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İsmail PEHLİVAN
Şükrü HATUN
Metin AYDOĞAN
Kadir BABAOĞLU
Gülcan TÜRKER
Ayşe Sevim GÖKALP

Maternal Serum Vitamin D Levels in the Third Trimester of Pregnancy

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Department of Pediatrics, Faculty of Medicine, Kocaeli University, Kocaeli - Turkey

Abstract: Aim: To measure serum vitamin D levels of pregnant women in the last trimester and to determine factors affecting serum levels.

Methods: Seventy-eight pregnant women, 19-39 years old and having their third trimester between March and May 2000, were enrolled. Serum Ca, P and alkaline phosphatase and 25-hydroxyvitamin D3 levels were measured in venous blood samples during the third trimester. Maternal age, education, socioeconomic status, number of gravida, nutrition, dressing habits and daily exposure time to sunlight were determined and their correlation with serum vitamin D levels were analyzed statistically.

Results: The mean age of mothers was 26.1±5.1 years. The mean serum 25-hydroxyvitamin D_3 level of the mothers was 17.5±10.3 nmol/L and 94.8% of the mothers had a 25-hydroxyvitamin D_3 level below 40 nmol/L (below 25 nmol/L in 79.5%). The risk factors associated with low maternal 25(OH)D were low educational level, insufficient intake of vitamin D from the diet and 'covered' dressing habits. No statistical significance was found between serum 25-hydroxyvitamin D3 levels and maternal age, socioeconomic status, daily exposure time to sunlight and parity.

Conclusions: Severe maternal vitamin D deficiency remains a commonly seen problem in Turkey. Pregnant women should be encouraged to expose themselves to sunlight and take vitamin D supplements. Fortification of certain foods with vitamin D will be a practical way of preventing maternal vitamin D deficiency and rickets in infants.

Key Words: Vitamin D supplementation, infancy, pregnancy

Introduction

Vitamin D and parathyroid hormone play important roles in calcium-phosphorus homeostasis and bone mineralization. Direct exposure to ultraviolet radiation and dietary intake are the two main sources of vitamin D. Inadequate exposure to sunlight and dietary intake in pregnancy and during lactation causes both inadequate body stores in the newborn and in breast milk (1). These factors impair bone growth and mineralization in early infancy and even may cause hypocalcemic convulsions (2-5).

In 1995, a series of 105 breastfed infants presenting with hypocalcemic convulsions due to rickets were reported from Turkey (6). In the last two years we also had four infants 3-6 months old presenting with hypocalcemic convulsions. Common characteristics of these four breastfed infants were their mothers' low serum vitamin D levels due to inadequate exposure to sunlight and no vitamin D supplementation during pregnancy. The data emphasizes the significance of the maternal factor especially in the early infancy period, in the development of rickets.

In this study, our aim was to measure serum vitamin D levels of pregnant women in the last trimester and determine the factors affecting serum levels.

Materials and Methods

Seventy-eight pregnant women, 19-39 years old and having their third trimester between 1st of March and 30th of May 2000, were enrolled. The women who had chronic diseases, or were taking medicines, or who had obstetric problems such as gestational diabetes, hypertension, preeclampsia, eclampsia or premature delivery were excluded from the study.

Serum Ca, P and alkaline phosphatase and 25-hydroxyvitamin D_3 levels were measured in venous blood samples during the third trimester. Enzyme binding protein assay (Biomedica Gruppe, Immunodiagnostic, Bensheim, Germany) was used for 25-hydroxyvitamin D_3 determinations, and values between 25 and 40 nmol/L were considered marginal, whereas levels below 25 nmol/l indicated severe vitamin D deficiency (7).

Maternal age, education, socioeconomic status, number of gravida, nutrition (especially consumption foods containing vitamin D), dressing habits, and daily exposure time to sunlight were determined and their correlation with serum vitamin D levels were analyzed statistically.

