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Research Article

Vitamin D Deficiency in Mothers of Vitamin D Deficient Newborns

Atiye Fedakar*

Department of Pediatrics, Afiyet Hospital Ümraniye, Ä°stanbul, Turkey

***Corresponding Author**: Atiye Fedakar, Department of Pediatrics, Afiyet Hospital Ümraniye, Ä°stanbul, Turkey.

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Abstract

Objective: The aim of this study is to review the clinical features of the prevalence of vitamin D deficiency in newborn mothers with vitamin D deficiency in our neonatal intensive care unit.

Materials and Methods: This study was a retrospective study conducted between August 2014 and January 2019. In the routine biochemical tests performed on the postnatal third day of the patients who were followed up and treated with different diagnoses, calcium (Ca), phosphorus (P), 25 (OH) vitamin D were examined for babies and mothers who had hypocalcemia. Mother's age, number of pregnancies, type of delivery, presence of additional diseases (premature rupture of membranes, thyroid, urinary tract infection, gestational diabetes), season and whether or not they received vitamin D support were recorded from the hospital files. Mothers age 15 - 24 years, 25 - 34 years 35 age and over to be divided into 3 groups. Serum 25 (OH) vitamin D levels were evaluated as> 30 ng/ml normal, 20 - 30 ng/ml deficiency, and < 20 ng/ml deficiency.

Results: A total of 523 infants in our hospital's neonatal intensive care unit were evaluated for 25 (OH) vitamin D due to hypocalcemia. Only the 25 (OH) vitamin D levels of 508 mothers were measured. The level of 25 (OH) vitamin D was determined as 7.54 ± 6.94 ng/ml in the infants and 10.53 ± 8.6 ng/ml in the mothers. The examination of vitamin D levels in infants revealed that 91% had deficiency, 7,9% had insufficiency and 0,6% had normal vitamin D levels. The examination of vitamin D levels in mothers revealed that 84.4% had deficiency, 12.4% had insufficiency and 3.2% had normal vitamin D levels. 311 of the mothers (59.5%) did not receive vitamin D supplementation during pregnancy. 24 (4.6%) mothers received vitamin D ampoules, 173 mothers received (33.1%) drops and 15 mothers (2.9%) received both ampoules and drops.

There was a positive correlation between vitamin D levels of mothers with vitamin D levels of babies and 74,6% (p: 0.000; $p < 0.05$). There was no statistically significant relationship between mothers' vitamin D levels and the number of pregnancies and age groups ($p > 0.05$).

Conclusion: In conclusion; vitamin D deficiency continues to be a global health problem both in the world and in our country. Vitamin D deficiency in the mother can cause effects that may last for life both in mother and newborn. Therefore, making the right vitamin D supplementation during pregnancy will prevent health problems in the early and late periods of mother and baby.

Keywords: *Vitamin D Deficiency; Maternal Vitamin D Deficiency; Newborn*

Introduction

Many recent studies have emphasized that vitamin D deficiency is a common problem for both mother and infant. It is frequently emphasized that maternal vitamin D deficiency is the most important risk factor for infantile rickets in newborn and infancy and may also exert permanent effects on the fetus [1-5].

Fetus and newborn are completely dependent on the mother for calcium and phosphorus, which are necessary for bone development, growth and function of tissues. Calcium actively passes through the placenta to ensure bone development during pregnancy, whereas 25 (OH) D passes passively and stored in the fetus to initiate vitamin D metabolism of the newborn [6,7].

Since there are limited natural sources of vitamin D, mothers mainly require sunlight and vitamin supplements for sufficient levels of vitamin D [8]. Maternal vitamin D level is crucial for bone development, growth and development of the fetus, as well as for maintaining the skeletal structure of the mother. In addition, it is suggested that maternal vitamin D level is associated with fetal neurological development in the postnatal and later periods, immune functions and chronic diseases [9,10].

