

# Vitamin D levels in maternal serum and umbilical cord blood in a multi-ethnic population in Antwerp, Belgium

Y. JACQUEMYN, M. AJAJI, N. KAREPOUAN

*Department of Obstetrics and Gynaecology, Antwerp University Hospital UZA, Wilrijkstraat 10, 2650 Edegem, Belgium.*

Correspondence at: Prof Dr Yves Jacquemyn. E-mail: Yves.jacquemyn@uza.be

Tel.: 00 32 3 8215945; fax: 00 32 3 4584774

## Abstract

**Objective:** To describe the status of vitamin D levels in maternal and umbilical cord blood in term pregnant woman in a mixed ethnic population in an inner-city European maternity.

**Methods:** A single centre prospective cohort descriptive study including all uncomplicated singleton term pregnancies from April 1, 2011 until May 31, 2011. Plasma 25-hydroxy vitamin D level was determined in maternal and umbilical cord blood and data on age, previous obstetric history, ethnicity, nutritional intake and use of vitamin supplements were registered.

**Results:** Complete data were collected in 94 patients. Mean maternal serum vitamin D was 16.6 ng/mL. Using a cut-off of 20 ng/mL, 66% of women were classified as deficient. Deficiency was present in all ethnic groups, but lower levels were noted in North-African, Central-African and Asian women. A strong correlation between maternal and umbilical cord levels was noted ( $R = 0.91$ ). Number of previous pregnancies and intake of supplements had no influence.

**Conclusion:** The majority of low risk pregnant women showed vitamin D deficiency which was strongly correlated with umbilical cord levels. The prevalence was highest in the immigrant non-European population and was not influenced by intake of vitamin supplements. It can therefore be questioned whether the proposed cut-off values are appropriate.

**Key words:** Vitamin D, pregnancy, foetus, hypovitaminosis, ethnicity.

## Introduction

Vitamin D is a fat-soluble vitamin obtained by the human body in two ways, through dietary intake mainly from fatty fish, eggs and fortified food and through endogenous production in the skin after ultraviolet-B exposure. Rising evidence suggests that vitamin D deficiency is associated with a higher risk of preeclampsia, growth retardation, multiple sclerosis, schizophrenia, diabetes and asthma (Scholl & Chen, 2009). There is currently no consensus what the correct reference values for serum Vitamin D in pregnancy are, whether these reference values should be the same for all ethnic populations nor what the physiologic changes during pregnancy are. Immigrants in northern countries, especially when they are dark skinned and/or wear total body covering clothes (e.g. the traditional muslim clothing),

are more prone to vitamin D deficiency, particularly in pregnancy (McCullough, 2007; Van der Meer et al., 2006). We studied the prevalence of vitamin D deficiency in maternal and umbilical cord blood in a pregnant population of mixed ethnic origin.

## Materials and Methods

This was a descriptive single center study performed at Antwerp University Hospital (Edegem, Belgium). From April 1<sup>st</sup> to May 31<sup>st</sup> 2011 all term pregnant women presenting with spontaneous term labour were asked to have a blood sample drawn for vitamin D. A venous maternal serum sample and a sample from the umbilical vein at delivery were collected. The study was approved by the local ethics committee and all patients signed a written informed consent. Term pregnancy was defined as from

37 weeks on; complications such as diabetes, hypertension, fetal growth retardation or any other maternal disorder necessitating special care during pregnancy (including bariatric surgery and a previous baby with a congenital malformation) were excluded. A short food questionnaire was presented including questions on previous pregnancy and delivery, birth weight of previous children, previous surgery, congenital anomalies in the family, use of vitamin supplements during pregnancy, any medication, eating eggs, meat, fish, vegetables, fruits and using alcoholic beverages. Patients were also asked for their self-identified ethnic group: autochthonous Belgian, Moroccan, Turkish, Central African, Western European (other than Belgian), (East)-Asian and "other".

25-hydroxy vitamin D was analysed with the Modular Analytics E170 (Roche Diagnostics, Belgium), the measurement area used was 4 to 100 ng/mL. A serum level below 20 ng/mL was considered vitamin B12 deficiency (IOM, 2010).

Statistics were performed with the SPSS 20.0 package. Differences between groups were compared with Student's t-test.  $P < 0.05$  was considered statistically significant. Spearman's rank correlation analysis was used to check for correlation between maternal and umbilical cord values. Linear regression was performed to evaluate other factors such as nutrition and use of supplements.

