

Journal of Human Lactation

<http://jhl.sagepub.com/>

Maternal Vitamin D Supplementation to Meet the Needs of the Breastfed Infant : A Systematic Review

Doria K. Thiele, Jeanine L. Senti and Cindy M. Anderson

J Hum Lact published online 4 March 2013

DOI: 10.1177/0890334413477916

The online version of this article can be found at:

<http://jhl.sagepub.com/content/early/2013/03/01/0890334413477916>

Published by:



<http://www.sagepublications.com>

On behalf of:



[International Lactation Consultant Association](http://www.ilca.org)

Additional services and information for *Journal of Human Lactation* can be found at:

Email Alerts: <http://jhl.sagepub.com/cgi/alerts>

Subscriptions: <http://jhl.sagepub.com/subscriptions>

Reprints: <http://www.sagepub.com/journalsReprints.nav>

Permissions: <http://www.sagepub.com/journalsPermissions.nav>

>> [OnlineFirst Version of Record](#) - Mar 4, 2013

[What is This?](#)

Maternal Vitamin D Supplementation to Meet the Needs of the Breastfed Infant: A Systematic Review

Journal of Human Lactation
XX(X) 1–8
© The Author(s) 2013
Reprints and permission:
sagepub.com/journalsPermissions.nav
DOI: 10.1177/0890334413477916
jhl.sagepub.com


Doria K. Thiele, MN, CNM, IBCLC^{1,2}, Jeanine L. Senti, MS, APRN-BC, CNS, IBCLC², and Cindy M. Anderson, PhD, WHNP-BC, FAAN²

Abstract

Maternal vitamin D insufficiency during lactation, related to lack of sun exposure and minimal intake of vitamin D from the diet, contributes to low breast milk vitamin D content and, therefore, infant vitamin D deficiency. The objective of this review was to examine the literature regarding evidence for achieving maternal vitamin D status that promotes sufficient vitamin D transfer from mother to infant exclusively from breast milk. PubMed and CINAHL databases were searched using the terms *lactation* or *breastfeeding* or *milk*, *human* and *vitamin D*. The resulting articles were further limited to those written in English, published within the last 10 years, and involving clinical or randomized controlled trials of humans. The search yielded 13 studies, 3 of which provide evidence for maternal intake of vitamin D and the correlation with exclusively breastfed infants' serum 25-hydroxyvitamin D level. A strong positive correlation exists between maternal vitamin D intake during exclusive breastfeeding and infant serum 25-hydroxyvitamin D levels. There is support to conclude that when maternal vitamin D intake is sufficient, vitamin D transfer via breast milk is adequate to meet infant needs. In the reviewed studies, doses up to 10 times the current recommended daily intake of vitamin D were needed to produce sufficient transfer from mother to breastfed infant. Further research is needed to refine the dose and gestational timing of maternal vitamin D supplementation. Due to the high rates of vitamin D deficiency during lactation and the correlations between vitamin D deficiency and multiple diseases, providers should consider monitoring lactating mothers' vitamin D status.

Keywords

25-hydroxyvitamin D, breastfeeding, breast milk, cholecalciferol, human milk, infant, lactation, vitamin D, vitamin D deficiency

Background

Vitamin D (cholecalciferol) is a steroid hormone photosynthesized in the skin when exposed to appropriate ultraviolet B wavelengths. Receptors for vitamin D are found throughout the body and are important for multiple functions beyond bone health. There has been a long-held belief that human breast milk contains such small amounts of vitamin D that it is inadequate to meet infant dietary vitamin D needs.^{1,2} However, research dating back to the 1980s demonstrated that breast milk vitamin D content was directly related to maternal serum vitamin D levels and can be increased by increasing maternal exposure to ultraviolet B radiation or maternal intake of vitamin D.^{3–5} More recent findings point to maternal vitamin D deficiency as the precursor to breast milk vitamin D inadequacy, supported by evidence linking adequate maternal vitamin D supplementation with increases in breast milk vitamin D content.^{6–9}

There continue to be gaps in evidence regarding appropriate maternal supplement dosing and serum 25-hydroxyvitamin D (25[OH]D) levels that correspond to adequate

infant intake of vitamin D received solely from breast milk. However, breast milk is considered the gold standard for infant nutrition, offering a complement of antibodies, macronutrients, and nutritional balance unsurpassed by any substitute. Therefore, maternal nutrition should be optimized to impart the best nutrition to exclusively breastfed infants. Additionally, mothers may become concerned about their breast milk's ability to supply everything that their infants need if told that it is inadequate in this way. It is imperative that we reduce barriers to exclusive breastfeeding and enable mothers to rely fully on their breast milk to meet the needs of their infants. The importance of vitamin D to infant health is underscored by recent findings demonstrating a correlation

Date submitted: September 11, 2012; Date accepted: January 17, 2013.