In this study, we aimed to investigate the prevalence of vitamin D deficiency among the mothers and infants in our neonatal intensive care unit, and to emphasize that maternal and fetal vitamin D deficiency still remains a critical public health issue.

Materials and Methods

This study was a retrospective study conducted between August 2014 and January 2019 our neonatal intensive care unit. İn the routine biochemical tests performed on the postnatal third day of the patients who were followed up and treated with different diagnoses, Ca, P, 25 (OH) vitamin D were examined for babies and mothers who had hypocalcemia. Mother's age, number of pregnancies, type of delivery, presence of additional diseases (premature rupture of membranes, thyroid, urinary tract infection, gestational diabetes), season and whether or not they received vitamin D support were recorded from the hospital files. Mother's age 15 - 24 years, 25 - 34 years 35 age and over to be divided into 3 groups.

Serum levels of 25 (OH) vitamin D > 30 ng/ml were taken as sufficient; insufficiency is said to be present between 20 - 30 ng/ml and < 20 ng/ml were designated as a deficiency. Hypocalcemia was defined as the total calcium level of below 7 mg/ dL in the blood sample. The levels of 25 (OH) vitamin D were also studied using electrochemiluminescence binding assay (ECLIA) with a Roche's Cobas e 411 analyzer (Roche Germany) in hospital laboratory.

Results

Our study included a total of 523 infants diagnosed with hypocalcemia upon the routine 3rd day biochemistry tests between August 2014 and January 2019. Of the babies included in the study, 348 (66.5%) were male, 175 (33.5%) were female, whereas 418 (79.9%) were delivered by cesarean section (C/S) and 105 (20.1%) were delivered by spontaneous vaginal delivery (SVD). 430 (82.3%) of the infants were full-term, 93 (17.7%) were premature and 68 (13%) were small for gestational age (SGA). The level of 25 (OH) vitamin D was 7.54 ± 6.94 ng/ml in the infants and 10.53 ± 8.6 ng/ml in the mothers (Table 1).

N = 523	Min-Max	Ort ± SS
Weight (gr)	720 - 4770	2828,37 ± 705,17
Gender (Female/Male)	175 348	(33,5%) (66,5%)
Type of delivery N,% (Normal/Cesarean)	105 418	(20.1%) (79,9%)
Gestasyonel age Term Preterm	276 247	(52,7%) (47,2%)
25(OH) D serum level (ng/mL)	2 - 35	7,54 ± 6,94
Ca (mg/dL)	4.3 - 9	7,22 ± 0,63
P (mg/dL)	3 - 10	6,88 ± 1,29
25(OH) D serum level (N = 523) Deficient İnsufficient Normal	479 41 3	91.5% 7,9% 0.6%

Table 1: *Demographic characteristics of newborn.*

Of the total 523 babies, 311 (59.5%) of the mothers had no vitamin D supplements during pregnancy, 24 (4.6%) received vitamin D ampoules, 173 received (33.1%) drops and 15 (2.9%) received ampoules + drops. The distribution of the mothers by age was as follows: 128 (24,4%) aged 15 - 24, 294 (56,2%) aged 25 - 34 and 101 (19,3%) aged 35 and over.

Only the mothers of 508 infants with hypocalcemia were evaluated for the level of 25 (OH) vitamin D, Ca and P. The mean age of the mothers (508) was 28,85 ± 5,78, with a mean parity of 2,2 ± 1,36.

A total of 124 (23.7%) mothers had a history of infection during pregnancy, 92 of which were urinary tract infections, 15 were respiratory tract infections (pneumonia, influenza infection) and 17 were other infections (discharge, fungal, etc). One of the mothers passed away immediately after delivery due to severe pneumonia.

14 (2.7%) of the mothers had gestational diabetes and 46 (9%) had additional diseases.

When the vitamin D levels of the mothers were examined, deficiency was observed in 84.4%, in 12.4% of the cases, in 3.2% of the cases, vitamin D levels were normal (Table 2).

