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Physiological Role of Vitamin D and Magnesium Deficiency in Modulating Glycemic Variability and Biochemical Profiles in Type 2 Diabetes Mellitus Patients

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Abstract

Vitamin D and magnesium exert critical regulatory influence on glucose metabolism. This experimental study evaluated the diagnostic significance of serum 25-hydroxyvitamin D, ionized magnesium, and their effects on glycemic variability and key biochemical parameters in Type 2 diabetes mellitus (T2DM). One hundred adult T2DM patients were prospectively recruited and stratified into deficiency and non-deficiency groups. Continuous glucose monitoring assessed glycemic variability metrics (SD, MAGE). Biochemical assays included fasting glucose, HbA1c, insulin resistance indices, lipid profile, and inflammatory markers. Vitamin D deficiency (< 20 ng/mL) and magnesium deficiency (< 1.7 mg/dL) were independently associated with significantly higher glycemic variability: SD (mean ± SD: 45.1 ± 6.3 vs. 32.8 ± 5.9 mg/dL, $p < 0.001$) and MAGE (80.2 ± 9.7 vs. 55.7 ± 8.2 mg/dL, $p < 0.001$). Deficient groups also had poorer glycemic control (HbA1c 8.9 ± 1.2 vs. 7.2 ± 0.9 %, $p < 0.001$), elevated HOMA-IR, dyslipidemia, and higher hs-CRP. Multivariate regression confirmed both deficiencies as independent predictors of increased glycemic variability ($p < 0.01$). These findings suggest that coexisting deficiencies of vitamin D and magnesium substantially exacerbate glycemic dysregulation and biochemical derangements in T2DM. Routine assessment and correction may offer a strategy to stabilize glucose fluctuations and improve metabolic outcomes.

Keywords: type 2 diabetes mellitus; vitamin D deficiency; magnesium deficiency; glycemic variability

Introduction

Type 2 diabetes mellitus (T2DM) is a metabolic disorder characterized by chronic hyperglycemia and insulin resistance, affecting millions worldwide. Glycemic control remains a primary goal, yet growing emphasis has shifted toward glycemic variability as an independent predictor of microvascular complications and oxidative stress. Understanding factors that modulate glycemic variability is therefore essential for optimizing diabetic care.1-3

Emerging evidence identifies vitamin D as a pleiotropic hormone with roles extending beyond calcium homeostasis. It influences insulin secretion via direct effects on pancreatic β-cells, interacts with insulin receptor expression, and modulates systemic inflammation. Meta-analyses reveal that low serum 25-hydroxyvitamin D is associated with insulin resistance and poor glycemic outcomes in T2DM, although effects on glycemic variability per se remain underexplored. Additionally, deficiency rates are disproportionately high in diabetic populations, owing to shared risk factors such as sedentary lifestyle and obesity.4-7

Magnesium is a cofactor for enzymes involved in glucose metabolism and insulin signaling. Hypomagnesemia, common in T2DM, impairs cellular glucose uptake and promotes endothelial dysfunction. Evidence links magnesium deficiency to increased insulin resistance, dyslipidemia, and inflammatory activation. However, its specific contribution to glucose excursions throughout the diurnal cycle requires further elucidation.8-11

Given the complementary roles of vitamin D and magnesium in modulating glucose homeostasis, it is plausible that concurrent deficiencies may synergistically elevate glycemic variability and biochemical disturbances in T2DM. Recent randomized and longitudinal studies published between 2022 and 2024 underscore the potential benefits of repleting these micronutrients, reporting attenuated variability and improved lipid and inflammatory profiles among supplemented cohorts.12

Despite these advances, no study has simultaneously quantified the impact of dual deficiency on glycemic variability using continuous glucose monitoring (CGM), correlating with comprehensive metabolic profiles in a diabetic cohort. Employing CGM provides granular insight into glucose fluctuations, while capturing biochemical markers offers mechanistic clarity. This integrative approach could inform future interventional strategies targeting micronutrient correction as adjunctive therapy in T2DM.

The objectives of this investigation were to examine the prevalence of vitamin D and magnesium deficiency in T2DM patients; quantify the extent to which each deficiency, alone or combined, influences glycemic variability metrics derived from CGM; and define their relationship with glycemic control, insulin resistance, lipid profile, and systemic inflammation. It was hypothesized that T2DM patients with dual deficiencies would exhibit significantly greater glycemic variability and biochemical dysregulation compared to those with adequate nutrient levels.

Methodology

A prospective, observational study was performed at Nawaz Shareef Medical College enrolling 100 adults aged 30 to 70 years with established T2DM. Sample size was determined via Epi Info, anticipating a prevalence of dual deficiency at 40%, effect size (difference in glycemic variability metrics) of 0.5, 80% power, and $\alpha = 0.05$, requiring 98 patients. Patients were stratified into four groups based on serum 25-hydroxyvitamin D (≥ 20 or < 20 ng/mL) and serum ionized magnesium (≥ 1.7 or < 1.7 mg/dL) levels. Exclusion criteria included type 1 diabetes, advanced renal impairment (eGFR < 30 mL/min/1.73 m²), hepatic failure, recent systemic steroid use, current micronutrient supplementation, or active infection. Approval was obtained from the institutional review board, and verbal informed consent was documented for all participants.

Baseline assessments entailed demographic data, clinical history, and anthropometry. CGM devices (Dexcom G6) were applied for 14 days to collect interstitial glucose readings. Glycemic variability indices calculated included standard deviation (SD), mean amplitude of glycemic excursions (MAGE), and coefficient of variation (CV). Fasting blood samples were drawn at baseline for measurement of 25-hydroxyvitamin D (chemiluminescent immunoassay), ionized magnesium (ion-selective electrode), fasting glucose, insulin, HbA1c, lipid panel (total cholesterol, LDL, HDL, triglycerides), homeostatic model assessment for insulin resistance

(HOMA-IR), and hs-CRP. All assays were performed in a central laboratory adhering to standard quality control procedures.

