High prevalence of vitamin D and calcium deficiency among pregnant women and their newborns in Chengdu, China

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Background: **Vitamin D and calcium deficiency is common in pregnant women and newborn infants. There are few data about the prevalence of hypovitaminosis D during pregnancy and infancy in China. We assessed vitamin D status of pregnant women and their neonates in Chengdu, Sichuan province, China.**

Methods: **Maternal serum and cord blood levels of calcium, 25-hydroxyvitamin D [25(OH)D], alkaline phosphatase, and parathyroid hormone (PTH) were studied in 77 urban and rural mother-neonate pairs at term.**

Results: **The mean level of maternal serum 25(OH)D was 35.95±19.7 nmol/L, and that of cord blood 25(OH)D was 40.98±18.89 nmol/L. The intake of calcium and vitamin D was uniformly low, although it was higher in urban (1010±450 mg/d, 237±169 IU/d) than in rural (320±210 mg/d, 62±66 IU/d) women. Maternal serum 25(OH)D was correlated positively with cord blood 25(OH)D (r=0.94, P<0.01).**

Conclusions: **There is a high prevalence of vitamin D and calcium insufficiency in pregnant women and neonates in Chengdu even when mothers are compliant with prenatal vitamin supplementation. Supplementation is needed to improve maternal and neonatal vitamin D and calcium nutrition.**

World J Pediatr 2010;6(3):265-267

Key words: **dietary calcium;**
newborn;
parathyroid hormone;
pregnancy;
vitamin D

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doi:10.1007/s12519-010-0224-x

Introduction

Vitamin D and calcium deficiency is prevalent in China, but it is unexpected since the nutritional status and living conditions of people improved in recent years. Deficient vitamin D and calcium have been shown to be the causes in a large proportion of childhood rickets in China.[1] In a population that already has a high prevalence of vitamin D deficiency and poor dietary calcium intake, the problem is likely to worsen during pregnancy because of the active transplacental transport of calcium to the developing fetus. There are few data from China on serum 25(OH)D concentration and the prevalence of vitamin D deficiency in pregnant women and their newborns.[2] This study was undertaken to determine the prevalence of maternal and fetal hypovitaminosis D in urban and rural areas of Chengdu and to study their correlations with the levels of calcium, serum 25(OH)D, and plasma parathyroid hormone (PTH).

Methods

Pregnant women were recruited from West China 2nd University Hospital and other two maternal and child health care hospitals in Sichuan Province. We recruited all women with a full-term pregnancy who presented to the hospital in a 2-week period in September 2007 and their infants. Exclusion criteria were chronic liver disease, renal disease, or treatment with antitubercular or antiepileptic drugs in the previous 3 months. Daily intake of vitamin D and calcium was assessed using a self-administered food frequency questionnaire. Any supplemental intake of calcium and/or vitamin D in pregnancy was also noted. Daily sun exposure was assessed by taking a detailed history of the daily routine including the time of outdoor activities and the type of clothing worn.Written informed consent was obtained from all subjects. The study was approved by the institutional ethics committee.

Maternal blood in the nonfasting condition before labor and cord blood sample were collected and

immediately transported on ice to the experiment center within 24 hours for assay of serum alkaline phosphatase (ALP), calcium, albumin, and phosphorus. The levels of serum total calcium, albumin, and inorganic phosphorus were analyzed spectrophotometrically (Sigma Diagnostics, St Louis, MO). Serum calcium was corrected for serum albumin. Serum ALP was measured spectrophotometrically (Boehringer Mannheim, Mannheim, Germany). The normal upper limit for maternal ALP was taken as that for total ALP in our laboratory for an adult population (110 U/L), and the normal upper limit for cord blood ALP was taken as 212 U/L. The serum PTH level was measured using the intact-PTH electrochemiluminescence immunoassay (Roche Intact PTH, Roche Group, Switzerland). The reference range for PTH is 1.60-6.90 pmol/L. Serum 25(OH)D was assayed using a commercial enzyme immunoassay kit (IDS, Bolden, UK) according to the manufacture's protocol. The reference range was 6-360 nmol/L. We defined vitamin D deficiency as [25(OH)D<37.5 nmol/L], vitamin D insufficiency as [25(OH)D 37.5-80 nmol/L] and vitamin D sufficiency as [25(OH)D>80 nmol/L].[3,4] The cutoffs were the same for both women and neonates.[3]

Data were presented as mean±SD. Statistical analysis was made using SPSS FOR WINDOWS software (version 9.0; SPSS, Chicago, USA). Proportions were compared using the Chi-square test. Group means were compared using independent-samples *t* test. Correlations were studied using Spearman's rank-order correlation coefficient. Significance at $P<0.05$ was taken for two-sided tests.

