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RESEARCH ARTICLE

A study on correlation between Vitamin D and glycated hemoglobin in Type 2 diabetes mellitus patients attending a tertiary care hospital in West Bengal

Vikash Raj[1], Shashank Kanchan[1], Richa[2]

[1]Department of Orthopedics, IQ City Medical College and Hospital, Durgapur, West Bengal, India, [2]Department of Community and Family Medicine, All India Institute of Medical Sciences, Deoghar, Jharkhand, India

Correspondence to: Richa, E-mail: drrichapsm@gmail.com

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ABSTRACT

Background: Vitamin D is a steroid hormone, responsible for calcium homeostasis. It has shown to affect insulin synthesis, secretion, and action. Diabetes is a non-communicable systemic disease caused by multiple factors cumulatively leading to insulin deficiency and insulin resistance. In this context, there was a research question to know the extent of association between Vitamin D levels and Type 2 diabetes mellitus. **Aim and Objective:** The study aims to establish an association between Vitamin D levels and glycosylated hemoglobin (HbA1c) levels in Type 2 diabetes mellitus patients. **Materials and Methods:** It was a hospital-based retrospective study done over a period of 3 months at a tertiary care center of West Bengal. The values of fasting blood sugar (FBS), postprandial blood sugar, HbA1c, and Vitamin D level were recorded. Statistical analysis of the data collected was done using SPSS ver. 20. **Results:** Out of a total of 148 patients, 74.3% had deficiency, 21.6% insufficiency, and 4.1% had normal levels of Vitamin D. Similarly, 83.1% of the patients had HbA1c level more than and equal to 6.5% and 16.9% had HbA1c levels less than 6.5%. A negative correlation between Vitamin D and FBS levels and HbA1c and Vitamin D was seen. **Conclusion:** There is a definite inverse correlation between Vitamin D and HbA1c levels.

KEY WORDS: Fasting Blood Sugar; Glycosylated Hemoglobin; Postprandial Blood Sugar; Vitamin D

INTRODUCTION

Vitamin D is a fat-soluble hormone synthesized in our skin from 7-dehydrochlesterol in the presence of UV B rays of sunlight.[1] It refers to a group of secosteroid compounds known to prevent rickets, osteodystrophy, and osteoporosis. It can be also obtained in some amounts from animal (Vitamin D_3 and cholecalciferol) and plant sources (Vitamin D_2 and ergocalciferol). Main dietary sources of Vitamin D are fatty fish, beef liver, egg yolk, cheese, soy, mushrooms, etc. The Vitamin D synthesized in the body or obtained from diet, is stored in adipose tissue as cholecalciferol (Vitamin D_3). When needed, Vitamin D_3 is converted to active form by two-step hydroxylation. The first step is the conversion to 25(OH) D in liver by the 25-hydroxylase enzyme (CYP2R1). This is the stable form of Vitamin D. It is found in blood bound to Vitamin D-binding protein (DBP). The second step hydroxylation takes place in the renal tubules by the 1α-hydroxylase enzyme (CYP27B1) to form 1, 25$(OH)_2$D which is the metabolically active form of Vitamin D. 1,25$(OH)_2$D, in turn, binds with nuclear receptors known as Vitamin D receptors (VDR) inducing various genes and leading to synthesis of different proteins roughly grouped as calcium-binding proteins (CBPs) involved in calcium

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homeostasis. CBP causes increase in calcium and phosphorus absorption in the intestines and renal tubules and thus increases the serum calcium levels. The activity of CYP27B1 gene is dependent on many factors. The parathyroid hormone, calcitonin, hypocalcemia, and hypophosphatemia increase its activity while 1,25$(OH)_2$D, fibroblast growth factor inhibits its activity. Besides intestine and renal tubules, VDR is expressed in various tissues such as cardiovascular tissues, liver and central nervous system, and autocrine and paracrine tissues.

