



# Serum Vitamin D Levels and Risk Factors for Cardiovascular Complication in Diabetes

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## Abstract

**BACKGROUND:** Diabetes is a significant contributor to dyslipidemia, which can contribute in cardiovascular complications. Vitamin D is crucial in preventing chronic metabolic diseases such as diabetes and heart disease (cardiovascular disease [CVD]).

**AIM:** The objective of this study was to determine the relationship between Vitamin D levels and cardiovascular risk in type 2 diabetes mellitus.

**MATERIALS AND METHODS:** This study is cross-sectional in nature. The study sampled 89 diabetic patients who met the study's inclusion and exclusion criteria. After a 10 h fast, a venous blood test is performed to determine Vitamin D levels, apolipoprotein-A levels, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride levels. The data are analyzed using SPSS. The Pearson correlation test ( $p > 0.05$ ) was used to determine the connection.

**RESULT:** Vitamin D levels were found to correlate with Apo-A1, TC, HDL-C, and triglyceride levels ( $p = 0.05$ ), but not with LDL-C levels ( $p > 0.05$ ).

**CONCLUSION:** Vitamin D supplementation may assist DM2 patients minimize their chance of developing CVD problems.

**Edited by:** Sasho Stoleski

**Citation:** Amelia R, Harahap J, Wijaya H, Fujiati I, Widjaja SS, Rusdiana R. Serum Vitamin D Levels and Risk Factors for Cardiovascular Complication in Diabetes. Open-Access Maced J Med Sci. 2021 Nov 12; 9(B):1394-1397.  
<https://doi.org/10.3889/oamjms.2021.7364>

**Keywords:** Vitamin D; Macrovascular complications; Diabetes mellitus type 2; Cardiovascular complications

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**Received:** 18-Sep-2021

**Revised:** 04-Oct-2021

**Accepted:** 02-Nov-2021

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**Funding:** This study was supported by the Ministry of Research and Technology/National Research and Innovation Agency (No. 12/E1/KP. PTNBH/2021, March 8, 2021)

**Competing interests:** The authors have declared that no competing interests exist

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## Introduction

Dyslipidemia is a metabolic disease characterized by an increase in total cholesterol (TC) or triglyceride levels in the blood and a reduction in high-density lipoprotein cholesterol (HDL-C) levels [1]. Chronic hyperglycemia associated with diabetes alters the metabolism of cholesterol, triglycerides, and their highly controlled metabolites, resulting in hypercholesterolemia and hypertriglyceridemia [2].

Vitamin D is a fat-soluble vitamin that is required for calcium homeostasis and bone growth. Vitamin D receptors are found in a number of tissues and play critical roles in the production of insulin, immune function, gene expression, and cardiovascular protection [3]. In addition, Vitamin D is critical in preventing chronic metabolic syndromes including diabetes and cardiovascular disease (CVD) [4]. Vitamin D's active form (1.25-hydroxyvitamin D) causes an insulin response to glucose transport by promoting the formation of insulin receptors in peripheral tissues [5].

Vitamin D and its metabolites are known to decrease blood lipid levels through lipogenesis. Vitamin D, on the other hand, enhances the activity of lipoprotein lipase in adipose tissue, resulting in a decrease in triglyceride-enriched lipoprotein in the blood, therefore decreasing the risk of developing CVD [6]. Vitamin D receptors identified in cardiac and vascular cells imply that Vitamin D-mediated activities contribute to the development of CVD [7]. Some clinical studies [4], [8] have discovered that Vitamin D has an effect on the lipid profile of diabetic patients. The objective of this study was to determine the relationship between blood Vitamin D levels and risk factors in individuals with type 2 diabetes mellitus (T2DM).

## Materials and Methods

### Research design

This is an analytical study using a cross-sectional design that was conducted in Medan.

### Ethical approval

The Research Ethics Committee at the University of North Sumatra in Indonesia approved this study (permission number: 280/KEP/USU/2020).

### Population and research samples

The study population is composed of DMT2 people seeking treatments at Medan's main health care institutions. A sample size calculation for the one-proportion hypothesis resulted in a sample size of 89 participants. Consecutive sampling is used to choose samples, with inclusion and exclusion criteria in place. This study is intended to patients who see their primary care physician and are willing to participate in research. Patients with a history of vascular abnormalities before diabetes, a history of stroke, or a history of blood issues are not eligible to enroll.

### Laboratory examination

After a 10 h fast, a venous blood test (up to 5 cc) is performed to determine the patient's Vitamin D and lipid profile. Vitamin D levels are determined using the ELISA technique and a human ELISA Vitamin D kit (catalog: E1543Hu; Brand: Bioassay TL). Apo-A1 levels are determined using the ELISA method using a human Apo-A1-ELISA kit (catalog: No E1535Hu; Brand: Bioassay TL). TC levels are determined using an enzymatic colorimetry approach (oxidase cholesterol method/CHOD PAP), whereas HDL-C, low-density lipoprotein cholesterol (LDL-C), and triglyceride levels are determined using the Group Policy Object-Trended method.

### Data analysis

SPSS for Windows is used to assess the data, and the findings are presented in tables and graphs. The Shapiro–Wilk test ( $p > 0.05$ ) was used to determine the average normal distribution of sample data. The Pearson correlation test is used to determine the association between Vitamin D and CVD complication indicators in a bivariate analysis ( $p < 0.05$ ).

## Results

In this study, 89 people were chosen. The total patients observed encompassing the sex, age, and length of diabetes suffering may be seen more clearly in Table 1.

According to Table 2, the largest group of responders was 69 women (77.5%). Diabetic patients have an average age of 55.2 years ( $SD \pm 8.9$ ) and have diabetes for an average of 4.4 years ( $SD \pm 4.3$ ).

