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Correlation between Vitamin D Deficiency in Pregnancy and Low Birth Weight Neonates

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Abstract

Background: Vitamin D is a steroidal prohormone that plays a significant role in calcium and phosphate metabolism. It reaches the body through synthesis in the skin or through food ingestion. The metabolites of this vitamin play key roles in metabolism of minerals. Requirement for calcium increases in 3rd trimester of pregnancy and for this reason it is vital to receive adequate vitamin D and calcium during pregnancy for fetal homeostasis.

Aim of Study: The objective of this study was to discuss the relation between maternal vitamin D level in pregnancy and development of low birth weight neonates.

Patients and Methods: This was a prospective cross-sectional study conducted on 60 pregnant female presented to Obstetrics and Gynecology Department of Damanhour Teaching Hospital during the period from November 2019 till November 2020 and were classified into group (A) and (B) each included 30 neonates (A) with birth weight <2500 gm and (B) with birth weight >2500gm.

Data were fed to the computer using IBM SPSS software package version 20.0.

Results: Our results revealed a non-significant statistical difference between both groups regarding demographic data of women. Also, there was a significant correlation between the level of vitamin D deficiency and the development of of low birth weight and the vitamin D categories and fetus weight either low or normal birth weight.

Conclusion: We can conclude that Vitamin D supplementation during pregnancy is essential to help in normal development of the fetus and prevent fertal growth retardation (FGR).

Key Words: *Vit-D: Vitamin D – VDR: Vitamin D receptor – LBW: Low birth weight – FGR: Fetal growth retardation.*

Introduction

VITAMIN D is a steroidal prohormone, the active type which plays a significant role in absorption of calcium and phosphate. It reaches the body through skin synthesis via ultraviolet rays when the sun exposure is adequate and can be ingested through food. Through influencing the absorption of calcium in the intestinal tissues and other effects on bone and other tissues of the body, the metabolites of this vitamin have key roles in regulating the metabolism of minerals **[1]**.

During pregnancy, fundamental changes occur in calcium and vitamin D metabolism. Requirement for calcium increases in the third trimester of pregnancy so that in the final stages of pregnancy, about 30g of the calcium for the fetal skeleton is created from the maternal skeleton and through hormonal intervention. So, it is vital to receive adequate vitamin D and calcium during the pregnancy for the fetal homeostasis, bone growth and mineral development **[2]**.

In pregnant women, 25(OH)D can cross the placenta and 1,25(OH)2D cross only at the low concentration. Nevertheless, in the placenta and decidua, the elevation of 1α hydroxylase activity caused increasing production of 1,25(OH)2D to supply to the mother and fetus **[3]**.

In pregnancy, maintain adequate Vitamin D concentration is pivotal. However, the optimal concentration of serum 25(OH)D is still debated. Now, the optimal concentration of Vitamin D is based on the level of the general population **[4]**.

Vitamin D deficiency brings about obvious damages to the growth and development of fetal bones. It can lead to osteomalacia in pregnancy, skeletal abnormalities and fetal mineral bone acquisition in childhood, and influences the neonatal skeletal development, bone size and impaired bone mass accrual **[5]**.

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Extra-skeletal consequences of vitamin D deficiency in pregnancy include potentially increase risks of gestational diabetes mellitus, pre-eclampsia and maternal bacterial vaginosis but not delivery by caesarean section. It increases the risk of intrauterine growth retardation, low birth weight and early-onset sepsis in infants. In addition, sufficient vitamin D concentration in pregnancy is supposed to have a positive influence on mother's and child's immune system **[6]**.

Vitamin D deficiency in pregnancy is prevalent, especially in women with limited access to sunlight due to minimal outdoor activity or heavy use of sunscreen, cultural practices or traditional clothing, and among women with dark skin pigmentation **[7]**.

Despite the controversies related to adverse outcomes, and lack of evidence of clear benefits of routine supplementation, most Western countries recommend vitamin D supplementation during pregnancy **[1]**.

Low birth weight (LBW) refers to term or preterm neonates with birth weight <2500gm **[8]**. These neonates may be small for gestational age or have intrauterine growth restriction. Mortality rate in such neonates is 40 times more than those with normal weight. Some investigations highlighted the effect of micronutrients on birth weight. Vitamin D (vit-D) has a key role in fetal growth by its interaction with parathyroid hormone and Ca^{2+} homeostasis **[9]**. Studies confirmed that insufficient prenatal and postnatal levels of vit-D have great effects on poor bone mineralization which have significant association with small for gestational age (LBW) births. Low birth weight births are reported more frequent in pregnancies occurring in the winter with vit-D deficiency **[10]**.

