Published in final edited form as:

J Am Coll Nutr. 2014 ; 33(5): 394–399. doi:10.1080/07315724.2013.879843.

Typical prenatal vitamin D supplement intake does not prevent decrease of plasma 25-hydroxyvitamin D at birth

Marlies K. Ozias, PhD¹, Elizabeth H. Kerling, MS, RD, LD¹, Danielle N. Christifano, MS¹, Susan A. Scholtz, PhD¹, John Colombo, PhD², and Susan E. Carlson, PhD^{1,3}

¹Department of Dietetics and Nutrition, University of Kansas Medical Center

²Department of Psychology, University of Kansas

Introduction

There is a high incidence of inadequate vitamin D status in pregnant women [1-4]. Studies report different rates of inadequacy, which may be due to stage of pregnancy when status is assessed or influence of non-dietary factors known to affect vitamin D status such as greater body mass index (BMI), latitude, season, skin pigmentation, and sun exposure. Dietary vitamin D intake of US women of childbearing age averages less than 160 IU/day [5] while the DRI RDA is 600 IU [6]. Many obstetricians recommend prenatal supplements, which contain vitamin D, to cover this gap. A recent study reported pregnant women in Canada consume a median of 400 IU/d in supplemental vitamin D throughout pregnancy [7]. A recent randomized controlled trial (RCT) conducted in pregnant women in South Carolina determined that a supplement of 400 IU/day of vitamin D maintains plasma 25-hydroxyvitamin D [25(OH)D] [8], while supplementation of 2000 and 4000 IU/d improves vitamin D status [9]. However, assessment of typical prenatal supplementation and its effect on vitamin D status (plasma 25(OH)D concentration) has not occurred in the United States. The aim of the present study was to determine if typical vitamin D supplemental intake maintained maternal vitamin D status at birth, relative to mid-pregnancy vitamin D status. Other maternal characteristics (race, season, BMI) known to influence vitamin D status were evaluated for their influence on status in addition to maternal docosahexaenoic acid (DHA) status. Our hypotheses were that typical intake of supplemental vitamin D intake would not sustain plasma 25(OH)D concentration during pregnancy and that women living at latitude 39 °N would have high prevalence of inadequate vitamin D status.

Methods

This longitudinal, cross-sectional study used tissue and data collected from consenting participants in the Kansas University DHA Outcome Study (KUDOS; NCT00266825). Women from the Kansas City metropolitan area (latitude 39 °N) were enrolled between January 2006 and November 2009 for this Phase III randomized trial funded by the National

³Corresponding author for requests and reprints: 3901 Rainbow Blvd, Mail Stop 4013, University of Kansas Medical Center, Kansas City, KS, 66160, USA; scarlon@kumc.edu, telephone (913) 588-5355, fax (913) 588-8946.

These data were presented as a poster at the 76th annual meeting of Experimental Biology, San Diego, CA, April 21-25, 2012.

Institute of Child Health and Human Development (R01HD047315) with co-funding from the Office of Dietary Supplements. A primary aim of the parent study was to determine if a daily supplement of 600 mg of DHA during pregnancy affected gestation duration and birth size, therefore we included red blood cell phospholipid DHA as percent of total fatty acids as a covariate [10]. Women enrolled were healthy, 16-36 years old with a singleton pregnancy, between 8 and 20 weeks gestation, BMI < 40, and willing to be randomized and ingest DHA or placebo capsules. BMI was determined by self-reported height and weight at enrollment. Exclusion criteria were diabetes, hypertension, or other maternal medical condition with the potential to adversely influence child development. Women consumed daily either three capsules of algal oil with a combined 600 mg DHA or three placebo capsules containing a mixture of corn and soybean oils starting between 8 and 20 weeks gestation and continuing to delivery. Medical records, health history, and socio-demographic information were collected for each subject. Race was self-reported as African-American (black), white, or other. Season of sample collection was defined as winter (December, January, February), spring, (March, April, May), summer (June, July, August), and fall (September, October, November).