## Results

Of 110 women included in the study, 90 (81.8%) completed the questionnaire. There were 54 (48.8%) primiparous and 56 (51.2%) multiparous women. Eighty three women (75.6%) were taking vitamin supplements. The only brand used was Omnibionta Pronatal® (Merck, Belgium) 10 microgram (400 IU) of vitamin D. There were 56 (51%) autochthonous Belgian women, 26 (24%) Moroccan, 8 (7%) Asian, 8 (7%) Central African, 10 (9%) Western European other than Belgian, and only 2 (2%) Turkish.

Maternal serum 25-hydroxy vitamin D was available for 94 (85.5%) of women; missing samples were almost all from women having signed the informed consent, but whose delivery was completed before blood samples were taken, mainly during night time. Mean serum 25-hydroxy vitamin D was 16.6 ng/mL (standard deviation 12.7 ng/mL, minimum 4 ng/mL, maximum 64 ng/mL). Vitamin D deficiency was noted in 62 (65.9%) of women. For the women with vitamin D deficiency 28 (45.2% of those deficient for vitamin D) was autochthonous Belgian, 20 (32.3%) Moroccan, 6 Asian (9.7%), 4 Central African (6.4%), 2 Western European other than Belgian (3.2%) and 2 Turkish (3.2%). This

means that for Belgian mothers 50%, for Moroccan 76.9%, for Asian 75%, for Central African 50%, for other European 20% and for Turkish women 100% was vitamin D deficient.

Umbilical cord blood samples were available for 84 cases (76.4%). Mean 25-hydroxy vitamin D was 20.5 ng/mL (standard deviation 10.1 ng/mL, maximum 35 ng/mL, minimum 4 ng/mL). In 42 cases (50%) the level was below 20 ng/mL. Correlation between maternal and umbilical cord levels was rather strong (Spearman's correlation coefficient  $R = 0.91$ ). Umbilical cord deficiency was present in 44 Belgian mothers (52.4% of deficiencies; 78.6% of Belgian mothers), 24 Moroccan (28.6% of deficiencies, 92.3% of Moroccan women), 4 Central African (4.7% and 50.0% respectively), 8 Asian (9.5% and 100% of Asian samples), 2 other European (2.4% and 20.0% respectively) and 2 Turkish (2.4%, including 100% of Turkish babies).

The only significant factor (except ethnicity) in the linear regression determining maternal serum levels for 25 hydroxy vitamin D was eating eggs: the more per week the less deficiency (eating 1 to 2 eggs per week;  $p = 0.025$ , eating 3 to 4 eggs per week;  $p = 0.016$ ). Using a vitamin supplement was not related to the maternal serum level of vitamin D.

## Discussion

Despite the fact that the majority of women in our sample was using vitamin supplementation, deficiency for vitamin D was present in the majority. This can be due both to biologic factors such as interference with food or absorption, but it can also be due to bias in reporting if women who report using vitamins fail to effectively take them. The brand used in our population, the most popular one, sold over the counter to pregnant women in Belgium, contains too low an amount of vitamin D to counter deficiencies, but the optimal dose and timing continue to be a matter of dispute (Hovdenak et al., 2012). Another possibility is that the available criteria for vitamin D deficiency, as we and others have used, are not reflecting true vitamin D deficiency.

Vitamin D deficiency is clearly more frequent in women from North African (Moroccan), Central African and Asian descent. We have previously described traditional clothing with a veil covering the face to be an independent risk factor for vitamin D deficiency (Vercruyssen et al., 2012), probably due to lower skin to sun contact. As all of our measurements have been performed in a short period during spring, a seasonal influence between groups has been excluded. Recently the amount of air pollution at the mother's home address was identified as an

other determining factor, but for this we have no data in our study (Baiz et al., 2012).

A recent review has summarized the impact of low vitamin D on pregnancy, demonstrating a correlation with preeclampsia, gestational diabetes, bacterial vaginosis and postpartum depression, which suggests a potential effect of vitamin D on several pregnancy outcomes (Christesen et al., 2012). It should be kept in mind though that this does not mean that vitamin D supplementation would lower the incidence of the above-mentioned pregnancy complications; published trials on supplementation have been of low quality and have only demonstrated none to borderline significant changes in outcome (De-Regil et al., 2012; Thorne-Lyman et al., 2012). In fact, there is as yet no sound scientific prove of any beneficial effect of vitamin D supplementation in pregnancy. This should be kept in mind before considering systematic supplementation with vitamin D.

