# Association between Vitamin D Deficiency and Risk of Cardiovascular Diseases among Type 2 Diabetes Mellitus Individuals in Bangladesh: A Case Control Comparative Study

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#### **Abstract**

Type 2 diabetes mellitus (T2DM) is a well-known healthcare problem globally. Several factors, including vitamin D level influence cardiovascular diseases. This study was aimed to determine the association of vitamin D (25 [OH] D) levels and serum lipid profiles with T2DM in Bangladesh. The data (n = 111) were collected from the patients' register record book of BIHS General Hospital (Mirpur, Dhaka). Clinical (age, gender) and biochemical (fasting glucose level, after meal glucose level, HbA1C, lipid profile (HDL, LDL, TG, cholesterol) and 25-hydroxy vitamin D information were included for analysis. Independent sample t-test (two-tailed) was used to compare diabetic (cases, n = 70) and nondiabetic (control, n = 41) groups. Correlation analysis and multiple linear regression assessed unadjusted and adjusted relations between vitamin D levels and other variables, respectively. There was a statistically significant (p <0.001) difference identified in vitamin D levels (mg/dl) between diabetic [mean (range): 23.3 (10.20-38.4)] and non-diabetic [mean (range): 26.9 (20.5-51.4)] subjects. Significantly higher triglyceride, total cholesterol and blood glucose (fasting and after meal) levels were observed in diabetic subjects compared to non-diabetic subjects. However, HDL level was significantly lower in diabetic patients than in non-diabetic patients ( $40.15 \pm 5.56$  vs.  $42.74 \pm 5.72$  mg/dl). Pearson correlation analysis exhibited a significantly positive correlation of vitamin D deficiency with glycated hemoglobin (HbA1C) (r = 0.195, p = 0.040), total cholesterol (r = 0.567, p = 0.046), and LDL (r = 0.897, p = 0.003) levels. Multiple regression analysis showed that vitamin D deficiency was significantly associated with higher glycated hemoglobin A1C ( $\beta$  = -0.097, p = 0.039), fasting blood glucose ( $\beta = -0.119$ , p = 0.011), total cholesterol ( $\beta = -0.160$ , p = 001) and triglyceride ( $\beta = -0.201$ , p < 0.001) levels. Additional extended and thorough randomized controlled clinical trials are required to draw a more definitive conclusion and accumulate more substantial evidence regarding the positive impact of vitamin D supplements on type 2 diabetes mellitus (T2DM).

**Key words**: Type 2 diabetes mellitus, cardiovascular diseases, vitamin D, lipid profile, haemoglobin level.

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#### Introduction

Vitamin D deficiency has emerged as a significant health concern globally, particularly in individuals with type 2 diabetes mellitus (T2DM) (Ghosh *et al.*, 2023; Paciaroni *et al.*, 2019). Type 2 diabetes mellitus (T2DM) is a persistent metabolic condition marked by elevated blood sugar levels due to compromised insulin secretion and/or insulin resistance (Alam *et al.*, 2022; Jannat *et al.*, 2022; Ahmmed *et al.*, 2024; Hossain *et al.*, 2024). This condition is connected with a higher likelihood of experiencing cardiovascular diseases (CVD). Several investigations have suggested a potential association between insufficient vitamin D levels and the onset and advancement of CVD in individuals with T2DM (Anderson *et al.*, 2011; Chitalia *et al.*, 2012).

Calciferol, commonly referred to as vitamin D, is a fat-soluble vitamin that is essential for maintaining bone health and regulating calcium level in the body. However, its functions extend beyond the skeletal health. Vitamin D receptors (VDR) are found in various tissues, including the myocardium and vascular cells, suggesting a potential role in cardiovascular health (Richter et al., 2019). Vitamin D has been shown to have anti-inflammatory, antithrombotic and vasoprotective effects, which may contribute to its cardioprotective properties (Chowdhury et al., 2019).

Several studies reported a high prevalence of vitamin D deficiency in individuals with T2DM. One study found that 22% of diabetic patients had deficient vitamin D levels, while 41% had sufficient levels (Altieri *et al.*, 2017; Liang *et al.*, 2021). The median vitamin D level in diabetic subjects was significantly lower than in non-diabetic subjects. This suggests that individuals with T2DM are at a higher risk of vitamin D deficiency, which may have implications for their cardiovascular health (Abugoukh *et al.*, 2022).

