# Correlation between Vitamin D and HbA1c in Type 2 Diabetic Patients

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**Abstract :**

**Introduction :** Diabetes is a metabolic disease that can affect nearly every organ system in the body. Recently, vitamin D has sparked widespread interest in the pathogenesis and prevention of diabetes. The goal of this study is to find out whether this correlation between vitamin D and diabetes is present or not. Mainly in this study we have tried to correlate vitamin D with HbA1c levels. **Materials & Methods :** Total 100 individuals with type 2 diabetes, aged between 30- 75 years, who visited GCS Hospital between September 2015 to March 2016, for diabetic checkup and who satisfy our inclusion criteria were enrolled for this study. Type 2 diabetic patients with diabetes of less than 5 year duration were enrolled. Those who were pregnant and those who had microvascular complications or were already on calcium or vitamin D supplements were excluded. **Results :** Out of the total 100 patients, 68 patients had a deficient vitamin D level, 19 patients had a vitamin D level in the insufficiency range and rest had normal vitamin D levels. There was an inverse correlation between HbA1c and vitamin D levels which was also found to be statistically significant. We additionally found an inverse correlation between vitamin D and FBS (fasting blood sugar level) and PP2BS (post prandial blood sugar level after two hours of meal)levels. **Conclusion :** There is an inverse correlation between vitamin D levels and control of diabetes as measured by HbA1c. Vitamin D supplementation should be considered in those with type 2 diabetes patients, when deficient or insufficient levels are found as this may help to improve the glycemic control.

**Key words :** Correlation, HbA1c, Type 2 Diabetes, Vitamin D

## Introduction :

Diabetes is a metabolic disease that can affect nearly every organ system in the body. [1] Diabetes continues to be a public health concern. It has been estimated that 380 million individuals would be affected with diabetes worldwide by the year 2025. [2] In India alone 41 million individuals are affected by this deadly disease, and this is likely to go up to 70 million by the year 2025.[3] Although important knowledge has been acquired on the aetiology of diabetes its precise etiopathogenesis is still under discussion. Inflammatory factors, reactive oxygen species and autoimmune reactions have all strongly emerged as the major pathogenic effectors for diabetes.

Recently, vitamin D has sparked widespread interest in the pathogenesis and prevention of diabetes. As the major regulator for calcium homeostasis, vitamin D directly and or indirectly improves insulin exocytosis via activating calcium-dependent endopeptidases. Vitamin D also improves glucose tolerance. [4] Vitamin D could also prevent type 2 diabetes through its role as an efficient antioxidant. Additionally, the steroid hormone form of vitamin D promotes suppressor cell activity and inhibits the generation of cytotoxic (Tc), macrophages, delayed hypersensitivity type and natural killer (NK) cells. Vitamin D also mediates several non-calcemic functions. It is a regulator of cellular proliferation, differentiation and replication, and mediator of autoimmune reactions, in a variety of organs and biological systems.[5] The discovery of receptors for 1, 25-dihydroxyvitamin D3 (1,25 (OH) 2D3), the activated form of vitamin D, in tissues with no direct role in calcium and bone metabolism (e.g., pancreatic beta-cells and cells of the immune system) has broadened our view of the physiological role of vitamin D. [6, 7]

Several animal studies have also shown that vitamin D plays an important role in the normal pancreatic insulin secretion.[8-10] Many studies have shown its role in increasing the insulin production and secretion in humans as well as decreasing insulin resistance. Low

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serum 25-hydroxyvitamin D (25(OH)D) levels were associated with surrogate f insulin resistance, many cardiovascular events, cancers, and all-cause mortality, at least in subjects with metabolic syndrome . Alternately high 25(OH) D levels were associated with a low risk of occurrence of diabetes as well as decrease in progression of impaired glucose tolerance to overt diabetes. Also studies have shown that giving vitamin D supplements in patients with uncontrolled diabetes have shown to improve the glycemic control to a certain extent. [6, 7]

The goal of this study is to find out whether this correlation between vitamin D and diabetes is present or not. Mainly in this study we have tried to correlate vitamin D with HbA1c levels.

The most beneficial serum concentrations of 25(OH) vitamin D are observed at levels >30ng/ml (>75nmol/L).These are considered sufficient levels. Most experts agree that vitamin D insufficiency is present with 25(OH) vitamin D levels of 20-30ng/ml. Levels <20ng/ml (<50nmol/L) is indicative of vitamin deficiency. [6]

**Materials & Methods:**

**Criteria for diagnosis of diabetes [11]**

| |
|---|
| A1C ≥6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.* |
| OR |
| FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.* |
| OR |
| 2-h plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.* |
| OR |
| In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L) |

*In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.

