Determinants of vitamin D status in pregnant women and neonates

Christy G. Woolcott, PhD,[1] Yves Giguère, MD, PhD,[2] Hope A. Weiler, RD, PhD,[3] Anne Spencer, MSc,[1] Jean-Claude Forest, MD, PhD,[2] B. Anthony Armson, MD, MSc,[4] Linda Dodds, PhD[1]

ABSTRACT

OBJECTIVES: Evidence suggests a beneficial effect of vitamin D on perinatal health; however, low vitamin D status is prevalent in pregnant women and neonates. The objective was to determine factors that are associated with vitamin D status of mothers in early pregnancy and neonates.

METHODS: The study comprised 1,635 pregnant women from Quebec City and Halifax, Canada, 2002–2010. Vitamin D status was based on the concentration of 25-hydroxy-vitamin D [25(OH)D] determined with a chemiluminescence immunoassay in maternal sera collected at a median of 15 weeks' gestation and in neonatal cord sera at delivery. A questionnaire with information on potential determinants was completed midpregnancy.

RESULTS: A total of 44.8% of mothers and 24.4% of neonates had 25(OH)D concentrations <50 nmol/L. Adjusted mean (95% confidence interval) maternal 25(OH)D levels were higher in summer than in winter by 16.1 nmol/L (13.6–18.7), and in those in the highest versus the lowest category of education by 6.1 nmol/L (0.5–11.8), in BMI <25 kg/m^2 versus BMI ≥35 kg/m^2 by 8.2 nmol/L (4.0–12.3), and in the highest versus the lowest physical activity category by up to 9.5 nmol/L (2.9–16.1). Determinants of neonatal 25(OH)D levels were similar but also included maternal age, dairy intake, supplement use and 25(OH)D level.

CONCLUSION: This study suggests that vitamin D status of pregnant women and/or neonates might be improved through supplementation, adequate dairy intake, a move towards a healthy pre-pregnancy body weight, and participation in physical activity. Controlled studies are needed to determine the effectiveness of interventions aimed at these factors.

KEY WORDS: Pregnancy; newborn; vitamin D; lifestyle; epidemiology; Canada

La traduction du résumé se trouve à la fin de l'article.

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Vitamin D has long been known to be essential for calcium-phosphorus homeostasis and bone health. The recognition that vitamin D metabolites influence other physiologic processes has prompted the examination of its effect on a range of disorders, including those in pregnancy.[1] Although results among studies can be heterogeneous, evidence suggests that better vitamin D status is associated with a lower risk of gestational diabetes, pre-eclampsia, bacterial vaginosis, preterm birth, small for gestational age infants, and later child health outcomes such as low bone density, asthma and type I diabetes.[2,3]

Using the concentration of 25-hydroxy-vitamin D [25(OH)D], a vitamin D intermediate with a half-life of approximately 20 days, as the best indicator of vitamin D status that accounts for all sources of exposure, the U.S. Institute of Medicine (IOM) and Health Canada suggest that achieving at least 30 nmol/L will prevent deficiency with respect to bone health and 50 nmol/L will ensure sufficiency in practically all individuals.[4] Other groups use different cutpoints. The Canadian Paediatric Society, for example, suggests <25, 25–<75, 75–<225, and ≥225 nmol/L to define deficiency, insufficiency, optimal and pharmacologic levels respectively in pregnant women and infants.[5] Although no joint consensus exists, concentrations <50 nmol/L have been associated with an increased risk of adverse perinatal outcomes.[2]

Vitamin D is derived both endogenously and exogenously (reviewed in ref.[4]). Endogenous production occurs with epidermal exposure to sunlight and can thus be influenced by factors such as latitude and season. Exogenous sources include fortified dairy products and supplements. Other factors that may serve as proxy indicators of exposure, or that may affect the sequestration of vitamin D within adipose tissue, include race/ethnicity, socio-economic status, body mass index (BMI) and physical activity

Author Affiliations

1. Perinatal Epidemiology Research Unit, Departments of Obstetrics & Gynaecology and Pediatrics, Dalhousie University and IWK Health Centre, Halifax, NS
2. CHU de Québec Research Centre and Department of Molecular Biology, Medical Biochemistry and Pathology, Université Laval, Quebec City, QC
3. School of Dietetics and Human Nutrition, McGill University, Ste. Anne de Bellevue, QC
4. Department of Obstetrics & Gynaecology, Dalhousie University and IWK Health Centre, Halifax, NS

Correspondence: Christy G. Woolcott, PhD, Perinatal Epidemiology Research Unit, 7th Floor, Women's Site, Room G7108, IWK Health Centre, 5980 University Avenue, PO Box 9700, Halifax, NS B3K 6R8, Tel: 902-470-7087, E-mail: christy.woolcott@dal.ca

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level.[4] Given the evidence suggesting a beneficial effect of vitamin D in pregnancy and fetal dependence on maternal 25(OH)D, it is important to determine which of these factors help to identify pregnant women at risk of low vitamin D status and to estimate the effect they could have on 25(OH)D levels to inform the nature of potential interventions. However, few large studies have been conducted,[6–11] and none were in Canada. Therefore, our objective in this study of over 1,500 pregnant Canadian women was to determine the association between maternal characteristics and vitamin D status. Our second objective was to determine the association among maternal, pregnancy and fetal characteristics and neonatal cord serum [25(OH)D].