Some research showed significant associations between vitamin D deficiency and various cardiovascular risk factors in individuals with T2DM. Evidence showed that vitamin D levels were

positively correlated with fasting blood sugar, HbA1c (glycated haemoglobin), cholesterol and LDLcholesterol levels (May et al., 2010; Pekkanen et al., 2015). These findings suggested that vitamin D deficiency may contribute to the development and progression of dyslipidaemia and hyperglycaemia in individuals with T2DM, increasing their risk of CVD. The exact mechanisms by which vitamin D deficiency contributes to CVD in individuals with T2DM are not yet fully understood. However, several potential mechanisms have been proposed. Vitamin D deficiency may lead to endothelial dysfunction, oxidative stress, inflammation, impaired insulin secretion and sensitivity, all of which are implicated in the pathogenesis of CVD (Mousa et al., 2015; Pokhrel et al., 2021). Furthermore, vitamin D deficiency may contribute to dyslipidaemia and abnormal lipid metabolism, further increasing the cardiovascular risk in T2DM patients.

Due to the significant occurrence of vitamin D deficiency among individuals with type 2 Diabetes (T2DM) and its potential influence on cardiovascular well-being, it is crucial to regularly assess and track vitamin D levels in this group. Hence, the study was aimed to explore the relationship between vitamin D deficiency and cardiovascular disease risk in T2DM patients in Bangladesh.

# **Materials and Methods**

Study design and settings: The study involved a cross-sectional case-control comparative analysis using randomly collected data from patients who had visited the Outpatient Department (OPD) and the Department of Clinical Biochemistry Laboratory at BIHS General Hospital in Mirpur, Dhaka, Bangladesh, from October 2022 to May 2023. A total of 111 individuals (diabetic cases = 70 and non-diabetic control = 41) were recruited in this study.

Inclusion and exclusion criteria: The human subjects were recruited by maintaining some inclusion and exclusion criteria. The eligibility criteria comprised individuals aged 35-65 years diagnosed with T2DM at least three months ago and

receiving regular follow-ups at BIHS General Hospital. Exclusion criteria encompassed those under 35 years old, recently diagnosed with T2DM, individuals with chronic metabolic disorders, pregnant individuals, and those undergoing vitamin D supplementation.

Data collection and parameters: All the data were collected from the BIHS General Hospital register record book and the participants were attending this hospital for their regular health follow-up check-up. Then, we finalized the total number of participants according to the selection criteria. Clinical (age, gender) and biochemical (fasting glucose level, after glucose level, HbA1c, lipid profile (HDL, LDL, TG, Cholesterol), and 25-hydroxy vitamin D parameters were included.

Measurements: The Dimension EXL 200 System clinical chemistry auto analyzer was utilized to measure the fasting blood sugar (FBS), total cholesterol (TC), high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol and triglycerides (TG). This was done by employing enzymatic methods on the serum sample, utilizing a commercially available kit designed explicitly for auto analyzer.

Statistical analysis: The study employed Statistical Package for Social Sciences (SPSS)

version 25.0 (IBM SPSS Statistics, Armonk, NY) for the purpose of data analysis. The results were expressed as their mean ± standard deviation (SD). The study involved univariate, bivariate and multivariate analysis and followed the proper statistical protocols (Jamil et al., 2023; Hossain et al., 2023). The study employed independent-sample ttests to compare groups and investigate the association between dependent and independent variables. Two-tailed tests were utilized for all statistical analyses. Pearson correlation analysis was used to evaluate the unadjusted relationship between vitamin D levels and other confounding variables, while a multiple linear regression model was employed to assess adjusted relationships. Statistical significance was defined as a p-value below 0.05.

#### **Results and Discussion**

A total of 111 subjects were included in this study. Among them, 37% (n = 41) and 63% (n = 70) were diabetic and nondiabetic subjects, respectively. The percentage (%) distribution of diabetic and nondiabetic subjects according to gender has been shown in figure 1, which revealed that 57% were male and 43% were female diabetic subjects. On the other hand, 61% were male and 39% were female in nondiabetic subjects (Figure 1).

