Relationship of Low Maternal Vitamin D3 Level and Adverse Early Neonatal Outcomes

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Abstract

Background: Low serum vitamin D [25 (OH) D] levels have been shown to have multiple health-related implications in females at childbearing age, during pregnancy, as well as in their children. **Aim of the study:** To assess the inverse relationship between vitamin D3 level and adverse neonatal outcomes using parameters such as fetal birth weight, head circumference, Apgar scores, fetal respiratory distress syndrome, and rate of neonatal admission.

Materials and methods: A prospective study was conducted on 100 early- and full-term pregnant women at Al-Elwiya Maternity Teaching Hospital in Baghdad from 1st of April 2017 to 31st of March 2018. Maternal vitamin D deficiency was confirmed based on levels <20 ng/mL.

Results: The vitamin D3 levels in the studied pregnant women were categorized as follows: normal (45%), insufficiency (31%) and deficiency (24%). The significant adverse neonatal outcomes associated with vitamin D3 deficiency were low Apgar score (54.2%), low birth weight (91.7%), small head circumference (91.7%), respiratory distress syndrome (66.7%), and neonatal intensive care unit admission (66.7%).

Conclusions: vitamin D3 deficiency among pregnant women is associated with prominent adverse neonatal outcomes.

***Keywords**: Vitamin D3, term pregnancy, neonatal outcome, apgar score*

Introduction

Hypovitaminosis D is prevalent worldwide, especially in Asia and the Middle East despite their tropical climate with abundance of sunlight. This suggests the prevalence of specific risk factors for hypovitaminosis D in these regions. These include the classic predictors and the conservative concealed clothing style in women in general and in men from Gulf countries in particular. The lack of governmental regulation regarding food fortification with vitamin D in these regions is also a potential risk factor. [1]

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Literature from Saudi Arabia, Kuwait, United Arab Emirates, and Iran revealed that 10-60% of mothers and 40-80% of their neonates had undetectable to low vitamin D levels (0-25 nmol/L) at the time of delivery. [2] In Iraq, hypovitaminosis D occurred in more than 65% women of childbearing age. [3]

A developing fetus is entirely dependent on the mother as a source of vitamin D. About 60 to 70% of the maternal plasma level of 25- hydroxyl-vitamin D [25(OH) D] acts as a source of vitamin D in the developing fetus. However, pregnant women have been reported with an unacceptably high prevalence of vitamin D deficiency and insufficiency. [4, 5] This, in turn, has been reported to increase the risk of adverse maternal and neonatal outcomes.[6]

Many observational studies have indicated that maternal hypovitaminosis D (as defined by maternal

25(OH) D levels <20 ng/ml) is a significant risk factor for adverse neonatal outcomes including underdevelopment according to gestational age, preterm birth, detrimental effect on bone and teeth development, etc.. [4, 7] Several studies have associated low 25(OH) D level to the risk of respiratory and other infectious diseases. [8] Vitamin D deficiency also puts children at a higher risk of diseases such as asthma and sepsis. [9, 10]

Many Iraqi researchers have reported significant adverse effects of hypovitaminosis D during pregnancy like preterm labor, preeclampsia and risk of gestational diabetes mellitus. [11, 12] In addition, optimum vitamin D level has been shown to have a vital role in limiting the occurrence of preeclampsia and other hypertensive disorders during pregnancy. [13]

Aim of Study

To assess the inverse relationship between vitamin D3 levels and adverse neonatal outcomes, especially regarding fetal birth weight, head circumference, Apgar scores, fetal respiratory distress syndrome, and neonatal admission.

Patients and method

Design, settings and sampling

This prospective clinical study was conducted at the **,** Al-Eleiya Maternity Teaching hospital, Baghdad, Iraq between first of April 2017 and 1st of March 2018.

Ethical consideration: Oral informed consent and signed paper was taken from each participant prior to their enrollment in the study.

All pregnant women admitted to the obstetrics wards at Al-Elwiya Maternity Teaching Hospital for elective cesarean section were enrolled in the study. A total of 100 term pregnant women were selected based on the inclusion and exclusion criteria.

The inclusion criteria included women with singleton and full-term healthy pregnancies.