METHODS

Study design and population

The participants in this analysis comprised the control group from a nested case-control study that had been conducted within two cohorts of Canadian women in Quebec City, Quebec[12] and Halifax, Nova Scotia[13] to examine the association between vitamin D and perinatal outcomes. Specifically, the controls did not experience pregnancy loss, gestational diabetes, pre-eclampsia, preterm delivery (<37 weeks), or delivery of an infant with low birth weight (<2500 g) or small for gestational age (<10th percentile). In Quebec City, women who presented at Centre Hospitalier Universitaire de Québec for their first routine prenatal visit (2005–2008) or a dating ultrasound (2008–2010) were approached and 85% agreed to participate. Participants filled out a questionnaire at a subsequent visit, which was either for a routine ultrasound or for gestational diabetes screening. Following delivery, medical charts were reviewed. In Halifax, women presenting for routine blood testing at the IWK Blood Collection Services Laboratory before 20 weeks' gestation (2002–2005) were approached and 95% agreed to participate. Participants filled out a questionnaire during the 20th week. Following delivery, medical record review and linkage to the Nova Scotia Atlee Perinatal Database were conducted. In both cities, blood was collected at the time of recruitment and processed in each institution's clinical laboratory with centrifugation at 4°C within 30–120 minutes. Serum aliquots were stored at −70°C or −80°C until they were shipped to the laboratory on dry ice for 25(OH)D assays. In Quebec City, a blood sample was also taken from the umbilical cord at delivery and similarly processed and stored. The study was approved by the research ethics boards of the IWK Health Centre in Halifax, the Centre Hospitalier Universitaire de Québec, and McGill University in Montreal. Written informed consent was obtained at enrolment.

Data collection

Women completed questionnaires at 20–28 weeks' gestation. Information collected in both cohorts included maternal age, relationship status, education, family income, pre-pregnancy weight, height, chronic medical conditions, smoking habits and caffeine intake. Self-reported weight and height were confirmed via medical chart review. Pre-pregnancy BMI was calculated as weight divided by the square of height (kg/m^2). A second digit of "0" in the postal code was used as an indicator of rural residence. Information collected only in Quebec City included ethnicity, intake of alcoholic beverages and dairy products, supplement use in the previous month, and frequency of doing leisure time physical activity for 20–30 minutes in the previous three months. Collected only in Halifax was current use of folate-containing supplements and the Kaiser Physical Activity Survey (KPAS).[14] With the KPAS, physical activity in pregnancy was assessed in three domains (household, active living and transport, and sports and exercise); a total score that ranged from 3 to 15 and a sport and exercise score that ranged from 1 to 5 were derived.

25(OH)D assay

Concentration of 25(OH)D was determined at McGill University in the laboratory of co-author HAW using a direct, competitive chemiluminescence immunoassay run on the DiaSorin LIAISON platform2 (DiaSorin, Stillwater, MN, USA). Assays were completed in 2013, a median of 5.8 and 8.8 years after maternal bloods were collected in Quebec City and Halifax respectively. Concentrations of 25(OH)D are known to be stable after long-term freezing.[15] The antibody used is co-specific for the two possible forms (25(OH)D_3 and 25(OH)D_2). Internal quality control measures included duplicate measures of high and low controls supplied in the manufacturer kits, and a pooled serum sample from non-pregnant healthy adults. The laboratory participated in the Vitamin D External Quality Assessment Scheme and obtained a Certificate of Proficiency. The laboratory also received a quality assurance certified value from the National Institute Standards for Technology (NIST). Accuracy was measured based on the NIST vitamin D controls: there was a 3.3% difference of the All Laboratory Trimmed Mean from the NIST reference measurement procedure in October 2012 and a 6.3% difference in January 2013. The intra-batch coefficient of variation (CV) ranged from 1.4% to 7.6% and the inter-batch CV was 5.7%.

