

## HIGH PREVALENCE OF VITAMIN D DEFICIENCY AMONG PREGNANT WOMEN AND THEIR NEWBORNS

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### ABSTRACT

An increasing number of studies suggest that vitamin D deficiency during pregnancy is associated with multiple adverse health outcomes in mothers, neonates, and children. There are no representative country data available on vitamin D status of pregnant women in Europe. The aim of this study was to estimate the prevalence of vitamin D deficiency among Belgian pregnant women and to assess the determinants of vitamin D status in the first and third trimester of pregnancy. The women were selected via a multi-stage proportionate-

to-size sampling design. Blood samples were collected and a questionnaire was completed face-to-face. 55 obstetric clinics were randomly selected and 1311 pregnant women participated in the study. The median serum 25-hydroxyvitamin D [25-(OH) D] concentration was significantly lower in the first trimester (20.4 ng/ml) than in third trimester (22.7 ng/ml). Of all women, 74.1% (95%CI = 71.8-76.5%) were vitamin D insufficient (25-(OH)D <30 ng/ml), 44.6% (95%CI = 41.9-47.3%) were vitamin D deficient (25-(OH)D <20 ng/ml), while 12.1% (95%CI = 10.3-13.8%) were severely vitamin D deficient (25-(OH)D <10 ng/ml). Of all women included, 62.0% reported taking vitamin D-containing multivitamins, of which only 24.2% started taking those before pregnancy. The risk of vitamin D deficiency (25-(OH) D <20 ng/ml) was significantly higher for less educated women and women who reported not going on holidays to sunny climates. The risk of severe vitamin D deficiency (25-(OH) D <10 ng/ml) decreased for women who reported alcohol consumption during pregnancy, decreased with more frequent use of sunscreen lotion and increased for smokers and women who reported preference for shadow. In conclusion, vitamin D deficiency is highly prevalent among pregnant women in Belgium and this raises concerns about the health consequences for the mother and the offspring. A targeted screening strategy to detect and

treat women at high risk of severe vitamin D deficiency is needed in Iraq and show and explain the reasons and treatments.

**KEYWORDS:** Prevalence, Deficiency, Newborns.

## INTRODUCTION

Vitamin D is a fat-soluble vitamin and steroid derivative. By itself, it has no physiological function; however, when converted into its active forms, vitamin D becomes an effective substance with many physiological activities. The active forms of vitamin D include 25-hydroxyvitamin D<sub>3</sub>, 1,25-hydroxyl vitamin D<sub>3</sub>, and 24,25-hydroxyl vitamin D<sub>3</sub>. Among these, 1,25-hydroxyl vitamin D<sub>3</sub> is the main form, with an active rate 500 to 1000 times higher than that of 25-hydroxyl vitamin D<sub>3</sub>.<sup>[1]</sup> However, because of its longer half-life, 25-hydroxyvitamin D<sub>3</sub> is considered the best biomarker of the vitamin D status. As an essential nutrient for the human body, vitamin D has the following main physiological functions: regulation of calcium and phosphorus metabolism, promotion of bone growth, and regulation of cell growth and differentiation. Studies have revealed that vitamin D deficiency is a worldwide problem.<sup>[2-6]</sup> Furthermore, vitamin D deficiency and inadequacy are very common during pregnancy,<sup>[7,8]</sup> and their incidence can reach up to 96.0% to 99.4%.<sup>[9,10]</sup> Studies have also shown that vitamin D deficiency in pregnant women is associated with various adverse pregnancy outcomes in the mother (preeclampsia, gestational diabetes, cesarean section, and infectious disease), fetus (gestational duration), and offspring (type 1 diabetes, eczema, and inflammatory and atopic disorders).<sup>[11-14]</sup> Previous studies have suggested that vitamin D deficiency among pregnant women is common in China.<sup>[15,16]</sup> However, the vitamin D status in the general population varies significantly among different areas of China because of diverse diets, dietary supplements, and sunlight exposure.<sup>[6]</sup> Therefore, the present study was designed to investigate the prevalence of vitamin D deficiency in pregnant women in Guizhou, China and explore the relationship between the vitamin D nutritional status and adverse perinatal outcomes in pregnant women.