Women presenting with preterm, multiple pregnancies, congenital abnormalities, taking any long-term drugs, smoking habit, obstetrical or medical complications (diabetes, pre-eclampsia, anemia, antepartum hemorrhage, premature rupture of membrane, polyhydramnios, etc.) were excluded.

Cesarean section of all participants was carried out under spinal anesthesia to eliminate any side effects of general anesthesia on the neonate. All participants were asked questions according to a special questionnaire prepared specifically for the study based on previous similar studies.

A detailed history was obtained from women, including the age, occupation, residence, and clothing style of selected pregnant women.

A detailed obstetrical history was taken from the participants : It included number of parities and antenatal care visits. Gestational age was determined according to last menstrual period and early ultrasound report; it was confirmed by late ultrasound (which was done to ensure viability and first-time pregnancy and exclude any congenital abnormalities). A thorough physical examination was performed for all the participants to exclude any other underlying pathology.

A 5 ml blood sample was drawn from each participant and was sent for cholecalciferol (25(OH) D_3) level analysis to the Laboratory of Al-Elwiya Maternity Teaching Hospital. High-performance liquid chromatography methods quantitated 25-hydroxy vitamin D_2 and D_3 levels. Confirmation of vitamin D deficiency diagnosis was based on levels <20 ng/mL; vitamin D insufficiency was defined as levels ranging from 20 to 29.9 ng/mL, while normal level was 30 ng/mL and more.

Each neonate was assessed and followed up by a senior pediatrician post delivery or after admission to the neonatal intensive care unit (NICU). All respondents were assessed for weight, head circumference, Apgar score at 1 and 5 minutes, respiratory distress syndrome, and admission to NICU. The Apgar score was classified according to WHO definition into <7 and >7. Neonates with Apgar scores of <7 had compromised vital functions (appearance, pulse, grimace, activity and respiration).

Neonatal weight less than 2.5 kg was regarded as low and was measured using the UNICEF weighing scale.

The head circumference of neonates was classified into small (<34.5 cm for males and <33.8 cm for

females) and normal values (>34.5 cm for males and >33.8 cm for females). Respiratory distress syndrome, NICU admission, and duration of NICU stay were also assessed.

Statistical Analysis

MS-Excel and Statistical Package for Social Sciences (SPSS) version 23 were used to collect and analyze the data. Chi-square test was used for comparison between categorical data (Fisher's exact test was applied when expected variable was less than 20% of total). One-way ANOVA analysis was used to compare more than two means. The level of significance (p value) was set as ≤ 0.05.

Results

Vitamin D3 levels of the participants were as follow; normal (45%), insufficiency (31%) and deficiency (24%). (***Figure*** 1)