Data analysis

Factors examined as determinants of maternal [25(OH)D] in early pregnancy were those assessed by questionnaire and medical chart review (listed above), city, and season of blood draw. Analyses were done first with determinants collected in both cities and then stratified to add factors collected exclusively in each cohort. Additional factors examined as determinants of [25(OH)D] in neonatal cord blood were season of delivery, infant birth weight, and gestational age at birth; subsequent models included maternal [25(OH)D].

Factors that were independently associated with the odds of having [25(OH)D] <50 nmol/L were identified using multiple logistic regression. We used a cutpoint of 50 nmol/L to define low vitamin D status in keeping with the IOM and Health Canada[4] and to allow comparison with other studies.[6,8,10] Multiple linear regression was used to identify factors independently associated with [25(OH)D], and the mean difference in [25(OH)D] between categories of each determinant was estimated. For both linear and logistic regression analyses, a backward stepwise approach was taken, starting with a saturated model including all factors associated with the [25(OH)D] outcome with $p < 0.10$ in unadjusted analyses. Then at each step, the factor with the weakest association with the outcome (i.e., highest p-value) was eliminated and factors eliminated in previous steps that became significant were re-introduced, until only factors with $p < 0.10$

remained. Collinearity among factors was checked with the variance inflation factor (VIF), which was <10 in all models. Overall statistical significance was set at $p < 0.05$.

A sensitivity analysis that incorporated the 1,398 case participants from the base case-control study was done but the results are not presented since they were very similar to the results reported herein based on 1,635 control participants alone. All analyses were conducted using SAS version 9.2 (Cary, NC).

RESULTS

Included in the analysis were 1,635 women, of whom 416 were from Halifax and 1,219 from Quebec City (Table 1). Early pregnancy [25(OH)D] was measured at a median of 15 weeks (interquartile range: 12–15). The mean ± SD concentration of maternal 25(OH)D was 52.7 ± 16.9 nmol/L and 732 (44.8%) of mothers had levels below 50 nmol/L. In 902 Quebec City participants with a cord serum sample, the mean ± SD concentration of 25(OH)D was 67.1 ± 23.9 nmol/L and 220 (24.4%) had levels below 50 nmol/L.

Determinants of maternal vitamin D status from the analysis of both cities combined are shown in Table 1. A winter (January to April) blood draw was strongly associated with the odds of [25(OH)D] <50 nmol/L (OR = 8.1; 95% CI: 5.7–11.4, relative to summer, i.e., July to September). The odds of [25(OH)D] <50 nmol/L were also increased with low education and income, and high BMI. Maternal age, smoking and caffeine intake were associated ($p < 0.10$) with the odds of [25(OH)D] <50 nmol/L in unadjusted but not adjusted analyses. In the analyses with [25(OH)D] as a continuous variable, similar determinants were found but also included city. The mean difference in [25(OH)D] between winter and summer was 16.1 nmol/L (95% CI: 13.6–18.7), and between women with a BMI ≥35 kg/m^2 and women with a BMI <25 kg/m^2 was 8.2 nmol/L (95% CI: 4.0–12.3). Determinants included in the model explained 18% in the variability of [25(OH)D] between women. Factors unrelated to maternal [25(OH)D] were relationship status, rural residence, pre-existing hypertension and diabetes, and gestational age at blood draw.

Factors collected only in Halifax that were found to be additional determinants of maternal early pregnancy [25(OH)D] are shown in Table 2. Participating in physical activity and taking a folate-containing supplement were associated with lower odds of [25(OH)D] <50 nmol/L.

Factors collected only in Quebec City that were found to be additional determinants of maternal [25(OH)D] are shown in Table 3 and included leisure time physical activity, intake of dairy products, and ethnicity. Small numbers precluded analyses to identify specific ethnic groups that were at risk of low vitamin D status. Although intake of vitamin D in supplements was associated with a higher mean [25(OH)D] with $p < 0.10$ (the criterion for inclusion in the model), it was not significant at the 0.05 level.

Determinants of neonatal cord blood [25(OH)D] in Quebec City participants are shown in Table 4. Before considering maternal early pregnancy [25(OH)D], determinants of neonatal cord [25(OH)D] were similar to the factors associated with maternal [25(OH)D] in early pregnancy but also included maternal age and intake of vitamin D in supplements. Maternal early pregnancy [25(OH)D], measured in blood drawn a median of 24.9 weeks (interquartile range: 23.9–26.0) before delivery, was correlated with, but lower than, cord blood [25(OH)D] ($r = 0.20$, $p < 0.001$; mean difference ± SD = 15.4 nmol/L ± 25.7; $p < 0.001$). In the regression model, relative to neonates of mothers with [25(OH)D] between 50 and 75 nmol/L in early pregnancy, neonates of mothers with [25(OH)D] <30 nmol/L had concentrations that were lower by a mean of 22.8 nmol/L (95% CI: 16.1–29.5). Factors unrelated to cord blood [25(OH)D] were mother's relationship status, education, rural residence, parity, pre-existing diabetes or hypertension, smoking, caffeine intake and alcohol consumption, and neonate's birth weight and gestational age at delivery.