This study aimed to correlate the relationship between vitamin D deficiency in pregnancy and low birth weight neonates and the importance of vitamin D in the growth of neonates.

Patients and Methods

This is a prospective cross-sectional study was carried out on 60 pregnant women at Damanhour Teaching Hospital from Nov. 2019 – Nov. 2020.

The following females (1) Singleton fetus (2) Full term fetus as diagnosed from LMP and 1st trimester ultrasound examination; all were included in the study. Women with (1) Pregnant <35 WG; (2) Multiple gestations; (3) Uncertain gestational age; (4) Systemic and chronic conditions, hematologic disorders, medications and drug abuse; (5) Cases with congenital anomalies and infections; (6) Accidental hemorrhage associated with moderate or severe bleeding were excluded from this study.

All cases signed a well-informed written consent to declare their agreement to be enrolled in the study as agreed upon by the ethical committee.

All cases in this study will subjected to; (1) History taking "personal, present, past, menstrual, obstetric histories"; (2) Complete clinical "general, local and gynecological examination including pelvic and rectal" examination; (3) Investigations "routine and ultrasonographic examination to assess last menstrual period and gestations age and weight of the fetus".

Data were analyzed using IBM SPSS software package version 20.0 (Belmont, Calf, 2013). Data were collected in tables then analyzed in regarding to Chi square (x^2) and *p*-value less than 0.05 were considered significant.

Results

The study was conducted on 60 pregnant female presented to the Obstetric and Gynecology Clinic, Damanhour Teaching hospital, in labor, their neonates after their birth were categorized into two groups, Group I: Neonates with birth weight <2500gm (n=30) and Group II: Neonates with birth weight >2500gm (n=30).

The maternal age in group I ranged from 25.0-36.0 years with mean of 30.2±3.5 years while in group II it ranged from 25.0-36.0 years with mean of 30.6±3.6 years and the statistical analysis revealed a non-significant statistical difference between the two groups regarding maternal age (*p*= 0.79), (Table 1).

In group I parity of women ranged from 1.0-4.0 pregnancies with mean of 2.0±0.9 pregnancies while in group II parity ranged from 1.0-4.0 pregnancies with mean of 2.4±1.0 pregnancies with no statistical significant difference between the two studied groups regarding parity (*p*=0.254), (Table 1). In addition, BMI in group I ranged from 25.9-30.9 Kg/m^2 with a mean of 28.2±1.5 Kg/m^2 and in group II it ranged from 25.8-30.8 Kg/m^2 with mean of 28.4±1.5 Kg/m^2 with also a non-significant statistical difference between the two studied groups regarding BMI (*p*=0.405), (Table 1).

Table (1): Comparison between the two studied groups regarding demographic data.

Variable	Group I (LBW) (n=30)	Group II (Normal fetal weight) (n=30)	*p*-value
Maternal age (Years):			
Range	25.0-36.0	25.0-36.0	0.79
Mean ± SD	30.2±3.5	30.6±3.6	(NS)
Parity:			
Range	1.0-4.0	1.0-4.0	0.254
Mean ± SD	2.0±0.9	2.4±1.0	(NS)
BMI (Kg/m^2):			
Range	25.9-30.9	25.8-30.8	0.405
Mean ± SD	28.2±1.5	28.4±1.5	(NS)

Comparing the mode of delivery in the studied groups, in group I were 12 babies (40%) delivered by normal vaginal delivery (NVD) and 18 babies (60%) delivered by CS while in group II 20 babies (66.7%) delivered by normal vaginal delivery and 10 babies (33.3%) delivered by CS and the statistical analysis revealed no statistical significant difference between the both groups regarding mode of delivery (*p*=0.121), (Table 2).

Table (2): Comparison between the two studied groups regarding mode of delivery.

Mode of delivery	Group I (LBW) (n=30)		Group II (Normal fetal weight) (n=30)		*p*
	No.	%	No.	%	
NVD	12	40	20	66.7	0.121
CS	18	60	10	33.3	(NS)
p	0.121 (NS)		0.121 (NS)		

Vitamin D level in group I ranged from 7.0-35.0nmol/L with mean of 12.6±5.7nmol/L while in group II it ranged from 12.0-54.0nmol/L with mean of 28.1±8.5nmol/L and the statistical analysis revealed a statistical significant increase in group II than group (*p*=0.001), (Table 3).

Table (3): Comparison between the two studied groups regarding vitamin D level.