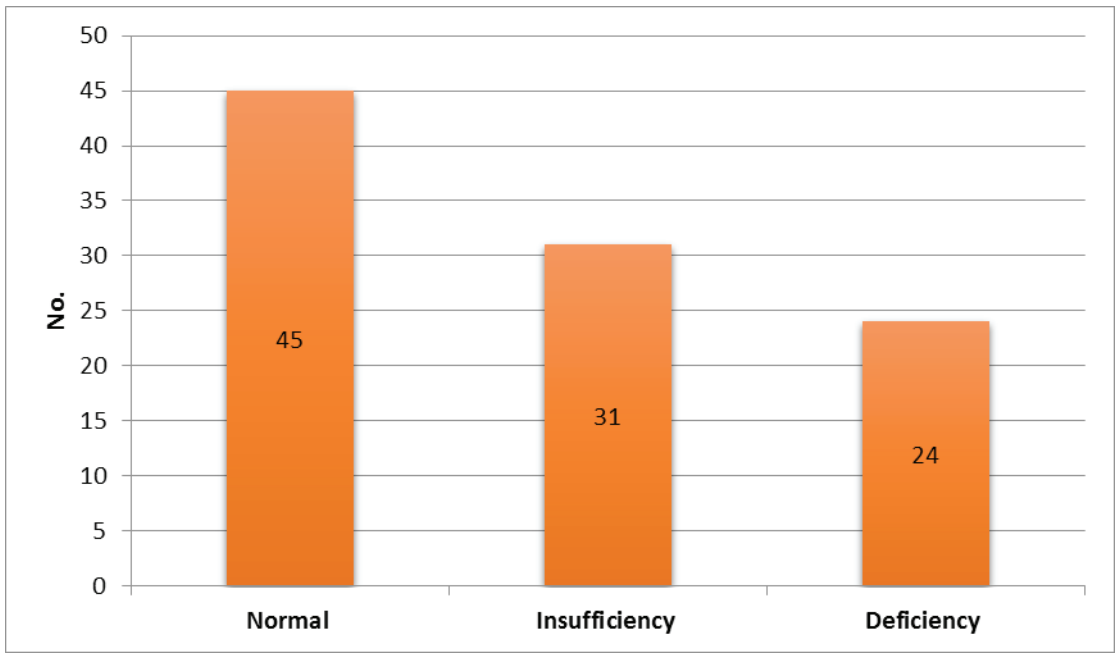

Figure 1: Vitamin D3 level distribution.

A highly significant association was observed between the age of the pregnant women and vitamin D3 insufficiency (p<0.001), as 96.8% of women with vitamin D3 insufficiency were in the younger age group. In addition, we found that 95.8% of women with vitamin D deficiency were housewives.

It was shown that women with abnormal BMI (overweight and obese) suffered from vitamin D3 deficiency (p<0.001). Pregnant women living in rural areas were significantly associated with vitamin D3 deficiency (p<0.001), (95.8%). A highly significant association was also observed between vitamin D3 deficiency and veiled pregnant women, high parity and irregular antenatal care visits (p<0.001) (***Table*** 1).

Table 1: Distribution of women's characteristics according to vitamin D3 level.

Maternal characteristics	Vitamin D3 level						P value	
	Normal		Insufficiency		Deficiency			
	No.	%	No.	%	No.	%		
Age of women								
20-29 years	9	20.0	30	96.8	10	41.7	**<0.001***	***Highly significant***
30-39 years	30	66.7	1	3.2	14	58.3		
≥40 years	6	13.3	0	-	0	-		
Occupation								
Employed	38	84.4	1	3.2	1	4.2	**<0.001****	***Highly significant***
Housewife	7	15.6	30	96.8	23	95.8		
BMI								
Normal	40	88.9	4	12.9	1	4.2	**<0.001***	***Highly significant***
Abnormal	5	11.1	27	87.1	23	95.8		
Residence								
Urban	38	84.4	1	3.2	1	4.2	**<0.001****	***Highly significant***
Rural	7	15.6	30	96.8	23	95.8		
Clothing style								
Veiled	8	17.8	30	96.8	23	95.8	**<0.001***	***Highly significant***
Unveiled	37	82.2	1	3.2	1	4.2		
Parity								
1 - 2	15	33.3	8	25.8	9	37.5		
3	19	42.2	23	74.2	4	16.7	**<0.001****	***Highly significant***
4	11	24.4	0	-	8	33.3		
5 and more	0	-	0	-	3	12.5		
Antenatal care visits								
Regular	44	97.8	3	9.7	1	4.2	**<0.001****	***Highly significant***
Irregular	1	2.2	28	90.3	23	95.8		

Fisher's exact test, **Chi-square test, * One-way ANOVA.*

A highly significant association was observed between neonates with low Apgar score at 1 and 5 minutes, low birth weight, small head circumference, respiratory distress syndrome (and maternal vitamin D3 deficiency ($p<0.001$). In addition, a highly significant association was observed between neonatal admission to NICU and maternal vitamin D3 deficiency ($p<0.001$) (***Table*** 2).

Table 2: Distribution of neonatal characteristics according to vitamin D3 level.

Neonatal characteristics	Vitamin D3 level						P value
	Normal		Insufficiency		Deficiency		
	No.	%	No.	%	No.	%	
APGAR score at 1 minute							<0.001** Highly significant
>7	44	97.8	30	96.7	11	45.8	
<7	1	2.2	1	3.3	13	54.2	
APGAR score at 5 minutes							<0.001** Highly significant
>7	44	97.8	30	96.8	16	66.7	
<7	1	2.2	1	3.2	8	33.3	
Weight							<0.001* Highly significant
Normal	42	93.3	1	3.2	2	8.3	
Low	3	6.7	30	96.8	22	91.7	
Head circumference							<0.001* Highly significant
Normal	42	93.3	1	3.2	2	8.3	
Small	3	6.7	30	96.8	22	91.7	
Respiratory distress syndrome							<0.001** Highly significant
Yes	1	2.2	1	3.2	8	33.3	
No	44	97.8	30	96.8	16	66.7	
NICU admission							<0.001** Highly significant
Yes	1	2.2	1	3.2	8	33.3	
No	44	97.8	30	96.8	16	66.7	