¹Oregon Health and Science University, Monmouth, OR, USA

²University of North Dakota, Grand Forks, ND, USA

Corresponding Author:

Doria K. Thiele, OHSU School of Nursing, 345 N Monmouth Ave,
Monmouth, OR 97361, USA
Email: thiele@ohsu.edu

between vitamin D deficiency and asthma/wheeze, atopic dermatitis, early infancy upper respiratory infection, type 1 diabetes, and innate immune response.¹⁰⁻¹⁶

Currently, the American Academy of Pediatrics recommends that all breastfed infants receive a supplement of 400 IU of oral vitamin D daily starting at birth because of the lack of adequate vitamin D transferred to infants through breast milk.¹⁷ All infants rely on external sources of vitamin D because direct sun exposure is minimized due to possible harm. Infant formulas contain vitamin D, negating the need for additional vitamin D supplementation for formula-fed infants. In fact, findings from a recently published longitudinal study demonstrate that breastfed infants receiving vitamin D supplement and infants receiving formula had similarly low rates of vitamin D deficiency at 4 months of age. Additionally, the authors reported that 40% of breastfed infants not receiving a vitamin D supplement were vitamin D deficient.¹⁸

Although referred to as a vitamin, vitamin D is actually a steroid hormone that acts on almost all body tissues.¹⁹ Vitamin D is naturally synthesized in the skin when exposed to ultraviolet B radiation from sunlight. The lighter a person's skin, the less time needed in the sun to synthesize the daily requirement of vitamin D. When synthesized in the skin or ingested in supplement form, vitamin D binds with the vitamin D-binding protein and travels to distant sites in the circulation. Once in circulation, vitamin D is converted in the liver to 25[OH]D, which is the major circulating form and is used for evaluating vitamin D status. To be biologically active, the 25[OH]D is further converted to 1,25 dihydroxyvitamin D (1,25[OH]₂D). This final conversion is completed by the enzyme 1- α -hydroxylase, which was known to exist in the kidney and has more recently been found in placental, breast, and immune system cells.²⁰⁻²² The active 1,25[OH]₂D binds with nuclear receptor sites on DNA, leading to protein synthesis and regulation.

Historically, it has been understood that the role of vitamin D in the body is to maintain calcium homeostasis. Vitamin D acts in the intestine to increase calcium absorption. As vitamin D levels drop, absorption of calcium and phosphorous from the intestine is similarly reduced. Subsequent lower blood calcium and phosphorous levels stimulate increased production of parathyroid hormone, which maintains blood calcium in a normal range by increasing bone resorption.²³ This negative feedback loop ensures blood calcium availability; however, chronic activation leads to osteoporosis, osteomalacia, and other bone diseases. Vitamin D deficiency is the primary culprit in rickets development, a bone-deforming disease particularly involving the legs, which affects infants and children. More subtle bone maladies related to vitamin D deficiency are currently being explicated.²⁴

As there have been general advances in understanding vitamin D physiology, there have been specific advances in understanding vitamin D physiology during pregnancy and

lactation.^{25,26} There is an almost immediate increase in maternal 1,25[OH]₂D during pregnancy that promotes the increased intestinal absorption of calcium.^{25,27} Maternal calcium absorption increases during pregnancy, with maximal rate of calcium absorption seen in the third trimester, as the fetal skeleton is being developed.²⁸ However, recent studies report that despite the 3- to 4-fold increase in 1,25[OH]₂D—which would promote increased calcium absorption—maternal serum and urine calcium levels remain in the normal range.²⁶ If a nonpregnant woman sustained such high 1,25[OH]₂D levels, she would experience hypercalcemia and hypercalcuria. Researchers postulate that instead of playing a calcium homeostasis role, these high levels of 1,25[OH]₂D are responsible for immune modulating effects.²⁶ Additionally, 25[OH]D crosses the placenta readily, but 1,25[OH]₂D does not cross it easily, leading to 25[OH]D deficiency in the fetus or neonate born to a 25[OH]D-deficient mother.²⁸ These pregnancy-specific physiologic changes related to vitamin D and calcium metabolism are not yet fully understood.²⁶

Unlike the process that occurs during pregnancy, very little 25[OH]D passes from the maternal circulation to breast milk. Instead, the neonate receives vitamin D in its parent form of cholecalciferol in breast milk.^{25,29,30} Therefore, it is critical that maternal serum cholecalciferol levels remain adequate, as this is the primary form passed to the neonate. However, cholecalciferol is quickly converted to 25[OH]D by the mother, thereby disabling it from transfer to the neonate and thus suggesting the need for daily dosing of vitamin D to achieve breast milk transfer.²⁵

To discuss the physiologic impact of maternal vitamin D status on breast milk vitamin D content, levels of circulating 25[OH]D must be defined as those corresponding to sufficiency, insufficiency, and deficiency. However, a lack of consensus exists regarding defined status based on levels of 25[OH]D in adults and infants.³¹⁻³⁶ Part of the lack of consensus stems from the lack of randomized controlled trials on which to base recommendations. Research on the physiologic benefits of vitamin D are almost exclusively observational and therefore do not provide sufficient evidence for generalized recommendations.^{32,37} Many researchers set a 25[OH]D level of 30 to 32 ng/mL (80 nmol/L) or greater as defining sufficiency, as this corresponds to the minimizing of serum parathyroid hormone.³⁸⁻⁴¹ This 25[OH]D level similarly corresponds with adequate bone mineral density.⁴² When 25[OH]D levels drop below 20 ng/mL (50 nmol/L), there is a corresponding drop in calcium absorption and a subsequent development of hyperparathyroidism.^{38-40,43} Therefore, there is fairly consistent recognition of 25[OH]D levels less than 20 ng/mL (50 nmol/L) as representing vitamin D deficiency, with some authors reporting levels less than 15 ng/mL as extremely deficient. Intermediate levels that fall between 20 and 32 ng/mL define the category of insufficiency (50-80 nmol/L).

