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Association of Vitamin D Deficiency with Gestational Diabetes

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ABSTRACT

Background: A common illness that presents serious risks to the mother and foetus is gestational diabetes mellitus. The hypothesis suggests that vitamin D insufficiency may serve as an etiological element in the development of gestational diabetes mellitus (GDM). The scope of its influence upon demographic and clinical parameters, including age, parity, and gestational age, remains undefined. **Objective:** To determine the association of vitamin D deficiency with gestational diabetes. **Design of the study:** The study utilized a case-control design. **Setting and Study Duration:** The study was conducted from July 2024 to January 2025 at the Obstetrics and Gynaecology Department of Lady Reading Hospital, Peshawar. **Methodology:** 107 women with a diagnosis of gestational diabetes mellitus (case group) and 107 healthy controls were among the 214 women between the ages of 18 and 40 who took part of the study. We measured serum vitamin D levels and administered an oral glucose tolerance test to all patients between weeks 24 and 28 of pregnancy. **Results:** The study found that the GDM cohort's vitamin D levels were significantly lower than those of the control group. In the GDM group, the mean vitamin D level was 24.04 ± 9.23 nmol/L, while in the non-GDM sample, it was 39.16 ± 11.26 nmol/L ($p < 0.000$). The coefficient of regression of -10.024 ($p < 0.001$) indicated that being a member of the case group was associated with a significant decrease in vitamin D levels, according to multivariate analysis. **Conclusion:** The study discovered a strong correlation between vitamin D deficiency and an increased risk of gestational diabetes mellitus.

INTRODUCTION

Gestational diabetes is diabetes that is acquired during pregnancy and disappears after giving birth. It is characterized by high glucose during pregnancy, often from the 24th to the 28th week of gestation.[2] There is no known cause that gestational diabetes is believed to stem from, but it is believed to be caused by the changes in hormone during pregnancy that cause the body to be less sensitive to the effects of insulin and thus cause resistance to insulin.[3] The condition increases the risk to both the child and the mother of developing complications, such as increased susceptibility to developing diabetes later in life in the form of type-2 diabetes in the mother and diabetes and overweight in the child.[4]

Vitamin D plays an essential role in maintaining calcium homeostasis and bone health and in immune system function.[5] Vitamin D during pregnancy plays a crucial role in maintaining proper fetal growth, particularly in bone growth and mineralization.[6] Vitamin D in adequate amounts is necessary to promote proper growth and health of the fetus and to prevent maternal health complications, such as preeclampsia and gestational diabetes.[7]

Vitamin D deficiency during pregnancy is increasingly considered to be a serious issue, as research has indicated that very high rates of pregnant women worldwide are lacking in this essential nutrient.[8] Vitamin D deficiency is linked with osteoporosis, infantile rickets, and susceptibility to infections. Vitamin D deficiency in pregnant females has been shown in some studies to lead to gestational diabetes, preterm labour, and to preeclampsia.[9] Mechanisms by which vitamin D is impacting pregnancy are not established yet, but vitamin D's role in immune function and its effect on glucose sensitivity are suspected to play some part in the prevention of gestational diabetes.[10]

Vitamin D deficiency has previously been indicated by studies to be associated with the onset of gestational diabetes.[11] Low vitamin D causes both impaired insulin sensitivity and failure of the β-cells and these are factors that contribute to diabetes.[12] Vitamin D has been reported in some research to have an anti-inflammatory effect, and this has been proposed to control the immune system and reduce the risk of resistance to insulin in pregnancy.[13]

In a study by Mahmood S, et al. found that the mean serum vitamin D level in patients with gestational diabetes mellitus (GDM) was 23.4 ± 17.4 ng/ml, while the mean level in patients without GDM was 29.7 ± 15.4 ng/ml.[14]

Vitamin D is implicated in glucose metabolism, and its insufficiency during pregnancy is associated with a heightened risk of gestational diabetes mellitus (GDM). Existing research indicates that the precise correlation between serum vitamin D levels and the onset of gestational diabetes mellitus (GDM) is challenging to evaluate, especially in varied groups. It is worth conducting such a study in order to continue investigating the association, identify populations-at-risk, as well as inform preventive strategies such as vitamin D supplementation. These findings could influence the quality of antenatal care as well as possibly reducing the incidence of GDM and its sequelae.