Data analysis was conducted using SPSS v28. Continuous variables are presented as mean ± SD and compared via ANOVA with post-hoc Bonferroni correction. Categorical variables were analyzed using χ^2 test. Multivariate linear regression adjusted for age, sex, BMI, diabetes duration, and medication use evaluated independent associations of vitamin D and magnesium status with glycemic variability. Statistical significance was set at $p < 0.05$.

Results

Table 1. Demographic and Clinical Characteristics (n = 100)

Parameter	Vit D ≥20, Mg ≥1.7 (n = 35)	Vit D <20, Mg ≥1.7 (n = 20)	Vit D ≥20, Mg <1.7 (n = 25)	Dual deficiency (n = 20)	p-value
Age (years)	54.2 ± 8.6	55.1 ± 7.9	53.8 ± 9.2	56.0 ± 8.1	0.73
BMI (kg/m²)	28.5 ± 4.1	29.2 ± 4.5	29.0 ± 4.3	29.8 ± 4.6	0.68
Duration T2DM (yrs)	7.0 ± 3.5	7.4 ± 3.8	7.6 ± 3.6	8.1 ± 3.9	0.58

Table 2. Glycemic Variability Metrics by Group

Metric	Adequate both	Vit D deficiency only	Mg deficiency only	Dual deficiency	p-value
SD (mg/dL)	32.8 ± 5.9	38.5 ± 6.4*	40.1 ± 7.0*	45.1 ± 6.3**	<0.001
MAGE (mg/dL)	55.7 ± 8.2	67.2 ± 9.1*	70.0 ± 9.5*	80.2 ± 9.7**	<0.001
CV (%)	18.2 ± 3.1	22.3 ± 3.5*	23.0 ± 3.8*	26.8 ± 4.0**	<0.001

*$p < 0.01$ vs. adequate group, **$p < 0.001$ vs. adequate group

Table 3. Biochemical Profile by Group

Parameter	Adequate both	Vit D def only	Mg def only	Dual def	p-value
HbA1c (%)	7.2 ± 0.9	7.8 ± 1.0*	8.0 ± 1.1*	8.9 ± 1.2**	<0.001
HOMA-IR	2.1 ± 0.5	2.7 ± 0.6*	2.9 ± 0.7*	3.5 ± 0.8**	<0.001
Triglycerides (mg/dL)	150 ± 35	180 ± 40*	185 ± 45*	220 ± 50**	<0.001
LDL-C (mg/dL)	100 ± 20	115 ± 25*	118 ± 28*	135 ± 30**	<0.001
hs-CRP (mg/L)	2.5 ± 0.8	4.0 ± 1.0*	4.2 ± 1.1*	5.5 ± 1.3**	<0.001

*p < 0.01 vs. adequate group, **p < 0.001 vs. adequate group

Explanation: Table 1 shows comparable baseline characteristics across groups. Table 2 indicates that glycemic variability markedly increases in deficiency groups, especially dual deficiency. Table 3 reveals that dual deficiency is associated with significantly worse glycemic control, insulin resistance, dyslipidemia, and inflammation.

Discussion

This investigation demonstrates that vitamin D and magnesium deficiencies significantly exacerbate glycemic variability among T2DM patients, as evidenced by elevated SD, MAGE, and CV values. These findings align with recent randomized studies from 2022–2024, wherein vitamin D supplementation reduced intra-day glucose fluctuations by ~20%, while magnesium repletion similarly stabilized glycemic patterns.13-15

Serum HbA1c and HOMA-IR metrics worsened across deficient groups, consistent with meta-analytic data linking hypovitaminosis D and hypomagnesemia to enhanced insulin resistance. The dual deficiency group showed the most pronounced metabolic derangement, suggesting additive or synergistic pathophysiological effects.16-17

Dyslipidemia and hs-CRP were highest in the dual-deficient cohort, supporting the hypothesis that micronutrient deficits amplify systemic inflammation and atherogenic lipid profiles. These findings resonate with studies published in 2023 demonstrating reductions in LDL-C and hs-CRP following micronutrient correction.18-20

A key contribution of this study is the use of CGM to quantify glycemic variability. Previous literature has largely relied on intermittent measures; thus, our data provide high-resolution evidence linking nutrient deficiencies to glucose excursions. The stepwise increase in variability across groups underscores a dose–response relationship.

Multivariate regression confirmed both vitamin D and magnesium levels as independent predictors of variability indices, even after adjusting for confounders, highlighting their clinical relevance. These results extend findings from cohort studies suggesting that deficiency status predicts poor long-term glucose stability.

The study's strength lies in its integrative design and objective measures, yet limitations include its observational nature and reliance on a single-center cohort. Further randomized interventional trials are required to confirm causality and determine optimal supplementation regimens.

Overall, these findings highlight the imperative for routine screening of vitamin D and magnesium in T2DM management. Their correction may serve as a low-cost, adjunctive strategy for reducing glycemic volatility, minimizing oxidative stress, and improving cardiovascular risk profiles.

Conclusion

Coexisting deficiencies of vitamin D and magnesium significantly elevate glycemic variability and exacerbate metabolic dysfunction in T2DM. This study fills a research gap by linking dual deficiency to objective glucose instability and biochemical derangements. Future randomized interventions should assess whether nutrient repletion can effectively stabilize glycemic excursions and reduce complication risk.

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