Because so few large randomized controlled trials have been conducted with pregnant and lactating participants,

Table 1. Vitamin D Content in Naturally Occurring Foods and Fortified Food Sources: Ergocalciferol and Cholecalciferol⁷⁰

Foods	International Units ^a	
	D ₂	D ₃
Naturally occurring		
Cod liver oil, tsp (highly variable)		400-1000
Salmon, fresh wild caught, 3 oz		375
Tuna, canned, 12.5 oz		148
Egg, hardboiled		44
Mushrooms		
Portabella exposed to ultraviolet B, cup	634	
Dried shiitake, 4 mushrooms	23	
Raw white, cup	5	
Fortified		
2% cow's milk, 8 oz		98
Cheddar cheese, 2 oz		14
Butter, tbsp		9
Yogurt, cup		127
Orange juice, cup		100
Breakfast cereal, cup (highly variable)		40
Infant formula, 8 oz		100

^aD₂, ergocalciferol; D₃, cholecalciferol.

there is also no consensus regarding dosing, timing, and type of vitamin D supplementation necessary to correct deficiency. Two types of vitamin D are typically used for supplementation: vitamin D₂ (ergocalciferol), which is made by plants in small quantities, and vitamin D₃ (cholecalciferol), which is made by animals and is considered more biologically available to convert to 1,25[OH]₂D.⁴⁴ As part of an extensive analysis of current evidence, the Institute of Medicine has updated the recommended daily intake of vitamin D for all adults, including pregnant and lactating women, to 600 IU.³² The American College of Obstetrics and Gynecologists has embraced this recommendation as well.³¹ The Endocrine Society recommends 600 IU for all pregnant and lactating women but suggests that 1500 to 2000 IU may be needed to maintain adequate serum 25[OH]D.³⁵

Contemporary research demonstrates widespread vitamin D deficiency among pregnant women and breastfed infants, despite consistent daily prenatal vitamin use and ingestion of vitamin D-containing foods (Table 1).^{9,19,29,45-51} Studies based in several US states document the extent of vitamin D deficiency among newborns. In Oakland, California, researchers found that 90% of neonates and 54% of mothers had 25[OH]D levels consistent with insufficiency.⁵² South Carolina researchers report that 65.5% of African American neonates and 24% of white neonates had cord blood 25[OH]D levels consistent with extreme deficiency.⁴⁵ In Massachusetts, researchers found that 58% of infants and 35.8% of mothers had 25[OH]D levels in the deficient range and that 38% of

infants and 23.1% of mothers had 25[OH]D levels in the extremely deficient range.⁴⁹ In the relatively sun-rich area of Sacramento, California, it was found that 28.3% of infants had insufficient 25[OH]D levels, with exclusive breastfeeding being a significant risk factor for vitamin D deficiency.⁵³ Infants who have darker skin pigmentation, are kept out of sunlight, are born in the winter, and are exclusively breastfed by a vitamin D deficient mother are at greatest risk for vitamin D deficiency.^{28,54,55} These studies provide support for the conclusion that maternal and infant vitamin D deficiency is prevalent and that further research is needed to explore methods to minimize this condition.

The rationale for this systematic review was to investigate current evidence regarding vitamin D transfer from mother to infant via breast milk and to identify gaps in knowledge warranting further research. The objective of this review was to evaluate contemporary intervention studies of lactating women regarding maternal vitamin D supplementation and the resulting infant 25[OH]D status among breastfed infants.

Methods

PubMed and CINAHL databases were searched using the terms *lactation* or *breastfeeding* or *milk*, *human* and *vitamin D*. Articles included in this review met the criteria of those published within the last 10 years, randomized controlled trials, intervention of maternal vitamin D supplementation, and outcome measures of maternal vitamin D status and breast milk or infant vitamin D status determined by vitamin D transfer via breast milk.

A minimum of 2 authors reviewed each study, extracting data independently. Consensus was reached through discussion, which included a third author if agreement was not achieved. Data abstraction included study design, sample characteristics, and dependent variables, including maternal vitamin D status, breast milk vitamin D content, and infant 25[OH]D levels. How the primary authors defined vitamin D status was noted to provide appropriate context and interpretation. Statistical analyses were extracted, including associations, relationships, and group differences, reported by measures of significance and variance.

Results

The search of the literature revealed 13 articles. Excluded articles pertained to direct infant supplementation and did not investigate the relationship between maternal 25[OH]D status or vitamin D intake and infant 25[OH]D status.⁵⁶⁻⁶⁵ Of those articles meeting inclusion criteria, only 4 were randomized controlled trials in which lactating mothers were supplemented with vitamin D and then followed for measurement of their 25[OH]D levels along with those of their infants.⁶⁻⁹ Additionally, one of these articles reported additional outcomes on the original data set found in Hollis

Table 2. Summary of the Intervention, Outcome Measures, and Conclusions from Reviewed Articles^a

Author	N	Maternal Dose: Vitamin D, IU	Maternal 25[OH]D, ng/mL		Breast Milk Vitamin D, IU/L		Infant 25[OH]D, ng/mL	
			Baseline	Outcome	Baseline	Outcome	Baseline	Outcome
Hollis and Wager ^{7,c}	18							
G1		2000 daily	27.6 (3.3)	36.1 (2.3) ^b	35.5 (3.5)	69.7 (3.0) ^b	7.9 (1.1)	27.8 (3.9) ^b
G2		4000 daily	32.9 (2.4)	44.5 (3.9) ^b	40.4 (3.7)	134.6 (48.3) ^b	13.4 (3.3)	30.8 (5.0) ^b
Wagner et al ^{9,d}	10							
G1		400 daily ^e	32.2	38.4	59.6	76.3	13	43 ^b
G2		6400 daily ^f	34	58.8 ^b	82.4	873.5 ^b	14	46 ^b
Saadi et al ^{8,g}	44							
G1		2000 daily	11.7 (4.1)	16.7 (5.6) ^b	Unable to detect ^h	50.9 (0-62.5) ⁱ	5.6 (3.4)	19.8 (7.4) ^b
G2		60 000 monthly	8.9 (4.0)	14.3 (4) ^b			5.48 (4.84)	17.8 (6) ^b

^a25[OH]D, 25-hydroxyvitamin D. Data presented as mean (standard deviation).