DISCUSSION

In this study of 1,635 pregnant women in Quebec City and Halifax (45–47°N) conducted between 2002 and 2010, 45% had concentrations of 25(OH)D below 50 nmol/L in early pregnancy (~15 weeks' gestation). As levels below 50 nmol/L are associated with an increased risk of many adverse perinatal outcomes,[2] the current study is important for showing that pregnant women have approximately 8 times the odds of having [25(OH)D] <50 nmol/L in winter than in summer. It also indicated the extent to which modifiable factors such as dairy and supplement intake, BMI and participation in physical activity influence 25(OH)D levels in an observational setting. Maternal vitamin D status was the strongest determinant of neonatal levels.

Season was strongly associated with vitamin D status in the current study. Levels were higher in summer than in winter by a mean of 16.1 nmol/L (95% CI: 13.6–18.7) in early pregnancy and of 28.8 nmol/L (95% CI: 24.4–33.1) in cord blood. Other studies conducted among pregnant women or women of reproductive age in Canada, the US and Europe show slightly lower summer-winter differences of between 7 and 12 nmol/L,[6,9,16,17] but others show very similar or slightly higher differences.[7,11,18,19] When UV radiation from the sun is not of sufficient strength to support endogenous vitamin D production,[20] reliance must be on exogenous sources. Therefore, seasonal differences can be blunted in populations with high intake of vitamin D.[19]

Supplement use among the Quebec participants in the current study was associated with a non-significant increase in mean maternal 25(OH)D concentration (5.4 nmol/L for supplement use of ≥400 IU/day vs. no use). In other observational studies, clinical trials examining women later in gestation, and the current study's examination of neonatal cord blood, significant differences over twice this magnitude have been found between supplement users and non-users.[3,7,8,17] In a recent clinical trial, a mean increase of 10.5 nmol/L from baseline (mean 14 weeks' gestation) to delivery was observed in pregnant women assigned to 400 IU/day.[21] Nevertheless, a substantial proportion of supplement users still have low vitamin D status.[8,10,17,22] In the current study, 38% of Quebec City mothers who reported supplementation above 400 IU/day had levels <50 nmol/L. This finding may be due to low adherence or a duration of use not yet long enough for circulating concentrations to reach a higher steady state.[8,23] Another explanation could be that the dose taken by these mothers was too low. Health Canada now recommends daily intake of 600 IU to ensure that almost all individuals have [25(OH)D] ≥50 nmol/L even if sun exposure is minimal,[4] and others support daily doses of 1000 IU in pregnancy.[5]

Table 1. Determinants of maternal vitamin D status in early pregnancy, Quebec City and Halifax

