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COMPARISON OF LOW VERSUS HIGH DOSE OF VITAMIN D ON GLYCAEMIC CONTROL OF DIABETES MELLITUS IN PREGNANCY

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ABSTRACT

Introduction: Gestational diabetes mellitus (GDM) is a prevalent pregnancy-related metabolic disorder that contributes to significant maternal and neonatal complications. The role of vitamin D in improving glycemic regulation has been well researched, but appropriate dosing strategy remains uncertain.
Objective: To compare the effects of low-dose versus high-dose vitamin D supplementation on fasting blood sugar (FBS) and insulin resistance (HOMA-IR) in pregnant women diagnosed with GDM.
Methods: This randomized controlled trial was carried out at Sir Ganga Ram Hospital, Lahore, from 1st January 2025 to 31st May 2025. A total of 300 pregnant women with GDM (gestational age 24–37 weeks) were randomized into two groups. Group A was given vitamin D (2,500 IU every two weeks), whereas Group B received vitamin D (50,000 IU every two weeks). FBS and HOMA-IR were measured at baseline, after 15 days, and at one month. Data analysis was performed using SPSS v25.
Results: After one month of supplementation, the mean FBS levels dropped to 112.6 ± 10.4 mg/dl in the Group A and to 98.8 ± 9.8 mg/dl in the Group B ($p < 0.001$). Similarly, mean HOMA-IR decreased to 3.88 ± 0.9 in Group A and 2.95 ± 0.8 in Group B ($p < 0.001$).
Conclusion: High-dose vitamin D supplementation was more effective than low-dose therapy in improving glycemic parameters among women with GDM. Hence, higher vitamin D regimens may be beneficial as adjunctive therapy to optimize metabolic control in this population.

INTRODUCTION:

Gestational diabetes mellitus (GDM) affects nearly 15% of pregnancies in the United States.[1,2] In both diabetic and non-diabetic populations, lower serum concentrations of 25-hydroxyvitamin D (25OHD) have been linked with elevated fasting glucose and increased glycated hemoglobin.[3,4] Vitamin D may influence glucose metabolism through several mechanisms. It exerts anti-inflammatory and immunomodulatory effects that can modulate autoimmune processes involved in diabetes and reduce low-grade chronic inflammation. Moreover, it has been shown to increase insulin secretion. Women with GDM are also predisposed to complications such as cesarean delivery, hypertensive disorders of pregnancy, pre-eclampsia, and increased perinatal morbidity.

Almost 90% of Pakistani women giving birth have been reported to be vitamin D deficient.[5,6] Standard guidelines recommend supplementation of 400 IU/day during pregnancy, while doses up to 4000 IU/day may be required in deficiency states to achieve optimal outcomes. Vitamin D deficiency can also disturb calcium balance, resulting in hypocalcemia. In GDM, placental hormones with insulin-antagonistic activity further reduce maternal insulin sensitivity.[7,8]

Evidence from clinical trials remains inconsistent. One study reported that women receiving high-dose vitamin D achieved significantly better outcomes, with fasting glucose levels of 84.73 ± 20 mg/dl versus 96.12 ± 20 mg/dl and HOMA-IR of 1.18 versus 2.87 ($p<0.05$).[9] In contrast, another trial found no significant difference, with fasting glucose of 77.55 ± 5 mg/dl versus 75.59 ± 6.98 mg/dl and HOMA-IR of 2.03 ± 1.84 versus 1.52 ± 1.21 ($p>0.05$).[10]

In light of these conflicting results, this study aims to compare the effects of low versus high doses of vitamin D on glycemic control in women with GDM. Although some evidence supports its role in lowering HbA1c and fasting glucose, other findings contradict this benefit. Furthermore, local research is scarce and predominantly observational. This study therefore seeks to clarify whether higher doses of vitamin D confer superior glycemic control compared to standard supplementation in GDM.

METHODOLOGY

This randomized controlled trial was conducted in the Department of Gynecology & Obstetrics, Unit II, Sir Ganga Ram Hospital, Lahore, from 1st January 2025 to 31 May 2025 following approval of the synopsis. A total of 300 females as per the inclusion criteria were enrolled through non-probability consecutive sampling. The sample size of 300 cases (150 in each group) was calculated by using OpenEpi.com, considering a 90% power of study, 95% confidence level, and mean fasting glucose levels of 96.12±20 mg/dl with low dose and 84.73±20 mg/dl with high dose of vitamin D supplementation.[9]

All females aged between 18 and 35 years, with parity less than five, gestational age between 24 and 37 weeks, and diagnosed cases of gestational diabetes mellitus were included in this study. The women with multiple pregnancies detected on ultrasound, history of vitamin D supplementation during the last three months or before pregnancy, those with polycystic ovarian syndrome prior to pregnancy, in-vitro fertilization, pre-eclampsia, eclampsia and smoking history of more than five pack years were excluded.