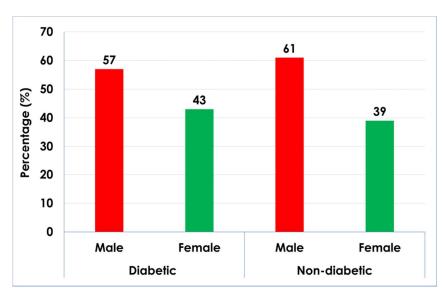


Figure 1. Percentage distribution of diabetic and non-diabetic subjects according to gender.

Table 1 showed the clinical and biochemical characteristics of the study. The group included individuals between 35 and 65 years old, with an average age of  $50.60 \pm 4.2$  years for those with diabetes and  $48.49 \pm 2.0$  years for those without diabetes.

Table 1 indicated a significant elevation in fasting blood sugar (FBS) (mmol/l) among individuals with diabetes in contrast to those without

diabetes (8.94  $\pm$  2.25 vs. 5.26 $\pm$  0.71; p < 0.001). Additionally, the after-breakfast blood sugar (ABFBS) (mmol/l) level was significantly increased in the diabetic participants compared to their non-diabetic counterparts (12.87 $\pm$ 3.08 vs. 6.92 $\pm$ 0.89; p < 0.001). Glycated haemoglobin A1C (HbA1C) (%) was also seen to be higher in diabetic than non-diabetic subjects (8.48 $\pm$ 1.59 vs. 5.74 $\pm$ 0.37; p < 0.001).

Table 1. Clinical and biochemical characteristics of the study subjects (n=111).

Variables	Diabetic, n=70 (63%)	Non-diabetic, $n = 41 (37\%)$	p-value
Age (years)	$50.60 \pm 4.2$	$48.49 \pm 2.0$	0.247
Gender			
Male	40 (57%)	25 (61%)	0.696
Female	30 (43%)	16 (39%)	0.696
FBS (mmol/L)	$8.94 \pm 2.25$	$5.26 \pm 0.71$	< 0.001
ABFBS (mmol/L)	$12.87 \pm 3.08$	$6.92 \pm 0.89$	< 0.001
HbA1C (%)	$8.48 \pm 1.59$	$5.74 \pm 0.37$	< 0.001
S. Cholesterol (mg/dl)	$181.23 \pm 4.74$	$172.02 \pm 1.96$	0.242
S. Triglycerides (mg/dl)	$163.85 \pm 7.0$	$141.73 \pm 4.78$	0.023
HDL Cholesterol (mg/dl)	$40.15 \pm 5.5$	$42.74 \pm 5.72$	0.022
LDL Cholesterol (mg/dl)	$112.76 \pm 4.12$	$98.85 \pm 3.60$	0.060
Vitamin D (ng/ml)	23.35 (10.20-38.4)	26.9 (20.5-51.4)	< 0.001

Results were expressed as mean  $\pm$  SD and n (%), n=number of subjects. Student 't' test was calculated for comparison between case and control subjects. FBS=Fasting blood sugar, ABFBS=After breakfast blood sugar, HDL=High density of lipoprotein, LDL=Low density of lipoprotein, HbA1C = Haemoglobin A1C. Vitamin D level was expressed as mean (range).

Furthermore, diabetic individuals exhibited significantly elevated level of triglycerides (mg/dl) in comparison to those who did not have diabetes (163.85  $\pm$  7.0 vs. 141.73  $\pm$  4.78; p = 0.023). On the other hand, HDL cholesterol level (mg/dl) was found to be significantly lower in diabetic subjects compared to non-diabetic subjects (40.15  $\pm$  5.5 vs. 42.74  $\pm$  5.72; p = 0.022). Finally, vitamin D (ng/mL) level [median (range)] was found to be significantly (p < 0.001) lower in diabetic subjects, 23.35 (10.20-

38.4) compared to 26.9 (20.5-51.4) non-diabetic subjects (Table 1).

Table 2 showed that the correlation coefficient of vitamin D level with other confounding variable in this study subjects. There is significantly positive correlation of vitamin D with FBS (r=0.186, p=0.051) HbA1C (r=0.195, p=0.040); total cholesterol (r=0.567, p=0.046) and LDL-cholesterol (r=0.897, p=0.003), respectively.

Table 2. The correlation coefficient of vitamin D with confounding variables in the study.