^b $P < .05$ (statistically significant increase from baseline data).

^cOutcome, 4 months postpartum. *Conclusions:* High-dose vitamin D intake by the mother for 3 months increased the 25[OH]D serum concentrations for mothers and infants without causing hypercalcemia or hypercalcuria.

^dOutcome, 7 months postpartum. *Conclusions:* Maternal intake of 400 IU daily was inadequate; maternal intake of 6400 IU elevated 25[OH]D in mother and nursing infant, with a 10-fold increase in breast milk vitamin D content. No adverse outcomes.

^eInfants received 300 IU daily.

^fInfants received placebo.

^gOutcome, 4 months postpartum. *Conclusions:* With deficiency defined as < 20 ng/mL, close to 100% of participants and their infants were vitamin D deficient at the beginning of the study. Significant improvements were seen in both groups, although deficiency remained prevalent.

^hSubset of 12 women (characteristic not provided).

ⁱSubset of 8 women (characteristic not provided). Range in parentheses.

and Wagner⁶; therefore, only their article is included in this review.⁶ In all, 3 articles met inclusion criteria and are reviewed here.

In 2004, Hollis and Wagner set out to examine the effectiveness of higher-dose vitamin D supplementation in lactating women.⁶ Participants were recruited in South Carolina for a 3-month study. Outcome measures included total 25[OH]D, serum calcium, parathyroid hormone, and urine calcium/creatinine levels in the mothers and 25[OH]D serum levels for the infants. A convenience sample of lactating women ($N = 64$) was randomized into 2 treatment groups, with only 18 women (9 in each group) completing the study after loss to follow-up and breastfeeding attrition. Of the 18 women completing the study, 13 were white and 5 were African American (group 1, $n = 3$; group 2, $n = 2$). Group 1 received 2000 IU of vitamin D (1600 IU as D_2 and 400 IU as D_3), and group 2 received 4000 IU of vitamin D (3600 IU as D_2 and 400 IU as D_3) daily for 3 months beginning at 1 month postpartum. Baseline mean (standard deviation) for 25[OH]D level did not differ statistically between the 2 groups: 27.6 ng/mL (3.3) in group 1 and 32.9 (2.4) in group 2. Both groups had significant increase in mean 25[OH]D levels to 36.1 ng/mL (2.3) and 44.5 (3.9), respectively ($P < .05$ and $P < .04$, respectively). Breast milk vitamin D content increased significantly: 35.5 IU/L (3.5) to 69.7 (3.0) ($P < .00001$) and 40.4 IU/L (3.7) to 134.6 (48.3) ($P < .00001$) in groups 1 and 2, respectively. Infants of mothers in both groups had significant increases in

circulating 25[OH]D. Infants in group 1 increased from a mean 25[OH]D level of 7.9 ng/mL (1.1) to 27.8 (3.9) after 3 months of maternal supplementation ($P < .02$). Infants of mothers in group 2 also had significant increase, from a mean 25[OH]D level of 13.4 ng/mL (3.3) to 30.8 (5.0) ($P < .003$). No participants demonstrated vitamin D toxicity, which was monitored by maternal serum calcium, infant serum calcium and phosphorus, and maternal urine calcium/creatinine ratio. This study was limited in scope owing to a small sample size; however, despite the small number of participants, the study still had adequate power to demonstrate statistical significance for maternal and infant 25[OH]D levels within groups. These findings underscore the large effect size of maternal vitamin D supplementation on transfer to the exclusively breastfed infant.

In follow-up to the Hollis and Wagner study findings,⁶ Wagner et al enrolled exclusively breastfeeding women at 1 month postpartum for a 6-month follow-up trial.⁹ Participants were recruited in South Carolina, and of the final 19 recruited participants, 15 were white, 2 were Hispanic, and 2 were African American. Participants were randomized to group 1, receiving 400 IU of vitamin D daily ($n = 10$), or group 2, receiving 6400 IU of vitamin D daily ($n = 9$). Of the 19 enrolled, 10 participants completed the study. Skin pigmentation was monitored and corresponded to warmer months but did not differ between the 2 groups, nor did ethnicity profile. Women in group 1 were assigned to give their infants

300 IU of vitamin D by liquid drop each day, and women in group 2 gave 1 drop of liquid placebo to their infants each day. This regimen was continued for 6 months after enrollment (postpartum months 1-7).

