

Evaluation of Vitamin D Status and Effective Maternal Factors on Vitamin D Levels in Cord Blood of Infants Born in Zahedan, Iran

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Abstract

Background: The available sources indicate our insufficient knowledge about vitamin D levels in infants born in Iran. Therefore, the aim of this study was to investigate the vitamin D status and effective maternal factors on vitamin D levels in cord blood of neonates born in south-east of Iran.

Materials and Methods: This descriptive-cross sectional study was performed on neonates who were born in Ali-Ibn-Abitaleb Hospital (Zahedan, Iran), and their mothers from August 2020 to January 2021. To assess the maternal serum and umbilical cord level of vitamin D, 5 ml of whole blood (umbilical cord blood and maternal venous blood) was evaluated by enzyme-linked immunosorbent assay. The relationship between different levels of the infants' vitamin D and some maternal vitamin D deficiency factors were evaluated.

Results: A total of 190 pregnant women & 190 infants participated in this study. The mean serum level of vitamin D in newborns was 37.90 ngr/ml, of which 41(21.8%) were vitamin D deficient. Vitamin D status of neonatal cord blood was significantly related to using vitamin D supplements by mother during pregnancy, parity, maternal literacy level, infant gender, maternal exposure to sunlight and maternal vitamin D status ($p < 0.05$ for all).

Conclusion: Our study showed that using vitamin D supplements by mother during pregnancy, parity, maternal literacy level, infant gender, maternal exposure to sunlight and maternal vitamin D status are related to the infants' vitamin D status. Further research is needed to determine the reason behind some established relationships in the present research including the relationship between parity and vitamin D in neonates.

Key Words: Infant, Mother, Pregnancy, Vitamin D Deficiency.

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1- INTRODUCTION

Vitamin D is one of the most important fat soluble vitamins involved in regulating the homeostasis of minerals and bone health. Vitamin D and its metabolites are actually hormones and have hormonal precursors, as they can be made up in body alongside their recipient from dietary intake or sun light (1). This fat soluble vitamin has many beneficial effects especially on the skeleton and bone mineralization. There are various risk factors described for vitamin D deficiency. Low dietary intake of vitamin D, obesity, smoking, low exposure to sunlight, and ethnicity are among the most important factors (2); while reduced level of vitamin D has unfavorable effects on different population, pregnant women's vitamin D status is an important issue and a global health problem (3, 4). Recently, it has been demonstrated that vitamin D deficiency in pregnancy is related to adverse clinical outcomes including preeclampsia, premature birth and intrauterine growth retardation (5).

Moreover, appropriate growth and development of fetus depends on the maternal supply of vitamin D and there are evidences indicating that vitamin D deficiency in mothers may be correlated with reduced level of vitamin D in fetus (2, 6); while it has been demonstrated that the placenta has the potential to activate vitamin D and regulate the vitamin D level in placenta; however, mothers reduce their contribution in providing the vitamin D supply of their fetus as their own serum vitamin D concentration becomes low (2, 7). Therefore, maintaining normal level of Vitamin D level in pregnant women is considered to be an important issue, especially in the countries facing vitamin D deficiency as a health concern. Many countries around the world including India, Afghanistan, and Pakistan are facing vitamin D deficiency as problematic health issue (8). It has been reported that vitamin

D deficiency is common in Iran and various health care policies have been conducted to prevent and treat vitamin D deficiency (9). A previous systematic review and meta-analysis on Iranian population demonstrated that the average concentration of vitamin D in pregnant women and infants in Iran is estimated to be 15.02 ng/ml and 14.59 ng/ml respectively. Based on this report, the average concentration of vitamin D in pregnant women and infants in Iran is considered to be low and should be addressed as an important health priority (10). Therefore, determination of the correlation of maternal and fetal vitamin D status is an important issue which is not widely studied in Iran. Moreover, the possible relationship between fetal vitamin D levels and some maternal factors including parity, vitamin D supplementation status and maternal educational status have been neglected in Iran. Therefore, the aim of the present study is the evaluation of the vitamin status in serum of mothers giving birth in Sistan and Baluchestan province and also to evaluate the possible relationship between umbilical cord vitamin D levels and maternal factors.