## Methods

Pregnant women who received perinatal care and delivered in the Obstetric Department of the Affiliated Hospital of Guizhou Medical University from 1 November 2014 to 30 April 2015 were enrolled in this retrospective study. The patients' baseline characteristics (age, gestational age, perinatal outcomes, and other parameters) were obtained from their medical records. The adverse perinatal outcomes assessed in this study were preeclampsia, gestational

diabetes, and similar conditions. All pregnant women were divided into two groups according to their pregnancy outcomes: the healthy group (Group A), which comprised patients who had good pregnancy outcomes and no pregnancy complications, and the adverse perinatal outcome group (Group B), which comprised patients who were healthy before their pregnancy and developed adverse outcomes during the perinatal period. Patients with the following diseases were excluded: primary hypertension, primary diabetes, chronic liver disease, hyperthyroidism, and connective tissue diseases. All participants provided written informed consent to participate in the study. This study was approved by the medical ethics committee of Guizhou Provincial Hospital.

### **Analysis of samples**

All participants received health education and guidance regarding standard clinical nutrition during perinatal care. With the patients' consent, 5 mL of fasting blood samples were collected from the antecubital vein in the early morning at 11 to 16 weeks of gestation and analyzed by a laboratory technician in the clinical laboratory of our hospital. The serum 25-hydroxyvitamin D [25-(OH)D] concentration was measured by enzyme-linked immunosorbent assay (Roche, Basel, Switzerland) according to the manufacturer's guidelines. According to the standard set by the National Institutes of Health, a serum 25-(OH)D concentration of <30 nmol/L (<12 ng/mL) was defined as vitamin D deficiency, that from 30 to 50 nmol/L (12 to 20 ng/mL) was defined as vitamin D inadequacy, and that of >50 nmol/L (>20 ng/mL) was defined as vitamin D sufficiency.

### **Statistical Methods**

Measurement data are expressed as mean  $\pm$  standard deviation. Data were analyzed using the statistical software SPSS 21.0 (IBM Corp., Armonk, NY, USA). The Wilcoxon signed-rank test and the Spearman rank correlations method were used to analyze the relationship between vitamin D and perinatal outcomes. The Wilcoxon signed-rank sum test is a nonparametric statistical hypothesis test and was used to compare the population mean ranks between Groups A and B. The Spearman rank correlations method was used to measure the strength and direction of the association between vitamin D levels in pregnant women in early pregnancy and perinatal infant and maternal outcomes. A *P* value of <0.05 was considered statistically significant.

**RESULTS**

In total, 220 pregnant women were enrolled in this study. Among these 220 women, 149 (67.7%) were assigned to Group A and 71 (32.3%) were assigned to Group B. The patients' ages ranged from 18 to 43 years (mean,  $29.3 \pm 4.5$  years). Four (1.8%) women were 18 to 21 years old, 188 (85.5%) were in 22 to 34 years old, and 28 (12.7%) were  $>35$  years old. The serum 25-(OH) D concentration was measured from 11 to 13 gestational weeks. The differences in the mean age and gestational weeks between Groups A and B were not statistically significant (Table 1).

Table 1.

Comparison of baseline characteristics of Groups A and B.

	Group		P
	A	B	
Age in years			
18–21	3	1	0.75
22–34	125	63	
$\geq 35$	21	7	
Age in years			
	$28.35 \pm 5.40$	$29.68 \pm 4.30$	0.0704
Gestational weeks			
11	51	25	0.89
12	53	23	
13	45	23	

Data for Groups A and B are presented as number of patients or mean  $\pm$  standard deviation.

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**Prevalence of vitamin D deficiency in pregnant women**

The mean serum 25-(OH) D concentration among all 220 pregnant women was  $29.5 \pm 5.8$  nmol/L. Vitamin D deficiency was found in 159 (72.3%) women, vitamin D inadequacy was found in 45 (20.5%) women, and vitamin D sufficiency was found in 16 (7.3%) women. Thus, overall, 92.8% of pregnant women in this study had vitamin D insufficiency.

### Relationship between vitamin D level and perinatal outcomes

In Group A, vitamin D deficiency was found in 103 (69.1%) women, vitamin D inadequacy was found in 30 (20.1%) women, and vitamin D sufficiency was found in 16 (10.8%) women. In Group B, vitamin D deficiency was found in 61 (85.9%) women and vitamin D inadequacy was found in 10 (14.1%) women; no women in Group B had vitamin D sufficiency. The Wilcoxon signed-rank test showed that the differences between these two groups were statistically significant ( $P < 0.05$ ). Overall, 38.4% of pregnant women with vitamin deficiency and 22.2% of pregnant women with vitamin inadequacy developed adverse perinatal outcomes.