The level of Vitamin D depends on various factors such as age, sex, race, latitude, season, nutritional status, and physical fitness.[2] Many chronic diseases such as diabetes, renal insufficiency, hypoalbuminemia, and cardiovascular diseases also affect the Vitamin D levels of an individual. The serum levels of 25(OH)D are measured to estimate Vitamin D status of an individual as it has a long half-life and is 500–1000 times more abundant as compared to 1,25$(OH)_2$D. Its values <20 ng/ml are termed to be Vitamin D deficiency, levels 21–20 ng/ml are termed as Vitamin D insufficiency, and >30 ng/ml is taken as normal Vitamin D level.[3,4]

It is estimated that 80–90% of the Indian population suffers from Vitamin D deficiency.[5] It is a global public health concern. People of all age group, ethnicity, and background are affected to various extents. Main causes can be reduced exposure to sunlight, lesser physical activity levels, poor dietary habits, poor intestinal absorption, chronic diseases of kidney and liver, etc.[6] Vitamin D deficiency makes the population prone to osteoporosis, sarcopenia, fractures, poor physical condition, chronic fatigue, cardiovascular problems, neurodegenerative diseases, cancers, autoimmune diseases, and infections.[7]

Diabetes mellitus is a systemic non-communicable disease characterized by raised blood sugar levels due to insulin deficiency and/or resistance due to any cause. Various factors such as age, sex, heredity, occupation, environment, and associated diseases are supposed to be responsible for the development of diabetes. Although important knowledge has been acquired on the etiology of diabetes, its precise etiopathogenesis is still under discussion. It can affect nearly every organ of the body. It has been estimated that 380 million individuals would be affected with diabetes worldwide by the year 2025.[8]

Diabetes is classified into two types – Type 1 DM and Type 2 DM.[9] Type 1 DM is an autoimmune disease characterized by destruction of β cells of pancreas, leading to complete absence of insulin in the patients. Type 2 DM is characterized by decreased secretion of insulin and/or increased insulin resistance in the target tissues.

Recent studies have shown a role of Vitamin D in the pathogenesis and prevention of diabetes.[10] Several studies have shown that Vitamin D plays an important role in the normal pancreatic insulin secretion by activating calcium-dependent endopeptidases in the β cells of pancreas as well as decreasing insulin resistance in target tissues, thus improving glucose tolerance.[11-14] In addition, it is also supposed to prevent type 2 diabetes through its role as an efficient antioxidant and anti-inflammatory activity caused by an increase in suppressor cell activity and inhibition of the generation of cytotoxic (Tc), macrophages, and natural killer (NK) cells, thus prevents apoptosis of β cells.[15-17] Low serum 25-hydroxyvitamin D (25(OH)D) levels have been associated with insulin resistance, many cardiovascular events, and even cancers.[18-21] High Vitamin D levels have been shown to decrease the incidence of overt diabetes in population with impaired glucose tolerance and improve the glycemic control in patients with uncontrolled diabetes in long-term studies.[22]

The rising cases of Type 2 diabetes mellitus patients call for measures to reduce its occurrence. At present, there are limited data on association between Vitamin D levels and glycosylated hemoglobin (HbA1c) levels in Type 2 diabetes mellitus patients and especially in western part of West Bengal. Keeping this in mind, the present study was contemplated in a tertiary care hospital of Durgapur, West Bengal, with the objective to determine the Vitamin D level in Type 2 diabetes mellitus patients and to establish an association between Vitamin D levels and HbA1c levels.

MATERIALS AND METHODS

It was a hospital-based retrospective study. After obtaining the ethical clearance from the Institute Ethical Committee, the records of Type 2 diabetes mellitus patients who had attended IQ City Medical College, Durgapur, from August 2019 to October 2019 were obtained from the Medical Record Department. The data of patients fulfilling the inclusion criteria were recorded. Patients with Type 2 diabetes mellitus (based on criteria of the American Diabetes Association) and without any complications due to diabetes were included in the study. Pregnant females and patients taking Vitamin D or calcium supplements were excluded from the study.

A total of 148 subjects matched the selection criteria. Their demographic characteristics, that is, the age and sex were recorded. Fasting blood sugar (FBS), postprandial blood sugar (PPBS), HbA1c, and Vitamin D levels were noted.

Based on Vitamin D levels, the subjects were divided into three groups: "Normal," that is, patients with the Vitamin D level > 30 ng/ml, "insufficiency" with Vitamin D level in the range of 20–29 ng/ml, and "deficient state" with Vitamin D ≤20 ng/ml.

On the basis of HbA1c levels, the subjects were divided into two groups, that is, with HbA1c levels less than 6.5% and ≥6.5%.

