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Effect of Vitamin D Supplementation during Pregnancy on Birth Weight: A Case-Control Study

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ABSTRACT

***Background*:** Previous studies revealed that maternal serum level of vitamin D can influence neonatal outcomes. In this controlled trial, we evaluated the effect of vitamin D supplementation during pregnancy on birth weight.
***Methods*:** In this interventional study, we enrolled 67 pregnant women (gestation: 10 weeks), who referred to Seyyed-al Shohada Hospital during two years (from January 2014) with vitamin D less than 30 ng/ml. From gestational age of 14-24 weeks, vitamin D (50,000 IU/week) was administered to the patients, and its level was measured again in the 24th week of gestation. At this time, patients with vitamin D more than 30 ng/ml served as the intervention group, while the remaining patients were excluded (n=55 patients). In the control group, the level of vitamin D was measured at the time of delivery.
***Results*:** The mean vitamin D level in the intervention group was 43.04±20.09 ng/ml. The baseline patient characteristics such as gravidity, parity, and the number of deliveries were not significantly different between the two groups. However, the two groups were significantly different regarding neonates' characteristics such as birth weight, height, and head circumference.
Conclusion: Our findings showed that administrating vitamin D during pregnancy increases the mean values of neonatal weight, head circumference, and height.

Keywords: Birth weight, Pregnancy, Vitamin D

Introduction

Vitamin D deficiency is a common global problem in pregnant women and neonates (1-3). The estimated prevalence rates of vitamin D deficiency among pregnant women and infants are about 60% and 15-65%, respectively (4, 5). A study revealed that vitamin D deficiency rates in Iranian pregnant women and infants were about 71% and 55%, respectively (6). Calcium and vitamin D are considered as two important factors during pregnancy, which can affect fetal skeletal growth (7), brain development (8), and neonatal immune function (9). Moreover, they are related to recurrence of some diseases such as gestational diabetes and hypertension (10).

25-hydroxy vitamin D [25(OH) D] is a major active metabolite of vitamin D, which is transferred from maternal circulation into fetal circulation via placenta to meet the fetal requirement for vitamin D (11). The exact impact of vitamin D on maternal, placental, and certain fetal tissues is not known yet (7). Besides, it is not clear whether the changes in maternal-fetal vitamin D status can affect maternal and neonatal outcomes or not (12, 13). On the other hand, previous trials are not sufficient to support or refute the efficacy of vitamin D supplementation during pregnancy (14, 15).

Low birth weight (LBW) refers to newborns with birth weight less than 2500 g. The rate of mortality and morbidity in these infants is higher than those with normal birth weight (16). Additionally, small gestational age (SGA) is prevalent in mothers with Vitamin D deficiency as it is the major cause of poor mineralization of the bones due to the release

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of parathyroid hormone and Ca^{2+} homeostasis (3, 4). Several studies have indicated that vitamin D deficiency is common in Iranian pregnant women (16). This interventional study aimed to examine the effect of vitamin D administration on pregnant women and birth weight.

Methods

In this interventional study, all the pregnant women (gestational age: 10 weeks), who referred to Seyyed-al Shohada Hospital were recruited. The pregnancy and gestational age were determined by ultrasonography. The patients with vitamin D levels less than 30 ng/ml (n=67 patients) were selected for the study. At week 14 of pregnancy, vitamin D 50,000 IU/weekly was administered to the women for 10 weeks (weeks 14-24). Vitamin D level was measured again in 24th week of gestation at the same center (Seyyed-al Shohada Hospital). Women with vitamin D more than 30 ng/ml participated in the study as the intervention group, while the ones with vitamin D less than 30 ng/ml were excluded from the study. Besides, five patients whose measured vitamin D level at the time of delivery was less than 30 ng/ml served as the control group. Gravidity among the patients varied between 1 and 4. More importantly, the women with preeclampsia, gestational diabetes, body mass index (BMI) above 28 kg/m^2, osteomalacia, active thyroid or parathyroid diseases, endocrine disorders, hypertension, use of diuretics, calcium blockers intake, chronic hypertension, and history of allergy to vitamin supplements were excluded from the study. The mean durations of pregnancy in the two groups were 39.45±2.21 weeks. After delivery, weight, length, and head circumference of the neonates were evaluated and recorded. The study protocol was explained to all the patients and the written informed consent was obtained from them. Ethic approval was not necessary as vitamin D administration is routine in pregnant women with vitamin D deficiency.

Statistical analysis

The data was statistically analyzed using SPSS, version 22. Categorical data is presented as numbers (percentages) and continuous data as mean±SD. Chi-square and t-test were run to compare the categorical and continuous variables, respectively. P-value less than 0.05 was considered statistically significant.

Results

In this study, 123 women, including 67 in the intervention group (treated with vitamin D for 10 weeks) and 55 in the control group, were compared. The mean level of vitamin D in the intervention group was 43.04±20.09 ng/ml. The baseline patient characteristics such as gravidity, parity, and the number of labors did not show a significant difference between the two groups (Table 1). In the intervention group, the mean of birth weight (3361.18 g), height (51.68 m), and head circumference (35.14 mm) were significantly higher than the control group (Table 2). Furthermore, we did not detect any adverse effects related to vitamin D consumption in the intervention group.