We asked women the brand and frequency of supplement intake and calculated their daily supplemental vitamin D intake from the reported number of weeks of supplement use during pregnancy and the vitamin D content claimed on the label of the supplement consumed. There was an average of 400 IU vitamin D/tablet. Out of the 301 women who completed the original study, 193 had blood collected at both time points and supplemental intake data.

Plasma 25(OH)D analysis

Blood was collected at mid-pregnancy and at birth. Plasma was separated from cells by centrifugation ($3000 \times g$, $4^{\circ}C$, 10 minutes) and stored at $-80^{\circ}C$ until analysis. Quantification of plasma 25(OH)D concentration was performed using a commercial EIA (Immunodiagnostik, Bensheim, Germany; Alpco Diagnostics, Salem, NH). The EIA was performed according to the manufacturer's guidelines which included a step to separate any bound 25(OH)D from the vitamin D binding protein. All samples were assayed in duplicate. The EIA detected 25(OH)D in the range of 12 to 240 nmol/L with a 100% and 68% specificity toward 25(OH)D₃ and 25(OH)D₂, respectively. Intra- and inter-assay CV were both 7.0%.

All samples obtained at mid-pregnancy had a 25(OH)D concentration in the range of the assay; 12 samples obtained at birth (of 193 available) had a 25(OH)D concentration below the range of the assay (12 nmol/L). These 12 were included in the category of vitamin D deficiency to estimate status but did not contribute to the mean 25(OH)D concentration at birth. Institute of Medicine (IOM) guidelines were used to categorize vitamin D status based on plasma 25(OH)D concentration: vitamin D deficiency (< 30 nmol/L), vitamin D insufficiency (30 – 49.9 nmol/L), vitamin D sufficiency (50 – 125 nmol/L) and vitamin D toxicity (> 125 nmol/L) [5].

Statistical analyses

Simple descriptive statistics were used to calculate the incidence of vitamin D deficiency, insufficiency, sufficiency, and toxicity. Repeated measures ANOVA was used to determine whether certain variables influenced the change in subjects' plasma 25(OH)D concentration at birth compared to their mid-pregnancy plasma 25(OH)D concentration. Variables included in the model were average daily supplemental vitamin D intake, pre-pregnancy BMI, race, DHA status, and season in which birth occurred. There were no missing variables in our data set. Because 25(OH)D concentration at mid-pregnancy and birth were skewed positively, a square-root transformation was employed to normalize the distributions before model building. The Box-Cox procedure was used to formally identify a transformation from the family of power transformations on Y. Model assumptions were verified using the Kolmogorov-Smirnov, Shapiro-Wilk, and Breusch-Pagan tests, and the effect of multicollinearity was examined. Oneway ANOVA was used to compare 25(OH)D concentration across season of blood collection at birth. Fisher's Least Significant Difference was used to conduct pairwise comparisons. All data were analyzed with SPSS Statistics 20.0 software (SPSS, Chicago, IL) and *P*-values ≤ 0.05 were considered significant.

Results

Using IOM 2011 guidelines for vitamin D status, 49% of women had inadequate vitamin D status [deficient (< 30 nmol/L) or insufficient (30 – 49.9 nmol/L)] at mid-pregnancy and 82% at birth (Table 1). On average, plasma 25(OH)D concentration dropped 61% from mid-pregnancy to birth, and this decline remained statistically significant ($F = 6.17$, $P = 0.014$) even when controlling for variables known to affect vitamin D status. The covariates we included in the analysis of change in plasma 25(OH)D concentration at birth compared to mid-pregnancy plasma 25(OH)D concentration were maternal race, pre-pregnancy BMI, supplemental vitamin D intake, season of birth, and DHA status at delivery. Of these covariates, only season of birth significantly interacted with the observed decline in plasma 25(OH)D concentration ($F = 7.86$, $P = 0.006$); women who delivered in the summer and fall had a 1.5-fold greater concentration than women who delivered in winter and spring (41.1 ± 23.1 and 40.7 ± 20.5 nmol/L summer and fall, respectively, versus 27.7 ± 17.9 and 29.3 ± 21.4 nmol/L in winter and spring, respectively, Figure 1).