There is no consensus on the clinically relevant values to use for defining vitamin D deficiency; Other studies have also demonstrated a very high prevalence of vitamin D deficiency in pregnant women both in Northern America and Western Europe (Van der Meer et al., 2006; Collins-Fulea et al., 2012; Vandevijvere et al., 2012; Vercruyssen et al., 2012).

Recently confusing and contradictory publications have been issued from the Institute of Medicine and from the Endocrine Society, demonstrating inadequate evidence to guide clinical management (Rosen et al., 2012). Before considering interventions major and convincing studies on the relation between vitamin D levels and pregnancy outcome should be available. The majority of women in our study had what is considered vitamin D deficiency although this was a selected low risk pregnancy group excluding preterm labour, growth retardation and hypertension. Furthermore one should consider the ethnic origin of the mother, as it seems rather inconsequent to consider almost all North and Central African women, having uncomplicated pregnancies and deliveries, as suffering from hypovitaminosis D (van Noord & Berghout, 2012).

## Conclusion

Women having an uncomplicated pregnancy and delivery in Antwerp, Belgium, frequently show

vitamin D deficiency which was correlated with lower umbilical cord vitamin D levels. Serum vitamin D levels are different between pregnant women of different ethnic origin. The prevalence of low vitamin D levels is highest in women from North African, Central African and Asian descent and is not influenced by the intake of the available over the counter vitamin supplements. We question the appropriateness of a vitamin D deficiency cut-off value of 20 ng/mL for a multiethnic population in Western Europe.

## References

- Baiz N, Dargent-Molina P, Wark JD et al. Gestational Exposure to Urban Air Pollution Related to a Decrease in Cord Blood. Vitamin D Levels. *J Clin Endocrinol Metab.* 2012;97:4087-95.
- Christesen HT, Elvander C, Lamont RF et al. The impact of vitamin D in pregnancy on extraskeletal health in children: A systematic review. *Acta Obstet Gynecol Scand.* 2012;91:1368-80.
- Collins-Fulea C, Klima K, Wegienka GR. Prevalence of low vitamin D levels in an urban midwestern obstetric practice. *J Midwifery Womens Health.* 2012;57:439-44.
- De-Regil LM, Palacios C, Ansary A et al. Vitamin D supplementation for women during pregnancy. *Cochrane Database Syst Rev.* 2012 Feb 15;2:CD008873.
- Hovdenak K, Haram K. Influence of mineral and vitamin supplements on pregnancy outcome. *Eur J Obstet gynecol Reprod Biol.* 2012;164:127-32.
- IOM (Institute of Medicine). *Dietary Reference Intakes for Calcium and Vitamin D.* Washington DC: The National Academies Press; 2010.
- McCullough ML. Vitamin D deficiency in pregnancy: bringing the issues to light. *J Nutr* 2007; 137: 305-6.
- Rosen CJ, Abrams SA, Aloia JF et al. IOM committee members respond to Endocrine Society vitamin D guideline. *J Clin Endocrinol Metab.* 2012;97:1146-52.
- Scholl TO, Chen X. Vitamin D intake during pregnancy: association with maternal characteristics and infant birth weight. *Early Hum Dev.* 2009; 85: 231-4.
- Thorne-Lyman A, Fawzi WW. Vitamin D during pregnancy and maternal, neonatal and infant health outcomes: a systematic review and meta-analysis. *Paediatr Perinat Epidemiol.* 2012;26 Suppl 1:75-90.
- Van der Meer IM, Karamali NS, Boeke AJ et al. High prevalence of vitamin D deficiency in pregnant non-Western women in The Hague, Netherlands. *Am J Clin Nutr.* 2006; 84:350-3.
- van Noord C, Berghout A. [Ethnic differences in laboratory results]. [Article in Dutch] *Ned Tijdschr Geneeskd.* 2012; 156(12):A4404.
- Vandevijvere S, Amsalkhir S, Van Oyen H et al. High prevalence of vitamin d deficiency in pregnant women: a national cross-sectional survey. *PLoS One.* 2012;7(8):e43868.
- 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;116:76-7.