**Table 1: The characteristics of 89 type 2 diabetes mellitus patients**

Characteristics	Frequency (n)	Percentage
Sex		
Male	20	22.5
Female	69	77.5
Age, years (mean, SD)	55.2 (8.9)	
Duration of illness, (mean, SD) years	4.4 (4.3)	

The average values of CVD compound parameters such as Apo-A1, TC, HDL-C, LDL-C, and triglyceride are shown in Table 2: 8.4 mg/dl, 220.1 mg/dl, 46.7 mg/dl, 126.4 mg/dl, and 244.4 mg/dl, respectively. The Pearson correlation test indicated a relationship between Vitamin D levels and Apo-A1, TC, HDL-C, and triglyceride levels ( $p > 0.05$ ). At the same time, there was no correlation ( $p > 0.05$ ) between Vitamin D levels and LDL-C levels.

**Table 2: Correlation of Vitamin D with CVD risk parameters**

Parameter	Mean	SD	Min	Max	p
Apo-A1 (mg/dl)	8.4	11.2	11.2	51.3	0.0001
Total cholesterol (mg/dl)	220.1	42.1	136	335	0.01
HDL-C (mg/dl)	46.7	11.7	24	77	0.001
LDL-C (mg/dl)	126.4	34.7	51	249	0.922
Triglyceride (TG)	244.4	124.0	11.2	51.3	0.034

LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol.

## Discussion

Vitamin D levels were found to be associated with Apo-A1, TC, HDL-C, and triglycerides, all of which are associated with diabetic CVD complications [9], [10]. Diabetes causes an increase in the release of free fatty acids (FFA) from insulin-resistant lipid cells, increasing the risk of dyslipidemia [11]. Increased triglyceride synthesis results in increased apolipoprotein B (Apo-B) and very low-density lipoprotein (VLDL) production. Apo-B and VLDL cholesterol levels are associated with an increased risk of heart disease. Hyperinsulinemia has been associated with decreased HDL and increased Apo-B and VLDL levels [12]. Hyperglycemia also has a detrimental effect on lipoproteins (particularly LDL and VLDL) by increasing glycosylation and oxidation, decreasing vascular compulsion, and actively encouraging the development of atherosclerosis [13].

According to Alkhatatbeh (2019), there is a favorable relationship between vitamin D levels and HDL. High vitamin D levels raise HDL levels, lowering the risk of cardiovascular disease. The study, however, found that vitamin D levels were unrelated to other lipid profiles such as LDL, triglycerides, and TC. They discovered a negative association between vitamin D and HbA1C levels in this study, and there is no relationship between vitamin D levels and blood sugar levels [14].

When renal impairment was included in people with T2DM, the connection between triglycerides, HDL-C, and cardiac events became negligible, indicating that kidney function plays a critical role in this interaction.

Due to the fact that the kidney is the primary site of calcitriol activation to physiologically active calcitriol, it is also inextricably linked to Vitamin D status. Megalin and cubilin are required in the kidneys for the filtering of Vitamin D-DBP complexes, and renal failure results in Vitamin D insufficiency as a result of urine loss and the prevention of future activation [15], [16]. Megalin is a member of the LDL receptor family that is specifically interested in lipoproteins containing Apo-B. Cubilin binds to Apo-A-I, which means that HDL is the ligand. Megalin and cubilin, as a result, are necessary for Vitamin D absorption and activation, as well as for the elimination of lipoprotein from circulation. Megalin expression is regulated by Vitamin D. This association may aid in elucidating the possible mechanisms behind the relationship between Vitamin D and blood lipid concentrations [17], [18].

When renal impairment was included in people with T2DM, the connection between triglycerides, HDL-C, and cardiac events was non-significant, indicating that kidney function plays a critical role in this interaction. Because the kidney is the primary site of calcitriol activation and conversion to physiologically active calcitriol, it is thus inextricably linked to Vitamin D status. Megalin and cubilin are necessary for the kidneys to filter Vitamin D-DBP complexes, and renal failure results in Vitamin D insufficiency as a result of urine loss and the inhibition of future activation [15], [16]. Megalin is a member of the LDL receptor family that has a special affinity for lipoproteins carrying Apo-B. Because Apo-A-I is the ligand for cubilin, HDL is the ligand. As a result, megalin and cubilin are necessary for Vitamin D absorption and activation, as well as lipoprotein clearance from the circulation. Megalin expression is controlled by Vitamin D. This association may aid in elucidating the possible mechanisms behind the relationship between Vitamin D and blood lipid levels [17], [18].

Another potential mechanism for changes in lipid and vitamin D levels is adiponectin. Adiponectin is a cytokine generated by adiposity with fat mass that has been shown to increase HDL levels while reducing VLDL and LDL concentrations. Adiponectin levels are connected to vitamin D levels, and dietary treatments to improve vitamin D status are associated to greater levels of adiponectin [19]. The presence of vitamin D has also been related to vascular adhesion and endothelial dysfunction [20]. Obesity prevalence, fat mass count, adipose differentiation and proliferation, insulin secretion and sensitivity, blood pressure modulation, blood lipid changes, and atherogenesis inhibition are all factors that can contribute to the link between vitamin D status and the risk of heart disease and death [21]. Vitamin D possesses anti-inflammatory properties that have been linked to its positive effects on a variety of inflammatory disease states, including diabetes and cardiovascular disease [22].

## Conclusion

Vitamin D levels are associated with Apo-A1, TC, HDL cholesterol, and triglyceride levels, all of which are associated with CVD. Vitamin D supplements, as well as the patient's autonomous behavior in controlling blood sugar to minimize complications, notably CVD, which increase mortality and morbidity in T2DM, may be an alternative for reducing CVD issues in DMT2 patients.

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