Similar to what many other clinical studies have published, season of birth ($F = 4.85$, $P < 0.029$), pre-pregnancy BMI ($F = 7.04$, $P = 0.009$), and maternal race ($F = 15.17$, $P < 0.001$) significantly influenced plasma 25(OH)D concentration at both time points while typical vitamin D supplement intake ($n = 334$ IU/d) from prenatal supplements did not have a significant effect ($F = 2.81$, $P > 0.05$). Finally, DHA status at delivery ($F = 5.38$, $P = 0.022$) significantly influenced plasma 25(OH)D concentrations ($F = 5.38$, $P = 0.022$).

Discussion

Our high rates of inadequate vitamin D status in mid-pregnancy are consistent with other reports in the United States [1-3]. While others have reported similar plasma 25(OH)D concentration in the first and third trimesters [1, 11], the 61% decline in plasma 25(OH)D concentration between mid-pregnancy and birth seen in our study has never been reported in

the United States. Coincidentally, this drop from mid-pregnancy to late in the third trimester is similar to a report from the Spanish Mediterranean coast (36 °N) [12, 13]. Because of the various factors that influence vitamin D status, it is difficult to elucidate influences of plasma 25(OH)D concentration in pregnancy. However, one of the strengths of our study was the demographic and detailed supplement intake data collected prospectively on each subject and the size of the study and the assessment of vitamin D status early and at birth. In doing so, we were able to identify season and vitamin D status at mid-pregnancy as the determinants that influenced the change in maternal vitamin D status from mid-pregnancy to birth while vitamin D intake from prenatal supplementation did not have an impact.

While race and pre-pregnancy BMI did not significantly interact with the decline in vitamin D status during pregnancy, these variables did influence 25(OH)D concentration at both time points. The effect of race (increased pigmentation) and obesity are been associated with lower vitamin D status in pregnant [1, 3, 14] as well as non-pregnant populations [15-17]. Another covariate that did not interact with the decline in vitamin D status was maternal DHA status. However, DHA status was associated with 25(OH)D concentration, a relationship also reported by Wu *et al.* [18] regarding dietary intake of DHA and vitamin D in pregnant women. Women enrolled in the KUDOS cohort were randomized to either placebo or 600 mg DHA/day and those supplemented with DHA had elevated red blood cell DHA ($7.3 \pm 2.2\%$ vs. $4.7 \pm 1.3\%$). Our cohort's consumption of fish known to contain substantial amounts of vitamin D and DHA is rather low (7% consumed tuna or salmon weekly; based on a nonstandardized food intake questionnaire to assess potential sources of dietary DHA); and therefore, dietary intake of vitamin D and DHA were similarly expected to be low. It is possible that there exists a mechanistic or regulatory relationship between 25(OH)D concentration and DHA status which should be further explored.

In this longitudinal study, we show that season of birth and the vitamin D status at mid-pregnancy (~14 weeks gestation) significantly influenced the change in vitamin D status from mid-pregnancy to birth while race, pre-pregnancy BMI, DHA status, and supplemental vitamin D intake do not. The impact of season (and ability to synthesize vitamin D) on vitamin D status is well documented [2, 19, 20]. Individuals living at latitudes greater than the 35th parallel are not able to synthesize vitamin D year round [21]. The rate of inadequate vitamin D status at the end of pregnancy in our white subjects is similar to a recent study in Sweden (58 °N) which showed season, use of prenatal supplements, and traveling to southern latitudes largely predicted maternal plasma 25(OH)D concentration at gestational weeks 35 to 37 [19]. One of our limitations in this present study is lack of data in regards to our subjects' exposure to sunlight, which is the major source of vitamin D [20]. We also only analyzed women who had given us supplemental intake information (99% of this cohort took a prenatal supplement). This precludes us from learning the effect of stage of pregnancy on vitamin D status in pregnant women who do not take supplemental vitamin D.

