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Original Article

Evaluation of the prevalence of vitamin d deficiency in pregnant women and its correlation with neonatal vitamin D levels

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SUMMARY

Background: Sufficient levels of vitamin D (25-hydroxyvitamin D, 25(OH)D) are required during pregnancy to maintain fetal developmental and reduce adverse outcomes in fetus/neonates and mother. The present study aimed to determine the levels of vitamin D in pregnant women and neonates and evaluate the corresponding effects of vitamin D supplementations.

Materials and Methods: This descriptive-analytical study, conducted in Asali Hospital, Khorramabad, included 77 pregnant women, between 15–45 years of the age, presented with the gestational age of 37–42. 5cc of the blood samples were obtained from the mothers during the labor and umbilical cord, postpartum. Demographic and medical data were obtained from the patients and results from the lab findings, based on the levels of 25(OH)D, were recorded in the questionnaire.

Results: The mean concentration of 25(OH)D in pregnant women was 13 ng/ml and their neonates was 15 ng/ml. Overall, 60.9% of the mothers and neonates were reported to be 25(OH)D deficient whereas, 89% of the mothers and their newborns had insufficient vitamin D levels. The levels of 25(OH)D in the umbilical cord had a significant relationship with serum vitamin D levels. Maternal age, gestational age, body mass index and occupational status had no

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effect on maternal and neonatal vitamin D levels. Women under vitamin D supplementations (4000IU/day) had higher levels of vitamin D levels.

conclusions: The mean concentration of vitamin D in pregnant women and infants is low and it is a direct correlated with umbilical cord blood vitamin D levels.

Introduction

During the third trimester of pregnancy, significant changes are seen in maternal calcium metabolism, given the need of calcium for skeletal development of the fetus. A high prevalence of vitamin D deficiency has been reported during pregnancy in The United Kingdom, India, Pakistan, Norway and Saudi Arabia. The low levels also correspond to vitamin D deficiency in neonates [1]. The risk factors of maternal vitamin D deficiency include; low exposure to sunlight and inadequate dietary vitamin D intake [2]. Furthermore, studies have also shown that pregnancy alone is a risk factor for vitamin D deficiency, particularly among women living in high altitude regions [3,4]. Adverse health outcomes associated with low levels of vitamin D are known to be gestational diabetes, preeclampsia, intrahepatic cholestasis of pregnancy, cesarean section, preterm labor, postpartum hemorrhage, inadequate fetal immune, neural and skeletal development, cardiovascular and respiratory dysfunction in newborn, type I diabetes and rickets [5–7]. Increased maternal 25(OH)D is associated with greater gestational age. Maternal 25 (OH) D concentrations < 40 ng/mL increases the risk of preterm birth risk by 60% among general obstetrical patients at an urban medical center [8].

The prevalence of vitamin D deficiency among pregnant women and neonates in the Middle Eastern region is reported to be 24.5–98% and 22–100%, respectively [5]. A recent clinical trial has reported that a daily intake of 30 μg of vitamin D in pregnant women can maintain a sufficient amount of vitamin D levels in mothers and neonates [9]. Furthermore, intake of vitamin D supplements can reduce maternal and fetal adverse outcomes [7]. The levels of vitamin D in breastfeed are also of great significance for adequate growth of the infant. Vitamin D supplementation in breastfeeding mothers can improve vitamin D status in infants [10].

The aim of this study to assess the prevalence of vitamin D deficiency among the pregnant women, its correlation with cord blood and neonatal vitamin D levels and corresponding risk factors.

Methods

This descriptive-analytical study was performed in Asali hospital, Khorramabad that included healthy pregnant women aged 15–45 years with gestational age of 37–42 weeks who consented to participate in the study.

Three types of data were collected from the participants: demographic data, medical data and clinical lab-based data.

Sampling was performed after obtaining a written consent. Women with fetal intrauterine death, chronic disease, diabetes (any type) and preeclampsia were excluded from the study.

A questionnaire including general information and current pregnancy status information, history of previous pregnancy, history of rickets during infancy, clinical symptoms of osteomalacia, and history of osteoporosis and fracture was completed for all participants. Medications and any supplements including calcium, vitamin D at 4000 IU/day dose and other vitamins during pregnancy were also recorded in the questionnaire. Daily intake of calcium and vitamin D was calculated based on the Food Frequency Questionnaire [11].

Clinical examinations and measurements of height and weight were performed and recorded on a questionnaire. After obtaining consent in the delivery room, 5cm blood was taken from the mother. 5cc of umbilical cord blood was also obtained after the birth. The samples were centrifuged and the sera was sent to the laboratory for the assessment. Maternal and umbilical cord blood samples were analyzed for 25-hydroxyvitamin D using a kit from IDS (Immunodiagnostic system, The United Kingdom) by enzyme immunoassay.