**Inclusion criteria:**

- Type 2 diabetics of less than 5 year duration and with out any complications.

**Exclusion criteria:**

- Non-diabetic patients
- Type 2 diabetics with microvascular complications
- Patients on vitamin D and calcium supplements
- Pregnancy

Here diabetics with especially renal complications have been excluded as vitamin D gets converted to its active metabolite through its metabolism in the kidney and this mechanism gets affected in diabetic kidney disease. Also those on supplements have been excluded as supplementation will alter the baseline level.

**Study subjects :**

Total 100 individuals with type 2 diabetes, aged between 30- 75 years, who visited GCS hospital between September 2015 to March 2016 for diabetic checkup, who satisfy our inclusion criteria were enrolled for this study.

**Study groups :**

Individuals were divided into three groups according to their plasma vitamin D levels [6] :

Group 1 : deficiency (<20 ng/ml),

Group 2 : insufficiency (20-30 ng/ml), and

Group 3 : normal (>30 ng/ml).

The same individuals were regrouped on the basis of HbA1c level. As per ADA guidelines the target in diabetic patients is to achieve an HbA1c of less than 7.[11] So on the basis of this data we classified the subjects into the following two groups:

Group 1 : less than 7

Group 2 : more than 7

Informed consent was obtained from every patient enrolled for the study before their participation. Ethical clearance was obtained prior to data collection from the institutional ethics committee of G.C.S. hospital.

**Sample collection and processing :**

Using aseptic precautions, 4ml of venous blood was collected in a syringe. It was equally distributed in red, grey and lavender vacutainers. Red capped vacutainers were used for estimation of total plasma vitamin D.

Grey capped vacutainers were used for estimation of blood sugar. FBS was measured as a morning sample after overnight fasting of minimum of 8 hours and PP2BS was measured 2 hours after a major meal. Lavender vacutainers were used for estimation of HbA1c.

Total vitamin D assay was estimated in Elecsys 2010 by ECLIA method. Glucose was estimated by Hexokinase method and HbA1c was measured in BIORAD variant II turbo using ion exchange High performance liquid chromatography method.

**Statistical analysis**

Data was compiled and statistical analysis was done using Statistical Package for the Social Sciences (SPSS) 16.0.Wherever appropriate, chi square test, pearsons' coefficient correlation was used. P value <0.05 was considered as statistically significant.

**Results :**

Out of a total of 100 patients enrolled for the study, 54 were males and 46 were females. The age group of the patients included 26-85 years. Mean age of the study population was 54.16. Mean age of the males was 55.5 years and of the females was 52.58 years. Out of the total 100 patients, 68 patients had a deficient vitamin D level that is vitamin D level less than 20, 19 patients had a vitamin D level in the insufficiency range that is between 20 to 29 while the rest 13 patients had sufficient vitamin D levels.

Among the males, 9 had sufficient vitamin D levels, 16 were in the insufficiency range while 29 had deficient levels. While among the females, 4 had sufficient vitamin D levels, 5 were in the insufficiency range while 37 had deficient levels. The mean vitamin D level in the study population was 15.86 ng/ml. The mean vitamin D level in males was 18.4 ng/ml while in females it was 12.8 ng/ml.

The mean HbA1c level in the study group was 9.47, with it being 8.97 in males and 10.0 in females. The mean FBS level in the study group was 174 mg/dl, with it being 163.5 mg/dl in males and 186.8 mg/dl in females. The mean PP2BS level in the study group was 262.6 mg/dl, with 249.9 mg/dl in males and 277.5 mg/dl in females. (Table 1)

**Table 1 : Primitive information of study subjects**

| Sr. No | Parameters | Mean + Standard deviation |
|---|---|---|
| 1. | Age | 54.16 + 10.5 |
| 2. | FBS | 174.2 + 66.3 |
| 3. | PP2 | 262.6 + 102.1 |
| 4. | BSHBA1c | 9.47 + 2.47 |
| 5. | Vitamin D | 15.86 + 9.69 |

**Table 2 : Association of Vitamin D levels with HbA1c values among study participants**

| Vitamin D | HbA1c < 7% | HbA1c > 7% | TOTAL |
|---|---|---|---|
| >30 ng/ml | 5 | 8 | 13 |
| 20-30 ng/ml | 7 | 12 | 19 |
| <20 ng/ml | 8 | 60 | 68 |
| Total | 20 | 80 | 100 |

The association between vitamin D groups and HbA1c group was done using chi square test. The p-value was 0.01099. (At chi square value of 9.02) This p value is less than 0.05 which says that there is only less than 5% chance that a correlation between the two parameters vitamin D and HbA1c is not present, thus in turn suggesting a high likelihood of the correlation between the two parameters being present.

