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ORIGINAL ARTICLE

Relation Between Vitamin D Deficiency and Bacterial Vaginosis in Women with Gestational Diabetes

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Abstract

Background: **A class of fat-soluble steroid hormones known as vitamin D is in charge of reabsorbing different ions including calcium, magnesium, and phosphate.**

Aim: **To research the link between vitamin D insufficiency and bacterial vaginosis in women with gestational diabetes mellitus (GDM) and the subsequent impact of vitamin D deficiency on maternal and fetal outcomes.**

Patients and methods: **A prospective cohort research was carried out from January 2020 to April 2022 on 100 pregnant women at Al Hussien University Hospital.**

Results: **Regarding the vitamin D status in second trimester among all patients, the present findings revealed that 58% of studied cases have vitamin D deficiency while regarding the vitamin D status during third trimester among all patients, the present study revealed improvement in vitamin D level and only 7% of the studied cases have vitamin D deficiency.**

Conclusion: **Deficiency of vitamin D seems to significantly affect the frequency or occurrence of BV and gestational diabetes mellitus during pregnancy.**

Keywords: Bacterial vaginosis, Gestational diabetes, Vitamin D

1. Introduction

Both reproductive and newborn health may be profoundly impacted by the vaginal microflora's makeup. Vaginal lactobacilli produce lactic acid, which decreases the phylogenetic diversity of the vaginal microbiome and creates a low pH environment in the vagina that, together with bacteriocins and maybe other chemicals, limits the colonization and proliferation of potentially dangerous microbes. The lactobacilli are reduced and replaced by a polymicrobial, anaerobic microflora that includes *Megasphaera, Gardnerella vaginalis, Sneathia, Prevotella* spp., *Atopobiumvaginae*, and others in the dysbiosis condition known as bacterial vaginosis (BV). Despite the fact that BV commonly has no symptoms, this dysbiotic condition is strongly linked to various clinical issues such as pelvic inflammatory illness, infertility, and spontaneous miscarriage.[1]

A class of fat-soluble steroid hormones known as vitamin D is in charge of reabsorbing different ions including calcium, magnesium, and phosphate. The most effective member of this family, vitamin D3, also known as cholecalciferol, is produced by a number of metabolic reactions including intake. In animals, it is created in the skin as 7-dehydrocholesterol under the impact of UV radiation on several provitamins. Previtamin D3 is created quickly during this process and is slowly transformed into vitamin D3's active form.[2]

There are three main changes to vitamin D homeostasis during pregnancy: a) increased calcitriol in the mother, b) optimum neonatal 25 (OH) D status requires maternal supply for 25 (OH) D, and c) a rise in the concentration of maternal

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vitamin D binding proteins. Both the systemic circulation and the placenta may see these alterations, indicating that the placenta is the primary location of vitamin D metabolism during gestation.[3]

Based on inadequacy and adequacy, vitamin D status in gestation has been divided into two categories: 25(OH)D less than 50 nmol/l (<20 ng/ml) and 25 (OH) D greater than or equal to 50 nmol/l (^{3}20 ng/ml), respectively. The Endocrine Society employs additional comparable cut-off criteria, which have also been utilized in earlier pregnancy research[4,5].

(1) Deficient values: less than 50 nmol/l (<20 ng/ml)
(2) Insufficient values: 50–74.9 nmol/l (20–29.9 ng/ml)
(3) Sufficient values: greater than or equal to 75 nmol/l (^{3} 30 ng/ml).

It is a remarkable observation that the concentration of 1, 25 (OH) 2D is rising in the mother's placenta and systemic circulation. By attaining a favorable calcium balance and providing immunosuppressive impacts as well as systemic and placental maternal tolerance for a healthy continued uncommon phenomenon supports normal in-utero bone formation.[6]

By the end of the first trimester, serum calcitriol level had doubled compared with nongravid women. After delivery, serum calcitriol returned to normal levels.[7]

The main reason for vaginal discharge is bacterial vaginosis (BV). In addition to an elevated risk of premature birth, pelvic inflammatory illness, and acquiring sexually transmitted diseases such the human immunodeficiency virus, *Chlamydia trachomatis, Neisseria gonorrhea, Trichomonas vaginalis,* and herpes simplex virus-2, it is also linked to an elevated risk of preterm birth.[8]

