



www.figo.org

Contents lists available at [SciVerse ScienceDirect](http://www.sciencedirect.com)

International Journal of Gynecology and Obstetrics

journal homepage: www.elsevier.com/locate/ijgo

SPECIAL COMMUNICATION

Low maternal vitamin D status during pregnancy requires appropriate therapeutic intervention

Faustino R. Pérez-López*

Department of Obstetrics and Gynecology, Faculty of Medicine, University of Zaragoza Hospital Clínico, Zaragoza, Spain

ARTICLE INFO

Keywords:

25-hydroxyvitamin D₃
 Deficiency
 Pregnancy outcome
 Sunlight
 Vitamin D

Humans obtain vitamin D via synthesis from sun exposure and a small contribution from certain foods. The major determinants of vitamin D status are the characteristics of the skin and ultraviolet action over keratinocytes. Over the years, lifestyle changes (e.g. reduced exposure to sunlight, dietary changes, increased weight), migration, poverty, and climate change have produced an increase in the prevalence of hypovitaminosis D. Vitamin D status is expressed by levels of serum 25-hydroxyvitamin D (25[OH]D)—the main precursor of the bioactive hormone calcitriol. Placental vitamin D receptors and the 1-alpha-hydroxylase (CYP27B1) activating enzyme contribute to vitamin D adjustments during pregnancy. Calcitriol levels and the calcitriol/25(OH)D quotient are higher in pregnant women to optimize appropriate fetal growth and development and calcium homeostasis.

In the January issue of IJGO, two articles are devoted to the study of vitamin D during pregnancy. Vercauysen et al. [1] studied vitamin D status in a group of pregnant women with a median gestational age of 24 weeks (range, 4–37 weeks), living in Antwerp, Belgium. The majority of those who wore clothes that partially or completely reduced sun exposure had mean serum 25(OH)D levels of less than 15 ng/mL compared with a mean of 23.6 ng/mL among uncovered women. In addition, 25(OH)D levels significantly differed by month of the year when sampling occurred. Fernández-Alonso et al. [2] studied a cohort of pregnant women living on the Spanish Mediterranean coast near Almería and found that serum 25(OH)D levels significantly decreased in the third trimester of pregnancy compared with the first trimester; no adverse impact on perinatal outcome was observed. Low serum levels during the first trimester of pregnancy were significantly associated with nonwhite ethnicity, high maternal body mass

index, tobacco use, and season when sampling occurred [3]. Obstetric and neonatal outcome did not differ by first trimester vitamin D level [2]. A recent study of a small group of pregnant women studied in Karachi, Pakistan, found that 89% of pregnant women who wore clothes that partly or completely covered their body had serum 25(OH)D levels below 30 ng/mL at delivery. A significant correlation ($r=0.68$) was reported between cord and maternal 25(OH)D levels [4].

Although comparisons are not possible between the 3 studies that were conducted at different latitudes with different social and medical circumstances, reduction of sun exposure seems to be a major factor determining maternal (and indirectly fetal) vitamin D levels rather than latitude alone. In addition, both the Pakistani and Spanish studies reported an inverse relationship between body mass index and serum 25(OH)D levels. This is supported by evidence that vitamin D fixates at the adipose tissue, which reduces its biologically active availability [5].

The second source of vitamin D is digestive intake. Women studied by Hossain et al. [4] and Fernández-Alonso et al. [2] were not receiving vitamin D supplementation or fortified food. In the study by Vercauysen et al. [1], 24.4% of women were taking multivitamins including vitamin D (400 IU per day), although this did not seem to influence 25(OH)D levels.

There is no agreement on the normal range of circulating vitamin D; however, to prevent the increase of parathyroid hormone and bone calcium mobilization, serum 25(OH)D levels should be higher than 30 ng/mL. It is likely that optimal/desirable maternal serum levels should be in the range of 30–80 ng/mL [6]. Maternal vitamin D deficiency is associated with a higher risk of pre-eclampsia, gestational diabetes, preterm birth, fetal growth restriction, neonatal hypocalcemia and tetany, low birth weight, and maternal osteomalacia and muscle weakness. In addition, pregnant women with low vitamin D levels are at higher risk of osteopenia and their offspring have a higher risk of rickets, asthma, and neurological diseases [2,7,8]. However, as discussed by Fernández-Alonso et al. [2], certain controversial obstetric results may relate to different baseline 25(OH)D levels, patient selection, and diagnostic criteria. It seems that lower 25(OH)D levels during early pregnancy are associated with adverse pregnancy outcomes [8].