METHODOLOGY

This case-control study was conducted at the Obstetrics and Gynaecology Department of Lady Reading Hospital Peshawar (MTI) over a minimum period of six months, following the approval of the study synopsis. The sample size was determined using the Open Epi calculator for unmatched case-control studies, considering the mean serum vitamin D level in patients with GDM to be 23.4 ± 17.4 ng/ml, and in patients without GDM to be 29.7 ± 15.4 ng/ml.[14] A total of 214 participants were enrolled, with 107 in the GDM group and 107 in the non-GDM group.

The inclusion criteria specified women aged 18 to 40 years with a singleton pregnancy, confirmed by ultrasound, and a gestational age between 24 and 28 weeks. Participants could have any parity. The GDM patients were assigned to the case group, while the non-GDM patients were placed in the control group. Exclusion criteria were applied to remove participants with pre-pregnancy diabetes, pregnancy complications such as anemia or gestational hypertension, and those with multiple pregnancies.

Subsequent to obtaining ethical approval from the hospital's ethics committee, all patients fulfilling the inclusion criteria were recruited via the Outpatient Departments at Lady Reading Hospital. All individuals provided informed consent prior to their involvement in the study. A thorough obstetric and medical history was obtained, and a clinical examination was conducted for each participant.

All participants underwent a test for oral glucose tolerance between 24 and 28 weeks of pregnancy, employing a 75-gram glucose load after an overnight fast. Plasma glucose concentrations were evaluated at fasting, 1 hour, and 2 hours, following the IADPSG criteria for the diagnosis of gestational diabetes mellitus. Gestational diabetes is identified when any of the following criteria are satisfied: fasting plasma glucose levels ≥ 92 mg/dL, 1-hour blood glucose ≥ 180 mg/dL, or 2-hour plasma glucose ≥ 153 mg/dL. Serum concentrations of vitamin D were also evaluated.

We used statistical analysis to determine the percentages and frequencies for categorical variables, and the mean and standard deviation for continuous data. Average vitamin D levels in both groups were categorized based on demographic factors. There was a multivariate investigation of the factors influencing vitamin D levels.

RESULTS

As shown in Table 1, the demographic characteristics of the two groups reveal that the case group had a slightly older mean age (31.94±4.47 years) compared to the control group (29.73±4.40 years). However, the gestational age was almost identical for both groups (26.09±1.36 weeks in the case group and 26.10±1.36 weeks in the control group). Parity was notably higher in the case group (2.36±1.31) compared to the control group (1.66±1.19).

Table 1

Demographics in Both Groups. (n=214)

Demographics	Group A (Case) n=107 Mean±SD	Group B (Control) n=107 Mean±SD
Age (years)	31.94±4.47	29.73±4.40
Gestational Age (weeks)	26.09±1.36	26.10±1.36
Parity	2.36±1.31	1.66±1.19

Table 2 shows a significant difference, with the case group (gestational diabetes) exhibiting a much lower mean Vitamin D level of 24.04±9.23 nmol/L, compared to the control group's mean of 39.16±11.26 nmol/L (t=-10.743, p<0.000). This significant deficiency in Vitamin D in the case group highlights a possible association with gestational diabetes.

Table 2

Comparison of Mean Vitamin D Levels in Both Groups

Vitamin D (nmol/L)	Group A (Case) n=107	Group B (Control) n=107	t	P value
	24.04±9.23	39.16±11.26	-10.743	<0.000

Table 3 further stratifies the Vitamin D levels according to various demographic factors. For women aged ≤30 years, the case group had a mean Vitamin D level of 33.42±6.34 nmol/L, significantly lower than the control group’s 47.16±7.22 nmol/L (p=0.000). Among women aged >30 years, the case group had an even lower mean of 17.98±4.50 nmol/L compared to the control group’s 28.13±4.29 nmol/L (p=0.000). Vitamin D levels were also significantly lower in the case group for both gestational age ≤26 weeks (24.04±10.36 nmol/L) and >26 weeks (24.03±7.51 nmol/L) compared to the control group at 38.91±12.41 nmol/L and 39.49±9.58 nmol/L, respectively (p=0.000). Parity also played a role, with the case group having significantly lower Vitamin D levels in both low parity (30.05±7.69 nmol/L) and high parity (16.65±4.25 nmol/L), compared to the control group at 44.40±8.63 nmol/L and 25.69±2.76 nmol/L, respectively (p=0.000).