Several health groups have differing opinions on optimal vitamin D status and supplemental intake. The IOM published general guidelines in 2011 which included vitamin D deficiency of 30 nmol/L and 600 IU/d for pregnant women and were considered conservative by many [6]. Recent 2013 guidelines by Central Europe [22] and the US Endocrine Society in 2012 [23] set a higher threshold for vitamin D deficiency as well as supplemental intake for

pregnant women. The American College of Obstetricians and Gynecologists (ACOG) 2011 guidelines concur with the latter groups, and consider a plasma 25(OH)D concentration < 50 nmol/L in pregnancy to be deficient and recommend a daily dietary supplement of 1000-2000 IU/d of vitamin D [24].

Regardless of the varying guidelines, even our subjects at known risk for vitamin D deficiency (black, high BMI, pregnant in winter and spring) were not evaluated for vitamin D status by their obstetrician. Awareness of vitamin D deficiency among US obstetricians may have improved since the years the study was conducted (2006-2010), however, a recent editorial from the American Journal of Perinatology [25] implies that because inadequate vitamin D status in pregnancy is common (i.e., normal) it cannot have adverse effects. In fact, a number of adverse functional outcomes have been linked to poor maternal vitamin D status including risk of maternal preeclampsia [26] and gestational diabetes mellitus [27, 28]. Additionally, inadequate vitamin D status in pregnant women is associated with offspring having a greater risk of: small-for-gestational age birth [29, 30], greater adiposity at 4 and 6 years of age [31], and asthma and low bone mineral content at 9 years of age [32, 33].

A recent report concluded that vitamin D status is a major determinant of health disparities in the United States [34]. In agreement with this study, we found disparities in illness between black and white children in our study that could be accounted for by differences in vitamin D status during gestation [35]. The idea has been suggested by others [36] that RCTs designed to improve vitamin D status during pregnancy linked to functional outcomes are vital to determine optimal health for both mother and child. Such evidence has recently been obtained by Hollis' group reporting greater 25(OH)D concentrations were associated with a decreased risk of pregnancy comorbidities [37].

Conclusions

In conclusion, women living at 39 °N in the Midwestern US are at risk for inadequate vitamin D status at mid-pregnancy and experience a further decline in vitamin D status at birth that is not prevented by usual intake of prenatal supplements. Furthermore, the season in which the women gave birth influenced their vitamin D status. The solution to improving vitamin D status in US pregnant women could start with targeted evaluation of women at greatest risk for deficiency (black, latitude > 35 °N, overweight/obese BMI, season) at the start of pregnancy and implement treatment according to ACOG guidelines. At present, most prenatal vitamin supplements contain 400 IU/tablet, however, prenatal vitamin supplements with higher concentrations of vitamin D may be required especially for women at high risk of deficiency.

Acknowledgments

This study was supported by the National Institutes of Health (grant number R01 HD047315), the Office of Dietary Supplements and the Sam E. and Mary F. Roberts Endowment. The authors acknowledge Dietetics and Nutrition Department Master's students who assisted with data collection and entry from 2006 – 2012; the nursing staffs at our participating clinics and hospitals whose support was essential to recruitment and availability of blood samples; and our subjects for their time.