N = 508	Min-Max	Ort ± SS
Mother age	15 - 46	28,85 ± 5,78
Number of pregnancy	1-8	2,2 ± 1,36
Ca (mg/dL)	2-19	8,61 ± 0,99
P (mg/dL)	2,8-8,5	4,08 ± 0,75
25(OH) D serum level (ng/mL)	2-26	10,53 ± 8,6
Deficient	429	84,4%
İnsufficient	63	12,4%
Normal	16	3,2%

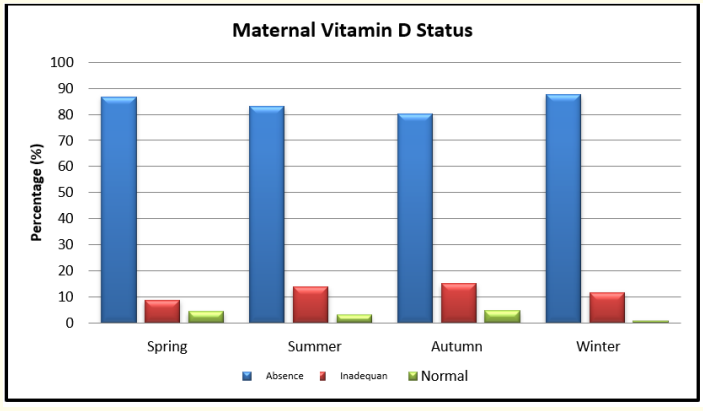
Table 2: *Demographic characteristics of mother.*

There was a positive correlation between vitamin D levels of mothers with vitamin D levels of babies and 74.6% (p: 0.000; $p < 0.05$) (Graph 1). There was no statistically significant relationship between mothers' vitamin D levels and the number of pregnancies and age groups ($p > 0.05$) (Table 3).

It was the first pregnancy of 220 women (43.3%) out of a total of 508 mothers. Either deficiency or insufficiency was detected in 93.2% of the mothers who underwent cesarean section and 97.5% of the mothers who had SVD in their first pregnancy. There was no statistically significant correlation between delivery type in the first pregnancy and maternal vitamin D levels ($p > 0.05$).

		Vitamin D Mother
Vitamin D Newborn	r	0,746
	p	0,000*
Number of Pregnancy	r	- 0,066
	p	0,139
	Spearman Rho Correlation Analysis	*p < 0.05

Table 3: *Evaluation of the correlation between vitamin D values of mothers with vitamin D values of infants and pregnancy numbers of mothers.*



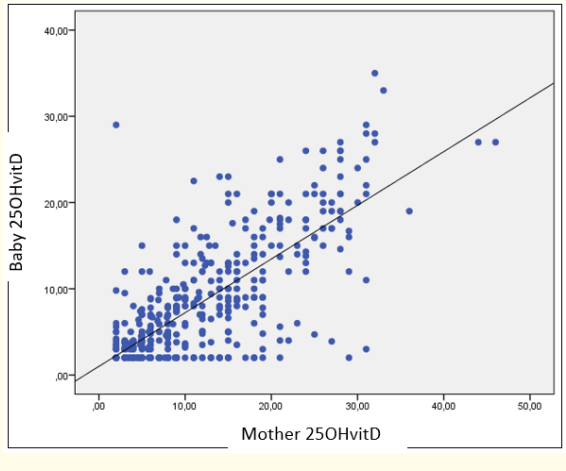
Graph 1: *Correlation between maternal vitamin D levels and fetal vitamin D.*

The evaluation of vitamin D deficiency (in newborns) according to the seasons revealed a statistically significant difference (p: 0.016; $p < 0.05$) (Table 4). The deficiency rate in winter (95.4%) was significantly higher than in autumn (86.6%). No statistically significant difference was found in vitamin D deficiency (mothers) according to seasons ($p > 0.05$) (Graph 2).

