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Effect of Prenatal Vitamin D Supplementation on Glucose Metabolism during Pregnancy: A Randomized Controlled Trial

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ABSTRACT

Background
The growing concern of gestational diabetes is its impact on a mother and her child's health. While a deficiency in vitamin D has been associated with glucose metabolism disturbances, strong evidence backing its preventive measures is still lacking. This study aimed to investigate if beginning oral vitamin D supplementation during the first trimester is capable of enhancing glucose metabolism and decreasing the incidence of gestational diabetes.

Methods
A randomized controlled trial was conducted at Khyber Teaching Hospital, Peshawar, from January 2022 to January 2023. One hundred and seven pregnant women in their first trimester were randomly divided into two groups: one received 2,000 IU of vitamin D daily, and the other received a placebo. Study participants were followed up to 28 weeks prenatal. Blood samples were analysed to assess fasting glucose, 2-hour OGTT, insulin, Hba1c, HOMA-IR, and serum vitamin D levels. GDM was diagnosed using IADPSG criteria.

Results
Participants in the vitamin D group exhibited significant enhancements in fasting glucose, Hba1c, and insulin resistance scores ($p < 0.001$) in comparison to other participants. GDM developed in 7.4% of the supplemented group participants versus 20.8% in the control group ($p = 0.018$).

Conclusion
It appears that gestational diabetes can be prevented with supplementation of Vitamin D in early pregnancy due to enhanced glucose metabolism. These results underscore the importance of including vitamin D testing and treatment in standard prenatal care.

Keywords: Vitamin D, gestational diabetes, pregnancy, insulin resistance, glucose metabolism, randomized trial.

INTRODUCTION

Pregnancy brings about considerable metabolic changes, including a natural rise in insulin resistance that peaks in the second and third trimesters. Although this change supports fetal growth, an exaggerated

response can result in 'gestational diabetes mellitus (GDM)'. Maternal and child health complications associated with GDM include, but are not limited to, childbirth difficulties and elevated risks of type 2 diabetes in later part of life[1-3].

Vitamin D, long known for its role in bone and mineral health, has recently gained attention for its involvement in other body systems, including regulating blood sugar. Researchers have discovered that vitamin D receptors are present in pancreatic beta cells and tissues involved in insulin action, suggesting it may influence how the body processes glucose. Low vitamin D levels have been linked with poor glucose control, and many pregnant women especially in regions with limited sun exposure or cultural practices that limit skin exposure are at risk of deficiency.[4-6].

Vitamin D deficiency among South Asian women is commonplace during pregnancy because of culturally prescribed dress, insufficient diet, and limited sunlight exposure. Concurrently, GDM is rising in prevalence, which poses a public health challenge requiring preventative measures. While supplementation is a simple and cost-effective intervention, its precise impact on glucose regulation during pregnancy still warrants clarification through well-designed clinical trials [7-9].

The objective of the study was "to assess the effect of daily oral vitamin D supplementation on glucose metabolism in women during the first and second trimester of pregnancy". The goal was to determine whether correcting the normal-deficient levels of vitamin D would ameliorate increased insulin resistance and decrease the prevalence of GDM in this particular high-risk group.

The diagnosis of PE is especially difficult in the setting of emergency care because its signs and symptoms overlap with other more common conditions like myocardial infarction, pneumonia, or heart failure. The use of D-dimer testing, CTPA, and clinical scoring like Wells and Geneva criteria has added value to the diagnosis; however, the problems of underdiagnosis and treatment delay continue to persist, especially in resource-constrained settings [2].

The evolution of PE management therapies has aligned with the increasing use of anticoagulation treatment. In cases exhibiting severe hemodynamic instability, systemic thrombolysis and directed thrombolytic catheter interventions may be necessary. Treatment algorithms now consider thrombus location, troponin and BNP levels, echocardiography results, and other additional markers, which incorporate stratification to improve outcomes. However, these still leave significant gaps with regards to advanced central or massive emboli [3].

Scant information is available regarding the acute real-time management and outcomes of patients diagnosed with acute PE in emergency departments in Pakistan. Most of the evidence is from retrospective studies or has been adapted from foreign studies which, due to differences in local patient population, comorbidity patterns, and healthcare practices, are not representative and may not be appropriate to use [4].