Since all the participants were residing in Khorramabad, in terms of weather and climate, the samples were homogenous. The samples for vitamin D analysis were obtained during the months of May to August. Due to insufficient and inaccurate data regarding the intake of sunlight from the participants, the variable was excluded from the study. This study was approved by the Research Ethics Board of Lorestan University of Medical Sciences.

The data was computerized and statistically analyzed using SPSS v18 (IBM, Chicago, USA). by correlation coefficient and linear regression. P-value<0.05 was considered to be statistically significant.

Results

In this study, 77 pregnant women with gestational age 37–42 weeks who referred to Asali Hospital for normal (vaginal) delivery were enrolled.

The mean and standard deviation of vitamin D level of mothers was 13 ± 8 ng/ml (minimum 3 ng/ml and maximum 17 ng/ml) whereas, the mean and standard deviation of vitamin D of neonates was 15±9 (minimum 4 ng/ml and maximum 39 ng/ml). Table 1 provides a description of the mean and standard deviation of maternal age, gestational age, maternal vitamin D, infant vitamin D and body mass index.

Vitamin D levels among housewives and their infants were not significantly different(Table 2). According to Table 3, women who consumed vitamin D supplements had significantly higher vitamin D levels. Similar findings were reported regarding neonates from the women ($P < 0.001$).

According to Table 4, maternal age, gestational age and maternal BMI were not correlated with maternal and neonatal vitamin D levels. But there was a statistically significant correlation between maternal vitamin D level and infant vitamin D level ($P = 0.001$).

Based on the results of Table 5, using regression model, it was concluded that maternal age, gestational age, body mass index and occupational status had no effect on maternal and neonatal vitamin D levels ($P \leq 0.05$).

It was also found that maternal vitamin D supplementation had no significant effect on the level of vitamin D in the infant, P=0.96.

Of all the participant, 28 (61%) of the mothers and infants had a severe vitamin D deficiency.

42 (89%) mothers and infants had insufficient vitamin D and only 7 mothers and infant had sufficient vitamin D levels(Table 6).

Discussion

With an increase in the calcium demand in the third trimester of pregnancy, vitamin D status is of great significance for adequate fetal growth, maternal health and early childhood pathologies. Pregnancy and lactation are characterized by the changes in the metabolism of vitamin D and calcium to provide the fetus with the calcium and vitamin D needed for growth and mineralization [12]. Studies

Table 1
Comparison of mean and standard deviation of maternal age, gestational age, maternal vitamin D, neonatal vitamin D and body mass index in subjects.

Variables	Mean ±SD
Age (years)	28±7
Gestational age (weeks)	39±1
Level of vitamin D in mother (ng/ml)	13±8
Level of vitamin D in neonate (ng/ml)	15±9
BMI (kg/m^2)	30±2

Table 2
Comparison of vitamin D levels in pregnant and housewives with vitamin D levels in their infants.

Employment status	Number	Maternal vitamin D			vitamin D in the infant		
		Mean±SD	t	p-value	Mean±SD	t	p-value
Employed	14	12±10	0.57	0.57	15±10	0.30	0.77
Housekeeper	86	14±8			15±9		

Table 3
Comparison of vitamin D supplementation status in mothers and their infants.

Groups	Use supplement vitamin D (4000IU)	Number	Mean ±SD (ng/ml)	T	p-value
Level of vitamin D in mother	Yes	16	24±8	6.91	0.001
	No	84	11±7	5.99	
Level of vitamin D in neonate	Yes	16	27±10	7.33	
	No	84	13±7	5.69	

Table 4
Comparison of correlation coefficients of quantitative variables (age, gestational age, body mass index) with maternal and neonatal vitamin D levels as well as maternal and neonatal.

Variables		Age	Gestational age (weeks)	BMI (kg/m2)	Level of vitamin D in mother (p-value)	Level of vitamin D in mother (p-value)
Level of vitamin D in mother	The correlation coefficient	−0.03	0.03	−0.133	1	0.96
Level of vitamin D in neonate	The correlation coefficient	−0.02	0.02	−0.145	0.96	1

Table 5
Comparison of the effect of other quantitative variables on maternal and neonatal vitamin D levels based on regression model.

Age	Gestational age	BMI	Employment status	Vitamin D supplementation	
0.78	0.77	0.53	0.74	0.05	p-value

Table 6
Relationship between maternal vitamin D levels and neonatal vitamin D levels.

Maternal vitamin D	vitamin D in the infant			
	severe deficiency 10>	Insufficient 10–30	Sufficient 30–100	Total
severe deficiency 10>	28(61%)	18(39%)	0(0.0%)	46(100%)
Insufficient 10–30	1(2%)	42(89%)	4(9%)	47(100%)
Sufficient 30–100	0(0%)	0(0.0%)	7(100%)	7(100%)
Total	29(29%)	60(60%)	11(11%)	100(100%)

have also revealed that vitamin D deficiency may persist till 12 months postpartum irrespective of seasonal factors and supplements [13]. A strong association between maternal serum 25 (OH) D concentration and neonatal cord vitamin D has also been reported. The source of vitamin D in infants and newborns depends on the storage of maternal vitamin D. Therefore, deficiency of maternal vitamin D can lead to vitamin D deficiency in neonates. Mothers with vitamin D deficiency will also have low

serum calcium and higher parathyroid hormones. The aim of this study was to evaluate the relationship between maternal and blood cord vitamin D levels, and the effects of vitamin D supplementations of neonatal vitamin D levels. Our study reports high prevalence of vitamin D deficiency in mothers and neonates in the study population.