Results

A comparison of urban and rural women is shown in the Table. Most (96.1%) of the women had elevated ALP (ALP>110 U/L) level. The mean level of serum 25(OH)D in women was low (35.95±19.70 nmol/L) and it was positively correlated with cord blood 25(OH)D ($r=0.94$, $P<0.01$). The mean level of cord blood 25(OH)D in neonates was low (40.98±18.89 nmol/L), and the mean level of serum 25(OH)D in urban neonates differed significantly from that in rural neonates (urban: 52.87±15.44 nmol/L; rural: 25.11±8.58 nmol/L; $P<0.01$). A large proportion of women (57.1%) and neonates (44.2%) showed vitamin D deficiency, and 97.4% of women and 96.1% of neonates showed vitamin D insufficiency. Maternal serum ALP was not correlated with blood cord ALP. Maternal serum PTH was negatively correlated with daily calcium intake.

Table. Biochemical indexes of urban and rural women

	Urban women (n=44)	Rural women (n=33)
Daily calcium intake (mg/d)	1010±450	320±210*
Daily vitamin D intake (IU/d)	237±169	62±66*
ALP (μ/L)	180±62	198±53
Serum 25(OH)D (nmol/L)	48.53±16.49	19.17±6.98*
Maternal PTH (pmol/L)	2.76±1.57	5.22±2.39*

*: compared with urban women, $P<0.05$. ALP: alkaline phosphatase; PTH: parathyroid hormone.

Discussion

The most unexpected finding in this study is the very high prevalence of hypovitaminosis D. The National Academy of Nutrition suggests 400 IU as the dietary reference intake for vitamin D during pregnancy.[5] However, several investigators worldwide are arguing for revised higher guidelines for vitamin D allowance during pregnancy and lactation.[6] Our study revealed that hypovitaminosis D in pregnant women is popular in Chengdu and the contributing factors might be low dietary intake and lack of sunshine. Another explanation could lie in the prolonged deficiency of dietary calcium intake because of the eating habits in China. It is reported that the annual milk per capita of China is low-down all over the world. Dietary calcium deficiency has been found to cause secondary vitamin D deficiency in rats.[7] Similar findings are also reported in humans.[8-11] A low calcium intake has been proposed to aggravate vitamin D deficiency through increased catabolism of 25-hydroxyvitamin D.[12]

Vitamin D sources in newborn infants are mainly from transplacental stores. Maternal vitamin D status is important in determining the amount of vitamin D transported across the placenta during fetal life and thereafter the size of vitamin D reserves at birth.[13,14] Cord blood 25(OH)D strongly correlated with maternal values.[15-18] Lee et al[19] reported that although a majority of mothers received a daily prenatal multivitamin, vitamin D deficiency was found in 50% of them and in 65% of their newborn infants; thus there is a positive correlation between maternal and infant plasma 25-hydroxyvitamin D concentrations. The cut-off values for hypovitaminosis D in neonates is still being debated. No evidence suggests that neonatal 25(OH)D concentrations are different from those in adults.

The most recent vitamin D intake guidelines formulated by the American Academy of Pediatrics recommend all infants and children, including adolescents, have a minimum daily intake of 400 IU of vitamin D beginning soon after birth.[20] Since the very low level of 25(OH)D in cord blood, we also suggest that vitamin D supplementation should be started in the first days of life. At present, the recommendation for vitamin D supplementation is 400 IU/d in China. Whether it is the suitable dosage for infants beginning a life with small stores as a result of maternal vitamin D deficiency still needs further investigation.

Our results are consistent with other studies,[21,22] showing that serum PTH concentration is inversely associated with calcium intake. In our study, 96.1% of mothers had elevated ALP level, which is one of the indicators for biochemical osteomalasia. Sachan et al[23] reported that although none of the women had clinical manifestations suggesting osteomalacia, 14% of them had elevated heat-stable alkaline phosphatase (HALP). Rab and Baseer[24] reported in the population with low vitamin D intake (88±14 IU/d) in the population, and the incidence of elevated total AP was 26%. Brook et al[15] found that 20% of their subjects with serum 25(OH)D<25 nmol/L had elevated HALP.

In conclusion, strategies should be developed to prevent maternal vitamin D and calcium deficiency and daily prenatal supplementation should be encouraged, especially in the third trimester, so that pregnant women may be healthy and provide enough vitamin D and calcium to their fetuses.

Funding: None.

Ethical approval: This study was approved by the data inspectorate of China and by the regional committee for medical research ethics.

Competing interest: No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

Contributors: Wang J proposed the study and wrote the main body of aritcle under the supervision of Yang F. Mao M is the guarantor. Liu DH and Yang HM provided advice on medical aspects. Yang SF analyzed the data.

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Received April 22, 2009
Accepted after revision December 30, 2009