Determinant†	Total (*n*‡)	[25(OH)D] <50 nmol/L					Mean [25(OH)D] (nmol/L)			
		<50 nmol/L (row %)	Unadjusted		Adjusted*		Unadjusted		Adjusted* mean difference (95% CI)	
			OR	(95% CI)	OR	(95% CI)	Mean	(SD)		
Maternal age (years)										
<25	168	(51.2)	1.3	(1.0–1.9)			48.5	(15.9)		
25–<30	571	(43.8)	1.0				53.3	(16.8)		
30–<35	558	(41.4)	0.9	(0.7–1.1)			53.8	(16.7)		
≥35	224	(48.2)	1.2	(0.9–1.6)			52.4	(16.6)		
Education										
≥Some university	711	(40.9)	1.0		1.0		54.0	(16.6)	0.0	(Ref.)
≥Some college	501	(44.9)	1.2	(0.9–1.5)	1.1	(0.9–1.5)	52.9	(17.2)	−0.2	(−2.4 to 1.9)
High school	260	(50.0)	1.4	(1.1–1.9)	1.4	(1.0–1.9)	50.6	(15.7)	−1.6	(−4.5 to 1.2)
<High school	49	(59.2)	2.1	(1.2–3.8)	2.3	(1.2–4.4)	46.9	(16.7)	−6.1	(−11.8 to −0.5)
Family income										
≥$40,000	1187	(42.2)	1.0		1.0		53.7	(16.5)	0.0	(Ref.)
<$40,000	334	(52.1)	1.5	(1.2–1.9)	1.4	(1.0–1.8)	49.9	(17.0)	−2.8	(−4.8 to −0.7)
Parity										
Nulliparous	696	(45.8)	1.0		1.0		51.8	(16.0)	0.0	(Ref.)
1	627	(40.7)	0.8	(0.7–1.0)	0.8	(0.6–0.97)	54.1	(17.2)	2.7	(0.8 to 4.6)
≥2	198	(51.0)	1.2	(0.9–1.7)	1.0	(0.7–1.5)	52.3	(17.2)	2.3	(−0.4 to 5.1)
BMI (kg/m^2)										
<25	1002	(40.1)	1.0		1.0		54.6	(16.8)	0.0	(Ref.)
25–<30	311	(47.9)	1.4	(1.1–1.8)	1.4	(1.1–1.9)	51.0	(15.6)	−3.6	(−6.0 to −1.3)
30–<35	124	(55.6)	1.9	(1.3–2.7)	2.0	(1.4–3.1)	48.2	(16.5)	−6.9	(−10.4 to −3.4)
≥35	84	(65.5)	2.8	(1.8–4.5)	2.8	(1.7–4.5)	45.7	(15.4)	−8.2	(−12.3 to −4.0)
Smoking in pregnancy										
No	1243	(42.9)	1.0				53.4	(16.6)		
Yes	274	(50.7)	1.4	(1.1–1.8)			50.6	(17.0)		
Caffeine (mg/day)										
0	554	(47.3)	1.0				§			
1–<150	572	(44.6)	0.9	(0.7–1.1)						
≥150	381	(40.4)	0.8	(0.6–0.98)						
Month at blood draw										
January to April	544	(62.3)	7.2	(5.2–10.0)	8.1	(5.7–11.4)	46.5	(15.4)	−16.1	(−18.7 to −13.6)
May to June	228	(49.1)	4.2	(2.9–6.1)	4.4	(3.0–6.5)	51.7	(16.9)	−10.1	(−13.2 to −7.0)
July to September	320	(18.8)	1.0		1.0		61.8	(14.1)	0.0	(Ref.)
October to December	429	(38.2)	2.7	(1.9–3.8)	2.7	(2.0–4.1)	54.8	(16.5)	−7.5	(−10.1 to −4.8)
City										
Quebec	1134	(45.1)	§				52.1	(15.7)	0.0	(Ref.)
Halifax	387	(42.4)					55.0	(19.1)	4.3	(2.5 to 6.1)

Note: [25(OH)D] = 25-hydroxy-vitamin D concentration; BMI = body mass index; CI = confidence interval; OR = odds ratio; SD = standard deviation.
* Adjusted results shown only for determinants independently associated with [25(OH)D] with $p < 0.10$ in the model. Adjusted for other determinants for which results are shown in the column.
† Results are shown only for determinants that were associated with [25(OH)D] in unadjusted analyses with $p < 0.10$.
‡ Women with missing values for the determinants in the adjusted models are excluded from all unadjusted analyses. The total sample size is 1521. Unadjusted results shown for a determinant not included in the final adjusted models may have a smaller sample size due to missing values for that determinant.
§ Unadjusted results are not shown for factors that were not associated with [25(OH)D] in unadjusted analyses with $p < 0.10$.

Table 2. Additional determinants of maternal vitamin D status in early pregnancy, Halifax

Determinant†	Total (*n*‡)	[25(OH)D] <50 nmol/L					Mean [25(OH)D] (nmol/L)			
		<50 nmol/L (row %)	Unadjusted		Adjusted*		Unadjusted		Adjusted* mean difference (95% CI)	
			OR	(95% CI)	OR	(95% CI)	Mean	(SD)		
Sport and exercise, KPAS score										
0–<1.5	107	(52.3)	1.0		1.0		50.3	(17.8)	0.0	(Ref.)
1.5–<2.5	113	(42.5)	0.7	(0.4–1.1)	0.7	(0.4–1.2)	55.3	(20.6)	4.6	(−1.2 to 10.4)
2.5–<3.5	97	(45.4)	0.8	(0.4–1.3)	1.1	(0.6–2.1)	55.4	(18.2)	2.2	(−3.8 to 8.3)
≥3.5	71	(23.9)	0.3	(0.1–0.6)	0.3	(0.1–0.6)	61.0	(18.4)	9.5	(2.9 to 16.1)
Total physical activity, KPAS score										
0–<7	172	(49.4)	1.0				51.9	(17.9)		
7–<9	147	(42.9)	0.8	(0.5–1.2)			54.8	(19.3)		
≥9	69	(24.6)	0.3	(0.2–0.6)			63.1	(19.6)		
Folate currently										
No	28	(64.3)	1.0		1.0		49.2	(26.4)		
Yes	360	(40.8)	0.4	(0.2–0.9)	0.4	(0.1–0.96)	55.5	(18.4)		