Bacterial vaginosis is caused by a disruption of the vaginal ecosystem, which includes a significant loss of lactobacilli after a substantial increase in the number of strict or facultative anaerobes that were previously in the minority in the vagina, including *Gardnerella vaginalis, Mycoplasma hominis, Atopobiumvaginae, Megasphaera, Prevotella, Ureaplasmaurealyticum, Mobiluncus, Peptoniphilus,* and additional meticulous or hitherto uncultivated bacteria.[9]

The varied populations of microorganisms found in the vaginal microbiome, or vaginal flora, have a significant impact on both the health of pregnant women and their unborn children. The vaginal microbiome is mostly dominated by bacteria. When a woman reaches reproductive age, she generates 1–4 ml of vaginal fluid, which has 10^8–10^9 bacterial cells/ml.[10]

A variety of bacteria, fungi, archaebacteria, eukaryotes, and viruses may be found in the vaginal microbiome. The majority of them are commensal species, which are present in human bodies from birth but which, under certain circumstances, might lead to illnesses.[11]

Insulin sensitivity, insulin insufficiency, and reduced biological function are all symptoms of the metabolic condition known as DM, which is brought on by hereditary and environmental causes. Considering how often the condition occurs, how often it results in disability and death, it has become a serious health problem for people all over the globe.[12]

Gestational diabetes mellitus (GDM) is DM that was not immediately apparent before becoming pregnant but was discovered in the second or third trimester.[13]

Women who were identified with DM in the first trimester would be labeled as having type 2 diabetes (type 2 DM)rather than GDM, which is a term used to describe DM that is not clearly type 1 or type 2 DM and is discovered in the second or third trimester of pregnancy.[14]

The following main categories apply to DM.

(1) Type 1 DM(owing to latent autoimmune DM of maturity and autoimmune β-cell death, which often results in absolute insulin insufficiency).
(2) Type 2 DM (because of a persistent lack of sufficient β-cell insulin production, which commonly occurs in the context of insulin resistance).
(3) Particular types of DM brought on by other factors, such as exocrine pancreas illnesses like cystic fibrosis and pancreatitis, monogenic DM syndromes (like neonatal DM and young-onset DM with maturity), and drug- or chemical-induced DM (such as after organ donation, when glucocorticoids are used, or while treating HIV/AIDS).
(4) Pregnancy-related DM.[13]

A background of persistent insulin resistance, to which the normal insulin resistance of pregnancy is somewhat additive, is what the great majority (~80%) of GDM patients first manifest as. As a result, afflicted women often have higher levels of insulin resistance than healthy pregnant women, which causes them to use glucose less effectively while producing more glucose and having higher quantities of free fatty acids (FFA).[15]

2. Patients and methods

Study setting: This research is a prospective cohort trial that will take place at Al Hussein University Hospital from January 2020 to April 2022.

Type of study and study population: A prospective cohort research involving 100 pregnant women was conducted.

Inclusion criteria of the cases: Age above 18 years old and below 40 years old, antenatal women of second and third trimester who developed GDM.

Exclusion criteria of the cases: Chronic conditions such as kidney, rheumatologic, hepatic, thyroid, and pregnancy in women who have previously had diabetes, as well as histories of vitamin D use and medications that interact with glucose metabolism.

Sample size calculation: The sample size, statistical calculator based on a 95% confidence interval, and research power calculations were performed utilizing the MedCalc version 12.3.0.0 software 'Ostend, Belgium' with an error of 5%.

Ethical and legal consideration: Approval from the department of Obstetrics and Gynecology, Al-Hussien Hospital, to review the records was obtained.

Confidentiality: Women are identified by their names in the data collection sheet, which is kept in privacy by the investigator.

2.1. Methods

Patients were subjected to:

Complete history taking: Menstrual history: including menarche age, menstrual disturbance, dysmenorrhea, and related symptoms. Obstetric history, such as parity and delivery mode Current medical history: chronic diseases and medications. HTN and DM history there is a family history of similar conditions or diabetes. Any medication allergy history surgical history, laparoscopic interference, laser therapy of hirsutism.

