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# Serum Vitamin D Status and its Relationship with Metabolic Parameters in Patients with Type 2 Diabetes Mellitus

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**Abstract**

Vitamin D is a fat-soluble vitamin with hormonal functions, which helps in calcium and phosphate homeostasis and bone metabolism. Beyond the role in bone health, vitamin D influences non-skeletal health problems and chronic diseases like obesity, hypertension, cardiovascular diseases, glucose intolerance and type 2 diabetes mellitus (T2DM). Low vitamin D impairs insulin synthesis and secretion resulting in glucose intolerance in T2DM. This study was carried out between July 2015 to June 2016 to assess vitamin D status in T2DM patients. In this study, vitamin D {25-hydroxycholecalciferol [25(OH)$D_3$]} was assessed in 65 type 2 diabetes mellitus patients and 70 healthy subjects of matching age and sex. Serum 25-hydroxycholecalciferol, fasting blood glucose (FBG), total cholesterol and serum creatinine were estimated. Data were analyzed with the help of the statistical package "R" (version 2.7). Serum 25-hydroxycholecalciferol in cases (Group A) was 55.73±9.02 ng/ml and in controls (Group B) was 53.77±10.86 ng/ml; there was no statistically significant difference between the two groups. Serum FBG was significantly different between the two groups, whereas serum total cholesterol and serum creatinine were not significantly different between the two groups. In type 2 diabetes patients, no significant correlation was found between serum 25-hydroxycholecalciferol with Body mass index (BMI), fasting blood glucose and total cholesterol. In healthy controls, there was no significant correlation of serum 25-hydroxycholecalciferol with BMI, fasting blood glucose and total cholesterol. Vitamin D level was sufficient in both type 2 diabetes patients and healthy individuals. Vitamin D was not associated with T2DM.

**Keywords:** 25-hydroxycholecalciferol [25(OH) $D_3$], Type 2 diabetes mellitus.

## Introduction

Diabetes is one of the main non-communicable chronic diseases. It is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Type 2 diabetes mellitus (T2DM) is characterized by insulin resistance and relative (or absolute) insulin deficiency and accounts for 90-95% of the total cases of diabetes. Defects in pancreatic β-cell function, insulin sensitivity and

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systemic inflammation - all contribute to the development of type 2 DM.[1,2] Obesity and other lifestyle factors such as exercise, alcohol consumption, smoking, and certain dietary habits can also play an important role. Vitamin D is an important nutritional factor for type 2 diabetes mellitus pathogenesis by modulating insulin receptor gene expression and insulin secretion.[3] Beyond the role of bone health maintenance, vitamin D is receiving increasing attention for its influence on non-skeletal health problems and chronic diseases. Low levels of serum 25-hydroxycholecalciferol are associated with increased risks of obesity, hypertension, cardiovascular disease, glucose intolerance and type 2 diabetes mellitus.[4] Vitamin D directly stimulates the expression of insulin receptors and enhances insulin action. The indirect effect of vitamin D is the regulation of extracellular $Ca^{2+}$ influx through the β-cell and improving insulin secretion.[5] Low vitamin D impairs insulin synthesis, and secretion resulting in glucose intolerance in T2DM.[6,7] Vitamin D is a fat-soluble vitamin with hormonal functions and helps in calcium and phosphate homeostasis. Vitamin D2 is synthesized by plants and is found mostly in nutrients supplemented with vitamin D or dietary supplements. Whether endogenously synthesized or ingested through diet or supplements, vitamin D in the circulation is bound to the vitamin D-binding protein (DBP), which transports it to the liver, where vitamin D is converted by 25-hydroxylase to 25-hydroxyvitamin D [25(OH)D]. This form of vitamin D is biologically inactive and must be converted primarily in the kidneys by 25-hydroxyvitamin D-1 alpha-hydroxylase to the biologically active form 1, 25-dihydroxyvitamin D [1,25(OH)2D]. 1, 25-dihydroxyvitamin D has a short half-life (about 4-5 hours) and 25-hydroxyvitamin D has long half-life.[8,9] 25-hydroxyvitamin D is the main circulating form of vitamin D and is an excellent biomarker. Because of its long half-life, 25hydroxycholecalciferol is used as a standard biomarker for the measurements of the vitamin D status of the individual.[8,10,11] Several studies found an association between vitamin D and T2DM. An inverse association between low levels of serum 25-hydroxycholecalciferol and incidence of T2DM has been found in a large cohort study.[12] In the prospective Ely-study inverse association between baseline serum 25-hydroxycholecalciferol and future glycemia and insulin resistance is found.[13] A prospective study in India found that serum 25(OH)D was lower in patients with T2DM as compared to the healthy controls. Levels of serum 25(OH)D had a negative correlation with HbA1c and fasting blood glucose.[14] Studies demonstrated that vitamin D supplementation significantly improved insulin sensitivity and insulin resistance.[15] Epidemiological studies showed a lower serum vitamin D concentration in the British Bangladeshi population of T2DM compared with normal individuals.[16] An observational study in India, found that a low level of vitamin D was not inversely associated T2DM.[17] A cross-sectional study in Indonesia demonstrated that vitamin D deficiency was not associated with T2DM.[18] A study in Turkey, reported that a low level of vitamin D was not associated with insulin resistance in T2DM and healthy controls.[19]