Discussion

Previous studies in Iran demonstrated that more than 50% of mothers suffer from vitamin D deficiency during pregnancy (6, 16). In this regard, the present study evaluated the impact of vitamin D on birth weight. Our findings indicated that birth weight, head

Table 1. Patient characteristics at baseline

Women's characteristics		Control group N=55	Intervention group N=67	P
Gravidity	1	30(44.8%)	36(65.5%)	0.14
	2	25(37.3%)	14(25.5%)	
	3	10(15%)	4(7.3%)	
	4	2(3%)	1(1.8%)	
Parity	1	26(38.8%)	14(25.5%)	0.13
	2	9(13.4%)	4(7.3%)	
	3	2(3%)	1(1.8%)	
The number of deliveries	1	26(38.8%)	14(25.5%)	0.15
	2	9(13.4%)	4(7.3%)	
	3	2(3%)	1(1.8%)	

Table 2. Patient characteristics and neonatal outcomes in the two groups

Neonates outcomes	Control group N=55	Intervention group N=67	P
Birth weight	3135.65±294.79	3361.18±350.70	0.001
Birth length	49.91±1.97	51.68±3.32	0.001
Head circumference	34.64±1.06	35.14±1.16	0.01

circumference, and height of the neonates in mothers treated with vitamin D were significantly higher than the control group. Hashemipour et al. also in an open-label study of 130 pregnant women with vitamin D less than 30 ng/ml (using vitamin D 200 and 400 IU daily) revealed that there was a significant difference between the two groups regarding maternal weight gain, as well as neonatal weight, height, and head circumference. They concluded that the administration of vitamin D supplement in pregnant women during pregnancy improves neonatal outcomes (17).

Sabour et al. in a cross-sectional study of 449 pregnant women examined the relationship of neonatal outcomes and maternal calcium supply with vitamin D intake. Their results revealed that the mean height at birth and 1-min Apgar score in a group of mothers with sufficient calcium and vitamin D intake were higher than neonates whose mothers had insufficient vitamin D and calcium intake (18). Besides, Khalessi et al. in another cross-sectional study corroborated our findings by revealing that about 48% of mothers suffer from vitamin D deficiency.

By and large, the frequency of LBW neonates with head circumference less than 33 cm in mothers with vitamin D deficiency was higher than mothers with normal level of vitamin D. It was concluded that maternal vitamin D deficiency increases the frequency of LBW neonates, while treatment with vitamin D improves maternal and neonatal outcomes (16). Gernand et al. conducted an observational cohort study in 12 medical centers in the USA during 1959-1965, the results of which substantiated our findings by highlighting the fact that mothers with 25(OH)D level of 37.5 nmol/l or more had neonates with higher birth weight and head circumference compared to mothers with 25(OH)D level of less than 37.5 nmol/l. In this respect, they indicated that birth weight and head circumference increased with the rise of 25(OH)D level up to 37.5 nmol/l. Furthermore, they emphasized that maternal 25(OH)D level of 37.5 nmol/l or more in the first trimester can affect the prevalence of SGA neonates. However, the same correlation was not observed in the second trimester (19).

In the same vein, a systemic review by Pérez-López (2015) also specified that the administration of vitamin D supplement during pregnancy increased the level of 25(OH)D circulation, birth weight, and birth length in neonates (20). Similarly, another systematic review by Galthen-Sørensen (2014) maintained the important role of 25(OH) D in fetal bone growth (21).

In line with a double-blind, placebo-controlled, randomized trial by Roth et al. in Bangladesh, which indicated the high dose of vitamin D3 administration in the third trimester of pregnancy did not correlate with the risk of adverse pregnancy and neonatal outcomes (22), the current controlled experiment did not show any adverse effects regarding vitamin D administration. Regardless of all the investigations on the beneficial role of vitamin D in maternal and neonatal outcomes with no remarkable adverse effects, the results of studies on the effect of vitamin D on maternal and neonatal outcomes are not consistent.

A randomized, controlled, triple-blind clinical trial on 126 pregnant women (in Iran) performed by Mohammad-Alizadeh-Charandabi et al. held that vitamin D did not have any impact on neonatal weight, height, and head circumference (23). More importantly, some studies indicated that vitamin D was correlated with placental vascular pathologies (19).

Consequently, although this study provided strong evidence in favor of vitamin D efficacy on neonatal outcomes, the results should be treated with cautious due to some limitations such as the relatively small sample size and the short duration of follow-up as they make the generalizability of the present findings impossible. Further randomized controlled studies with longer follow-ups and larger sample sizes are recommended to determine whether maternal vitamin D level can conclusively predict neonatal outcomes. These investigations will answer the question of whether vitamin D is a true modifier regarding maternal and neonatal outcomes or not.

Conclusion

This controlled trial revealed that administration of vitamin D in pregnant women increased the means of neonatal weight, head circumference, and height with no remarkable adverse effects. Further sufficiently powered randomized controlled trials are required to evaluate whether maternal vitamin D supplementation can increase fetal growth.

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