Vitamin D level	Group I (LBW) (n=30)	Group II (Normal fetal weight) (n=30)	*p*-value
Range	7.0-35.0	12.0-54.0	0.001
Mean ± SD	12.6±5.7	28.1±8.5	(S)

Regarding vit-D categories in both groups, in group I, deficient vit.D (<25nmol/L) category was 10 women (33.%), insufficient (25-50nmol/L) was 19 women (63.3%) and sufficient (>50nmol/L) was present in only one woman (3.3%) while in group II, there were 19 women (63.3%) had insufficient vitamin D and 11 women (36.7%) belonged to sufficient vitamin D level without any woman had deficient vitamin D level and the statistical analysis revealed the significant increase in normal weight with normal vitamin D levels and also, significant increase in LBW with advancement in vitamin D level decrease (*p*=0.001), (Table 4).

Table (4): Comparison between the two studied groups regarding Vit. D category.

Vit. D category	Group I (LBW) (n=30)		Group II (Normal fetal weight) (n=30)	
	No.	%	No.	%
Deficient	10	33.3	0	0.0
Insufficient	19	63.3	19	63.3
Sufficient	1	3.3	11	36.7
p	0.001*			

Table (5) shows correlation between vitamin D level and birth weight in both groups and all over the study group, Correlation coefficient in group I was 0.362, in group II was 0.321 and in all cases was 0.511. There was statistical significant difference between vitamin D level and birth weight in both groups and all over the study group (Table 5).

Table (5): Correlation between vitamin D level and birth weight in both groups and all over the study group.

Birth weight and Vit-D level	Group I (LBW) (n=30)	Group II (Normal fetal weight) (n=30)	All cases (n=60)
Correlation coefficient	0.362	0.321	0.511
p-value	0.026*	0.038*	0.001*

Discussion

Vitamin-D (Vit-D) deficiency has significant health impacts particularly related to calcium and bone metabolism. Significant calcium deposition in the fetal skeleton occurs in utero during the third trimester; thus preterm infants are at risk of osteopenia, which can predispose to fractures **[11].**

Approximately 10-20% of preterm infants <1000g have radiographically defined rickets. Optimizing calcium and phosphorus intake should prevent osteopenia of prematurity in majority of cases but requires sufficient levels of Vit-D **[12]**.

Vit-D receptors thus are thought to have multiple functions, many of which have not yet been fully elucidated, including roles in regulating genes that are involved in cell growth, immune function, and cardiovascular health. Given the widespread biologic effects of Vit-D it is reasonable to postulate that Vit-D deficiency in humans during the fetal and neonatal period may have long lasting health consequences **[13]**.

Maternal Vit-D deficiency has been shown to be detrimental to the fetus with increased risk of intrauterine growth restriction, pre-eclampsia, gestational diabetes mellitus, and preterm birth, all of which can have significant health impacts on the fetus and neonate. Studies have also shown that low cord blood levels of Vit-D were associated with an increased risk of respiratory infection during the first few months of life and increased risk of recurrent wheeze in early childhood **[11]**.

Low birth weight (LBW) is a multifaceted problem that increases the risk of hypoxemia, acidemia, preterm deaths, and maternal distress, and disposes the infant to a number of metabolic disorders, polycythemia, lung problems, intraventricular hemorrhage, cognitive dysfunction, and cerebral palsy, which occur in both term and preterm infants. Some of the effective factors on the occurrence of LBW include: the history of chronic maternal diseases (blood pressure, renal diseases, diabetes mellitus, anemia, etc), higher body mass index (BMI), maternal weight gain during pregnancy, maternal age during pregnancy, occupation, different types of fetal infections and chromosomal abnormalities, birth rank, delivery interval, neonatal sex, age of the uterus, placental abruption and placenta previa **[14]**.

The aim of this work was to study and investigate the relation between maternal vitamin-D level in pregnancy and development of low birth weight neonates in Damanhour Teaching Hospital.

This study was a prospective cross-sectional study carried out in Department of Obstetrics and Gynecology, Damanhour Teaching Hospital on 60 pregnant female come in labor. Their neonates after their birth was categorized into two groups, neonates with birth weight <2500gm (n=30) and neonates with birth weight >2500gm (n=30).

The results of this study showed that no significant difference between the two groups regarding basic demographic data including maternal age, parity, BMI, gestational age and mode of delivery.

In this study there was statistical significant difference between the two studied groups regarding vitamin D level. Also, here was statistical significant difference between the two studied groups regarding Vit-D categories "Deficient, insufficient and sufficient".

The findings of this study are in agreement with several studies, Dror and his coworkers, (2011), showed that low maternal vitamin D levels during pregnancy may be associated with an increased risk of low birth weight, gestational diabetes mellitus and preterm birth **[15]**.