2.2. Examination

(1) : The inclusion and exclusion criteria among all participants were carefully examined and evaluated, paying particular attention to them as follows:
   (a) A general checkup that includes temperature and breathing rate.
   (b) By dividing weight (kg) by height, the body mass index (BMI) was calculated (m^2) and classified as high (^{3} 25 kg/m^2), normal (<18.5–24.99 kg/m^2),or low (18.5 kg/m^2). Women with high BMIs were further classified as overweight (25.0 kg/m^2) or obese (^{3} 30.0 kg/m^2), depending on their weight.
   (c) Obstetric check.

2.3. Quantitation of 25 (OH) D

We collected whole blood samples, put them in vacutainers that had been treated with EDTA, and centrifuged them to separate the plasma. Prior to measuring total circulating 25 (OH) D utilizing a commercially available radio-immunoassay, the plasma was kept at− 80 °C (Diasorin, Stillwater, MN). Vitamin D levels were evaluated and classified.

Analysis of data: All data was collected and tabulated and statistically analyzed.

Ethical Consideration: The research protocol had been submitted to the Institutional Research Board of Al Azhar University's faculty of medicine for approval. Each research participant had given their verbal consent after being informed. Confidentiality and personal privacy were respected at all stages of research.

2.4. Statistical analysis

The SPSS program version 20.0 was used to tabulate and statistically analyze the collected data. For numerical parametric data, descriptive statistics were calculated as mean, SD, minimum and maximum of range, median, and first and third interquartile ranges, and for categorical data, as number and %. The level of significance was set at *P* value less than 0.050, which indicates whether or not the data is significant. *P* value is a statistical indicator of the chances that study findings may have been accidental.

3. Results

This table showed that 42 (42%) patients had normal VIT D in second trimester, 58 (58%) patients had deficiency Vit D in second trimester, its mean was 22.54 with range from 12 to 27 Table 1.

Table 1. Vit D in second trimester among all patients.

	No (%)
Vit D second	
Normal	42 (42.0%)
Deficiency	58 (58.0%)
Mean ± SD	22.54 (6.24)
Range	12 (37)

Table 2. Vit D in third trimester among all patients.

	No (%)
Vit D third	
Normal	93 (93%)
Deficiency	7 (7%)
Mean ± SD	26.37 (4.34)
Range	19 (37)

Table 3. Swab for bacterial vaginosis in second and third trimester among all patients.

	No (%)
Swab second	
Negative	49 (49.0%)
Positive	51 (51.0%)
Swab third	
Negative	77 (77.0%)
Positive	23 (23.0%)

Table 4. Maternal complication (postpartum hemorrhage, postpartum sepsis, wound infection) and neonatal Complication (neonatal respiratory distress, neonatal sepsis) among all patients.

	No (%)
Maternal complication	
Negative	58 (58.0%)
Positive	42 (42.0%)
Neonatal Complication	
Negative	64 (64.0%)
Positive	36 (36.0%)

This table showed that 7 (7%) patients had Deficiency Vit D in third trimester and 93 (93%) patients had normal VIT D, its mean was 26.37 with range from 19 to 37 Table 2.

This table showed that 49 (49%) patients had negative swab second, 51 (51%) patients had positive swab in second trimester, 77 (49%) patients had negative swab in third trimester, 23 (23%) patients had positive swab in third trimester Table 3.

This table showed that 42 patients (42%) had maternal complication and 36 patients (36%) had neonatal Complication Table 4.

This table shows that there was no statistically substantial relation between Vit D in second trimester and swab in second trimester Table 5.

Table 5. Comparison between in Vit D 2nd and swab 2nd trimester.

	Vit D second			
	Normal No (%)	Deficiency No (%)	Chi square test	
			χ^2	*P* value
Swab 2nd				
Negative	17 (40.5%)	32 (55.2%)	2.105	0.147
Positive	25 (59.5%)	26 (44.8%)		

Table 6. Comparison between Vit D 3rd and swab 3rd.

	Vit D 3rd			
	Normal No (%)	Deficiency No (%)	Chi square test	
			χ^2	*P* value
Swab third				
Negative	74 (79.6%)	3 (42.9%)	4.954	0.026
Positive	19 (20.4%)	4 (57.1%)		

Table 7. Comparison between Vit D and swab.

