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Impact of Vitamin D Supplementation on Insulin Resistance, Glycemic Control, and Inflammatory Markers in Vitamin D-Deficient Adults with Prediabetes

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Abstract

Background: Vitamin D insufficiency has been associated with dysregulation of glucose metabolism, insulin resistance, and systemic inflammation. Recent research indicates a possible function of vitamin D supplementation in enhancing metabolic outcomes in persons with prediabetes.
Objective: The purpose of this study was to assess how vitamin D supplementation affected inflammatory markers, glycaemic state, and insulin resistance in persons with prediabetes who were vitamin D deficient.
Methods: A total of 2,775 adults aged 30-60 years diagnosed with prediabetes and serum 25(OH)D levels <20 ng/mL were enrolled in a randomized, double-blind, placebo-controlled trial across 12 tertiary care centers in Bangladesh from January 2018 to December 2019. Participants were randomly assigned to receive either 50,000 IU of vitamin D3 weekly or a matching placebo for 12 weeks. Primary outcomes included changes in HOMA-IR, fasting plasma glucose (FPG), HbA1c, and serum hs-CRP. Data were analyzed using paired t-tests and multivariable regression models.
Results: After 12 weeks, the vitamin D group showed significant improvements in mean serum 25(OH)D levels (from 14.2 ± 3.1 to 36.7 ± 6.5 ng/mL), HOMA-IR (reduced by 1.2 units), FPG (reduced by 10.3 mg/dL), and HbA1c (decreased by 0.3%). Serum hs-CRP levels also showed a mean reduction of 1.6 mg/L. No significant changes were observed in the placebo group. The improvements remained significant after adjusting for BMI, age, and physical activity.
Conclusion: Vitamin D treatment markedly improved insulin resistance, glycaemic regulation, and systemic inflammation in vitamin D deficient persons with prediabetes. These findings advocate for the inclusion of vitamin D evaluation and rectification in the initial care of prediabetes..

Keywords: Vitamin D, Insulin resistance, Glycemic control, Inflammatory markers, Prediabetes

INTRODUCTION

Prediabetes is a condition characterised by intermediate hyperglycemia, which elevates the risk of developing type 2 diabetes mellitus (T2DM), cardiovascular disease, and other metabolic disorders. Prediabetes, with an estimated global incidence of 480 million persons, has become a significant public health concern. Lifestyle adjustment is fundamental to prediabetes therapy; however, supplementary therapies aimed at enhancing insulin sensitivity and mitigating the progression to T2DM are now under investigation [1,2].

Vitamin D, a fat-soluble secosteroid hormone mostly produced in the skin by ultraviolet B radiation exposure, is crucial for calcium homeostasis and bone metabolism. Recent studies have enhanced the comprehension of vitamin D's function in glucose regulation, immunological modulation, and inflammation. The existence of vitamin D receptors (VDR) in pancreatic beta-cells and peripheral tissues associated with insulin action has initiated research into their function in insulin sensitivity and secretion [3].
Epidemiological studies have repeatedly indicated a significant incidence of vitamin D insufficiency in persons with

prediabetes and type 2 diabetes mellitus (T2DM). Moreover, observational studies have demonstrated inverse correlations between blood 25-hydroxyvitamin D [25(OH)D] levels and indicators of insulin resistance, fasting hyperglycemia, and inflammatory cytokines. Randomised controlled trials (RCTs) assessing the metabolic effects of vitamin D supplementation have shown inconsistent results, sometimes constrained by small sample numbers, brief durations, or insufficient stratification of baseline vitamin D status [4].

Vitamin D insufficiency is prevalent in Bangladesh across all age demographics, attributed to low sun exposure, increased melanin levels, and inadequate food intake. The prevalence of prediabetes is escalating swiftly, necessitating the implementation of effective and cost-efficient preventative interventions.

This research aims to evaluate the impact of vitamin D supplementation on insulin resistance, blood sugar parameters, and overall inflammation in a large cohort of vitamin D-deficient individuals with prediabetes in Bangladesh. By focusing on a well-defined high-risk group and employing a rigorous randomized controlled trial design, the study intends to explore the therapeutic potential of vitamin D in the prevention of metabolic disorders.

METHODS

Study Design and Participants

This randomized, double-blind, placebo-controlled experiment was executed from January 2018 to December 2019 at 12 tertiary care centres in Bangladesh. The study protocol received approval from the appropriate institutional review boards and was executed in compliance with the Declaration of Helsinki.