The dressing habits of the women were as follows: group I (n = 4), covering their head and hands with a black scarf, no covering on the face; group II (n = 49), wearing a black scarf on their head, no covering of the hands or facei and group III (n = 25), no covering on the head, face or hands.

Statistical analyses were performed using SPSS in Windows 6.1. version 8.0. The Mann Whitney U test, Kruskal-Wallis test and Student's t-test were used for evaluation.

Results

Serum Ca, P, ALP levels were studied in 74 women. Mean serum Ca level was 8.7 ± 0.6 mg/dL and 17.9% (n = 14) had low levels. Mean serum P was 3.1±0.7 mg/dL and 23.1% (n = 18) had low levels and only one woman 1.3% (n = 1) had a high level. Mean serum ALP levels were 126 ± 54 IU/L and all values were within normal levels.

Mean 25-hydroxyvitamin D_3 levels were 17.5 ± 10.3 nmol/L (n = 78) and 74 mothers (94.8%) had low levels (< 40 nmol/L). Median vitamin D level was 16.3 nmol/L. Vitamin D deficiency was marginal in 15.3% (n = 12, 25-hydroxyvitamin D3=25-40 nmol/L) and severe in 79.5% (n = 62, 25-hydroxyvitamin D_3 < 25nmol/L). Only 4 mothers (5.2%) had normal serum 25-hydroxyvitamin D3 levels.

Mean age of the mothers was 26.1 ± 5.1 years. Fifty percent (n = 39) were younger than 25. The socioeconomic status of the women was classified as follows: 38 (48.7%) were of low, 28 (35.9%) of moderate and 12 (15.4%) of high socioeconomic status. The number of gravida was 1 in 31 women (39.7%), 2-3 in 36 women (46.1%), and ≥ 4 in 11 women (14.2%). When correlations of serum Ca, P, ALP and 25-hydroxyvitamin D_3 levels were analyzed with age, socioeconomic status and numbers of gravida, no significant difference was found between the groups younger than 25 and older than 25 ($p > 0.05$), different socioeconomic status ($p > 0.05$) and numbers of gravida ($p > 0.05$).

Educational levels of the women were as follohws: 46 (58.9%) were illiterate or had completed elementary school, and 32 (41.1%) had completed at leastsecondary school. When 25-hydroxyvitamin D_3 levels were correlated with the education level of the mothers, graduates of high school and university had higher serum 25-hydroxyvitamin D_3 levels ($p = 0.042$).

When antenatal medical care was evaluated, 59 (75.6%) women had received medical care and 19 (24.4%) had received no medical care and no vitamin D supplementation.

Mean daily vitamin D intake was 185 ± 117 IU. Forty-two subjects (53.8%) had never taken vitamin D supplementation during their pregnancies. No statistical significance was found between vitamin D intake and educational and socioeconomic status and maternal age. Total vitamin D intake from the diet and supplementation was below the recommended level. Although women who had received vitamin supplementation during pregnancy had higher serum 25-hydroxyvitamin D_3 levels (19.4 nmol/L versus 16.1 nmol/L), no significance was found statistically ($p = 0.09$).

When serum Ca, P, ALP and 25-hydroxyvitamin D_3 levels were compared in groups with total daily vitamin D intake above or below 100 IU/day, 25-hydroxyvitamin D_3 levels were significantly lower in the group with vitamin intake below 100 IU/day (respectively 19.3 ± 10.2 nmol/L, 15.4 ± 10.1 nmol/L, $p = 0.02$).

This study revealed that 47.5% (n = 37) of women never exposed themselves to sunlight during pregnancy. Most of the pregnancies took place in winter. When the time spent in and out of the house was evaluated in this group, 47.5% (n = 37) stayed at home all day and 52.5% (n = 41) spent at least one hour out of the house. No difference was detected between 25-hydroxyvitamin D_3 levels and daily exposure to sunlight ($p > 0.05$).