Note: [25(OH)D] = 25-hydroxy-vitamin D concentration; CI = confidence interval; KPAS = Kaiser Physical Activity Survey; OR = odds ratio; SD = standard deviation.
* Adjusted results shown only for determinants independently associated with [25(OH)D] with $p < 0.10$. Adjusted for other determinants for which results are shown in the column plus education, income, parity, BMI, and month at blood draw.
† Results are shown only for additional determinants that were associated with [25(OH)D] in unadjusted analyses with $p < 0.10$.
‡ Women with missing values for the determinants in the adjusted models are excluded from all unadjusted analyses. The total sample size is 388. Unadjusted results shown for a determinant not included in the final adjusted models may have a smaller sample size due to missing values for that determinant.

Table 3. Additional determinants of maternal vitamin D status in early pregnancy, Quebec City

Determinant†	Total (*n*‡)	[25(OH)D] <50 nmol/L					Mean [25(OH)D] (nmol/L)			
		<50 nmol/L (row %)	Unadjusted		Adjusted*		Unadjusted		Adjusted* mean difference (95% CI)	
			OR	(95% CI)	OR	(95% CI)	Mean	(SD)		
Caucasian										
Yes	1049	(44.1)	1.0				52.3	(15.6)	0.0	(Ref.)
No	29	(62.1)	2.1	(1.0–4.4)			44.1	(17.6)	−6.9	(−12.2 to −1.6)
Physical activity in leisure time										
Never	121	(53.7)	1.0		1.0		48.4	(16.3)	0.0	(Ref.)
>0–3 times/week	849	(44.3)	0.7	(0.5–1.0)	0.7	(0.4–1.0)	52.2	(15.5)	3.4	(0.3 to 6.4)
≥4 times/week	108	(37.0)	0.5	(0.3–0.9)	0.5	(0.3–0.9)	55.7	(15.9)	6.6	(2.4 to 10.7)
Dairy products (servings/day)										
≤1	70	(58.6)	1.0		1.0		48.7	(16.1)	0.0	(Ref.)
>1–3	470	(45.7)	0.6	(0.4–0.99)	0.7	(0.4–1.3)	51.5	(15.8)	0.9	(−3.0 to 4.8)
>3	538	(41.8)	0.5	(0.3–0.8)	0.5	(0.3–0.9)	53.1	(15.5)	3.0	(−0.9 to 6.8)
Vitamin D in supplements (IU/day)										
0	131	(50.4)	1.0				49.4	(17.9)	0.0	(Ref.)
>0–400	918	(44.0)	0.8	(0.5–1.1)			52.4	(15.3)	1.8	(−1.1 to 4.8)
>400	29	(37.9)	0.6	(0.3–1.4)			55.6	(15.5)	5.4	(−1.0 to 11.9)

Note: [25(OH)D] = 25-hydroxy-vitamin D concentration; CI = confidence interval; IU = international units; OR = odds ratio; SD = standard deviation.
* Adjusted results shown only for determinants independently associated with [25(OH)D] with $p < 0.10$. Adjusted for other determinants for which results are shown in the column plus education, income, parity, BMI, and month at blood draw.
† Results are shown only for additional determinants that were associated with [25(OH)D] in unadjusted analyses with $p < 0.10$.
‡ Women with missing values for the determinants in the adjusted models are excluded from all unadjusted analyses. The total sample size is 1078. Unadjusted results shown for a determinant not included in the final adjusted models may have a smaller sample size due to missing values for that determinant.