A study by Y. Jacquemyn *et al.* reported a strong corelation between maternal and umbolical cord vitamin D levels [14]. March, Chen [15] reported that initiation of 50 μg/d vitamin D supplementations from the 13 to 24 weeks of gestation till 8 weeks postpartum can lead to normalization of vitamin D levels in neonates. In a clinical trial, Rodda, Benson [16] reported that everyday intake of 2000–4000 IU cholecalciferol from 12–16 weeks of gestation is associated with higher Umbilical cord serum 25-OH vit D levels as compared to the women without supplementations. Hollis, Johnson [17] also concluded that 4000 IU of vitamin D per day is safe and most effective dose to achieve vitamin D sufficiency in infants and mothers, irrespective of the race. Maxium 1,25(OH)2D3 concentration of vitamin D can be maintained throughout the pregnancy with this dose. In another study, Wagner and Hollis [18] suggested that women at the beginning of their pregnancy should maintain their vitamin D levels at 40 ng/mL at least, which can significantly reduce adverse maternal and fetal outcomes. They further suggested the dose of 4000 IU per day, which is equal to the amount of vitamin D obtained by sun exposure. Low levels of maternal vitamin D have known to be a risk factor of Vitamin D deficiency/insufficiency in infants and breastfeeding children [19].

In the study, Ekonomova reported that the cord of 25-hydroxyvitamin D was lower than that of mothers who received vitamin D supplementation during pregnancy. Brooke and colleagues also found that 25(OH)D levels were significantly higher in pregnant women who received vitamin D supplementation than controls. Our study reported that a significant correlation between maternal vitamin D supplementation and vitamin D levels in neonates.

Maghbooli, Hossein-Nezhad [1] reported the prevalence of vitamin D deficiency as 66.8% and 93.3% in mothers and cord blood, respectively. In our study, 60.9% of mothers and neonates had vitamin D deficiency and 89.4% of mothers and neonates had insufficient vitamin D levels.

There is also a significant relationship between maternal and cord level 25 (OH) D in our study. In a study by Whitey and colleagues, vitamin D levels were seen to increase gradually in the second and third trimesters of pregnancy compared to the first trimester, which was likely due to the intake of nutrients and supplements and exposure to the sunlight. In the present study, based on t-test, maternal and cord blood vitamin D levels in women who received vitamin D supplementation were higher than those who did not. However, based on the regression model, the no significant correlation was found. Our study did not find the correlation between maternal vitamin D status and BMI. A study with the opposite results regarding the influence of BMI on the level of Vitamin D, carried out in pregnant women in the third trimester reported that BMI and season, obese had lower 25(OH)D compared with non-obese in winter: 9±1 vs 12±4 ng / ml ($p = 0.03$), and summer: 22±8 vs 29±8 ng / ml ($p = 0.01$). They concluded that high-risk pregnant in the third trimester have significantly lower vitamin D in winter than in summer and in obese than in non-obese. Patients with obesity in winter should be considered high risk of vitamin D deficiency [20].

The results of the present study did not correlate the mean vitamin D level with maternal age, gestational age, and employment status and are consistent with the results of the above study.

This study does not include the developmental effects of vitamin D in newborns. Furthermore, correlation of vitamin D levels with calcium and parathyroid hormone is also not indicated in our study. Beside laboratory findings, the data of the study are relied on the patient-based information that can be misleading and inaccurate. These findings are based on small sample size, and patients with similar characteristics. Overcoming these limitations of the study can help us to obtain a better conclusion.

Conclusion

The results of this study showed that the mean vitamin D concentration in pregnant women and their neonates is low and there is a direct relationship between the levels of maternal vitamin D at delivery and neonatal cord blood vitamin D. Maternal vitamin D reserves are dependent and vitamin D supplementation during pregnancy, that are likely to provide beneficial outcomes. However,

recommendations regarding the intake of vitamin D supplementations need to be drawn. Furthermore, the results also showed that vitamin D levels were not significantly related with maternal age, gestational age, BMI and employment status.

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Availability of data and material

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Contributors' Statement Page

Dr. Masoumeh Ghafarzadeh: conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript.

Dr. Amir Shakarami and Dr. Fariba Tarhani: Designed the data collection instruments, collected data, carried out the initial analyses, and reviewed and revised the manuscript.

Dr. Fatemeh Yari: Coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content.

Conflict of interest

The authors deny any conflict of interest in any terms or by any means during the study.

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