	25(OH) vitamin D	Spring n (%)	Summer n (%)	Autumn n (%)	Winter n (%)	p
	Deficient	108 (92,3%)	148 (90,2%)	95 (85,6%)	125 (95,4%)	0,016*
Newborn (N = 523)	İnsufficient	9 (7,7%)	13 (8,1%)	13 (11,7%)	6 (4,6%)	
	Normal	0 (0%)	3(1.8%)	3 (2,7%)	0 (0%)	
	Deficient	99 (86,8%)	132 (83%)	85 (80,2%)	113 (87,6%)	0,386
Mothers (N = 508)	İnsufficient	10 (8,8%)	22 (13,8%)	16 (15,1%)	15 (11,6%)	
	Normal	5 (4,4%)	5 (3,1%)	5 (4,7%)	1 (0,8%)	

Table 4: *Evaluation of vitamin D deficiencies of mothers and newborns by seasons.*

*Ki-kare test; * $p < 0.05$.*



Graph 2: *Seasonal distribution of vitamin D levels in mothers.*

Either deficiency or insufficiency was detected in 97.6% of mothers aged 15 - 24 years, 95.7% of mothers aged 25-34 years, and 99% of mothers aged 35 years and older. There was no statistically significant difference in maternal vitamin D levels between different age groups ($p > 0.05$). There was no statistically significant difference in maternal vitamin D levels according to parity ($p > 0.05$). There was either deficiency or insufficiency in 96.5% of parity 1 mothers, 94.8% of parity 2 mothers, 98.9% of parity 3 mothers and 98.6% of mothers of parity 4 and over.

The level of 25 (OH) vitamin D was below the laboratory detection limit of < 3 ng/mL in a total of 203 (38.8%) infants and 128 mothers (25.1%).

There was a positive, 74.6% and statistically significant correlation between maternal vitamin D levels and fetal vitamin D levels (p: 0.000; $p < 0.05$). There was no statistically significant difference in maternal vitamin D levels according to the presence of gestational diabetes ($p > 0.05$). However, all gestational diabetic mothers had either deficiency or insufficiency.

Statistical analyses

While evaluating the results obtained from the study, IBM SPSS Statistics 22 (SPSS IBM, Turkey) software was used for the statistical analyses. For the evaluation of the study data, the Shapiro-Wilk normality test was used to assess whether the parameters follows a normal distribution. A value of $p < 0.05$ was considered as the level of significance.

Discussion

In our study, there was a positive correlation of 74.6% between maternal and fetal vitamin D levels, which was consistent with the literature. 25 (OH) vitamin D deficiency was higher compared to the literature. The mean level of 25 (OH) vitamin was 7.54 ± 6.94 in the infants, whereas the mean level of 25 (OH) vitamin D was 10.53 ± 8.6 in the mothers. 99.4% of the infants had vitamin D deficiency/insufficiency, whereas 96.8% of the mothers had vitamin D deficiency/insufficiency.

One of the causes for high vitamin D deficiency was because 59.5% of the mothers had not received any vitamin D supplements before. However, no information were obtained regarding the clothing style or sunlight exposure of the mothers due to the retrospective nature of the study. Nevertheless, another study carried out in the same unit in 2014 revealed vitamin D deficiency/insufficiency in all 78 mothers and infants who were measured for vitamin D due to hypocalcemia. The mean level of 25 (OH) vitamin D was 4,57 ± 1,5, in the mothers, whereas the mean level of 25 (OH) vitamin D was 4.76 ± 0.7 in the infants. In this study, 80% of the mothers wore hijab and long sleeve clothes outside the home. In the 5-year period, we have managed to slightly increase the rate and intake of vitamin D by frequently informing gynecologists, in particular, about the significance and adverse effects of vitamin D deficiency for mothers and newborns. Daghan., *et al.* carried out a study investigating the level of knowledge and application regarding vitamin D intake among mothers and revealed that 88.1% of the mothers who were educated about vitamins used vitamin D supplements, whereas 55.7% of the mothers who were not educated did not take vitamin D [17]. Many studies have reported that maternal vitamin D deficiency is the major factor associated with fetal vitamin D deficiency. 25 (OH) vitamin D passes from the placenta to the fetus with a half-life of 2-3 weeks. A sufficient amount of vitamin D can be found in newborns even a few weeks after the delivery given that the level of maternal vitamin D is sufficient [15,18]. For this reason, we think that vitamin D deficiency should no longer be an important health problem provided that health care professionals inform mothers about the importance of vitamin D in maternal and fetal health.