** Chi-square test, ** Fishers exact test.*

Discussion

The present study showed that 31% of term pregnant women had vitamin D3 insufficiency and 24% had vitamin D3 deficiency. These findings were lower than the findings of Al-Jebory et al. [14] done in Iraq, which reported that 38% of term pregnant women had vitamin D3 insufficiency and 40% had vitamin D3 deficiency. Moreover, it is lower than another Iraqi study by Hilali et al., [3] in which 50-65% of Iraqi women of childbearing age had vitamin D3 deficiency while 25% of them had vitamin D3 insufficiency.

The vitamin D3 findings in our study were lower than the results of Naseh et al. [15] who found that 37% of pregnant women had vitamin D3 deficiency and 63% of pregnant women had vitamin D3 insufficiency in Iran.

Our study results were consistent with the results of Bassil et al [10] who reported 30.8% deficiency and 40% insufficiency. They also stated that vitamin D3 deficiency and insufficiency were prevalent in the Middle East countries, especially among children and women of childbearing age.

Vandevijvere et al. [16] reported that 74.1% of women were vitamin D3 insufficient, 44.6% were vitamin D3 deficient and 12.1% were severely vitamin D3 deficient.

Choi et al. [17] found that total prevalence of vitamin D3 deficiency among pregnant women in South Korea was 77.3%. Nageshu et al. [18] found that 58.3% of pregnant women in India had vitamin D3 insufficiency and 13.8% pregnant women were deficient in vitamin D3.

The discrepancies in vitamin D3 prevalence between different countries have been attributed to differences in culture, nutritional habits, altitudes, sun exposure, and quality of antenatal care services. The deficiency and insufficiency of vitamin D3 are common worldwide. Many authors detected high prevalence of vitamin D3 deficiency in women, particularly during pregnancy and lactation periods.

Our study showed a highly significant association between pregnant women of younger age and vitamin D3 insufficiency ($p<0.001$), as 96.8% of pregnant women with vitamin D3 insufficiency were aged 20-29 years. This finding is consistent with the results of Ginde et al.'s [19] study, which reported that adolescent and younger age pregnant women represented 95% women in the USA with vitamin D3 insufficiency. Fouda et al. [20] carried out a study on women of childbearing age in Saudi Arabia and revealed that severe vitamin D deficiency was higher (92%) among younger age women. High prevalence of vitamin D3 deficiency in younger age pregnant women may be because women in their adolescence and younger age have a higher need for vitamin D for their growth and maturation, while pregnancy increases the burden and severity of vitamin D3 deficiency. [21]

The current study revealed a highly significant association between housewives and vitamin D3 deficiency (95.8%; $p<0.001$). This is similar to the results of Bener et al.'s [22] study done in Qatar who reported that pregnant housewives showed a higher prevalence of vitamin D3 deficiency and 88% of pregnant housewives had vitamin D3 deficiency. Dave et al. [23] conducted a study on 110 pregnant women in India and documented that 98% of the pregnant housewives had a higher prevalence of vitamin D3 deficiency.

The strength of the present study was the prospective design while the main limitations of this study were inconsistent follow-up and a single-center study.

Conclusion

This study successfully showed that vitamin D3 deficiency among pregnant women can be directly linked with adverse neonatal outcomes like low Apgar score, low birth weight and head circumference, and respiratory distress syndrome. Monitoring the vitamin D3 levels can be beneficial both to the mother (pre and post pregnancy) and the newborn.

Recommendations

Emphasis on regular vitamin D and calcium monitoring of pregnant women during antennal period and vitamin D supplementation campaigns for pregnant women should be encouraged.

Younger age, housewives, obese, rural residents, high parity and veiled pregnant women must be labeled as high-risk patients who require regular monitoring and vitamin D supplementations.

Further large nation-wide studies are needed to assess the relation between the effect of D3 deficiency on the mother and her own neonate.

Conflicts of Interest: None

Source of funding: Self

Ethical Clearance: Ethical clearance was taken from the scientific committee of the Iraqi Ministry of health and from Al-Eleiya Maternity Teaching hospital, Baghdad, Iraq

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