The 2 groups did not differ in demographics or adherence to protocol, with about 80% compliance with maternal vitamin supplementation and 61% compliance with infant vitamin supplementation. Results showed that group 1 had maternal 25[OH]D serum levels slowly decrease over the first 5 months of the study and then increase slightly, as increased sun exposure was experienced for the last 2 months of the study (baseline, 32.2 ng/mL; 5 months, 25.9 ng/mL). Corresponding directly to maternal serum 25[OH]D levels, the mean vitamin D content of breast milk showed the same pattern (baseline, 59.6 IU/L; 5 months, 45.7 [nadir]; 7 months, 76.3). Participants in group 2 had increases in maternal 25[OH]D serum levels (mean at enrollment, 34.0 ng/mL; 6 months later, 58.8) that stabilized around postpartum month 4 and were maintained over the course of the study. Participants in group 2 had a 10-fold increase in the amount of vitamin D in their breast milk (82 IU/L to 873), which was a significant difference compared to women in group 1 ($P < .0003$). This resulted in their infants having a steady rise in circulating 25[OH]D serum levels nearly equivalent to the infants receiving 300 IU of vitamin D directly via supplementation. Participants were monitored for vitamin D toxicity through maternal and infant serum calcium and urine calcium and creatinine levels. There was no difference in these measures between the 2 groups, and the authors reported no adverse events. This study demonstrated that infants can receive doses of vitamin D through breast milk that are equivalent to oral dosing of 300 IU per day or greater. This study was limited by small sample size but regardless was able to demonstrate a significant improvement in breast milk vitamin D content for participants in group 2.

In 2009, Saadi et al undertook a larger study involving 90 breastfeeding women in the United Arab Emirates.⁸ The authors stated that vitamin D deficiency is particularly common among lactating Middle Eastern women because of minimal intake of vitamin D in the diet as well as norms of dress that include covering most of the body when in public. Women who planned to exclusively breastfeed for the next 3 months (the study period) were recruited at their first postnatal visit. Once recruited, the participants were randomly assigned to receive 2000 IU of vitamin D₂ daily in oral capsule form ($n = 45$) or 60 000 IU monthly in oral tablet form ($n = 45$) for 3 months. Neither the participants nor the researchers were blinded to the treatment allocation. All infants were supplemented with 400 IU of vitamin D₂ daily for 3 months. The participants and their babies had baseline 25[OH]D levels measured at entry to the study. Follow-up blood analysis was completed on participants in the 2000 IU daily group after 3 months of supplementation and in the monthly group (60 000 IU) before each monthly dose. All infants had a second 25[OH]D measurement at the end of

the 3-month study. The authors set the vitamin D deficiency level at ≤ 15 ng/mL (≤ 37.5 nmol/L) based on 2 older reports regarding physiologic measures.^{66,67} Baseline 25[OH]D levels were available on 92 infants (2 sets of twins) and revealed 95% incidence of deficiency. Participants had an 88% incidence of deficiency, even with the use of a cutoff value lower than the more widely accepted conservative definition of < 20 ng/mL. After 3 months of the assigned regimens, infants had drastically increased their mean serum 25[OH]D levels; however, 23% in the daily regimen group and 38% in the monthly regimen group still met the definition of deficiency. Circulating vitamin D levels in the mothers had shown improvement as well, although 36% of participants in the daily regimen group and 50% of participants in the monthly regimen group continued to meet the authors' definition of deficiency. Differences in mean maternal 25[OH]D levels between groups did not reach statistical significance. The researchers also analyzed vitamin D levels in the breast milk of a subset of 12 women at baseline and 8 women at the end of the study intervention. Characteristics on these subsets of participants were not provided. Breast milk vitamin D levels were undetectable at the beginning of the study and increased to a median of 50.9 IU/L. No serum or urine markers of toxicity were measured in either participants or their infants. Although this study concluded that significant increases were seen in maternal and infant serum vitamin D levels, the increases were not sufficient over the 3-month study period to correct a majority of the deficiency seen. This study was limited by the use of vitamin D₂ for supplementation, which is less effective at raising serum 25[OH]D levels.⁴⁴ It was additionally limited by lack of blinding and lack of control group.

Discussion

Findings from this systematic review reveal a very strong effect size of maternal vitamin D supplementation on the vitamin D status of exclusively breastfed infants. In the 3 studies reviewed, maternal and infant serum 25[OH]D levels increased in direct relationship to maternal vitamin D intake. Women's health care providers, particularly lactation consultants, are in a unique position to influence the health of their clients as well as that of the next generation. This review demonstrates that the long-held notion that women are unable to pass vitamin D to their infants through breast milk should be dismissed. As the gold standard for infant nutrition and the ideal infant feeding method, breastfeeding should be encouraged for all women, and barriers should be removed. Describing breast milk as being "deficient" or "lacking" vitamin D may lead mothers to doubt the ability of their breast milk to provide everything their babies need. The issue of vitamin D inadequacy in breast milk has been addressed by encouraging mothers to provide infants a vitamin D supplement, but this does not address the high levels of deficiency that persists in pregnant and breastfeeding

women themselves. If maternal vitamin D supplementation improves the health status of the mother and her breastfeeding infant, it is clearly the better choice.

This review revealed a lack of studies in which participants started vitamin D supplementation during pregnancy and continued through lactation. It is possible that researchers began the intervention during the lactation period (1) to avoid the high attrition from breastfeeding in the first month postpartum and (2) because of the relative difficulty in doing intervention studies with pregnant or newly lactating participants. However, the initiation of supplementation during lactation does not address the significant need for vitamin D adequacy during pregnancy. Reports from meta-analyses of randomized controlled trials of vitamin D supplementation during pregnancy provide evidence of the association of maternal vitamin D supplementation and reduced frequency of infants weighing less than 2500 g, although there is a dearth of studies available to determine the influence on other outcomes, including preterm birth, neonatal intensive care treatment, Apgar scores, or maternal death.⁶⁸ As vitamin D is involved in critical systemic functions beyond bone, the full implications of vitamin D deficiency in mothers and offspring is yet to be determined.