2- MATERIALS AND METHODS

2-1. Study design and population

The present cross sectional study was conducted in Ali Ibn Abitaleb hospital (Zahedan, Iran), from August 2020 to January 2021. The participants were asked to fill a researcher made checklist about their age, parity status, drug history, smoking and addiction status, receiving any vitamin D supplementation, and their infant's gender.

2-2. Method

All women meeting the inclusion criteria were entered to the study and after filling an informed consent form and the researcher made checklist, 5ml of whole

blood samples were taken from them and the umbilical cord after clamping. The samples from both the mother and the umbilical cord were then evaluated for vitamin D status.

2-3. Laboratory measurements

Five milliliters of umbilical cord blood was taken from each fetus after clamping the cord. Simultaneously, 5 milliliters of venous blood was taken from the mother as well. The blood samples was then sent to the laboratory of Ali-Ibn-Abitaleb Hospital for the evaluation of the vitamin status. The 25(OH) Vitamin D level was assessed by Vitamin D enzyme-linked immunosorbent assay kit (Pishtaz Teb, Iran), according to the manufacturer's guide. The vitamin D status was reported as follows: Vitamin D deficiency: <20 ngr/ml; Vitamin D insufficiency: 20-29 ngr/ml; sufficient vitamin D: 30-100 ngr/ml; and Vitamin D intoxication as >100 ngr/ml (4).

2-4. Inclusion and exclusion criteria

The inclusion criteria included the mothers who did not have any previous history of any medical disease, had singleton pregnancy, and their infant was not a preterm baby and did not have any congenital anomalies or intrauterine growth restriction. Women who did not agree to have blood samples taken from herself or cord blood were excluded from the study.

2-5. Ethical consideration

Ethic Committee of Zahedan University of Medical Sciences approved the study protocol (ethic committee approval code: IR.ZAUMS.REC.1399.319). During the study period, all women who gave birth in the hospital and their infants were enrolled in the present study after filling an informed consent form.

2-6. Data Analyses

The collected data were entered in the SPSS software (version 16.0). Chi-square test was used to evaluate the nominal variables and Fisher's exact test was used if necessary. Kolmogorov-Smirnov test was used to evaluate quantitative variables. The Mann-Whitney test was used to compare the status of vitamin D with nominal variables and Summers d test was used to compare the status of vitamin D with sequential and scale variables. P-value less than 0.05 were statistically significant.

3- RESULTS

A hundred and ninety women with their infants with mean \pm standard deviation of 27.25 ± 5.63 years were evaluated for serum (in mothers), and cord blood (in infants) vitamin D levels. Demographic data of the study participants is summarized in **Table.1**.

Table-1: Demographic data of mothers and their neonates (n=190).

Variables		Frequency	Percentage
Level of education	Primary school	28	14.9
	Secondary school	60	31.9
	High school	61	3.4
	University	39	20.7
Parity	1	26	13.9
	2	47	25.1
	3	41	21.9
	4	23	12.3
	5	14	7.5
	6	13	7
	7	14	7.5
	8	7	3.7

	9	2	1.1
Infants' gender	Male	92	48
	Female	98	52
Taking vitamin D supplementation		118	63.8
Vitamin D status	Insufficiency	65	34.6
	Inadequate	59	31.4
	Sufficient	64	34
	Intoxication	0	0
Sun exposure, minutes	50 minutes	1	0.5
	60 minutes	124	66.7
	90 minutes	47	25.3
	100	2	1.1
	120	12	6.5

A hundred and twenty-four women (66.7%) had sun exposure for at least 60 minutes and 47 women (25.3%) had sun exposure for at least 90 minutes each day. The mean of vitamin D among the women was 27.72 ± 17.5 ngr/ml, which was lower than the sufficiency level. Sixty five women (34.6%) had vitamin D deficiency. The mean of vitamin D among the infants was 37.90 ± 22.5 ngr/ml, which was within

the sufficient level. Forty one infants (21.8%) had vitamin D deficiency, 41 (21.8%) had insufficient level of vitamin D, and one infant (0.5%) was at risk of developing vitamin D intoxication. The mothers age was not correlated with infants vitamin D level ($P=0.945$). The relationship between infants' vitamin D level and different study variables is demonstrated in **Table.2**.

Table-2: Evaluation of the effective maternal factors on infants' vitamin D status (n=190).