	Vit D		Chi square test	
	Deficiency No (%)	Normal No (%)	χ^2	*P* value
Swab				
Negative	22 (38.6%)	104 (72.7%)	20.367	<0.001
Positive	35 (61.4%)	39 (27.3%)		

This table shows that there was no statistically substantial relation between Vit D in third trimester and swab in third trimester Table 6.

This table shows that there was no statistically substantial relation between Vit D and swab Table 7.

4. Discussion

In addition to being a steroid hormone that may be produced endogenously, vitamin D is a lipid-soluble vitamin. Preeclampsia, GDM, and premature delivery are just a few of the negative pregnancy outcomes that may emerge from vitamin D inadequacy during gestation Christoph and colleagues.[16]

Thus, the current study's objective is to identify the connection between BV and vitamin D deficit in women with GDM and the consequent influence of vitamin D shortage on maternal and fetal health.

This prospective cohort study included 100 pregnant women; all of them were diagnosed as having GDM. Cases were split into two groups according to the vitamin D status; group A included 50 patients who have vitamin D level less than or equal to 20 ng/ml and as a result, they received 4400IU vitamin D3/day, and group B that included 50 pregnant women who have vitamin D level greater than 20 ng/ml and received 400 IU vitamin D3/day. They were recruited and assessed for eligibility from Al-Azhar University maternity hospital.

The current research revealed that the median age of the studied cases was 30.12 ± 5.78 years old and the median BMI was 30.88 ± 2.91 kg/m^2 31% of cases have two times parity and 29% have parity for one time while 18% have zero times parity.

Similarly, a previous research by Bodnar and colleagues[17] evaluating the connection between vitamin D insufficiency and BV revealed that most women were 20–29 y old, multiparous, and overweight or obese. Skowrońska-Jóźwiak and colleagues[18] The average age of pregnant women was found to be 30.5 ± 4.9 years after research on the impact of maternal vitamin D deficiency on pregnancy outcomes.

Contrarily, a previous study by Yang and colleagues[19] indicated 40.7% had vitamin D deficiency,

25.1% had insufficient vitamin D, and just 2.4% had acceptable vitamin D levels in their late second or third trimester of pregnancy. Moreover, Ghafarzadeh and colleagues[20] revealed that The average values of 25 (OH) D in pregnant women was 13 ng/ml, while that of their neonates was 15 ng/ml. Overall, 60.9% of the mothers (gestational age of 37–42 weeks) and newborns were found to be 25 (OH) D deficient. While the vitamin D levels of 89% of the moms and their neonates were inadequate.

The present study revealed a statistically significant decrease HbA1C levels during third trimester of pregnancy (6.41 ± 0.47) in comparison with the HbA1C levels during second trimester of pregnancy (6.65 ± 0.52) (P value = 0.001). Such improvement in HbA1C level could be explained by the improvement in vitamin D levels during third trimester of pregnancy.

Additionally, Akoh and colleagues[21] revealed that Given that pregnant teenagers with 25 (OH) D levels below 30 ng/ml were more likely to test positive for BV ($P = 0.02$), poorer maternal vitamin D status may raise risk of infection during labor.

Similarly, Skowrońska-Jóźwiak and colleagues[18] demonstrated that it is possible that vitamin D has a function in the protection of certain infections since vitamin D insufficiency in pregnant women promotes the development of BV during pregnancy and subsequent respiratory infections in children.

Contrarily, cross-sectional research by Turner and colleagues[22] A study that looked at the relationship between BV and vitamin D inadequacyin pregnant and nonpregnant women found no connection between low vitamin D values and an elevated prevalence or incidence of bacterial vaginosis, and neither did vitamin D values less than or equal to 30 ng/ml.

Moreover, Powell and colleagues[23] study revealed that both early pregnancy vitamin D shortage and vitamin D supplementation had no effect on BV prevalence, and negative pregnancy outcomes were the same for women with and without BV.

4.1. Conclusion

The incidence or prevalence of BV and GDM during pregnancy seems to be significantly influenced by vitamin D deficiency. Furthermore, difficulties for the mother and the newborn are linked to vitamin D insufficiency and BV in pregnant GDM women. In order to improve health outcomes for this group, it may be required to identify vitamin D insufficiency as a modifiable risk factor for BV in pregnant GDM women.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

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Conflicts of interest

The authors declared that there were No conflicts of Interest.

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