In our review, we found compelling evidence to suggest that maternal vitamin D supplementation during lactation has an equivalent effect on infant 25[OH]D status as direct infant supplementation but also the potential to benefit both mother and child. There is no evidence to suggest that maternal vitamin D supplementation that results in physiologic 25[OH]D levels in the mother and breastfeeding infant lead to any ill effects, as demonstrated by no change in vitamin D toxicity markers. Next steps in research should include larger randomized controlled trials starting vitamin D supplementation early in pregnancy and continuing through lactation. This would allow for vitamin D adequacy to be attained by pregnant participants and their fetuses prior to birth, as opposed to the reviewed studies, which started with vitamin D-deficient women and infants at 1 month postpartum, essentially negating breast milk vitamin D transfer to the infant during the critical first month of development. However, the challenges inherent in building the body of evidence to provide substantial support for practice change provide a barrier to advancement. Many women begin early formula supplementation, to varying degrees and for varying reasons, thus limiting the ability to truly identify the impact of maternal vitamin D supplementation on breast milk transfer and infant vitamin D status. While initiation and duration rates of breastfeeding are improving, the barriers to breastfeeding and early attrition are likely major contributors to the low retention rates reported.⁶⁹ While the effect of vitamin D supplementation on maternal and infant status is significant, the small sample sizes and large variation in supplementation protocols in these 3 randomized controlled trials limit ability to suggest specific practice changes.

Conclusions

Maternal vitamin D supplementation during lactation increases vitamin D transfer in breast milk, consistent with improvements in vitamin D status in the exclusively breastfed infant. The ambiguity around definitions of vitamin D status, combined with the lack of consistent recommendations regarding the dosage and gestational timing of maternal vitamin D supplementation, represents a significant barrier to the advancement of guidelines for vitamin D supplementation to improve the short- and long-term health of mothers and children. Well-designed and powered clinical trials to generate new knowledge and establish best practice in the care of women and children for lifelong health are now needed to supplement the findings from these small studies. If larger clinical trials have similar findings and further demonstrate the safety of vitamin D supplementation for mothers and infants, then practice changes could be made.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This project was supported by the Robert Wood Johnson Foundation Nurse Faculty Scholar Award (CMA; 64202) and the Association of Women's Health, Obstetrics and Neonatal Nurses (DKT).

References

1. Hillman LS. Mineral and vitamin D adequacy in infants fed human milk or formula between 6 and 12 months of age. *J Pediatr*. 1990;117(2)(pt 2):S134-S142.
2. Specker BL. Do North American women need supplemental vitamin D during pregnancy or lactation? *Am J Clin Nutr*. 1994;59(2):484S-490S.
3. Ala-Houhala M, Koskinen T, Parviainen MT, Visakorpi JK. 25-hydroxyvitamin D and vitamin D in human milk: effects of supplementation and season. *Am J Clin Nutr*. 1988;48(4):1057-1060.
4. Greer FR, Hollis BW, Cripps DJ, Tsang RC. Effects of maternal ultraviolet B irradiation on vitamin D content of human milk. *J Pediatr*. 1984;105(3):431-433.
5. Specker BL, Tsang RC, Hollis BW. Effect of race and diet on human-milk vitamin D and 25-hydroxyvitamin D. *Am J Dis Child*. 1985;139(11):1134-1137.
6. Basile LA, Taylor SN, Wagner CL, Horst RL, Hollis BW. The effect of high-dose vitamin D supplementation on serum vitamin D levels and milk calcium concentration in lactating women and their infants. *Breastfeed Med*. 2006;1(1):27-35.
7. Hollis BW, Wagner CL. Vitamin D requirements during lactation: high-dose maternal supplementation as therapy to prevent hypovitaminosis D for both the mother and the nursing infant. *Am J Clin Nutr*. 2004;80(6):1752S-1758S.