References

1. Bodnar L, Simhan H, Powers R, Frank M, Cooperstein E, Roberts J. High prevalence of vitamin D insufficiency in black and white pregnant women residing in the northern United States and their neonates. *J Nutr.* 2007; 137(2):447–52. [PubMed: 17237325]
2. Ginde A, Sullivan A, Mansbach J, Camargo C. Vitamin D insufficiency in pregnant and nonpregnant women of childbearing age in the United States. *Am J Obstet Gynecol.* 2010; 202(5): 436.e1–8. [PubMed: 20060512]
3. Johnson D, Wagner C, Hulsey T, McNeil R, Ebeling M, Hollis B. Vitamin D deficiency and insufficiency is common during pregnancy. *Am J Perinatol.* 2011; 28(1):7–12. Epub 2010 Jul 16. [PubMed: 20640974]
4. Sloka S, Stokes J, Randell E, Newhook LA. Seasonal variation of maternal serum vitamin D in Newfoundland and Labrador. *J Obstet Gynaecol Can.* 2009; 31(4):313–21. [PubMed: 19497150]
5. Institute of Medicine. Dietary reference intakes for calcium and vitamin D. Washington, DC: The National Academies Press; 2011.
6. Medicine IIo. , editor. Dietary reference intakes for calcium and vitamin D. Washington, DC: The National Academies Press; 2011.
7. Gomez MF, Field CJ, Olstad DL, Loehr S, Ramage S, McCargar LJ. Use of micronutrient supplements among pregnant women in Alberta: results from the Alberta Pregnancy Outcomes and Nutrition (APrON) cohort. *Matern Child Nutr.* 2013
8. Hollis BW, Johnson D, Hulsey TC, Ebeling M, Wagner CL. Vitamin D supplementation during pregnancy: double-blind, randomized clinical trial of safety and effectiveness. *J Bone Miner Res.* 2011; 26(10):2341–57. [PubMed: 21706518]
9. Wagner CL, McNeil R, Hamilton SA, Winkler J, Rodriguez Cook C, Warner G, Bivens B, Davis DJ, Smith PG, Murphy M, Shary JR, Hollis BW. A randomized trial of vitamin D supplementation in 2 community health center networks in South Carolina. *Am J Obstet Gynecol.* 2013; 208(2):137 e1–13. [PubMed: 23131462]
10. Carlson SE, Colombo J, Gajewski BJ, Gustafson KM, Mundy D, Yeast J, Georgieff MK, Markley LA, Kerling EH, Shaddy DJ. DHA supplementation and pregnancy outcomes. *Am J Clin Nutr.* 2013; 97(4):808–15. [PubMed: 23426033]
11. Milman N, Hvas A, Bergholt T. Vitamin D status during normal pregnancy and postpartum. A longitudinal study in 141 Danish women. *J Perinat Med.* 2011; 40(1):57–61.10.1515/JPM.2011.120 [PubMed: 22098305]
12. Perez-Lopez FR, Fernandez-Alonso AM, Ferrando-Marco P, Gonzalez-Salmeron MD, Dionis-Sanchez EC, Fiol-Ruiz G, Chedraui P. First trimester serum 25-hydroxyvitamin D status and factors related to lower levels in gravids living in the Spanish Mediterranean coast. *Reprod Sci.* 2011; 18(8):730–6. [PubMed: 21285449]
13. Fernandez-Alonso AM, Dionis-Sanchez EC, Chedraui P, Gonzalez-Salmeron MD, Perez-Lopez F. First-trimester maternal serum 25-hydroxyvitamin D(3) status and pregnancy outcome. *Int J Gynaecol Obstet.* 2012; 116(1):6–9. Epub 2011 Sep 28. [PubMed: 21959069]
14. Bodnar LM, Catov JM, Roberts JM, Simhan HN. Prepregnancy obesity predicts poor vitamin D status in mothers and their neonates. *J Nutr.* 2007; 137(11):2437–42. [PubMed: 17951482]
15. Gutierrez OM, Farwell WR, Kermah D, Taylor EN. Racial differences in the relationship between vitamin D, bone mineral density, and parathyroid hormone in the National Health and Nutrition Examination Survey. *Osteoporos Int.* 2011; 22(6):1745–53. [PubMed: 20848081]
16. Ginde AA, Liu MC, Camargo CA Jr. Demographic differences and trends of vitamin D insufficiency in the US population, 1988–2004. *Arch Intern Med.* 2009; 169(6):626–32. [PubMed: 19307527]
17. Lagunova Z, Porojnicu AC, Lindberg F, Hexeberg S, Moan J. The dependency of vitamin D status on body mass index, gender, age and season. *Anticancer Res.* 2009; 29(9):3713–20. [PubMed: 19667169]
18. Wu BT, Dyer RA, King DJ, Innis SM. Low fish intake is associated with low blood concentrations of vitamin D, choline and n-3 DHA in pregnant women. *Br J Nutr.* 2013; 109(5):936–43. [PubMed: 22691303]