Figure 1

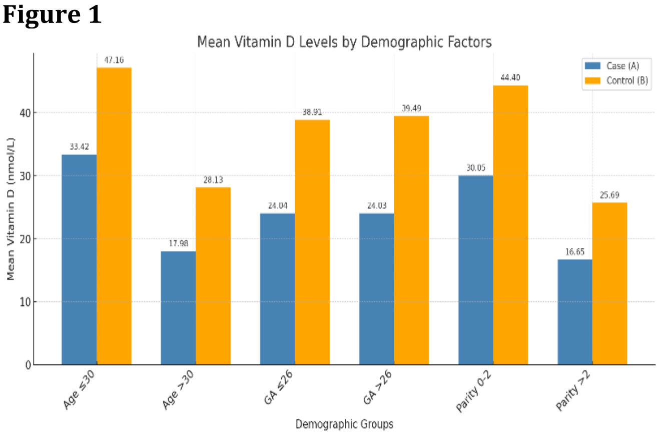

Table 3
Stratification of Mean Vitamin D Levels with Respect to Demographic Factors in Both Groups

Demographic Factors		Groups	Mean Vitamin D (nmol/L)	P Value
Age (years)	≤30	A (Case) (n=42)	33.42±6.34	0.000
		B (Control) (n=62)	47.16±7.22	
	>30	A (Case) (n=65)	17.98±4.50	0.000
		B (Control) (n=45)	28.13±4.29	
Gestational Age (weeks)	≤26	A (Case) (n=62)	24.04±10.36	0.000
		B (Control) (n=62)	38.91±12.41	
	>26	A (Case) (n=45)	24.03±7.51	0.000
		B (Control) (n=45)	39.49±9.58	
Parity	0-2	A (Case) (n=59)	30.05±7.69	0.000
		B (Control) (n=77)	44.40±8.63	
	>2	A (Case) (n=48)	16.65±4.25	0.000
		B (Control) (n=30)	25.69±2.76	

The regression coefficients indicate that lower Vitamin D levels are strongly associated with higher age (-1.714), gestational age (-0.477), and parity (-1.883). Notably, being in the case group (gestational diabetes) is associated with a significant decrease in Vitamin D levels (-10.024). The model explains a substantial portion of the variance in Vitamin D levels, with an R^2 value of 0.951, emphasizing the significant role of Vitamin D deficiency in gestational diabetes. (Table 4)

Table 4
Multivariate Analysis of Factors Affecting Vitamin D Levels

Parameter	Regression Coefficient	Std. Error	t	Sig.	95% CI
Age	-1.714	0.151	-11.379	0	-2.011, -1.417
Gestational Age (weeks)	-0.477	0.143	-3.327	0.001	-0.759, -0.194
Parity	-1.883	0.534	-3.529	0.001	-2.935, -0.831
GROUP=Case	-10.024	0.403	-24.851	0	-10.819, -9.228

R^2 = 0.951 (Adjusted R^2 = 0.950)

DISCUSSION

There is a substantial correlation between vitamin D insufficiency and gestational diabetes mellitus, according to the study. GDM cases had considerably lower vitamin D levels (24.04 ± 9.23 nmol/L) than controls (39.16 ± 11.26 nmol/L). This aligns with evidence that vitamin D enhances insulin sensitivity by modulating pancreatic β-cell function and reducing systemic inflammation, thereby mitigating hyperglycemia in pregnancy. The case group's older mean age (31.94 ± 4.47 years) and higher parity (2.36 ± 1.31) likely exacerbated deficiency, as aging reduces cutaneous vitamin D synthesis, and repeated pregnancies deplete maternal stores. Notably, vitamin D levels were consistently lower in GDM women across all gestational ages, suggesting deficiency precedes—rather than results from—dysglycemia. The multivariate analysis underscores this independence, with GDM status alone predicting a 10.024 nmol/L drop in vitamin D levels, possibly due to disrupted placental conversion of 25(OH)D to active $1,25(OH)_2D$ in insulin-resistant states.