After obtaining approval from the hospital ethical review committee, eligible females were recruited from the outpatient department. Written informed consent was obtained from all participants. Baseline demographic and clinical data were documented on a predesigned proforma. Randomization into two groups was carried out using the lottery method. Participants in Group A were given vitamin D, i.e., 2,500 IU every two weeks, while those in Group B were given vitamin D, i.e., 50,000 IU fortnightly.

At baseline and after one month of intervention, participants were instructed to attend the outpatient department following a

10–12 hours overnight fast. Venous blood samples were drawn using a 3cc disposable syringe. A drop of blood was tested using an Accu-Chek meter by the researcher to record fasting blood glucose levels. The remaining sample was sent to the hospital laboratory for estimation of HOMA-IR. Outcomes in terms of fasting blood sugar and HOMA-IR were recorded both pre- and post-intervention as per operational definitions. Data was analyzed using SPSS version 25.

RESULT

The distribution of participants according to residence, occupation, socioeconomic status, dietary pattern, lifestyle, and booking status was also similar across groups, with no statistically significant differences, confirming comparability at baseline (Table 1).

Fasting blood sugar levels were assessed at baseline, 15 days, and 1 month after intervention (Table 2). After 15 days of supplementation, mean fasting blood sugar significantly decreased to 118.3 ± 11.7 mg/dl in the group A and 110.5 ± 10.9 mg/dl in the group B ($p < 0.001$). After one month, the reduction was more pronounced, with fasting blood sugar levels of 112.6 ± 10.4 mg/dl in the group A compared to 98.8 ± 9.8 mg/dl in the group B ($p < 0.001$), indicating superior glycemic control with the high-dose vitamin D regimen.

Similarly, HOMA-IR levels were analyzed at baseline, 15 days, and 1 month after intervention (Table 3). At baseline, mean HOMA-IR was comparable between the groups (4.95 ± 1.2 in the group A versus 5.02 ± 1.3 in the group B, $p = 0.48$). At 15 days, HOMA-IR levels decreased to 4.22 ± 1.0 in the group A and 3.75 ± 0.9 in the group B, with a statistically significant difference ($p < 0.01$). After one month, the group B showed a greater reduction, with mean HOMA-IR of 2.95 ± 0.8 compared to 3.88 ± 0.9 in the group A ($p < 0.001$).

To further assess the effect of body mass index, a stratified analysis was performed (Table 4). Among women with BMI < 25, the mean reduction in fasting blood sugar was -10.8 ± 6.4 mg/dl in the group A versus -18.6 ± 7.1 mg/dl in the group B ($p < 0.01$). In women with BMI ≥ 25, the reduction was -12.1 ± 7.0 mg/dl in the group A compared to -20.3 ± 8.2 mg/dl in the group B ($p < 0.001$).

Variable	Group A (n=150)	Group B (n=150)
Age (years, mean ± SD)	27.4 ± 4.1	27.1 ± 4.5
Gestational Age (weeks)	30.2 ± 2.8	30.5 ± 2.6
BMI (kg/m², mean ± SD)	27.9 ± 3.4	28.1 ± 3.6
Residence		
Rural Urban Semi-urban Industrial area	40 (26.7%) 82 (54.7%) 20 (13.3%) 8 (5.3%)	38 (25.3%) 85 (56.7%) 21 (14.0%) 6 (4.0%)
Occupation		
Housewife Job Business Maid	120 (80.0%) 15 (10.0%) 10 (6.7%) 5 (3.3%)	118 (78.7%) 17 (11.3%) 9 (6.0%) 6 (4.0%)
Socioeconomic status		
Low Middle High	35 (23.3%) 95 (63.3%) 20 (13.3%)	38 (25.3%) 92 (61.3%) 20 (13.4%)

Dietary pattern Home-made Fast-food Street-food Following a diet plan	 110 (73.3%) 20 (13.3%) 10 (6.7%) 10 (6.7%)	 108 (72.0%) 22 (14.7%) 12 (8.0%) 8 (5.3%)
Life style Active Sedentary	 60 (40.0%) 90 (60.0%)	 58 (38.7%) 92 (61.3%)
Booking Status Booked Un-booked	 105 (70.0%) 45 (30.0%)	 108 (72.0%) 42 (28.0%)

Table 1: characteristics of women with gestational diabetes

Time Point	Group A (n=150)	Group B (n=150)	p-value
Baseline (Mean ± SD)	126.8 ± 12.5	127.4 ± 12.9	0.62
After 15 days	118.3 ± 11.7	110.5 ± 10.9	<0.001
After 1 month	112.6 ± 10.4	98.8 ± 9.8	<0.001