Table 4. Determinants of neonatal cord vitamin D status, Quebec City

Determinant‡	Total (*n*§)	<50 nmol/L (row %)	Mean [25(OH)D] (nmol/L)					
			Unadjusted		Adjusted* mean difference (95% CI)		Adjusted† mean difference (95% CI)	
			Mean	(SD)				
Maternal age (years)								
<25	102	(24.5)	65.6	(23.9)	0.4	(−5.1 to 6.0)	1.5	(−3.7 to 6.6)
25–<30	358	(29.3)	64.7	(23.6)	0.0	(Ref.)	0.0	(Ref.)
30–<35	299	(19.4)	69.8	(23.8)	4.4	(0.6 to 8.3)	4.1	(0.5 to 7.7)
≥35	98	(19.4)	70.6	(23.5)	7.2	(1.6 to 12.9)	7.0	(1.8 to 12.2)
BMI (kg/m^2)								
<25	573	(22.5)	69.2	(24.4)	0.0	(Ref.)		
25–<30	175	(27.4)	63.7	(21.7)	−3.5	(−7.8 to 0.8)		
30–<35	61	(26.2)	61.4	(22.0)	−6.1	(−12.8 to 0.5)		
≥35	48	(29.2)	64.5	(23.5)	−4.5	(−11.9 to 2.9)		
Caucasian								
Yes	825	(23.5)	67.9	(23.8)	0.0	(Ref.)	0.0	(Ref.)
No	32	(40.6)	51.5	(18.9)	−14.5	(−22.0 to −7.0)	−10.7	(−17.7 to −3.8)
Physical activity in leisure time								
Never	100	(35.0)	62.2	(24.7)	0.0	(Ref.)		
>0–3 times/week	669	(22.9)	67.8	(23.7)	4.0	(−0.9 to 8.8)		
≥4 times/week	88	(21.6)	69.2	(23.4)	5.0	(−1.6 to 11.6)		
Dairy products (servings/day)								
≤1	66	(30.3)	63.2	(22.7)	0.0	(Ref.)	0.0	(Ref.)
>1–3	362	(26.8)	65.0	(24.1)	3.9	(−2.1 to 9.9)	3.0	(−2.6 to 8.5)
>3	429	(21.0)	69.8	(23.5)	7.9	(2.0 to 13.8)	5.8	(0.3 to 11.3)
Vitamin D in supplements (IU/day)								
0	110	(36.4)	61.0	(24.1)	0.0	(Ref.)	0.0	(Ref.)
>0–400	722	(22.3)	68.0	(23.5)	7.3	(2.5 to 12.1)	6.5	(2.1 to 10.9)
>400	25	(24.0)	75.1	(27.9)	12.3	(2.1 to 22.6)	10.1	(0.7 to 19.6)
Month of delivery								
January to April	291	(38.5)	56.7	(20.1)	−28.8	(−33.1 to −24.4)	−35.0	(−39.4 to −30.6)
May to June	161	(19.3)	67.5	(20.4)	−17.5	(−22.5 to −12.5)	−21.0	(−25.9 to −16.1)
July to September	207	(5.8)	85.7	(23.5)	0.0	(Ref.)	0.0	(Ref.)
October to December	198	(26.3)	63.3	(20.3)	−21.3	(−26.1 to −16.5)	−23.7	(−28.3 to −19.2)
Maternal [25(OH)D] (nmol/L)								
<30	57	(50.9)	52.3	(23.2)	–		−22.8	(−29.5 to −16.1)
30–<50	331	(27.5)	65.6	(23.8)	–		−9.9	(−13.4 to −6.4)
50–<75	410	(19.5)	69.1	(22.4)	–		0.0	(Ref.)
≥75	59	(11.9)	78.2	(26.1)	–		11.9	(5.5 to 18.3)

Note: [25(OH)D] = 25-hydroxy-vitamin D concentration; BMI = body mass index; CI = confidence interval; IU = international units; OR = odds ratio; SD = standard deviation.
* Model not considering maternal early pregnancy [25(OH)D]. Adjusted for other determinants for which results are shown in the column.
† Model incorporating maternal early pregnancy [25(OH)D]. Adjusted results shown only for determinants independently associated with [25(OH)D] with $p < 0.10$. Adjusted for other determinants for which results are shown in the column.
‡ Results are shown only for determinants that were associated with [25(OH)D] in adjusted analyses with $p < 0.10$.
§ Women with missing values for the determinants included in the fully adjusted model are excluded from all analyses. The total sample size is 857.

Vitamin D status improves with other healthful behaviours. In Canada, where milk is fortified with 100 IU vitamin D per 250 mL, dairy intake increases 25(OH)D levels.[16,17] Maternal vitamin D status has been shown in our study and others to be inversely associated with BMI across its continuum;[6,10] therefore, if the relation is found to be causal, preconception weight loss may have a beneficial effect even if women do not achieve a normal BMI. Participation in physical activity is associated with a small but significantly higher concentration of 25(OH)D in some[7,11] but not all studies,[8] possibly due to its relationship to time spent outdoors and BMI. Results from other studies have suggested that smoking is related to lower vitamin D status,[6,7,10,11] but in the current study, smoking had no relation after accounting for income and education.

Given that the fetus does not produce vitamin D but 25(OH)D crosses the placenta,[24] very high correlations have been observed between maternal levels, at or near the time of delivery, and neonatal levels.[25–28] The current study and others demonstrate that maternal levels in early pregnancy are also associated with neonatal levels.[28,29] In contrast with most other studies, which tended to examine maternal-neonatal samples closer in time[26,28–30] (except for one[25]), the concentration of 25(OH)D was not lower in neonates than in mothers in the current study. We also found that some maternal characteristics had a residual association with neonatal 25(OH)D after accounting for maternal 25(OH)D, although, unlike in another study,[30] pre-pregnancy BMI was not one such characteristic. This finding may reflect the difference in timing of the samples in the current study, but could also suggest that transfer of 25(OH)D across the placenta varies by maternal characteristics; this hypothesis would need to be tested in a large sample of maternal-neonatal dyads with contemporaneous 25(OH)D assessment.