## Methodology

This cross-sectional study was carried out in the Department of Biochemistry at Sylhet MAG Osmani Medical College, Sylhet from July 2015 to June 2016. The study included patients diagnosed with T2DM who attended the Outpatient Department of Medicine, SOMCH & Sylhet Diabetic Hospital. After fulfilling the inclusion and exclusion criteria, a total of 135 subjects were selected and categorized into two groups: 65 individuals with type 2 diabetes mellitus and 70 age and sex-matched healthy subjects. Diabetes mellitus was confirmed by clinical history and laboratory investigation. Height, Weight and BMI were measured. The levels of 25-hydroxycholecalciferol in the serum of each sample were determined by ELISA. Serum fasting blood glucose, serum total cholesterol and serum creatinine were estimated by

enzymatic colorimetric assay. Data were analyzed with "R" statistical Package version 2.7. Then data were presented in different tables as necessary.

## Results

Total of 135 study subjects were divided into two groups. Group A, 65 type 2 diabetes patients and Group B, 70 healthy subjects without DM. Table 01 shows the age, sex and anthropometric parameters of study subjects. The age range was 35 to 50 years. There was no significant difference in age and sex distribution and BMI between the two groups. Table 02 shows serum 25-hydroxycholecalciferol, FBG, total cholesterol, and serum creatinine in study subjects. Type 2 diabetes patients had nonsignificant serum 25-hydroxycholecalciferol levels than control subjects. There was a significant difference in serum FBG level in type 2 diabetes subjects compared to healthy controls. There was no significant difference in total cholesterol and serum creatinine observed between the two groups. Table 03 shows Pearson's correlation between serum 25-hydroxycholecalciferol, BMI, FBG, and total cholesterol in study subjects. There was no significant correlation of 25-hydroxycholecalciferol with BMI, fasting blood glucose, and total cholesterol in all the study subjects.

**Table 01: Distribution of the study subjects according to age, sex and BMI**

| Parameters | Cases (n=65) | Controls (n=70) | P-value* |
|---|---|---|---|
| Age (yrs), Mean±SD | 42±3.29 | 41±3.97 | 0.284 |
| Male | 33 (49.76%) | 35 (50%) | |
| Female | 32 (49.23%) | 35 (50%) | |
| BMI, Mean±SD | 23.59±1.78 | 23.17±2.47 | 0.259 |

*Unpaired t-test was done, $p<0.05$ was considered significant

**Table 02: Biochemical Parameters of the study subjects**

| Parameters (Mean±SD) | Cases (n=65) | Controls (n=70) | P-value* |
|---|---|---|---|
| $25(OH)D_3$ | 55.73±9.02 | 53.77±10.86 | 0.255 |
| FBG | 161.98±62.47 | 86.92±15.74 | <0.001 |
| TC | 211.26±50.04 | 222.45±46.24 | 0.180 |
| S. creatinine | 1.14±0.29 | 1.06±0.25 | 0.096 |