This study was therefore undertaken to explore the clinical features, 'management strategies, and in-hospital outcomes of patients diagnosed with acute pulmonary embolism in the emergency department of a tertiary care hospital'. By identifying common presentation patterns and outcome predictors, the study aims to contribute to better clinical recognition, timely interventions, and overall improvement in patient care in similar settings.

METHODOLOGY

This study was conducted as a randomized controlled trial at the Department of Obstetrics and Gynaecology, Khyber Teaching Hospital, over one year (January 2022–January 2023). The focus of the study was on how daily supplementation of vitamin D may improve glucose metabolism and decrease the prevalence of gestational diabetes amongst expectant mothers.

"Through consecutive sampling from the antenatal outpatient department, 107 women in their first trimester were recruited" All subjects were informed of the requirements and attested to the criteria stipulated in the consent form. From this pool, women participants were randomly 'allocated to receive either 2,000 IU of vitamin D3 daily' or a matching placebo from the time of enrollment till the second trimester."

Inclusion Criteria

- Pregnant women aged 18–40 years
- Gestational age ≤ 14 weeks confirmed by ultrasound
- No history of diabetes or chronic illness• Willingness to participate and comply with follow-up

Exclusion Criteria

- Known cases of pre GDM
- Existing endocrine or metabolic disorders
- Vitamin D supplementation in the past three months
- Multiple pregnancies or known fetal anomalies

Using computer-generated random numbers, participants were randomly allocated into two groups. The intervention group was given oral supplements of vitamin D3 (cholecalciferol 2,000 IU daily) 'from enrollment until 28 weeks of gestation'. The control group was given a placebo that was identical in appearance to the treatment. All participants were instructed to maintain regular antenatal care, consisting of iron and folic acid supplementation.

Compliance with supplementation was assessed through verbal feedback and by counting the remaining tablets during follow-up visits. Participants were followed monthly until the end of the second trimester. Baseline data, including age, BMI, gravidity, parity, educational status, family history of diabetes, dietary habits, and sun exposure, were collected through structured interviews. Anthropometric measurements were taken using standard equipment. 'Fasting blood samples were collected at enrollment and 28 weeks of gestation'.

The following biochemical markers were analysed: 'Fasting Plasma Glucose (FPG), 2-hour Oral Glucose Tolerance Test (OGTT), Hba1c, Fasting Insulin, HOMA-IR (calculated as [FPG × Insulin]/405), Serum 25-hydroxyvitamin D levels'

All laboratory investigations were performed using standardised methods at the hospital's central biochemistry laboratory.

The study's different outcomes were changes in glucose metabolism parameters (FPG, OGTT, insulin levels, Hba1c, and HOMA-IR) in both groups. The secondary outcome was the occurrence of GDM, which was detected using the criteria set by the International Association of Diabetes and Pregnancy Study Groups (IADPSG).

Data obtained was input into SPSS version 25 in order to perform a statistical analysis. The demographic data was summarized using descriptive statistics. The means of both groups and continuous variables were analyzed using independent t-tests which calculated the mean and standard deviation values, as well. For categorical data, frequencies and percentages were calculated and evaluated through chi-square analysis. A statistical significance was determined using a value of $p < 0.05$.

RESULT

Following the intervention, women who received vitamin D exhibited clear improvements across multiple metabolic parameters. Their fasting glucose levels, post-load glucose readings, and Hba1c were 'significantly reduced compared to those in the control group'. 'Insulin resistance, measured by HOMA-IR' was also noticeably lower. A significant increase in vitamin D levels confirmed effective absorption and compliance. These outcomes suggest that initiating vitamin D supplementation early in pregnancy may contribute to healthier glucose control and potentially reduce the onset of gestational diabetes.