8. Saadi HF, Dawodu A, Afandi B, et al. Effect of combined maternal and infant vitamin D supplementation on vitamin D status of exclusively breastfed infants. *Matern Child Nutr.* 2009;5(1):25-32.
9. Wagner CL, Hulsey TC, Fanning D, Ebeling M, Hollis BW. High-dose vitamin D3 supplementation in a cohort of breastfeeding mothers and their infants: a 6-month follow-up pilot study. *Breastfeed Med.* 2006;1(2):59-70.
10. Camargo CA Jr, Ingham T, Wickens K, et al. Cord-blood 25-hydroxyvitamin D levels and risk of respiratory infection, wheezing, and asthma. *Pediatrics.* 2011;127(1):e180-e187.
11. Hyponen E, Laara E, Reunanen A, Jarvelin MR, Virtanen SM. Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study. *Lancet.* 2001;358(9292):1500-1503.
12. Karatekin G, Kaya A, Salihoglu O, Balci H, Nuhoglu A. Association of subclinical vitamin D deficiency in newborns with acute lower respiratory infection and their mothers. *Eur J Clin Nutr.* 2009;63(4):473-477.
13. Lagishetty V, Liu NQ, Hewison M. Vitamin D metabolism and innate immunity. *Mol Cell Endocrinol.* 2011;347(1-2):97-105.
14. Peroni DG, Piacentini GL, Cametti E, Chinellato I, Boner AL. Correlation between serum 25-hydroxyvitamin D levels and severity of atopic dermatitis in children. *Br J Dermatol.* 2011;164(5):1078-1082.
15. Waterhouse JC, Perez TH, Albert PJ. Reversing bacteria-induced vitamin D receptor dysfunction is key to autoimmune disease. *Ann N Y Acad Sci.* 2009;1173:757-765.
16. Akbar NA, Zacharek MA. Vitamin D: immunomodulation of asthma, allergic rhinitis, and chronic rhinosinusitis. *Curr Opin Otolaryngol Head Neck Surg.* 2011;19(3):224-228.
17. Wagner CL, Greer FR; American Academy of Pediatrics Section on Breastfeeding, American Academy of Pediatrics Committee on Nutrition. Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. *Pediatrics.* 2008;122(5):1142-1152.
18. Merewood A, Mehta SD, Grossman X, et al. Vitamin D status among 4-month-old infants in New England: a prospective cohort study. *J Hum Lact.* 2012;28(2):159-166.
19. Mulligan ML, Felton SK, Riek AE, Bernal-Mizrachi C. Implications of vitamin D deficiency in pregnancy and lactation. *Am J Obstet Gynecol.* 2010;202(5):429.e1-429.e9.
20. Adams JS, Hewison M. Extrarenal expression of the 25-hydroxyvitamin D-1-hydroxylase. *Arch Biochem Biophys.* 2012;523(1):95-102.
21. Liu NQ, Hewison M. Vitamin D, the placenta and pregnancy. *Arch Biochem Biophys.* 2012;523(1):37-47.
22. Welsh J. Vitamin D metabolism in mammary gland and breast cancer. *Mol Cell Endocrinol.* 2011;347(1-2):55-60.
23. Holick MF. Vitamin D: evolutionary, physiological and health perspectives. *Curr Drug Targets.* 2011;12(1):4-18.
24. Winzenberg T, Jones G. Vitamin D and bone health in childhood and adolescence. *Calcif Tissue Int.* 2013;92(2):140-150.
25. Wagner CL, Taylor SN, Johnson DD, Hollis BW. The role of vitamin D in pregnancy and lactation: emerging concepts. *Womens Health (Lond Engl).* 2012;8(3):323-340.
26. Hollis BW, Wagner CL. Vitamin D and pregnancy: skeletal effects, nonskeletal effects, and birth outcomes. *Calcif Tissue Int.* 2013;92(2):128-139.
27. 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):2341-2357.
28. Thandrayen K, Pettifor JM. Maternal vitamin D status: implications for the development of infantile nutritional rickets. *Rheum Dis Clin North Am.* 2012;38(1):61-79.
29. Hollis BW, Wagner CL. The vitamin D requirement during human lactation: The facts and IOM's "utter" failure. *Public Health Nutr.* 2011;14(4):748-749.
30. Wagner CL, Taylor SN, Hollis BW. Does vitamin D make the world go "round"? *Breastfeed Med.* 2008;3(4):239-250.
31. Vitamin D: screening and supplementation during pregnancy. Committee Opinion No. 495. American College of Obstetricians and Gynecologists.
32. Institute of Medicine. *Dietary Reference Intakes for Calcium and Vitamin D.* Washington, DC: National Academies Press; 2011.
33. Bischoff-Ferrari HA, Giovannucci E, Willett WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. *Am J Clin Nutr.* 2006;84(1):18-28.
34. Hollis BW. Circulating 25-hydroxyvitamin D levels indicative of vitamin D sufficiency: implications for establishing a new effective dietary intake recommendation for vitamin D. *J Nutr.* 2005;135(2):317-322.
35. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2011;96(7):1911-1930.
36. Holick MF. Vitamin D deficiency. *N Engl J Med.* 2007;357(3):266-281.
37. Rosen CJ, Adams JS, Bikle DD, et al. The nonskeletal effects of vitamin D: an endocrine society scientific statement. *Endocr Rev.* 2012;33(3):456-492.
38. Gloth FM 3rd, Tobin JD, Sherman SS, Hollis BW. Is the recommended daily allowance for vitamin D too low for the homebound elderly? *J Am Geriatr Soc.* 1991;39(2):137-141.
39. Lips P, Wiersinga A, van Ginkel FC, et al. The effect of vitamin D supplementation on vitamin D status and parathyroid function in elderly subjects. *J Clin Endocrinol Metab.* 1988;67(4):644-650.
40. Gloth FM 3rd, Gundberg CM, Hollis BW, Haddad JG, Jr, Tobin JD. Vitamin D deficiency in homebound elderly persons. *JAMA.* 1995;274(21):1683-1686.
41. Vieth R, Ladak Y, Walfish PG. Age-related changes in the 25-hydroxyvitamin D versus parathyroid hormone relationship suggest a different reason why older adults require more vitamin D. *J Clin Endocrinol Metab.* 2003;88(1):185-191.