Limitations and strengths

This study had some limitations. We did not have information on other known determinants of vitamin D status such as time spent outdoors, vacations at low latitude, sunscreen use, skin colour, and total dietary intake. Our observation that education and income persisted as independent determinants of vitamin D status suggests that either the behavioural factors need to be measured with greater precision or that other unmeasured factors also play a role in the socio-economic disparities in vitamin D status. Our determinants were also largely self-reported at a single point in time, which may not have represented the most biologically relevant time to influence 25(OH)D when it was measured. Women were recruited between 2002 and 2010, and with an expanding variety of foods being fortified, dairy intake may now have a greater impact on vitamin D status. Because participants were recruited from urban centres at 45–47°N latitude and were mostly Caucasian, the results may not be generalizable to other populations. Finally, the women included in the analyses comprised volunteers; although the recruitment rates were high, there is the possibility that the results for the associations differ somewhat from those in the women who chose not to participate.

This study had several strengths. Our sample of over 1,500 women makes it one of the largest studies of vitamin D status in pregnancy and permitted the simultaneous consideration of many potential determinants. We were able to examine determinants of both maternal and neonatal vitamin D status. Measurement of 25(OH)D was done with a valid method in a certified laboratory with strict quality control processes.

CONCLUSION

A substantial proportion of mothers and neonates in Halifax and Quebec City had [25(OH)D] <50 nmol/L. In Canada, where vitamin D status is not routinely tested, all pregnant women and particularly those whose pregnancies span the winter months and with risk factors such as low socio-economic status, non-Caucasian ethnicity, high BMI, and low physical activity, should be encouraged to ensure optimal vitamin D status. This study suggests that vitamin D status may be improved through supplementation, adequate dairy intake, moving towards a healthy pre-pregnancy body weight, and participating in physical activity, but controlled studies are needed to determine the effectiveness of interventions aimed at these factors.

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RÉSUMÉ

OBJECTIFS : Les données semblent indiquer que la vitamine D a un effet bénéfique sur la santé périnatale, mais un faible statut en vitamine D prévaut chez les femmes enceintes et les nouveau-nés. Nous avons voulu déterminer les facteurs associés au statut en vitamine D de mères en début de grossesse et de nouveau-nés.

MÉTHODE : L'étude a compris 1 635 femmes enceintes de Québec et de Halifax, au Canada, de 2002 à 2010. Le statut en vitamine D était fondé sur la concentration de 25-hydroxyvitamine D [25(OH)D], déterminée grâce à un immunoessai par chimiluminescence dans le sérum maternel prélevé à la durée médiane de 15 semaines de grossesse et dans le sérum du cordon ombilical des nouveau-nés à l'accouchement. Au milieu de leur grossesse, les femmes ont rempli un questionnaire donnant de l'information sur les déterminants potentiels.

RÉSULTATS : En tout, 44,8 % des mères et 24,4 % des nouveau-nés avaient des concentrations de 25(OH)D <50 nmol/L. Chez les mères, les concentrations moyennes ajustées (intervalle de confiance de 95 %) de 25(OH)D étaient plus élevées de 16,1 nmol/L (13,6–18,7) l'été que l'hiver; plus élevées de 6,1 nmol/L (0,5–11,8) chez les femmes ayant le plus haut niveau d'instruction par rapport au plus bas; plus élevées de 8,2 nmol/L (4,0–12,3) chez les femmes ayant un IMC <25 kg/m^2 contre un IMC ≥35 kg/m^2; et pouvaient être plus élevées de 9,5 nmol/L (2,9–16,1) chez les femmes ayant le plus haut niveau d'activité physique par rapport au plus bas. Pour les concentrations de 25(OH)D chez les nouveau-nés, les déterminants étaient semblables aux déterminants maternels, mais incluaient aussi l'âge, l'apport en produits laitiers, l'utilisation de suppléments et la concentration de 25(OH)D des mères.

CONCLUSION : Notre étude indique que le statut en vitamine D des femmes enceintes et/ou des nouveau-nés pourrait être amélioré par la supplémentation, par un apport suffisant en produits laitiers, par un effort pour atteindre un poids-santé avant la grossesse et par la participation à l'activité physique. Il faudrait mener des études contrôlées pour déterminer l'efficacité des interventions ciblant ces facteurs.

MOTS CLÉS : grossesse; nouveau-né; vitamine D; style de vie; épidémiologie; Canada