Table 1: Association of Vitamin D with sex and HbA1c levels (*n*=148)

Vitamin D	Sex		Glycosylated hemoglobin	
	Male (*n*=73)	Female (*n*=75)	Normal (≤6.5%)	Raised (>6.5%)
Normal (≥30 ng/ml)	4	2	2	4
Insufficiency (21–29 ng/ml)	24	8	9	23
Deficiency (≤20 ng/ml)	45	65	14	96

The data thus generated were entered into SPSS ver.20. Wherever appropriate Chi-square test, Pearson's coefficient correlation was used. $P < 0.05$ was considered to be statistically significant.

RESULTS

A total of 148 subjects were selected for the study, of which 73 were male while 75 were female. The subjects were in the age group of 25–75 years and their mean age was 50.01 ± 13.6 years. The mean age of males was 52.6 ± 13.3 years whereas that of females was 47.92 ± 18.4 years.

The mean Vitamin D level of the study subjects was 18.5 ± 5.08. The mean Vitamin D level in males was 19.3 while in females, it was 17.9. Only six subjects had Vitamin D level within normal range (i.e., >30 ng/dl). One hundred and ten subjects had a deficient level of Vitamin D (i.e., ≤20 ng/dl), among which two-thirds were female and one-thirds were male. The corresponding figures for insufficient Vitamin D (20–29 ng/dl) were 24 and 8 among males and females, respectively. There was a significant association between Vitamin D level and sex of the subjects [Table 1].

A total of 123 patients out of 148 had raised HbA1c levels out of which 96 (78%) had deficient level of Vitamin D [Table 1]. The basic information on blood levels of FBS, PPBS, and HbA1c is mentioned in Table 2.

The "r" value between Vitamin D and HbA1c was – 0.175 suggesting an inverse correlation between the two parameters. There was also an inverse correlation between Vitamin D and FBS [Table 3]. This indicates that lower the HbA1c level, higher is the Vitamin D level and vice versa.

Table 2: The mean quantitative variables in patients studied (*n*=148)

Parameters	Mean±standard deviation
Age (in years)	50.01±13.56
Fasting blood sugar (in mg/dl)	133.89±24.9
Postprandial blood sugar (in mg/dl)	222.31±45.72
Glycosylated hemoglobin (in %)	7.9±1.3
Vitamin D (in ng/ml)	18.55±5.08

Table 3: Correlation between Vitamin D with fasting blood sugar and glycosylated hemoglobin levels (*n*=148)

Correlation between	Pearson correlation values
Vitamin D and FBS	–0.097
Vitamin D and HbA1c	–0.175

DISCUSSION

It is essential for patients with Type 2 diabetes mellitus to be aware of high prevalence of Vitamin D inadequacy and its adverse effect on glycemic control and bone health. The present study was a retrospective, hospital based, which was conducted in a tertiary care hospital of West Bengal.

About 74.3% of the patients with Type 2 diabetes mellitus were deficient in Vitamin D. This was more than Ghavan *et al*.[23] The disparity can be explained due to geographical distribution, sun exposure, and dietary habits of the study subjects. The study shows a definite negative correlation between Vitamin D and HbA1c levels. A negative correlation was also seen between Vitamin D and FBS levels in the study group. Similar findings were seen in studies done by Kotwal *et al*.,[24] Mehta *et al*.,[25] and Mohpatra *et al*.[26]

It has been shown in various studies in the past that Vitamin D has a role in control of blood glucose levels and its utilization in the target tissues. Various animal and human studies have established the role of Vitamin D in insulin synthesis and secretion from β cells.[27] It has been seen that glucose intolerance and insulin resistance are responsible for the development and progression of Type 2 DM. Hence, logically diabetes can be prevented to some extent by providing adequate Vitamin D supplementations, especially to high-risk population.[28] Vitamin D has also been shown to delay the complications arising due to long-standing DM. Thus, there must be screening of all pre-diabetics and diabetic patients for Vitamin D deficiency. Vitamin D supplementation should be included in standard treatment protocol to prevent the harmful effects of Vitamin D deficiency and progression of DM. The recommended dosage of 4000 IU of Vitamin D to have these benefits is debatable and further studies are warranted in this respect.[29]

The study has a small sample size; hence, the findings of this study cannot be extrapolated to the whole population. For this, studies with larger sample size are advocated.

CONCLUSION

There is a definite inverse correlation between Vitamin D and HbA1c levels.

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