Variable	Diabetic (r/p)	Non-diabetic (r/p)
Age (years)	0.145/0.129	0.345/0.529
Sex	0.121/0.204	0.221/0.604
FBS (mmol/l)	0.186/0.051	0.566/0.541
ABF (mmol/l)	0.140/0.142	0.560/0.144
HbA1C (%)	0.195/0.040	0.156/0.123
Total cholesterol	0.567/0.046	0.567/0.432
Triglycerides	0.105/0.273	0.129/0.498
HDL	0.133/0.165	0.334/0.465
LDL	0.897/0.003	0.245/0.265

Data are expressed as correlation coefficient= r, p=significance level analysed by Pearson correlation test.

Table 3 showed multiple regression analysis for adjusted risk variables which are associated to development of diabetes. It is observed that vitamin D deficiency was significantly associated with higher HbA1C ( $\beta$  = - 0.097, p = 0.039), FBS ( $\beta$  = - 0.119, p = 0.011), total cholesterol (TC) ( $\beta$  = - 0.160, p = 001) and triglyceride (TG) ( $\beta$  = - 0.201, p < 0.001) levels.

Table 3. Multiple linear regression analysis for vitamin D and lipid profile.

Variables	β-coefficient	P value
HbA <sub>1</sub> C (%)	-0.097	0.039
FBS (mmol/l)	-0.119	0.011
TC (mmol/l)	-0.160	0.001
TG (mmol/l)	-0.201	< 0.001
LDL-C (mmol/l)	0.009	0.577

A standardized beta coefficient comparison of the strength of the effect of each individual independent variable to the dependent variable.

The present study delved into the association of lipid profiles and vitamin D levels with diabetes in a cohort of 111 subjects. The findings revealed compelling insights that contribute to our understanding of the interplay between these variables.

The demographic distribution among diabetic and non-diabetic subjects showed no significant differences in age and sex. This aligns with previous research by Zhou *et al.* (2021), supporting the notion that age and sex may not be primary factors influencing diabetes prevalence.

Significantly elevated levels of FBS, ABFBS, and HbA1C were observed in diabetic subjects compared to non-diabetic counterparts. These findings were consistent with numerous studies, including the study conducted by Ghazanfari *et al.* (2010), reinforcing the association between glycaemic control and diabetes.

Lipid profile analysis indicated elevated triglycerides and reduced HDL cholesterol in diabetic subjects, aligning with the established link between dyslipidaemia and diabetes (Zhou *et al.*, 2022). However, LDL cholesterol showed a marginal increase in diabetic subjects, emphasizing the nuanced relationship between LDL and diabetes (Sabahelkhier *et al.*, 2016). The study uncovered a substantial vitamin D deficiency in diabetic subjects compared to non-diabetic subjects. This aligned with research by Abugoukh *et al.* (2022), highlighting the prevalence of vitamin D deficiency in diabetic populations.

Understanding intricate connections the highlighted in this study holds implications for diabetes management. Addressing vitamin deficiency may serve as a potential intervention strategy to improve glycaemic control and lipid profiles in diabetic individuals. Supplementation with vitamin D may be considered to maintain optimal vitamin D levels and potentially reduce the risk of CVD in T2DM patients. However, further research, including long-term randomized controlled trials, is needed to establish the efficacy and safety of vitamin D supplementation in this context. Besides further study is needed to better understand the mechanisms underlying this association and to determine the optimal strategies for the prevention and treatment of vitamin D deficiency in individuals with T2DM. Nonetheless, it is important to recognize the potential cardiovascular implications of vitamin D deficiency in T2DM and consider appropriate screening and management strategies to optimize cardiovascular health in this population.

#### **Conclusions**

This study contributes valuable insights into the associations between diabetes, lipid profiles and vitamin D levels. It is revealed that a notable correlation exists between insufficient vitamin D levels and elevated levels of HbA1C, fasting blood glucose, total cholesterol and triglycerides. These findings underscore the multifaceted nature of these relationships, emphasizing the need for holistic approaches in diabetes management. Nevertheless, additional studies and interventions focused on addressing low vitamin D levels could be pivotal in improving the overall health results for people with diabetes.

#### Conflict of interest

No author has any conflict of interest to be declared.

## **Ethical statement**

The data for the study was gathered from the patient record book of the BIHS General Hospital, Mirpur, Dhaka, Bangladesh, with the data being acquired anonymously. As a result, ethical approval for the study was deemed unnecessary.

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