Table 1: Demographic and Baseline Characteristics of Participants

Variable	Intervention Group (n=54)	Control Group (n=53)	p-value
Age (years, mean ± SD)	27.6 ± 4.3	28.1 ± 4.7	0.462
'BMI (kg/m², mean ± SD)'	26.9 ± 3.2	27.1 ± 3.5	0.721
Gestational Age (weeks)	12.5 ± 1.4	12.7 ± 1.3	0.538
Gravidity ≥ 3	22 (40.7%)	20 (37.7%)	0.743
Parity ≥ 2	18 (33.3%)	16 (30.2%)	0.713
Urban Residence	39 (72.2%)	37 (69.8%)	0.774
Education ≥ Secondary	32 (59.2%)	31 (58.5%)	0.938
Family History of DM	15 (27.8%)	14 (26.4%)	0.872

After receiving vitamin D supplementation, women in the intervention group showed marked improvements in several metabolic indicators. Their fasting blood glucose levels, '2-hour post-load

glucose readings, and Hba1c values were significantly lower than the control group, all with highly significant p-values (<0.001)'. These outcomes point toward enhanced glycemic control as a result of the intervention. Additionally, a notable reduction in fasting insulin and HOMA-IR scores was observed, reflecting improved insulin sensitivity. The 'substantial rise in serum 25(OH) vitamin D concentrations further confirms that the supplementation effectively addressed the deficiency'. These results indicate that early vitamin D supplementation may support regulating glucose metabolism 'during pregnancy and in lowering the likelihood of developing gestational diabetes'.

Table 2: Biochemical and Metabolic Outcomes after Intervention.

'Variable'	'Intervention Group (n=54)'	'Control Group (n=53)'	p-value
'Fasting Plasma Glucose (mg/dL)'	84.5 ± 7.2	90.2 ± 8.1	0.001 **
2-h OGTT (mg/dL)	118.4 ± 16.7	134.9 ± 17.3	<0.001 **
HbA1c (%)	5.1 ± 0.3	5.4 ± 0.4	<0.001 **
Fasting Insulin (µIU/mL)	9.8 ± 2.1	12.5 ± 2.6	<0.001 **
HOMA-IR	2.04 ± 0.52	2.78 ± 0.61	<0.001 **
Serum 25(OH) Vitamin D (ng/mL)	36.2 ± 6.3	19.8 ± 5.4	<0.001 **

The rate of gestational diabetes was significantly reduced in the group that received vitamin D supplementation. In this group, only 4 out of 54 women developed GDM, compared to 11 cases in the control group. The difference observed was statistically significant, thus reinforcing the hypothesis about the beneficial effect of vitamin D intake early in pregnancy on the risk of vitamin D deficiency-associated glucose intolerance.

Table 3: Incidence of GDM.

Group	Developed GDM	Did Not Develop GDM	p-value
Intervention (n=54)	4 (7.4%)	50 (92.6%)	0.018 *
Control (n=53)	11 (20.8%)	42 (79.2%)	