19. Brembeck P, Winkvist A, Olausson H. Determinants of vitamin D status in pregnant fair-skinned women in Sweden. *Br J Nutr.* 2013;1–9.
20. Holick MF. Environmental factors that influence the cutaneous production of vitamin D. *Am J Clin Nutr.* 1995; 61(3 Suppl):638S–45S. [PubMed: 7879731]
21. Tsiaras WG, Weinstock MA. Factors influencing vitamin D status. *Acta Derm Venereol.* 2011; 91(2):115–24. [PubMed: 21384086]
22. Płudowski P, Karczmarewicz E, Bayer M, Carter G, Chlebna-Sokół D, Czech-Kowalska J, Dębski R, Decsi T, Dobrzańska A, Franek E, Głusko P, Grant WB, Holick MF, Yankovskaya L, Konstantynowicz J, Książek JB, Książkowska-Orłowska K, Lewiński A, Litwin M, Lohner S, Lorenc RS, Łukaszewicz J, Marcinowska-Suchowierska E, Milewicz A, Misiorowski W, Nowicki M, Povoroznyuk V, Rozentryt P, Rudenka E, Shoenfeld Y, Socha P, Solnica B, Szalecki M, Tałała M, Varbiro S, Wójcikowski MA. Practical guidelines for the supplementation of vitamin D and the treatment of deficits in Central Europe — recommended vitamin D intakes in the general population and groups at risk of vitamin D deficiency. *Endokrynologia Polska.* 2013; 64(4):319–27. [PubMed: 24002961]
23. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH, Weaver CM. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2011; 96(7):1911–30. [PubMed: 21646368]
24. ACOG Committee Opinion. Vitamin D: Screening and supplementation during pregnancy. *Obstet Gynecol.* 2011; 118:197–8. [PubMed: 21691184]
25. Saade GR. Reflections on 2011 from the obstetrical perspective. *Am J Perinatol.* 2012; 29(10): 755–8. [PubMed: 23080376]
26. Bodnar LM, Catov JM, Simhan HN, Holick MF, Powers RW, Roberts JM. Maternal vitamin D deficiency increases the risk of preeclampsia. *J Clin Endocrinol Metab.* 2007; 92(9):3517–22. [PubMed: 17535985]
27. Zhang C, Qiu C, Hu FB, David RM, van Dam RM, Bralley A, Williams MA. Maternal plasma 25-hydroxyvitamin D concentrations and the risk for gestational diabetes mellitus. *PLoS One.* 2008; 3(11):e3753. [PubMed: 19015731]
28. Burris HH, Rifas-Shiman SL, Kleinman K, Litonjua AA, Huh SY, Rich-Edwards JW, Camargo CA Jr, Gillman MW. Vitamin D deficiency in pregnancy and gestational diabetes mellitus. *Am J Obstet Gynecol.* 2012; 207(3):182 e1–8. [PubMed: 22717271]
29. Bodnar LM, Catov JM, Zmuda JM, Cooper ME, Parrott MS, Roberts JM, Marazita ML, Simhan HN. Maternal serum 25-hydroxyvitamin D concentrations are associated with small-for-gestational age births in white women. *J Nutr.* 2010; 140(5):999–1006. [PubMed: 20200114]
30. Burris H, Rifas-Shiman S, Camargo C, Litonjua A, Huh S, Rich-Edwards J, Gillman M. Plasma 25-hydroxyvitamin D during pregnancy and small-for-gestational age in black and white infants. *Ann Epidemiol.* 2012; 31:31.
31. Crozier SR, Harvey NC, Inskip HM, Godfrey KM, Cooper C, Robinson SM. Maternal vitamin D status in pregnancy is associated with adiposity in the offspring: findings from the Southampton Women's Survey. *Am J Clin Nutr.* 2012; 96(1):57–63. [PubMed: 22623747]
32. Gale CR, Robinson SM, Harvey NC, Javaid MK, Jiang B, Martyn CN, Godfrey KM, Cooper C. Maternal vitamin D status during pregnancy and child outcomes. *Eur J Clin Nutr.* 2008; 62(1):68–77. [PubMed: 17311057]
33. Javaid MK, Crozier SR, Harvey NC, Gale CR, Dennison EM, Boucher BJ, Arden NK, Godfrey KM, Cooper C. Maternal vitamin D status during pregnancy and childhood bone mass at age 9 years: a longitudinal study. *Lancet.* 2006; 367(9504):36–43. [PubMed: 16399151]
34. Weishaar T, Vergili JM. Vitamin D status is a biological determinant of health disparities. *J Acad Nutr Diet.* 2013; 113(5):643–51. [PubMed: 23415504]
35. Moukarzel, S. Master's thesis. Master's thesis, University of Kansas Medical Center; Kansas City, KS: 2011. The relation between maternal vitamin D status in pregnancy and incidence of infection in infants up to one years of age. Retrieved from http://kuscholarworks.ku.edu/dspace/bitstream/1808/9716/1/Moukarzel_ku_0099M_11826_DATA_1.pdf
36. Bodnar LM, Simhan HN. Vitamin D may be a link to black-white disparities in adverse birth outcomes. *Obstet Gynecol Surv.* 2010; 65(4):273–84. [PubMed: 20403218]