**Table 3 : Correlation between vitamin D and various diabetic parameters (using pearson's correlation coefficient)**

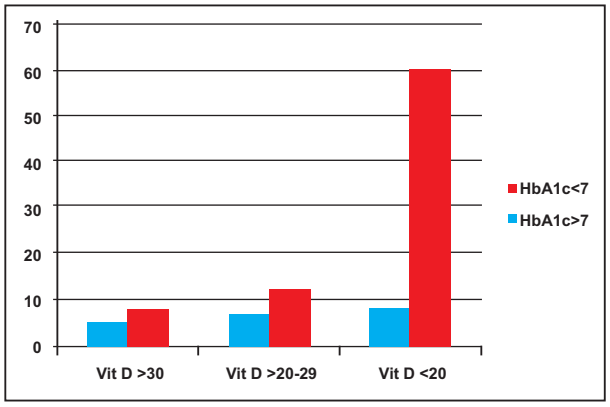
| Correlation between the two parameters | R value |
|---|---|
| Vitamin D and HBA1C | - 0.1205 |
| Vitamin D and FBS | - 0.0109 |
| Vitamin D and PP2BS | - 0.1146 |

The 'r' value between vitamin D and HbA1C was –0.1205, which suggested that there was an inverse correlation between the two parameters.The 'r' value between vitamin D and FBS was - 0.0109 . This suggested that there was an inverse correlation between the two parameters. Also the 'r' value between vitamin D and PP2BS was - 0.1146 , thus suggesting an inverse correlation between the two vitamin D and PP2BS.

The 'r' value calculated between the two parameters of vitamin D and HbA1C showed an inverse correlation

between them, which means that as HbA1C rises, the vitamin D is found to be low in the same. This suggests that patients with uncontrolled hyperglycemia had low vitamin D levels. Thus giving vitamin D supplements in such patients might help to improve the glycemic control to a certain extent.

**Figure 1: Bar diagram depicting correlation of vitamin D level with HbA1c**




Also from the above graph it is shown that the tallest bar is representing vitamin D levels less than 20 and HbA1c levels of more than 7. This also establishes that the correlation present between both these parameters is an inverse correlation.

## Discussion :

Thus this study shows an inverse correlation between vitamin D levels and HbA1c levels.[12,13] This suggests that keeping vitamin D concentration in the normal range may help in maintaining the glucose homeostasis. These findings also highlight the need to consider screening for vitamin D insufficiency in individuals with an elevated HbA1c level and vice versa. This is important in populations at high risk for both conditions. Whether vitamin D supplementation can delay the onset of diabetes remains to be established. Therefore, future studies to clarify the efficacy of vitamin D supplementation in preventing diabetes and pre-diabetes are warranted, especially in populations at high risk.

Also shown by this study is the prevalence of vitamin D deficiency in the diabetic population. Though it is a small population of only 100 patients, 68 out these have vitamin D deficiency which suggests a prevalence of 68%.

Other studies have shown that maintaining vitamin D levels above the sufficiency range will help to decrease the incidence of occurrence of diabetes [14,15] and maintain the beta cell functioning. [16]

Also studies have shown that the vitamin D level was lower in patients with type 2 diabetics in comparison to normal levels found in those without diabetes. [17,18]

Studies have also shown that giving vitamin D supplements have helped in improving insulin resistance present in the diabetics. [19]

## Conclusion :

In type 2 diabetic patients, low vitamin d levels are associated with high HbA1c levels . Thus an inverse correlation is present between the two parameters. Vitamin D screening can be carried out in diabetic patients on a regular basis. Vitamin D supplementation should be considered in patients with type 2 diabetes, when deficient or insufficient levels are found as this may help to improve the glycemic control. Vitamin D fortified diabetic diets may be of additional help.

This study was an observational study from a single centre. The limitation of the study was that the correlation between HbA1c and vitamin D levels after giving vitamin D supplements was not undertaken. More information regarding this subject can be attained if such studies are carried out on a multicentric basis on a larger sample.

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