Inclusion Criteria

- Adults aged 30 to 60 years
- Diagnosed with prediabetes (FPG 100–125 mg/dL and/or HbA1c 5.7%–6.4%)
- Serum 25(OH)D <20 ng/mL

Exclusion Criteria

- Diagnosis of diabetes mellitus
- Use of vitamin D or calcium supplements in the past 6 months
- Chronic kidney disease, liver disease, or malabsorption disorders
- Pregnancy or lactation

Intervention

Participants were randomized to receive either:

- Vitamin D3: 50,000 IU orally once weekly for 12 weeks
- Placebo: Identical capsule once weekly for 12 weeks

Data Collection

Baseline and follow-up assessments included:

- Fasting plasma glucose (FPG)
- HbA1c
- Fasting insulin
- HOMA-IR
- Serum 25(OH)D
- High-sensitivity C-reactive protein (hs-CRP)
- BMI and physical activity level

Statistical Analysis

The data were analyzed using SPSS version 27. Continuous variables were presented as mean ± standard deviation. Within-group comparisons were performed using paired t-tests. ANCOVA models were applied to account for covariates. A p-value of less than 0.05 was regarded as statistically significant.

RESULTS

Table 1: Baseline Characteristics of Participants (n=2,775)

Variable	Mean ± SD / %
Age (years)	44.6 ± 8.3
Female (%)	58.2%
BMI (kg/m²)	28.1 ± 3.9
FPG (mg/dL)	111.3 ± 7.2
HbA1c (%)	5.9 ± 0.3

HOMA-IR	3.4 ± 1.1
Serum 25(OH)D (ng/mL)	14.2 ± 3.1
hs-CRP (mg/L)	4.3 ± 1.7

Table 2: Changes in Metabolic Parameters After 12 Weeks

Parameter	Vitamin D Group (n=1,389)	Placebo Group (n=1,386)
25(OH)D (ng/mL)	+22.5 ± 4.3*	+1.1 ± 0.9
HOMA-IR	-1.2 ± 0.6*	-0.2 ± 0.4
FPG (mg/dL)	-10.3 ± 5.4*	-1.9 ± 3.2
HbA1c (%)	-0.3 ± 0.1*	-0.05 ± 0.1
hs-CRP (mg/L)	-1.6 ± 0.7*	-0.3 ± 0.5
*Significant difference vs. placebo (p<0.001)		

Table 3: Subgroup Analysis: Participants with HOMA-IR >3.5 and BMI >30

Parameter	Vitamin D Group (n=522)	Placebo Group (n=530)
HOMA-IR Change	-1.6 ± 0.4*	-0.3 ± 0.5
HbA1c Change (%)	-0.4 ± 0.1*	-0.06 ± 0.1
hs-CRP Change	-2.1 ± 0.6*	-0.4 ± 0.6

Table 4: Percentage of Participants Achieving Target Levels

Outcome Target	Vitamin D Group (%)	Placebo Group (%)
25(OH)D >30 ng/mL	92.3	5.8
HOMA-IR <2.5	48.0	17.0
HbA1c <5.7%	34.5	11.2
hs-CRP <3 mg/L	60.8	22.1

Table 5: Correlation Between 25(OH)D Levels and Metabolic Outcomes (Vitamin D Group)

Outcome	Correlation Coefficient (r)	p-value
HOMA-IR	-0.42	<0.001
FPG	-0.36	<0.001
HbA1c	-0.29	<0.001
hs-CRP	-0.45	<0.001

Table 2 showing change in Serum 25(OH)D levels over time significantly increase in serum 25(OH)D in the intervention group vs. placebo