Dressing habits had no correlation with Ca, P or ALP levels. But when serum 25-hydroxyvitamin D_3 levels were evaluated, the difference was significant between groups I and III ($p = 0.014$) and groups II and III ($p = 0.029$), whereas no difference was found between groups I and II ($p = 0.089$). Mean serum 25-hydroxyvitamin D_3 levels were 10.0 ± 4.8 nmol/L in group I (n = 4), 16.8 ± 10.1 nmol/L in group II (n = 49) and 20.1 ± 10.4 nmol/L in group III (n = 25) (Table).

Table. Serum 25-hydroxyvitamin D_3 levels in pregnant women in relation to maternal age, socioeconomic status, education, number of gravida, total daily vitamin D intake and daily exposure time to sunlight.

	n	25-hydroxyvitamin D_3 levels nmol/L (mean ±SD)	p value
All women	78	17.5 ± 10.3	-
Age			
< 25 years	39	17.1 ± 10.4	0.651
> 25 years	39	18.2 ± 10.2	
Socioeconomic status			
Low	38	17.1 ± 10.3	0.727
Moderate	28	17.8 ± 10.9	
High	12	18.6 ± 9.3	
Education			
Illiterate or completed elementary school	46	16.4 ± 10.4	0.042
Secondary school and above	32	19.3 ± 9.9	
Numbers of gravida			
1	31	18.9 ±11.5	0.606
2-3	36	16.4 ±9.5	
≥ 4	11	18.1 ±9.3	
Total daily vitamin D intake			
< 100 IU/day	33	15.4 ±10.1	0.020
> 100 IU/day	45	19.3 ±10.2	
Daily exposure time to sunlight			
< 1 hour/day	37	17.9 ±11.5	0.893
> 1 hour/day	41	18.2 ±11.9	

Discussion

Vitamin D and parathyroid hormone have an important role in Ca-P homeostasis and bone mineralization. Vitamin D deficiency causes rickets in children and osteomalacia in adults. Although vitamin D deficiency is generally asymptomatic in adults, asymptomatic even mild vitamin D deficiency may lead to serious problems in the fetus or newborn (1). The results of several studies suggest that the bone mass of the newborn may be related to the vitamin D status of the mother (7). Bone ossification of the fetus may be impaired and the infant may present with congenital rickets. Craniotabes, a large fontanel, enamel hypoplasia of the teeth, and hypocalcemic tetany may be observed (5,7,8). Low fetal Ca levels cause hyperplasia of fetal parathyroid glands, excessive PTH secretion and enhanced Ca resorption from the bone. Serum Ca levels in newborns and during early infancy are closely related to maternal Ca metabolism. The newborn consumes its vitamin D stores in the first 8 weeks (1,8). If vitamin D deficiency of the mother continues during lactation, the risk of rickets increases in breastfed infants.

Physiologically, 1,25-dihydroxyvitamin D levels are increased from the beginning of pregnancy, whereas no increase in 25-hydroxyvitamin D_3 level occurs. Since the half-life of 25-hydroxyvitamin D_3 is approximately one month, it is considered to be the best indicator of vitamin D status (9). In humans, endogenous synthesis from sunshine exposure is an important source of vitamin D, but large seasonal variations in serum 25-hydroxyvitamin D concentrations have been observed in adults and infants (7).

In 1981, Hasanoglu et Al. found low serum 25-hydroxyvitamin D_3 levels in 20% of mothers who had their pregnancies in winter months, whereas mothers having their pregnancies in sunny months had normal levels (10). In 1989, in 55% of mothers serum 25-hydroxyvitamin D_3 levels measured just after delivery were low. These incidences were similar to maternal

vitamin D deficiency reported from Pakistan (48%) and Saudi Arabia (59%) (11,12).