Variables	Infants Vitamin D status				P-value	
	Insufficiency	Inadequate	Adequate	Intoxication		
Median (QR) of mothers age (years)	28 (22-35)	25 (21-30)	27 (25-29)	24 (24-24)	0.954	
Median (QR) of parity	5 (2-7)	3 (2-6)	3 (2-4)	3 (3-3)	<0.001	
Receiving supplementation	4 (3.4%)	22 (18.6%)	91 (77.1%)	1 (0.8%)	<0.001	
Not-receiving supplementation	36 (53.7%)	19 (28.4%)	12 (7.9%)	0 (0%)		
Infants' Gender	Male	28 (31.1%)	20 (22.2%)	42 (46.7%)	0 (0%)	0.003
	Female	13 (13.3%)	21 (21.4%)	63 (64.3%)	1 (1%)	
Median (QR) of sun exposure	60 (60-60)	60 (60-60)	90 (60-90)	120 (120-120)	<0.001	
Mothers' vitamin D status	Deficiency	30 (46.2%)	20 (30.8%)	15 (23.1%)	0 (0%)	<0.001
	Insufficient	7 (11.9%)	17 (28.8%)	35 (59.3%)	0 (0%)	
	Sufficient	4 (6.3%)	4 (6.3%)	55 (85.9%)	1 (1.6%)	

QR: The interquartile range.

4- DISCUSSION

The present study showed that the level of vitamin D in umbilical cord blood is less than the desired values and 43.6% of the infants born in the Ali-Ibn-Abitaleb referral hospital in Zahedan-Iran, had

vitamin D deficiency or insufficiency. Moreover, we demonstrated that infants' gender, mothers exposure to sunlight, mothers' vitamin D status, mothers' receiving vitamin D supplementation, mothers' parity are correlated with infants

vitamin D status. Although low levels of vitamin D has been a global concern for several decades, some people are considered to be at greater risk for vitamin D deficiency. Pregnant women are among the populations requiring more attention regarding their vitamin D status (11).

On the other hand, vitamin D seems to have multifaceted effects on pregnancy that go beyond the specific activities of calcium and bone metabolism. Low levels of vitamin D during pregnancy is associated with various health problems and consequences from pre-implantation stages to adulthood, and it is now accepted that maternal vitamin D deficiency affects maternal and fetal calcium homeostasis as well as bone development of the fetus (12-14). As a result of the rapid growth and development of the fetus, there is a possibility of vitamin D deficiency in pregnant mothers that results in reduced vitamin D in the mothers' blood and breast milk. Vitamin D deficiency is an important public health concern in Iran and based on different cutoff points including 10, 20, and 30 ng/ml, 42.42%, 55.84% and 80.82% of pregnant women are considered to have abnormal vitamin D levels, respectively (15).

In the most recent systematic review study conducted by Hajizadeh et al., the prevalence of vitamin D deficiency and its side effects on pregnant women and their infants in the Middle East was assessed (16). The prevalence of vitamin D levels below 25 nmol/L in pregnant women and their infants was reported to be between 16.7-80% and 22-82%, respectively. The results of the study showed that the predictors for reducing vitamin D concentration in mothers and infants include reduced vitamin D synthesis due to reduced sun exposure and reduced vitamin D intake. Also, a predictor of neonatal vitamin D depletion was reported to be low maternal vitamin D level. The authors conclude that the high prevalence of

vitamin D deficiency in pregnant women in the Middle East indicates the need for national planning and prevention strategies (16). It has been previously demonstrated that the maternal vitamin D levels are correlated with the blood cord's vitamin D status (17-19). In our study, we could identify some maternal factors related to the infants' vitamin D levels in Iran. Based on our results, at higher parities, more babies were born with low levels of vitamin D. It has been previously demonstrated that Caucasian women with multiparity are more likely to face vitamin D deficiency (20). A study by Ahmed et al. on Bangladeshi pregnant women demonstrated that vitamin D deficiency is higher among nulliparous women (21).

Moreover, they demonstrated that vitamin D deficiency is higher among younger women (21). In contrast to our study, Veena et al.'s study demonstrated that parity is not associated with the fetal vitamin D status (22). However, our result about the non-significant relation between maternal age and fetal vitamin D status was the same (22). Another important related factor to vitamin D status among our population was maternal vitamin D supplementation. We demonstrated that infants who had vitamin D deficiency were born to mothers who did not take vitamin D supplements during pregnancy. The beneficial effects of vitamin D supplementation especially in those mothers who are vitamin D deficient have various maternal and fetal benefits including reduced risk of preeclampsia, preterm birth and neonatal death (23).