It was determined that maternal vitamin D deficiency was associated with maternal infection, increased cesarean rate/first birth by cesarean section, premature birth, SGA, gestational diabetes and preeclampsia [19-22]. There are studies in the literature which reported a lower risk of premature birth followed by increased vitamin D concentration [23,24]. The rate of gestational diabetic mothers was determined to be normal, but vitamin D deficiency/insufficiency was detected in all of them. There were no preeclamptic mothers. In the literature, Bi., *et al.* reported that vitamin D supplementation during pregnancy reduced the risk of SGA, fetal and neonatal mortality [25]. This meta-analysis which included twelve studies noted that maternal vitamin D deficiency might increase the risk of SGA [26]. In our study, the rate of SGA (13%) and premature birth (17,7%) were found higher than the overall rate in our country [27].

In the literature, some studies reported that vitamin D deficiency increased the risk of cesarean section (especially in first births). It was noted that this was because skeletal muscle contained vitamin D receptors and lead to proximal muscle weakness and reduced suboptimal muscle performance in case of deficiency [19]. The cesarean section rate was 79.9%, which was quite high. Vitamin D deficiency or insufficiency was detected in 93.2% of the mothers who had cesarean section in their first pregnancy. A total of 124 (23.7%) mothers had a history of infection during pregnancy. We lost one of the mothers due to severe pneumonia. The high rate of cesarean section and infection was consistent with the literature.

Maternal 25 (OH) vitamin D levels are also closely linked to the season in which birth takes place. The level of 25 (OH) D vitamin was particularly higher in mothers who gave birth in summer and autumn than those who gave birth in winter and spring [28]. In our study, there were no seasonal differences between the mothers. However, the fetal deficiency rate was significantly higher in winter (95.4%) than in autumn (86.6%). We believe that the outcome was linked to the fact that women in our country prefer traditional style of clothing and spend most of the day at home.

Daily doses of 600 IU can not prevent vitamin D deficiency in pregnant women. Their daily regimen should contain at least 1000 IU of vitamin D. Daily regimens should include a prenatal vitamin containing 400 IU of vitamin D and a supplement containing at least 1000 IU of vitamin D [15,18]. In our country, it is recommended that vitamin D support (1200 IU/day) should be given by the Ministry of Health within the scope of the vitamin D support program from the 12th week and 6 months after birth [15].

Vitamin D supplementation in pregnant women seems to be sufficient in our country, which is contradictory with the high rate of maternal and fetal vitamin D deficiency detected in our study. Therefore, it is important to make sure that mothers take and use vitamin D regularly, as well as whether they get sufficient sunlight and calcium intake. The outcome of our study may also be attributed to the traditional style of clothing, individual differences, skin color and socio-economic status [29].

Conclusion

In conclusion, vitamin D deficiency is still a major global health problem both in the world and in our country. Maternal vitamin D deficiency can sometimes cause lifelong effects in both mother and newborn. It is necessary that health professionals inform and monitor mothers regarding vitamin D intake throughout the pregnancy.

Conflıct of Interest

The authors declare no conflict of interest financial or otherwise.

Ethıcs Approval and Consent to Partıcıpate

The study was approved by the Ethics committee of Afiyet Hospital. Informed written consent was obtained from the parents/guardian of the children providing all the necessary information about the study.

This study was presented as an oral presentation in the 7th International Fetal Life to Childhood First 1000 Days Mother-Child-Nutrition Congress.

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