Our study results were consistent with those found in several previous studies that investigated the relationship between vitamin D deficiency and gestational diabetes mellitus (GDM). The demographic characteristics of the two groups revealed that the case group had a slightly older mean age (31.94 ± 4.47 years) compared to the control group (29.73 ± 4.40 years). This is similar to the findings of Zhang T, et al.[14] where the average age of the participants was 28.5 years, and there was a slight variation in age between groups, with older women showing a higher prevalence of GDM. The gestational age in our study was almost identical for both groups (26.09 ± 1.36 weeks in the case group and 26.10 ± 1.36 weeks in the control group), which aligns with the findings of Ali HS, et al,[15] who also found no significant differences in gestational age between GDM and control groups. However, parity was notably higher in the case group (2.36 ± 1.31) compared to the control group (1.66 ± 1.19), which is consistent with previous studies.[16]

The analysis of mean Vitamin D concentrations between the case and control groups in our study revealed a statistically significant disparity, with the case group demonstrating markedly lower Vitamin D levels (24.04 ± 9.23 nmol/L) in contrast to the control group's mean of 39.16 ± 11.26 nmol/L ($t = -10.743$, $p < 0.000$). The pronounced deficit of Vitamin D in the case group suggests a potential correlation with gestational diabetes mellitus (GDM), corroborating the findings of Milajerdi A, et al.,[17] who documented a reduced mean vitamin D level in women with GDM (OR = 1.15, 95% CI: 1.07–1.23). Wang L[18] similarly identified a substantial disparity in Vitamin D levels between women with gestational diabetes mellitus (GDM) and healthy individuals, revealing that women with GDM exhibited lower Vitamin D levels than healthy controls (SMD = -0.71, 95% CI: -0.91, -0.50).

Our study further stratified Vitamin D levels according to various demographic factors. For women aged ≤30 years, the case group had a mean Vitamin D level of 33.42 ± 6.34 nmol/L, significantly lower than the control group's 47.16 ± 7.22 nmol/L (p = 0.000). Among women aged >30 years, the case group had an even lower mean of 17.98 ± 4.50 nmol/L compared to the control group's 28.13 ± 4.29 nmol/L (p = 0.000). This finding is consistent with the results of Ali HS, [15] where women with vitamin D deficiency were more likely to be older and at greater risk for GDM. Furthermore, vitamin D levels were also significantly lower in the case group for both gestational age ≤26 weeks (24.04 ± 10.36 nmol/L) and >26 weeks (24.03 ± 7.51 nmol/L), compared to the control group at 38.91 ± 12.41 nmol/L and 39.49 ± 9.58 nmol/L, respectively (p = 0.000). This result mirrors the findings of Zhang T, et al., [14] who also found that vitamin D deficiency was significantly associated with GDM, with women diagnosed with GDM showing lower vitamin D levels across all gestational periods.

In our study, parity also played a role, with the case group having significantly lower Vitamin D levels in both low parity (30.05 ± 7.69 nmol/L) and high parity (16.65 ± 4.25 nmol/L), compared to the control group at 44.40 ± 8.63 nmol/L and 25.69 ± 2.76 nmol/L, respectively (p = 0.000). These findings are consistent with Milajerdi A, et al., et al., [17] who found a relationship between lower vitamin D levels and higher parity in women with GDM.

The multivariate analysis in our study further confirmed the negative association between Vitamin D levels and gestational diabetes. The regression coefficients indicated that lower Vitamin D levels were strongly associated with higher age (-1.714), gestational age (-0.477), and parity (-1.883). Notably, being in the case group (gestational diabetes) was associated with a significant decrease in Vitamin D levels (-10.024). These results align with those found by Milajerdi A, et al., [17] and Zhang T, et al., [14] both of which confirmed that lower vitamin D levels are independently associated with a higher risk of developing GDM. The model in our study explains a substantial portion of the variance in Vitamin D levels (R^2 = 0.951), emphasizing the significant role of Vitamin D deficiency in gestational diabetes.

By comparing the effects of vitamin D deficiency across various demographic groups, our study underscores the need for routine monitoring of vitamin D levels in pregnant women, particularly those at higher risk for GDM. Given the potential for vitamin D supplementation to mitigate this risk, further research in larger, diverse populations is warranted to confirm these findings and guide clinical recommendations.

Nonetheless, our study has several drawbacks. As a single-center study, the findings may lack full generalizability across diverse groups with differing demographics or geographic contexts. The absence of follow-up about the long-term effects of vitamin D supplementation in pregnant women complicates the evaluation of its enduring influence on gestational diabetes mellitus and overall maternal health.

CONCLUSION

Our research has determined that vitamin D insufficiency is highly correlated with a heightened risk for developing gestational diabetes mellitus (GDM). The results correspond with prior studies, emphasizing the significance of vitamin D in regulating insulin sensitivity and metabolism of glucose during pregnancy. Considering the found correlation, sustaining sufficient vitamin D levels may be a crucial approach in preventing gestational diabetes mellitus (GDM).

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