In August 1998, in a study performed in Istanbul, Alagol et al. reported low serum 25-hydroxyvitamin D_3 levels in 66.6% of women of reproductive age (13). In a recent study performed in Ankara, Andiran et al. also found low serum 25-hydroxyvitamin D_3 levels in mothers who delivered in October and November; 85% had 25-hydroxyvitamin D_3 levels lower than 40 nmol/L and 46% lower than 25 nmol/L (14). Vitamin D deficiency was even more marked in our study, with third trimester levels lower than 25 nmol/L in 79.5% of the group.

Our city, Kocaeli, has intensive industrial air pollution, which prevents optimal exposure to sunlight. In addition to mothers' dressing habits, low dietary vitamin D intake, no vitamin supplementation during pregnancy, spending most of the day time at home and air pollution contribute to vitamin D deficiency.

In India, in a study enrolling 9-24-month-old infants who had the same socioeconomic conditions and no vitamin D supplementation, the group living in the region with intensive air pollution had lower serum 25-hydroxyvitamin D_3 levels than those living in the countryside with no air pollution (12.6 nmol/L versus 28.2 nmol/L). In the same study, serum ALP and PTH levels of infants exposed to intensive air pollution (ALP: 663 IU/L and PTH: 42.9 pg/mL) were higher than those of infants living in the countryside (ALP: 404 IU/L and PTH: 14.7 pg/mL)(15).

We found no significance difference in maternal serum Ca, P, ALP and 25-hydroxyvitamin D_3 levels between various socioeconomic levels. However, Andiran et al. found vitamin D deficiency in the low socioeconomic class (14). We also found a positive correlation between serum 25-hydroxyvitamin D_3 level and educational status. In a study carried out in Pakistan, Atiq et al. found lower serum 25-hydroxyvitamin D_3 levels in mothers and their infants from the upper socioeconomic group. The women of the upper socioeconomic group, who mostly preferred to live indoors, had reduced exposure to direct sunlight (11). Although more vitamin consumption is expected in frequent pregnancies, we found no correlation between the number of pregnancies and vitamin D deficiency.

If exposure to sunlight is not optimal, the vitamin D content of the diet must be 400 IU/day (16). Dietary intake or vitamin supplementation is important, especially in winter. In countries where dairy products are not supplemented with vitamin D, where sunshine exposure is low, or when presentation for antenatal care is delayed, 1000 IU/d should be given during the last 3 months of pregnancy or 100 000 IU in one dose at the beginning of the last trimester (8,17,18).

In many developed countries, rickets is prevented by enriching foods, especially milk products, with vitamin D. This application makes vitamin D supplementation unnecessary in pregnant women (8,16). In our study, we found that women from all ages, and socioeconomic and educational levels had inadequate dietary vitamin D intake. We think that vitamin D supplementation is necessary for all pregnant women in Turkey and it is critically essential in winter.

Dressing habits (black covering on head, face and hands) play a role in serum vitamin D levels. In a study by Alagol et al., women in black dress covering their hands and face had lower 25-hydroxyvitamin D levels. They found no statistical difference between women in black dress covering their hands and face and those with their head, face and hands uncovered (13). However, in our study the difference was significant between the groups whose only heads are covered and those with their head, face and hands uncovered ($p = 0.029$), whereas no difference was found between women in black dress covering their hands and face and the groups whose only heads are covered ($p = 0.89$).

In conclusion, similar to our results, studies performed in Istanbul and Ankara reveal that there is serious maternal vitamin D deficiency in Turkey even in summer, and the problem is gradually becoming more severe. Pregnant women should be encouraged to expose themselvesto sunlight and vitamin D supplementation. Certainly an improvement in the nutritional status of mothers during pregnancy will lead in turn to an improvement in the vitamin D status of newborns. Fortification of certain foods with vitamin D will be a practical approach to prevent maternal vitamin D deficiency and rickets in infants.

Correspondence author:
İsmail PEHLİVAN
Department of Pediatriscs
Faculty of Medicine
Kocaeli University,
Derince, Kocaeli - Turkey

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