Spearman's correlation analysis was performed to further explore the relationship between vitamin D levels in pregnant women in early pregnancy and perinatal infant and maternal outcomes. The results revealed that the vitamin D level was negatively correlated with adverse pregnancy outcomes (Spearman correlation =  $-0.433$ ,  $P < 0.05$ ).

### DISCUSSION

Vitamin D is a fat-soluble vitamin. Its deficiency increases the risk of metabolic syndromes, including abnormal glucose metabolism, obesity, hypertension, and cardiovascular and cerebrovascular disease.<sup>[2]</sup> For example, vitamin D deficiency increases the incidence of preeclampsia and the rate of cesarean section, and it is closely associated with gestational age, neonatal hypoglycemia and hyperinsulinemia,<sup>[17,18]</sup> and decreased birth height, weight, and head circumference of the offspring.<sup>[19]</sup>

Studies have revealed that the average 25-(OH)D concentration in pregnant women in early pregnancy in the Middle East is  $<25$  nmol/L.<sup>[20,21]</sup> In China, a study conducted in the Beijing area revealed that the mean 25-(OH)D concentration in healthy women was  $27.28 \pm 6.64$  nmol/L; women with 25-(OH)D deficiency and inadequacy accounted for 99.4%, and women with adequate levels of 25-(OH)D accounted for only 0.6%.<sup>[6]</sup> Wang *et al.*<sup>[22]</sup> reported that the mean serum 25-(OH)D level in pregnant women was  $38.54 \pm 17.18$  nmol/L in the urban district of Xi'an city, Shanxi Province, and nearly 90% of pregnant women had 25-(OH)D deficiency. In addition, Xie *et al.*<sup>[23]</sup> reported that in Nanjing city, Jiangsu Province, the mean 25-(OH)D concentration in pregnant women was  $26.4 \pm 10.7$  nmol/L in summer and  $22.7 \pm 4.8$  nmol/L in winter. These studies showed that  $>96\%$  of pregnant women had low levels of vitamin D. Because the vitamin D status in pregnant women varies prominently among different areas because of different diets, dietary

supplements, and sunlight exposure,<sup>[6]</sup> the present study was performed to determine the vitamin D status in pregnant women in Guizhou, China. We found that the mean level of vitamin D in pregnant women was  $29.5 \pm 5.8$  nmol/L, and >90% of pregnant women had vitamin D insufficiency.

Furthermore, the incidence of adverse perinatal outcomes was significantly higher in pregnant women with vitamin D deficiency than in women with vitamin D sufficiency. In addition, the vitamin D level in pregnant women was negatively correlated with the incidence of adverse perinatal outcomes.

Therefore, for adequate prenatal care, guidance regarding nutrition and appropriate interventions are necessary during pregnancy. However, no unified standard guidelines on supplementation of vitamin D during pregnancy are currently available.

The American College of Obstetricians and Gynecologists recommends that for women with risk factors (vegetarians, populations with inadequate sun exposure due to living in the north or wearing protective clothing, and ethnicity, especially women with dark skin), daily supplementation with 1000 to 2000 IU of vitamin D is safe.<sup>[24]</sup> However, no adequate studies have been performed to evaluate the safety of large doses of additional supplements.

For women without an increased risk of vitamin D deficiency, enough vitamin D can be obtained by taking prenatal vitamins. In 2010, the US Institute of Medicine established that daily supplementation with 600 IU of vitamin D is sufficient for pregnant and lactating women.

Most prenatal vitamins contain at least 400 IU of vitamin D per tablet. The 2013 version of the “dietary reference intake for Chinese residents” recommends that the reference nutrient intake value of vitamin D in pregnant women in early pregnancy is 10 µg/day (1 IU = 0.025 µg; that is, 400 IU/day). Whether this reference value can meet the requirement of pregnant women needs to be further verified in the clinical setting.

Although this study provides a glimpse of the vitamin D status of pregnant women in Guizhou, China, the sample size was rather small. Moreover, this study was conducted in one hospital, which may have led to bias. Therefore, to more accurately guide the daily intake of vitamin D in pregnant women and further decrease adverse pregnancy outcomes from a

nutritional perspective, multicenter prospective cohort studies are needed to guide perinatal nutrition and health care.

### **Declaration of conflicting interest**

The authors declare that there is no conflict of interest.

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