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COMMON PREGNANCY COMPLICATIONS IN RELATION TO VITAMIN D DEFICIENCY

By

Mostafa Ahmed Essawi El-Zahaby, Ismail Mohammed Abd El-Azeam Mira, Hani Maged Abd El-Aal, Abd El-Aleem Abd El-Aleem El-Gendy*

Departments of Obstetrics and Gynecology and Clinical Pathology*, Faculty of Medicine, Al-Azhar University

E-mail: mostafa.elzahaby@yahoo.com

ABSTRACT

Background: Maternal vitamin D deficiency is a widespread public health problem as the prevalence of inadequate and deficient vitamin D status in pregnant women ranges from 5 to 84% globally.

Objective: To assess risk factors for vitamin D deficiency and investigate the relation between maternal vitamin D level, and development of gestational diabetes mellitus, gestational hypertension, intrauterine growth retardation, and preterm labor.

Patients and methods: Our prospective observational study included 100 pregnant women divided into 2 equal groups: group A had insufficient vitamin d level and group B had sufficient vitamin D level in serum with no risk factors. Vitamin D levels were measured on the MiniVidas (Biomerieux, France).

Results: The incidence of preterm labor was 22%. There was a statistically significant association between hypovitaminosis D and preterm labor. There was no significant association between hypovitaminosis D and gestational diabetes mellitus, gestational hypertension and intrauterine growth retardation.

Conclusion: There was an association between hypovitaminosis D in pregnancy and preterm deliveries, No association between vitamin D deficiency and common pregnancy complications as gestational diabetes, gestational hypertension and intra uterine growth retardation.

Keywords: Hypovitaminosis D, preterm labor, gestational diabetes mellitus, gestational hypertension and intrauterine growth retardation.

INTRODUCTION

Vitamin D deficiency in pregnancy is prevalent *(ACOG, 2019)*, 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.

Vitamin D receptor gene is one of the genes that have been extensively studied in relation to osteoprosis. It is responsible for a broad range of actions of 1, 25 (OH) 2 vitamin D3, including its effect on calcium transport, homeostasis and bone resorption. Vitamin D interacts with its receptor and affects calcium homeostasis by regulating bone cell growth and differentiation, calcium absorption and PTH secretion *(McCarthy et al., 2011)*. Serum 25-hydroxyvitamin D [25(OH) D] of less than 30ng/ml is considered an insufficient level *(ACOG, 2019)*.

Cord concentrations of 25(OH) D are lower than maternal concentrations. The fetus relies entirely on the vitamin D stores of the mother. Vitamin D may be an

important factor in preeclampsia causation *(Adams et al., 2014)*. Vitamin D deficiency may also elevate blood pressure ,This effect may be related to the ability of 1,25 (OH) 2D to down regulate the renin– angiotensin–aldosterone system, Vitamin D may play a functional role in the preservation of glucose tolerance through its effects on insulin secretion and insulin sensitivity. There may be an autocrine /paracrine role of vitamin D in insulin target tissues *(Adorini , 2015)*. As the osteoblasts have 1, 25-(OH) 2D receptors and several osteoblast specific genes that are also 1,25-(OH)2D responsive, low 25-(OH) D concentrations in mother and, therefore, low 25-(OH) D and/or 1, 25- (OH)2D in the fetus may lead to reduced osteoblastic activity, affecting long bone growth *(Pereira et al., 2015)*.

The aim of this study was to investigate the relation between maternal vitamin D level and develop of gestational DM, gestational hypertension, intrauterine growth retardation, and preterm labor.

PATIENTS AND METHODS

This observational prospective study was done in Gynecology and Obstetrics Department in Sayed Galal Hospital.

This study included 100 pregnant women who attended outpatient clinics in Sayed Galal Hospital with the following criteria: Age: 16-45 and gestational age 20~26 weeks with living fetus. We excluded cases who were pregnant less than 20 weeks of gestation, multiple gestation, uncertain gestational age, very obese patient (BMI > 40) for prevention of sonography false results, severe medical condition leading to termination of pregnancy, accidental hemorrhage associated with moderate or severe bleeding and cases suffering from polyhydramnios and oligohydramnios.

Patients were investigated by vitamin D level in blood and divided according to results (Table 3) into 2 equal groups: Group A have insufficient vitamin d level, and group B included 50 pregnant women have sufficient vitamin d level in serum.

Patients were followed up thorough pregnancy till delivery after taking their consent to participate in the study for development of gestational hypertension, gestational diabetes mellitus, intrauterine growth retardation and preterm delivery by gathering information on the mothers such as age, weight, height, parity, socio-economic status, occupation, daily sun exposure, daily usual duties, duration of daily exposure to the sun, sleep habits and time of sleep through day, Body mass index (BMI) was calculated by the formula [weight (kg)/height $(m)^2$] then blood samples for vitamin D were examined on the same day, and the vitamin D levels was measured on the MiniVidas, in The Clinical Pathology Department, Sayed Galal Hospital.

Statistical Methods:

The collected data were coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 22.0, IBM Corp., Chicago, USA, 2013.