The vitamin D level of 50 nmol/l or above is suggested for prevention of vitamin D deficiency in newborns (24). Another important factor increasing the vitamin D concentration is exposure to sun light which is another effective factor in increasing the vitamin D status in pregnant women. Based on our results, mothers who were less exposed to sunlight were more

likely to give birth to infants with low levels of vitamin D. A study by Akhlaghi et al., reported that 14.7% of mothers had normal vitamin D levels and vitamin D level was not significantly related to maternal age and parity in North-East of Iran (25). Moreover, they reported a relationship between vitamin D status and the average daily exposure of the mothers to the sun light (25).

In contrast to our study, they reported a higher percentage of infants with normal vitamin D levels while we both demonstrated that infants' vitamin D level is not related to the maternal age, but is significantly related with mothers' exposure to sunlight. Higher number of mothers with sufficient vitamin D levels in our study may be related to the demographic differences of the studied samples, especially since the latitude of Zahedan is lower than that of Mashhad and higher levels of vitamin D is not far from expectations. Regarding the relationship between parity and the level of vitamin D in the baby's umbilical cord blood, it seems that more studies need to be done to achieve a more conclusive result. However, the higher vitamin D deficiency in mothers with higher parity, which was observed in our study, may be due to the loss of part of the mothers' vitamin D sources in each pregnancy, which leads to a decrease in vitamin D levels in higher parity. Hatami et al.'s study from southern Iran reported that the prevalence of vitamin D deficiency (less than 20 ng / ml) was 76% among pregnant women (26).

Also, they reported that, there was no significant correlation between serum vitamin D levels and maternal age, although serum vitamin D levels were significantly different among those who were younger than 30 years (26). In our study, the rate of vitamin D deficiency in pregnant women was lower than in this study. Also, in our study, no significant relationship was found between maternal

age and vitamin D deficiency in cord blood. The reason for the improvement of vitamin D status in pregnant mothers could also be related to use of more vitamin D supplements by pregnant mothers in recent years because during these years with the expansion of cyberspace and social networks, pregnant mothers' information has increased. Elmee et al., evaluated the effect of vitamin D supplementation on birth outcomes during pregnancy and demonstrated that administration of 50,000 IU/week of vitamin D from 14-24 weeks of gestation increases the neonatal weight, height and head circumferences (27).

Although the beneficial effect of vitamin D supplementation during pregnancy has been reported in the literature, the exact dose of vitamin supplementation providing the most beneficial effects has not been clearly addressed, yet (5). Maqbooli et al.'s study from the Center of Iran demonstrated that 93.3% of infants and 66.8% of mothers had vitamin D deficiency (28). It has been previously demonstrated that vitamin D deficiency is prevalent in Zahedan (29).

Moreover, in this study, maternal age was not significantly associated with vitamin D levels, but the relationship between vitamin D levels in neonatal cord blood and serum levels of maternal vitamin D was significant. In our study, a smaller percentage of infants and mothers were deficient in vitamin D, which may be due to the increase in public awareness about vitamin D intake over the years. Also in this study, vitamin D levels less than 35 ng/ ml were considered as vitamin D

4-1. Limitations of the study

One of the main limitations of the present study alongside the limited sample size is unknown status of vitamin D levels in mothers prior and during the pregnancy. Moreover, the present study only evaluated the vitamin level of umbilical blood cord

and further studies can evaluate the blood level of vitamin D in infants.

5- CONCLUSION

The present study showed that 43.6% of infants born in a referral hospital in Zahedan have insufficient or efficient levels of vitamin D, and vitamin D deficiency is still common in these people and there is a need to take steps to improve their vitamin D levels. Considering the significant relationship between the level of umbilical vitamin D and taking vitamin D supplements and also increasing the time of sun exposure, creating a culture in the community in this regard can reduce the prevalence of vitamin D deficiency in pregnant mothers and their babies. Further research is needed to determine the significant relationship between parity and vitamin D status in infants.

6- ABBREVIATION

Vitamin D: Cholecalciferol (Vitamin D3).

7- ACKNOWLEDGMENTS

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8- CONFLICT OF INTEREST

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