Similarly, another vital meta-analysis suggested that vitamin D insufficiency was associated with an increased risk of low birth weight, pre-eclampsia and bacterial vaginosis **[16]**.

However, Dror and his coworkers, (2011), in their study included both case-control and prospective cohort studies and did not include the most recently published cohort studies; additionally, they did not evaluate the association using specific subgroup analysis. Moreover, the cut-off vitamin D levels differed between different studies. Thus, conduction this meta-analysis to provide stronger evidence for the association between vitamin D and low birth weight **[15]**.

This result is consistent with another randomized controlled trial in Pakistan by Hossain and his colleagues, (2011), in two studies, low vitamin D levels during pregnancy increased the risk of low birth weight, however vitamin D supplementation did not significantly reduce the risk of low birth weight **[17]**.

In another study by Gernand and his coworkers, (2013), maternal vitamin D level in the second trimester of the pregnancy was related to the risk of low birth weight in the white and non-obese women, while this relationship was not seen in the black or obese women. Low birth weight are likely associated with weight at birth <2500gm. **[18]**.

Vitamin D deficiency during pregnancy causes potentially harmful implications in the mother and the fetus. Several studies have referred to the relationship between vitamin D deficiency and the incidence of low birth weight **[19]**.

Some studies have shown that increasing the amount of 25-hydroxy vitamin D in the bloodstream

before and during pregnancy contributes to nesting and causes stability in pregnancy, as well as increased calcium uptake required for fetal growth and development. Studies have also indicated that the decreased expression of vitamin D receptors results in functional impairment and limitation in the beneficial effects of vitamin D in regulating the fetus-placental growth. In the study of Hutabarat and his colleagues, (2007), maternal vitamin D deficiency was observed in all pathological pregnancies with a decrease in the staining levels of placental VDR in low birth weight **[19]**.

As Zhang and his coworkers, (2008), have shown that severe vitamin D deficiency may play an important role in placental inflammation, which in turn may lead to a higher risk of low birth weight and other neonatal side effects **[20]**.

Conclusion:

We can conclude that Vitamin D supplementation during pregnancy is essential to help in normal development of the fetus and prevent fertal growth retardation (FGR). So, we recommend vit-D supplementation for pregnant women to prevent these events.

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الربط بين نقص فيتامين د فى الحمل وإنخفاض وزن المواليد عند الولادة

الخلفية : العلمية فيتامين (د) هو هرمون أو ليهورمونات الستيرويدية التى تلعب دوراً فى استقلاب الكالسيوم والفوسفات.يصل إلى الجسم من خلال التوليف فى الجلد أو من خلال تناول الطعام. تلعب مستقلبات هذا الفيتامين أدواراً رئيسية فى عملية التمثيل الغذائى للمعادن. تزداد متطلبات الكالسيوم فى الثلث ٣ من الحمل ولهذا السبب من الضرورى الحصول على ما يكفى من فيتامين (د) والكالسيوم أثناء الحمل من أجل توازن الجنين.

الهدف من البحث : كان الهدف من هذه الدراسة هو مناقشة العلاقة بين مستوى فيتامين (د) للأمهات أثناء الحمل وتطور حديثى الولادة منخفضى الوزن عند الولادة.

المرضى وطرق البحث : كانت هذه دراسة مقطعية استشرافية أجريت على ٦٠ امرأة حامل تم تقديمها إلى قسم أمراض النساء والتوليد فى مستشفى دمنهور التعليمى خلال الفترة من نوفمبر ٢٠١٩ حتى نوفمبر ٢٠٢٠ وتم تصنيفها إلى المجموعة (أ) و (ب) شملت كل منها ٣٠ مولوداً جديداً (أ) بوزن الولادة – ٢٥٠٠جم و (ب) بوزن الولادة – ٢٥٠٠جم. تم تغذية البيانات إلى الكمبيورتر باستخدام حزمة برامج SPSS IBM الإصدار ٢٠.٠.

النتائج : كشفت نتائجنا عن وجود فرق إحصائى غير معنوى بين المجموعتين فيما يتعلق بالبيانات الديموغرافية للنساء. كما أن هناك علاقة كبيرة بين مستوى نقص فيتامين (د) وتطور انخفاض الوزن عند الولادة وفئات فيتامين (د) ووزن الجنين أما منخفض أو طبيعى عند الولادة.

الخلاصة : يمكننا أن نستنتج أن مكملات فيتامين (د) أثناء الحمل ضرورية للمساعدة فى التطور الطبيعى للجنين ومنع تأخر النمو الوحشى (FGR).