Inferential analyses were done for quantitative variables using Shapiro-Wilk test for normality testing, independent t-test in cases of two independent groups with normally distributed data. In qualitative data, inferential analyses for

independent variables was done using Chi square test for differences between proportions and Fisher's Exact test for variables with small expected numbers with Post Hoc Bonferroni test. The level of significance was taken at P value < 0.050 is significant.

RESULTS

There were no significant differences in demographic and clinical characteristics between the 2 groups although sun exposure was lower among the deficiency group and development of gestational DM and gestational hypertension were higher in deficiency group but the difference was not significant **(Table1)**.

Table (1): Comparison between the studied groups regarding demographic and clinical characteristics

Variables \ Groups		Deficiency (N=50)	Normal (N=50)	^P
Age (years)	**Mean±SD**	30.6±3.6	30.4±4.7	>0.05
	Range	24.0–38.0	21.0–40.0	
BMI (kg/m^2)	**Mean±SD**	31.6±2.2	31.3±2.3	>0.05
	Range	24.2–34.9	24.7–36.6	
Parity	**Mean±SD**	3.2±0.9	3.1±1.1	>0.05
	Range	1.0–5.0	1.0–5.0	
GA (weeks)	**Mean±SD**	22.9±1.4	22.7±1.8	>0.05
	Range	20.0–25.0	20.0–26.0	
Sun exposure (hours)	**Mean±SD**	2.3±1.1	2.7±0.9	>0.05
	Range	0.0–4.5	0.9–4.9	
Vitamin 25(OH)D level	**Mean±SD**	19.2±6.6	40.5±5.1	**<0.001**
	Range	5.2–29.2	30.8–54.1	
Getational DM	**Present**	9 (18.0%)	5 (10.0%)	>0.05
	Absent	41 (82.0%)	45 (90.0%)	
Getational HTN	**Present**	4 (8.0%)	3 (6.0%)	>0.05
	Absent	46 (92.0%)	47 (94.0%)	

The development of intrauterine growth retardation and development of low birth weight were higher among the deficiency group as shown in table 2 but the difference was not significant between the 2 groups .There were significant differences in developing preterm deliveries among the 2 groups as among the deficiency group 11 cases developed preterm delivery in comparison to the normal group only 3 cases developed preterm delivery **(Table 2)**.

Table (2): Intrauterine growth retardation , low birth weight and preterm deliveries among the studied groups

Groups Variables	Findings	Deficiency (N=50)	Normal (N=50)	P
Intra uterine growth retardation	**Present**	3 (6.0%)	0 (0.0%)	>0.05
	Absent	47 (94.0%)	50 (100.0)	
Low birth weight	**Present**	6 (12.0%)	0 (0.0%)	>0.05
	Absent	44 (88.0%)	50 (100.0)	
Preterm delivery	**Present**	11 (22.0%)	3 (6.0%)	**0.021**
	Absent	39 (78.0%)	47 (94.0%)	

DISCUSSION

Vitamin D deficiency in pregnant women and their children is a major health problem, with potential adverse consequences for overall health. Vitamin D deficiency has been associated with several adverse pregnancy outcomes, including pre-eclampsia, gestational diabetes mellitus, intrauterine growth restriction and preterm birth. The studies on this subject showed conflicting results on the association between vitamin D levels in pregnancy and adverse effects on maternal and fetal health, both skeletal and non-skeletal like autoimmune diseases, cardiovascular diseases and diabetes *(Makrides et al., 2016).*

Maternal vitamin D deficiency is common during pregnancy and a widespread public health problem. A high prevalence of vitamin D deficiency has been observed among pregnant women, with prevalence rates varying by ethnicity and sunlight exposure. According to *(ACOG, 2019)* there is currently a lack of information and data to draw any definitive conclusions regarding vitamin D role in adverse pregnancy outcomes. Intake of vitamin D supplements during pregnancy has also been reported to decrease a subsequent risk for adverse pregnancy outcomes *(Masvidal et al., 2013).*

The current study found that cases developed preterm labor in hypovitaminosis D group were 22% while in normal group were 3% that declared Preterm delivery was significantly more frequent among deficiency group than among normal group. Two studies confirmed current findings. *Letícia et al. (2014)* declared increasing incidence of adverse neonatal outcomes and recommended a daily intake dose of vitamin D, taking into account the needs of the fetus and maternal milk output. *Faustino et al. (2015)* showed that Vitamin D supplementation during pregnancy was associated with increased circulating vitamin D levels, birth weight, and birth length, and was not associated with other maternal outcomes. Study).

The current study found that cases developed gestational diabetes mellitus in hypovitaminosis D group were 18% while in normal group were 10% that declare getational diabetes mellitus was non-significantly more frequent among deficiency group than among normal group.