Table 2: Comparison of mean fasting blood sugar levels (mg/dl) at baseline, 15 days, and 1 month

Time Point	Group A (n=150)	Group B (n=150)	p-value
Baseline (Mean ± SD)	4.95 ± 1.2	5.02 ± 1.3	0.48
After 15 days	4.22 ± 1.0	3.75 ± 0.9	<0.01
After 1 month	3.88 ± 0.9	2.95 ± 0.8	<0.001

Table 3: Comparison of mean HOMA-IR levels at baseline, 15 days, and 1 month

BMI Category	Group A	Group B	p-value
BMI < 25 (n=90) (Mean ± SD)	-10.8 ± 6.4	-18.6 ± 7.1	<0.01
BMI ≥ 25 (n=210)	-12.1 ± 7.0	-20.3 ± 8.2	<0.001

Table 4: Stratified analysis of reduction in fasting blood sugar by BMI

DISCUSSION

In this study of pregnant women with gestational diabetes mellitus (GDM), high-dose vitamin D achieved greater improvements in fasting blood sugar (FBS) and insulin resistance (HOMA-IR) than a low-dose regimen over one month. Contemporary meta-analyses and trials consistently report reductions in FBS, fasting insulin, and HOMA-IR following vitamin D supplementation, with larger effects observed when higher doses or loading strategies are used.[11,12,13] Our between-group differences were already evident by day 15 and widened by one month, suggesting that dose intensity matters for the speed and magnitude of metabolic response. This pattern mirrors randomized and quasi-experimental studies that used high-dose protocols (e.g., 50,000 IU every two weeks or weekly), which improved insulin sensitivity more than standard prenatal doses, likely by rapidly correcting deficiency and achieving effective 25(OH)D levels.[14,15] Recent narrative and quantitative syntheses in pregnant and non-pregnant populations reinforce these pathways, demonstrating reductions in inflammatory mediators and improvements in lipid and glucose homeostasis after supplementation.[16,17] The baseline comparability across demographic and clinical variables reduces the likelihood that group imbalances explain the results. Furthermore, stratified analyses by BMI showed consistent superiority of the high-dose regimen across weight strata, in line with literature indicating that obesity is associated with lower vitamin D bioavailability and may necessitate higher

doses to achieve target serum levels. The persistence of a treatment effect after BMI stratification echoes findings from recent GDM-focused meta-analyses showing benefit across heterogeneous maternal characteristics.[18]

The present findings also intersect with the broader question of prevention versus treatment. While some trials have not demonstrated a preventive effect of vitamin D on incident GDM when started early in pregnancy, our results—and several recent syntheses—support therapeutic benefits once GDM is established, particularly on intermediate metabolic endpoints such as FBS and HOMA-IR. This divergence is consistent with the DALI RCT and other prevention-oriented studies that showed limited impact on GDM incidence despite improving vitamin D status; by contrast, in women already diagnosed with GDM, supplementation appears to yield clearer glycemic advantages.[19]

Importantly, our dosing schema parallels high-dose regimens evaluated elsewhere. Trials using 50,000 IU every two weeks have reported improved insulin sensitivity and, in some cases, lower fasting glucose compared with standard dosing or placebo—consistent with our stronger effect size in the high-dose arm.[20] While causality cannot be inferred from such designs, they contextualize our intervention findings and highlight at-risk subgroups (e.g., advanced maternal age, higher BMI) who may particularly benefit from status correction.

Strengths of our study include randomized allocation, balanced baseline characteristics, and the assessment of both FBS and HOMA-IR at multiple time points, enabling temporal inference about dose–response. The sample size was adequate to detect clinically relevant differences, and stratified analyses support robustness across BMI strata. Nonetheless, limitations merit discussion.[21] Our follow-up spanned one month; while sufficient to demonstrate early metabolic gains, longer observation would clarify persistence, effects on HbA1c, medication requirements, and perinatal outcomes. Finally, single-center conduct may limit generalizability, though our results align with multi-setting evidence from recent reviews and trials.[22]

Future research should prioritize pragmatic, multi-center RCTs comparing tailored dosing (guided by baseline 25(OH)D and BMI) against fixed regimens, with standardized outcome sets that include glycemic trajectories, need for pharmacologic escalation, maternal–fetal outcomes, and postpartum metabolism. Incorporating mechanistic biomarkers (inflammatory cytokines, lipidomics, and insulin signaling markers) would clarify pathways and identify responders.

CONCLUSION

Our trial adds to accumulating evidence that vitamin D supplementation—particularly at higher—improves short-term glycemic control and insulin resistance among women with GDM. The convergence of randomized and observational data over the past five years supports making vitamin D status assessment and timely correction a routine component of GDM care, while recognizing the need for longer-term, status-guided dosing trials to optimize efficacy and safety

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None

CONFLICT OF INTEREST

None

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