*Unpaired t-test was done, $p<0.05$ was considered significant

**Table 03: Correlation of Serum 25-Hydroxycholecalciferol with BMI, Fasting Blood Glucose, Total Cholesterol**

| Correlation | | Cases (n=65) | | All subjects (n=135) | |
|---|---|---|---|---|---|
| parameters | | r- value | p-value* | r-value | p-value* |
| $25(OH)D_3$ | BMI | 0.03 | 0.977 | -0.027 | 0.754 |
| | FBG | 0.010 | 0.943 | 0.095 | 0.268 |
| | TC | - 0.007 | 0.952 | 0.052 | 0.506 |

*Pearson's correlation test was done, $p<0.05$ was considered significant

## Discussion

Vitamin D has a pivotal role in bone health and calcium metabolism. Recently, studies have suggested pieces of evidence that the role of vitamin D is associated with diabetes mellitus and other chronic diseases. This study evaluated vitamin D status in DM patients. In this study, the mean age of T2DM patients (Group A) was 42.02±3.29 years and the mean age of the healthy controls (Group B) was 41.35±3.99 years; there was no significant difference between the two age groups. This result is similar to the study[20] where the mean age of cases was 53.4±15.6 years as compared to the controls with a mean age of 48.9±15.9 years. A similar result was also observed in another study[21] where the mean age of cases was 49.7±9.7 years and controls 48.3±11.4 years. The mean BMI of cases (Group A) was 23.59±1.87 ($Kg/m^2$) and the mean BMI of controls (Group B) was 23.17±2.47 ($Kg/m^2$). This result is similar to a study[21] where the mean BMI of cases was 30.6±5.4 ($Kg/m^2$) and controls had a mean BMI of 29.8±5.0 ($Kg/m^2$). The difference regarding mean BMI was not statistically significant. Another study[22] observed that the mean BMI was significantly higher in cases than in controls.

Hidayat et al.[18] found that BMI was a statistically significant variable in the development of vitamin D deficiency. The greater the BMI, the higher the occurrence of vitamin D deficiency; especially in the obese group. The mean serum FBG was 161.98±62.47 mg/dl in cases (Group A) and 86.92±15.74 mg/dl in controls (Group B). There was a significant difference in serum FBG levels between the two groups. This result is similar to a study21 where the mean FBG of cases was 224±99.1 mg/dl and in controls, it was 95±8.9 mg/dl. Serum total cholesterol was 211.26±50.05 mg/dl in cases (Group A) and 222.45±46.24 mg/dl in controls (Group B). There was no significant difference in total cholesterol level between the two groups.

Slightly lower total cholesterol may be due to lipid-lowering drugs by most diabetic subjects. This observation is similar to the studies where the mean total cholesterol of cases was 170.8±45.5 mg/dl and in controls was 185.5±42.2 mg/dl.[23-25] The mean serum 25-hydroxycholecalciferol in cases (Group A) was 55.73±9.02 ng/ml and in controls (Group B) was 53.77±10.86 ng/ml. Surprisingly, T2DM patients, though non significantly, had higher 25-hydroxycholecalciferol levels than the controls. Different studies with vitamin D deficiency or insufficiency in both cases and controls showed a statistically non-significant difference in vitamin D status.[17,18] Some authors found a statistically significant difference in vitamin D level between diabetic patients and non-diabetic subjects, with more hypovitaminosis D in the patients.[21,22,26] In this study vitamin D levels in both groups were higher. Slightly higher vitamin D levels in cases may be an attempt to synthesize more vitamin D in DM patients to produce more insulin to overcome DM. The high vitamin D value may be due to seasonal effects, physical activity and sun exposure during our study period.

## Conclusion

In this study, the physically active subjects were exposed to sunlight in a similar proportion, so their $25(OH)_2$ D level was sufficient in both diabetic and nondiabetic subjects. Though theoretically, hypovitaminosis D might be associated with uncontrolled DM, in our study population, hypovitaminosis D was not associated with causation or maintenance of DM. Due to the seasonal variation in UV light intensity, a variation is also observed in 25(OH)D concentrations, such that the concentrations are highest in late summer and early autumn and lowest in late winter and early spring. In this study, we collected our data during the summer season from March to June 2016 which may cause a high 25(OH)D level.

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