37. Wagner CL, McNeil RB, Johnson DD, Hulsey TC, Ebeling M, Robinson C, Hamilton SA, Hollis BW. Health characteristics and outcomes of two randomized vitamin D supplementation trials during pregnancy: a combined analysis. *J Steroid Biochem Mol Biol.* 2013; 136:313–20. [PubMed: 23314242]

Figure 1.

Influence of season on plasma 25-hydroxyvitamin D [25(OH)D] concentration at birth compared to plasma 25(OH)D at mid-pregnancy. Values are mean $\pm$ SD, $n = 181$: summer births $n = 40$; fall births $n = 47$; winter births $n = 53$; and spring births $n = 41$. Data were square-root transformed before repeated measures ANOVA was employed to test for differences between time points using covariates BMI, race, supplemental vitamin D intake, season of delivery plasma 25(OH)D concentration. Fisher's Least Significant Difference was used to conduct pairwise comparisons. Significance was set at $P < 0.05$. Dotted line indicates cut-off for sufficiency from IOM guidelines; columns bearing different letters are significantly difference.

Table 1
Characteristics of study participants

Mid-pregnancy (n = 193)		
	Mean ± SD	Range
Age (year)	26 ± 5	16 - 36
BMI (kg/m ²)	27 ± 5	17 - 43
BMI categories (%)		
Underweight (< 18.5)	1*	
Normal (18.5 – 24.9)	37	
Overweight (25.0 – 29.9)	39	
Obese (> 30)	22	
Education level (year)	14 ± 3	8 - 20
Race (%)		
White	72 ^a	
Black	27	
Other	2	
Gestational age (weeks)	14 ± 4	8 - 22
25(OH)D concentration (nmol/L)	56.7 ± 33.2	5.1 – 226.2
Deficient status (< 30 nmol/L) (%)	21	
Insufficient (30 – 49.9 nmol/L)	28	
Sufficient (50 – 125 nmol/L)	51	
At birth		
Supplemental vitamin D intake (IU/d) ^b	334 ± 123	37 – 917
25(OH)D concentration (nmol/L) ^c	34.4 ± 21.4	0.26 – 104.8
Deficient status (%)	48	
Insufficient	34	
Sufficient	18	
Gestational weight gain (kg)	14 ± 6	(-4) - 29

^a Rounding percentages to whole numbers prevented sum 100.

^b Mean supplemental intake calculated from reported brand prenatal vitamin and additional supplements reported on dietary recalls.

^c n = 181, 12 subjects had undetectable plasma 25(OH)D concentration at birth.