

## Letter to the Editor

First published online 18 January 2017

### Maternal gestational vitamin D supplementation and child health: looking to the future

Madam

Pregnancy is a period of susceptibility to vitamin D deficiency. This is because there is increased demand for this hormone to meet the needs of pregnant woman and maintain reserves, as well as to meet the demands of regulation and cell differentiation for development and fetal growth<sup>(1)</sup>.

The available epidemiological evidence indicates that vitamin D deficiency in pregnant women is associated with the occurrence of pre-eclampsia, genitourinary infections and gestational diabetes<sup>(2)</sup>. In the newborn, intra-uterine exposure to vitamin D deficiency may increase the risk of low birth weight and prematurity, and of rickets, osteomalacia, and asthma and wheeze during childhood<sup>(1)</sup>. Therefore, vitamin D supplementation in pregnant women has been suggested in order to improve maternal vitamin D status and increase availability of this vitamin to the fetus and/or newborn.

In this context, the WHO/FAO has recommended a vitamin D intake (RDA) of 15 µg/d (600 IU/d) for pregnant women, irrespective of age, to maintain the serum concentration of 25-hydroxyvitamin D (25(OH)D) at about 50 nmol/l<sup>(3)</sup>. This recommendation is controversial, since it is based on vitamin D intake for bone health maintenance, not considering possibly different needs in pregnant women. Thus, there is still need for discussion in order to clarify some questions. What is a safe dose of supplemental vitamin D for pregnant women? Should vitamin D supplementation during pregnancy be recommended in clinical practice to prevent childhood diseases?

Clinical trials and cohort studies with pregnant women and children have been conducted to address these questions. The Antenatal Vitamin D in Dhaka (AViDD) trial<sup>(4)</sup> reported by Perumal and colleagues in *Public Health Nutrition* investigated the effects of supplementation with 875 µg (35 000 IU) of cholecalciferol (vitamin D<sub>3</sub>) per week during the third trimester of pregnancy on infant serum 25(OH)D concentration measured at <1, 2, 4 and 6 months of age<sup>(4)</sup>. The authors found that supplementation significantly increased infant 25(OH)D within 1 month of delivery. At 2 months, 25(OH)D remained significantly higher in the group with supplementation, yet the difference was attenuated by 4 months postpartum<sup>(4)</sup>. These results<sup>(4)</sup> can be questioned because of the sample size, absence of maternal dietary pattern analysis, and weight gain during pregnancy and postpartum. Obesity or excessive weight gain may influence the concentration of vitamin D<sup>(5)</sup>. Another limitation is that the concentration of

vitamin D-binding protein was not measured, because haemodilution during pregnancy and increasing vitamin D-binding protein concentration may significantly reduce the concentration of free 25(OH)D in the circulation<sup>(6)</sup>.

Level of vitamin D supplementation should also be based on the effects of vitamin D supplementation on children's health. Cohort studies have recorded increased risk of developing allergic diseases, such as food allergies, in children of mothers with higher maternal or cord blood vitamin D<sup>(7)</sup>. On the other hand, evidence from a recent meta-analysis suggests that increased *in utero* exposure to 25(OH)D is inversely associated with the risk of asthma and wheeze during childhood<sup>(8)</sup>. From this perspective, vitamin D supplementation during pregnancy should consider other factors besides maintaining the mother's and the child's bone health.

Evaluating the influence of high vitamin D concentrations during pregnancy on the child's health will require prospective cohort studies with a well-defined follow-up period. Another methodological aspect to be considered is the appropriate cut-off for classifying levels of vitamin D. Overall, current evidence shows controversial results, and little is known about the safe dose during pregnancy. Moreover, it is unclear whether vitamin D supplementation should be a routine part of prenatal care for women, or only in cases of vitamin D deficiency, to improve maternal and perinatal outcomes. It will be appropriate to develop new clinical trials and systematic reviews with meta-analysis to assess the clinical effects and safety of vitamin D supplementation during pregnancy and its effects in later periods of childhood or later in life.

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