Recently, the US Institute of Medicine recommended a dietary intake of 600 IU per day for adults, without distinction for pregnancy [9]. In 2007, the Canadian Pediatric Society recommended the administration of 2000 IU per day for pregnant and breastfeeding women to maintain vitamin D and calcium sufficiency. This recommendation

* Department of Obstetrics and Gynecology, Facultad de Medicina, Universidad de Zaragoza Hospital Clínico, Domingo Miral s/n, Zaragoza 50009, Spain. Tel.: +34 976 761734; fax: +34 976 761735.

E-mail address: faustino.perez@unizar.es.

was reaffirmed in 2010. In addition, the Society has recommended 25 (OH)D and calcium level screening [6].

The effect of vitamin D supplementation on mothers and children has recently been addressed in a randomized trial [10]. Pregnant women were randomized during the first trimester to receive 400 IU, 2000 IU, or 4000 IU of vitamin D₃ per day until delivery. Mean levels of 25(OH)D reached 1 month before and at delivery were significantly different among the groups. The percentage of women who achieved sufficient levels of 25(OH)D was significantly higher in the group that received 4000 IU per day. These women and their babies were less likely to have deficient or insufficient vitamin D serum levels. The relative risk of achieving a level of 32 ng/mL within 1 month of delivery was significantly different between the 2000 vs 400 IU groups and the 4000 vs 400 IU groups, but there was no difference between those who received 4000 IU and 2000 IU. It is important to mention that there were no adverse events related to the dose of vitamin D supplementation or the serum 25(OH)D level reached [10].

Pregnant women should probably consume 5–10 times more vitamin D supplement than has been recommended during the last decades. Organizations involved in women's health care, such as the World Health Organization and the International Federation of Gynecology and Obstetrics (FIGO), should make recommendations focused on pregnant and breastfeeding women to maximize maternal and child health, given the almost epidemic status of hypovitaminosis D.

Conflicts of interest

The author has no conflicts of interest.

References

- [1] Vercruyssen J, Jacquemyn Y, Ajaji M. Effect of sun exposure and 25-hydroxyvitamin D status among pregnant women in Antwerp, Belgium. *Int J Gynecol Obstet* 2012.
- [2] Fernández-Alonso AM, Dionis-Sánchez EC, Chedraui P, González-Salmerón MD, Pérez-López FR. First trimester maternal serum 25-hydroxyvitamin D status and pregnancy outcome. *Int J Gynecol Obstet* 2012.
- [3] Pérez-López FR, Fernández-Alonso AM, Ferrando-Marco P, González-Salmerón MD, Dionis-Sánchez EC, Fiol-Ruiz G, et al. 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.
- [4] Hossain N, Khanani R, Hussain-Kanani F, Shah T, Arif S, Pal L. High prevalence of vitamin D deficiency in Pakistani mothers and their newborns. *Int J Gynecol Obstet* 2011;112(3):229–33.
- [5] Wortsman J, Matsuoka LY, Chen TC, Lu Z, Holick MF. Decreased bioavailability of vitamin D in obesity. *Am J Clin Nutr* 2000;72(3):690–3.
- [6] First Nations, Inuit and Métis Health Committee, Canadian Paediatric Society. Vitamin D supplementation: Recommendations for Canadian mothers and infants. Reference No. FNIMH 07–01. Available at: www.cps.ca/english/statements/ii/fnim07-01.htm. Accessed September 12, 2011.
- [7] Radhika AG, Goel M, Radhakrishnan G, Arora S, Guleria K. Severe osteomalacia presenting as numerous fractures in late pregnancy. *Int J Gynecol Obstet* 2008;100(1):92–3.
- [8] Nassar N, Halligan GH, Roberts CL, Morris JM, Ashton AW. Systematic review of first-trimester vitamin D normative levels and outcomes of pregnancy. *Am J Obstet Gynecol* in press [Epub ahead of print].
- [9] Institute of Medicine (US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium; Ross AC, Taylor CL, Yaktine AL, Del Valle HB, editors. *Dietary Reference Intakes for Calcium and Vitamin D*. Washington DC, USA: National Academies Press (US); 2011.
- [10] 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.