: maternal age, clothing, ever drinking milk during pregnancy, and maternal medical problem.

V. Discussion and Interpretation of Findings

A. Conclusions to be drawn from findings

We found that, in a population of inner-city new mothers with a high proportion of dark-skinned women, vitamin D deficiency was present in 36% of newly delivered mothers, and 58% of newborn infants. Severe deficiency was present in 23% of mothers and 38% of infants. Giving birth in winter, and dark skin, were highly predictive of vitamin D deficiency in the mother, and the mother's own deficiency was strongly correlated with her infant's deficiency. In addition, we found that women with severe vitamin D deficiency were more likely to have a cesarean birth. The level of vitamin D deficiency present was worryingly high. Such low status in the maternal population, although seasonally related, indicates the probability of ongoing, chronic deficiency in an inner city community. Although the proportion of mothers who are deficient is lower than the proportion of infants, potentially it represents a greater threat, as these women are at risk for the many chronic morbidities associated with ongoing deficiency. Infant deficiency may potentially lead to rickets, however it is also possible that it represents a reflection of maternal status, and with time the infant's own status may change more quickly than the mother's status.

We were particularly interested in our unusual findings regarding low vitamin D and cesarean birth. At the turn of the 20th century "rachitic pelvis" was a common cause of obstructed labor and death in childbirth.[43] In addition, poor muscular performance[44-50] is an established symptom of vitamin D deficiency. The current US cesarean birth rate is 30.2%,[51] a "record high for the Nation;"[51] and characterized by steep increases in primary as well as repeat cesareans.[52] Common reasons for cesareans in industrialized nations include dystocia,[53] and failure to progress.[54] Recent research suggests that maternal calcium status plays a role both in preterm labor[55] and in the initiation of labor.[56] Further investigation is needed before any causal link can be made between vitamin D deficiency and cesarean birth, but theoretical possibilities exist for a potential link. Skeletal muscle contains the vitamin D receptor,[46,57] and vitamin D deficiency has been associated with proximal muscle weakness,[46] as well as with suboptimal muscle performance and strength.[44-50] Moreover, vitamin D deficiency is a possible risk factor for pre-eclampsia [58,59] Serum calcium status, which is regulated by vitamin D, plays a role in smooth muscle function in early labor.[56,60] Papandreou, et al, reported significantly higher serum calcium levels in pregnant women at the time of vaginal delivery compared to term women not in labor or women who did not labor but delivered by scheduled cesarean.[56] It was speculated that the higher serum calcium levels played a role in the mechanism of initiation of labor. Since vitamin D is important for the maintenance of calcium homeostasis, it is possible that vitamin D deficiency, which causes a slight lowering of the serum calcium, is related to both skeletal muscle and smooth muscle strength and may play a role in initiation of early labor. It is also possible that vitamin D deficiency might be related to specific types of cesareans (such as,

cephalopelvic disproportion or failure to progress) than to others (such as breech), although we did not have a large enough sample to be able to analyze this. This would be a critical area for future research.

B. Explanation of study limitations

Because our population was restricted to Black, Hispanic, and White infant mother pairs from the Greater Boston area, our results may not be generalizable to the entire population.

We chose to use 20 ng/mL as the standard for vitamin D deficiency, as this is the clinically accepted standard used in our hospital, and children with 25(OH)D below 20 ng/mL are now treated for deficiency. However, few clinical markers have been linked with vitamin D deficiency in children beyond rickets, thus the use of 20 ng/mL to describe deficiency is not necessarily indicative of clinical implications in the infant population.

C. Comparison with findings of other studies

Our rates of deficiency, especially in infants, are particularly high. Recently, using the same standard of deficiency (20 ng/mL) in a Boston population of infants in the first year of life, Gordon found a 12% rate of deficiency.[42] Since Gordon's population is also primarily African American, these results seem incompatible. We suggest however that the difference arose because our population was exclusively newborns, whereas hers included a range of infants under one year of age. It is possible that newborn levels are strongly related to maternal levels, and that later in the first year of life, levels increase.

No other studies thus far have linked cesarean birth with vitamin D deficiency and this is a novel finding.

D. Possible application of findings to actual MCH health care delivery situations

In 2008, the American Academy of Pediatrics revised its guidelines on vitamin D supplementation for infants and children. The original guidelines recommended 200 IU per day beginning in the first year of life;[14] the revised guidelines recommend 400 IU per day beginning in the early days of life.[61] Our data clearly show that large proportion of children are already deficient at birth, which should be taken into consideration by pediatricians, and should motivate them to comply with AAP guidelines regarding prescription of vitamin D supplements. Our findings should also make practitioners more aware of high risk groups, particularly dark skinned women, and especially those who are veiled, and prompt practitioners to recommend vitamin D supplements for women who are potentially at risk of chronic deficiency.

E. Policy implications

We note that although prenatal vitamin use in the third trimester protected women from deficiency, a large number of women who took the prenatal vitamin were still vitamin D deficient at term. There may be a need for policy change as to the recommended amount of vitamin D contained in the prenatal vitamin.

In addition, our findings on infants contain implications for future supplementation policy by the AAP and other bodies.

F. Suggestions for further research

One of the burning questions of the day is what actually constitutes vitamin D deficiency, especially in infants and young children. It is critical that some kind of

biological markers are established for the child population, in order for the numbers currently being used to describe deficiency are actually considered valid and validated. With regard to our own research, we believe that our discovery of the association between vitamin D deficiency and cesarean section merits in depth further research to explore causality. If causality is established, interventions to potentially prevent cesareans, by increasing vitamin D status in high risk pregnant women, could potentially be adopted and help to decrease the soaring cesarean birthrate.

VI. List of products

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