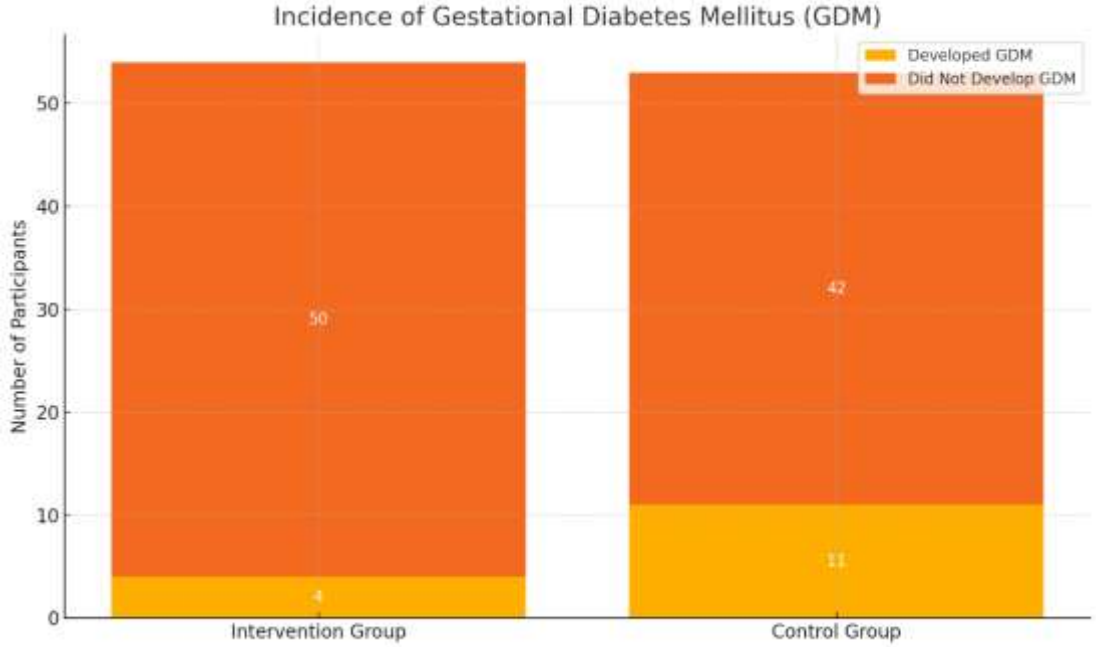

Figure 1

The bar graph compares gestational diabetes occurrence between the vitamin D intervention and control groups. 'It shows that a notably smaller number of participants developed GDM in the intervention group compared to the control group'. While most participants in both groups did not develop GDM, the cases were visibly lower in those who received vitamin D supplementation. This visual representation reinforces the statistical findings from 'Table 3, highlighting the possible protective role of vitamin D against glucose intolerance during pregnancy'. Although illustrated in simple numerical terms, the difference has significant implications for prenatal care and GDM prevention strategies.

DISCUSSION

The results from this randomized controlled trial indicate that the supplementation of vitamin D during the first trimester of pregnancy positively impacts glucose metabolism while reducing the risk for GDM. Women receiving vitamin D3 daily demonstrated lower fasting glucose, Hba1c, insulin concentrations, and HOMA-IR indices compared to the placebo group. These results prove the metabolic benefits of maintaining adequate vitamin D levels during pregnancy.

The outcomes of our trial are consistent with prior investigations that have explored how vitamin D influences insulin function and blood sugar control during pregnancy. Various studies have reported enhanced insulin sensitivity and a lower occurrence of GDM in women who received supplementation. [10-12]. Research conducted in Iranian populations also demonstrated a decline in fasting glucose and insulin resistance following vitamin D intake, reinforcing its regulatory role in maternal glucose metabolism [13-15].

The improvement in serum 25(OH) D levels in our intervention group confirms the effectiveness of the supplementation dose and adherence. Furthermore, the significantly lower GDM incidence among supplemented participants highlights the clinical relevance of early vitamin D correction in at-risk pregnant populations. While our study focused on early gestation, evidence suggests that even mid-pregnancy supplementation may confer glycemic benefits, though early intervention appears more protective [16-18].

Interestingly, our baseline comparison showed that both groups were matched across major demographic and obstetric variables, eliminating potential confounders and strengthening the trial's internal validity. This aspect underscores that the observed metabolic differences were likely due to the vitamin D intervention rather than pre-existing group differences [19, 20].

However, our study has certain limitations. First, despite regular follow-up, compliance was assessed through self-reporting and pill counts, which could introduce reporting bias. 'Second, we did not explore long-term neonatal outcomes related to maternal glucose control, which could provide further insight into the broader implications of vitamin D supplementation'. Lastly, while the study was powered for metabolic outcomes, a larger sample might have strengthened subgroup analysis, such as effects stratified by BMI or sunlight exposure.

Despite these limitations, the study contributes important evidence from a South Asian population where both vitamin D deficiency and GDM are highly prevalent. 'It highlights the need for incorporating vitamin D status assessment and supplementation into routine antenatal care, especially in regions with limited sunlight exposure or cultural practices that reduce skin exposure'.

CONCLUSION

The outcomes of this study indicate that vitamin D supplementation in early pregnancy may offer protective effects against GDM. Participants who received daily vitamin D demonstrated better control over blood sugar levels, improved insulin responsiveness, and experienced a significantly lower incidence of GDM than those who received a placebo. These findings suggest that timely detection and 'correction of vitamin D insufficiency during pregnancy could be valuable, especially for populations at increased risk due to lifestyle or geographic limitations'. Introducing vitamin D screening and supplementation into standard prenatal care may be a practical and low-cost approach to improving maternal metabolic health. Further investigations should explore long-term maternal and neonatal effects and help establish precise supplementation protocols for broader clinical adoption.

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