The current study found that cases developed gestational hypertension in hypovitaminosis D group were 8% while in normal group were 6% that declared getational hypertenson was non-significantly more frequent among deficiency group than among normal group. And the cases developed intra uterine growth retardation in hypovitaminosis D group were 6% while in normal group were 0% that declared intra uterine growth retardation was non-significantly more frequent among deficiency group than among normal group. While, in contrary with current findings, there were a nested case-control study at United States to assess relationship between midge station vitamin D deficiency and severe preeclampsia between 43 cases and 198 controls and found that maternal midgestation vitamin D deficiency was associated with increased risk of severe preeclampsia *(Baker et al., 2010). Xu et al. (2014)* found that the mean concentration of vitamin D was lower in preeclamptic women, so it was hypothesized that the plasma concentrations of maternal vitamin D measured at an average of 35 week gestational age were statistically significantly lower in women with adverse pregnancy outcomes compared to non-complicated controls

CONCLUSION

There was an association between hypovitaminosis D in pregnancy and preterm deliveries. No association between vitamin D deficiency and common pregnancy complications as gestational diabetes, gestational hypertension, and intra uterine growth retardation.

Conflicts of interest: No conflicts of interest were encountered.

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نقص فيتامين د في الحمل وعلاقته بحدوث مضاعفات أثناء الحمل

مصطفي أحمد الذهبي، اسماعيل عبد العظيم ميرة، هاني ماجد عبد العال، عبد العليم الجندي*

قسمي النساء والتوليد والباثولوجيا الاكلينيكية*، كلية الطب، جامعة الأزهر، القاهرة

خلفيـــة البحـــث: يعـــد نقـــص فيتـــامين د مشـــكلة صـــحية واســـعة الانتشـــار حيـــث ان معـــدل نقـــص فيتـــامين د ف الســـيدات الحوامـــل يتـــراوح مـــن 5 الـــي 84% عالميـــا و يـــؤدّي نقـــص فيتـــامين د عنـــد المـــرأة إلـــى ضـــعف الحمـــل وتكـــرار عمليّـــات الإجهـــاض، أو التعـــرّض لـــولادةٍ مبكـــرة. كمـــا يمكـــن لـــنقص فيتـــامين د أن يـــؤثر علـــى نُمـــو الطّفـــل ووزنـــه، بســـبب نقـــصٍ فـــي إمـــداد الـــدّم للمشـــيمة مـــن خـــلال إصـــابة الأم الحامـــل بتســـمُّم الحمل.

الهـــدف مـــن البحـــث: تحديـــد العوامـــل التـــي قـــد تـــؤدي الـــي نقـــص فيتـــامين د ف الحمـــل واثبـــات وجـــود علاقـــة بـــين نقـــص فيتـــامين د عنـــد الام والعديـــد مـــن المشـــاكل التـــي قـــد تصـــاحب المـــرأة الحامـــل مثـــل ســـكر الحمـــل و ضـــغط الحمـــل ونقـــص النمـــو الجنينـــي والولادة المبكرة.

المريضـــات وطـــرق البحـــث: تـــم اختيـــار مائـــة ســـيدة مـــن الســـيدات الحوامـــل فـــي 20-26 اســـبوعا مـــن الحمـــل مـــن اللاتـــي يتـــابعن فـــي قســـم النســـاء والتوليـــد بمستشـــفى ســـيد جـــلال .وتقسيمهم الي مجموعتين رئيسيتين:

المجموعـــة الاولـــي: تتضـــمن الحـــالات التـــي تعـــاني مـــن نقـــص حـــاد فـــي مســـتوي فيتامين د في الدم.

المجموعـــة الثانيـــة: تتضـــمن الحـــالات التـــي تحـــافظ علـــي مســـتوي طبيعـــي مـــن نسبة فيتامين د ف الدم.

وتـــم أخـــذ موافقـــه علـــي الاشـــتراك فـــي البحـــث مـــن كـــل المشـــاركين فـــي الدراســـة ومعرفـــة تـــاريخهم الطبـــي كـــاملا ثـــم تـــم عمـــل تحليـــل نســـبه فيتـــامين د بالـــدم لكـــل

المشـــاركين فـــي الدراســـة بمعمـــل الكيميـــاء قســـم الباثولوجيـــا الاكلينيكيـــة بمستشـــفى ســـيد جلال ومتابعتهم بصورة دوريه حتي نهاية الحمل والولادة.

نتـــائج البحـــث: وجـــود علاقـــة بـــين نقـــص فيتـــامين د ف الحمـــل والـــولادة المبكـــرة. ولكـــن اظهـــرت الدراســـة انـــه لا توجـــد علاقـــة بـــين نقـــص فيتـــامين د فـــي الحمـــل وظهـــور العديـــد مـــن المشـــاكل المصـــاحبة للحمـــل مثـــل مـــرض الســـكري المصـــاحب للحمـــل او ارتفـــاع ضغط الدم المصاحب للحمل او تأخر النمو الجنيني داخل الرحم.

الاســـتنتاج: الاكتشـــاف المبكـــر لـــنقص فيتـــامين د عنـــد الام وتعويضـــها بالنســـبة اللازمـــة اثناء الحمل قد يساعد على تخفيض نسبة حدوث الولادة المبكرة.