42. Bischoff-Ferrari HA, Dietrich T, Orav EJ, Dawson-Hughes B. Positive association between 25-hydroxy vitamin D levels and bone mineral density: a population-based study of younger and older adults. *Am J Med.* 2004;116(9):634-639.
43. Heaney RP, Dowell MS, Hale CA, Bendich A. Calcium absorption varies within the reference range for serum 25-hydroxyvitamin D. *J Am Coll Nutr.* 2003;22(2):142-146.
44. Heaney RP, Recker RR, Grote J, Horst RL, Armas LA. Vitamin D(3) is more potent than vitamin D(2) in humans. *J Clin Endocrinol Metab.* 2011;96(3):E447-E452.
45. Basile LA, Taylor SN, Wagner CL, Quinones L, Hollis BW. Neonatal vitamin D status at birth at latitude 32 degrees 72: evidence of deficiency. *J Perinatol.* 2007;27(9):568-571.
46. Hollis BW. Vitamin D requirement during pregnancy and lactation. *J Bone Miner Res.* 2007;22(suppl 2):V39-V44.
47. Hollis BW. Nutrition: US recommendations fail to correct vitamin D deficiency. *Nat Rev Endocrinol.* 2009;5(10):534-536.
48. Lee JM, Smith JR, Philipp BL, Chen TC, Mathieu J, Holick MF. Vitamin D deficiency in a healthy group of mothers and newborn infants. *Clin Pediatr (Phila).* 2007;46(1):42-44.
49. Merewood A, Mehta SD, Grossman X, et al. Widespread vitamin D deficiency in urban Massachusetts newborns and their mothers. *Pediatrics.* 2010;125(4):640-647.
50. Robinson CJ, Alanis MC, Wagner CL, Hollis BW, Johnson DD. Plasma 25-hydroxyvitamin D levels in early-onset severe preeclampsia. *Am J Obstet Gynecol.* 2010;203(4):366.e1-366.e6.
51. Collins-Fulea C, Klima K, Wegienka GR. Prevalence of low vitamin D levels in an urban midwestern obstetric practice. *J Midwifery Womens Health.* 2012;57(5):439-444.
52. Dror DK, King JC, Durand DJ, Allen LH. Association of modifiable and nonmodifiable factors with vitamin D status in pregnant women and neonates in Oakland, CA. *J Am Diet Assoc.* 2011;111(1):111-116.
53. Liang L, Chantry C, Styne DM, Stephensen CB. Prevalence and risk factors for vitamin D deficiency among healthy infants and young children in Sacramento, California. *Eur J Pediatr.* 2010;169(11):1337-1344.
54. Agarwal N, Faridi MM, Aggarwal A, Singh O. Vitamin D status of term exclusively breastfed infants and their mothers from India. *Acta Paediatr.* 2010;99(11):1671-1674.
55. Greer FR. 25-hydroxyvitamin D: functional outcomes in infants and young children. *Am J Clin Nutr.* 2008;88(2):529S-533S.
56. Siafarikas A, Piazena H, Feister U, Bulsara MK, Meffert H, Hesse V. Randomised controlled trial analysing supplementation with 250 versus 500 units of vitamin D3, sun exposure and surrounding factors in breastfed infants. *Arch Dis Child.* 2011;96(1):91-95.
57. Ponnappakkam T, Bradford E, Gensure R. A treatment trial of vitamin D supplementation in breast-fed infants: universal supplementation is not necessary for rickets prevention in southern Louisiana. *Clin Pediatr (Phila).* 2010;49(11):1053-1060.
58. Kim MJ, Na B, No SJ, et al. Nutritional status of vitamin D and the effect of vitamin D supplementation in Korean breast-fed infants. *J Korean Med Sci.* 2010;25(1):83-89.
59. Madar AA, Klepp KI, Meyer HE. Effect of free vitamin D(2) drops on serum 25-hydroxyvitamin D in infants with immigrant origin: a cluster randomized controlled trial. *Eur J Clin Nutr.* 2009;63(4):478-484.
60. Saadi HF, Dawodu A, Afandi BO, Zayed R, Benedict S, Nagelkerke N. Efficacy of daily and monthly high-dose calciferol in vitamin D-deficient nulliparous and lactating women. *Am J Clin Nutr.* 2007;85(6):1565-1571.
61. Al-Mustafa ZH, Al-Madan M, Al-Majid HJ, Al-Muslem S, Al-Ateeq S, Al-Ali AK. Vitamin D deficiency and rickets in the eastern province of Saudi Arabia. *Ann Trop Paediatr.* 2007;27(1):63-67.
62. Lovelady CA, Stephenson KG, Kuppler KM, Williams JP. The effects of dieting on food and nutrient intake of lactating women. *J Am Diet Assoc.* 2006;106(6):908-912.
63. Lorini R, Minicucci L, Napoli F, et al. Screening for type 1 diabetes genetic risk in newborns of continental Italy. primary prevention (prevefin Italy): preliminary data. *Acta Biomed.* 2005;76(suppl 3):31-35.
64. Gartner LM, Greer FR; Section on Breastfeeding and Committee on Nutrition, American Academy of Pediatrics. Prevention of rickets and vitamin D deficiency: new guidelines for vitamin D intake. *Pediatrics.* 2003;111(4)(pt 1):908-910.
65. Picaud JC, Boucher P, Lapillonne A, et al. Influence of dietary cholesterol on vitamin D metabolism in formula-fed preterm neonates. *J Pediatr Gastroenterol Nutr.* 2002;35(2):180-184.
66. Gessner BD, Plotnik J, Muth PT. 25-hydroxyvitamin D levels among healthy children in Alaska. *J Pediatr.* 2003;143(4):434-437.
67. Thomas MK, Lloyd-Jones DM, Thadhani RI, et al. Hypovitaminosis D in medical inpatients. *N Engl J Med.* 1998;338(12):777-783.
68. De-Regil LM, Palacios C, Ansary A, Kulier R, Pena-Rosas JP. Vitamin D supplementation for women during pregnancy. *Cochrane Database Syst Rev.* 2012;2:CD008873.
69. Centers for Disease Control and Prevention. <http://www.cdc.gov/breastfeeding/data/reportcard.htm#Rise>. Updated 2012. Accessed August 2012.
70. Agricultural Research Service. USDA National Nutrient Database for Standard Reference [release 25]. Washington, DC: US Department of Agriculture; 2012. <http://www.ars.usda.gov/ba/bhnrc/ndl>.