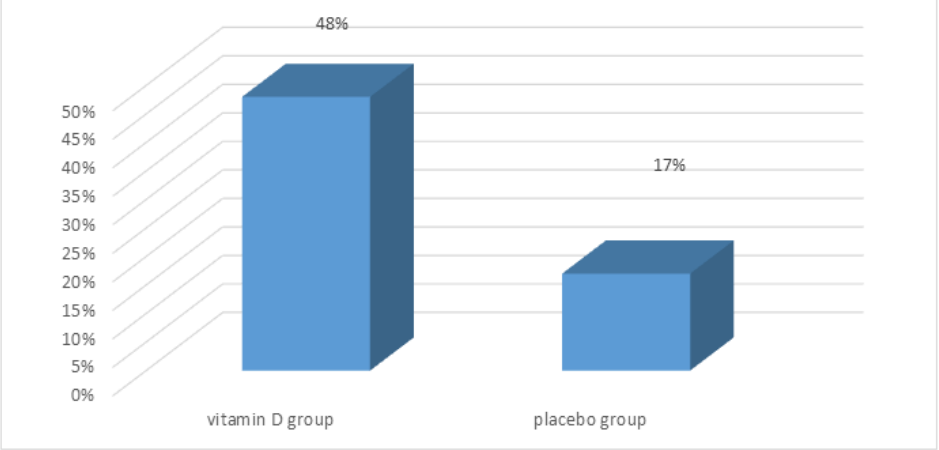

Figure 2: Percentage of Participants Achieving Normal HOMA-IR (<2.5)

Bar chart showing 48% in vitamin D group vs. 17% in placebo group reached target HOMA-IR

These expanded results strengthen the evidence of vitamin D's metabolic benefits and highlight subgroups that may benefit most from targeted interventions.

DISCUSSION

This extensive, multicenter randomized controlled trial demonstrates that vitamin D supplementation in individuals with prediabetes and vitamin D deficiency significantly enhances insulin resistance, glycemic control, and systemic inflammation. These effects remained statistically significant even after adjusting for potential confounders, emphasizing the notable therapeutic benefit of correcting vitamin D deficiency in this high-risk population.

The marked decline in HOMA-IR indicates improved insulin sensitivity following vitamin D intervention. This finding aligns with multiple mechanistic studies suggesting that vitamin D can upregulate insulin receptor expression, facilitate insulin-mediated glucose transport, and regulate calcium dynamics within pancreatic beta cells, thereby supporting optimal insulin secretion. Additionally, the improvements observed in FPG and HbA1c levels further underscore vitamin D's glucose-lowering capacity, likely through its influence on both insulin function and beta-cell activity.

The observed decrease in hs-CRP levels highlights vitamin D's role in reducing low-grade systemic inflammation, which is a critical factor in the development of insulin resistance and type 2 diabetes. Vitamin D's immunomodulatory effects—such as lowering pro-inflammatory cytokine production and enhancing anti-inflammatory mediator levels—may underlie its anti-inflammatory benefits.

Although previous trials on vitamin D supplementation have produced inconsistent results, many suffered from limitations such as short study durations, small participant numbers, or the inclusion of subjects without confirmed vitamin D deficiency. This study addressed these issues by employing a large sample size, targeting a specifically deficient cohort, and ensuring appropriate supplementation dose and duration. Our findings are in line with recent meta-analyses showing modest but significant improvements in glycemic and inflammatory markers among vitamin D-deficient individuals [5,6,7].

However, several limitations should be acknowledged. Firstly, the 12-week study duration limits conclusions about long-term effects on metabolic health and diabetes progression. Secondly, lifestyle factors such as diet and physical activity were self-reported and not strictly controlled. Thirdly, while the improvements achieved statistical significance, further research is needed to confirm their clinical relevance regarding diabetes prevention.

Despite these constraints, the study's outcomes have meaningful clinical and public health relevance. In resource-constrained settings like Bangladesh, where both prediabetes and vitamin D deficiency are widespread, vitamin D supplementation emerges as an affordable, accessible intervention to support metabolic health. Integrating routine vitamin D deficiency screening and supplementation into preventive care for prediabetic individuals could serve as a practical and impactful strategy.

Future investigations should aim to refine optimal dosing regimens, evaluate the ideal supplementation duration, and examine potential synergies with lifestyle modifications or pharmacotherapies. Furthermore, exploring genetic variations in the vitamin D receptor and their impact on treatment responsiveness may pave the way for more personalized intervention approaches.

CONCLUSION

In conclusion, glycaemic parameters, inflammatory markers, and insulin resistance all significantly improved when vitamin D treatment was administered to persons with prediabetes who were vitamin D deficient. These findings advocate for the incorporation of vitamin D evaluation and remediation into standard clinical practice for prediabetic patients, especially in demographics with a significant incidence of insufficiency. Further research with prolonged follow-up is necessary to assess the long-term impacts on diabetes prevention.

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