Correlation of Vitamin D3 Levels and the Blood Sugar Parameters among the Patients with type 2 Diabetes Mellitus

Kirubhakaran Kanakaraju[1], Rangabashyam Seetharaman Ranganathan[2], Shankar R[3]

ABSTRACT

Introduction: The extra-skeletal effects of vitamin D3 have attracted considerable interest. The identification of 1,25(OH)2D receptors and 1-α-hydroxylase expression in pancreatic beta cells, in cells of the immune system, and in various others tissues, besides the bone system support the role of vitamin D3 in the pathogenesis of type 2 diabetes. Vitamin D3 deficiency appears to be related to the development of diabetes mellitus type 2 and the metabolic syndrome. Vitamin D3 may affect glucose homeostasis, vitamin D3 levels having been found to be inversely related to glycosylated hemoglobin levels. Study aimed to assess the vitamin D3 levels among the type 2 diabetic patients and to correlate the vitamin D3 levels with the various blood sugar parameters.

Material and methods: Fasting blood glucose, post-prandial blood glucose, glycosylated hemoglobin (HbA1c) and 25(OH) D3levels were measured in a group of 100 type 2 diabetes mellitus patients. 25(OH)D3was measured by radioimmunoassay and glycosylated hemoglobin (HbA1c) was measured by high-performance liquid chromatography. The socio-demographic details, duration of diabetes status and the usage of OHA's and insulin were collected through a standardized questionnaire.

Results: The mean age of the patients was 55 years and the male : female ration was 0.92. The mean duration of diabetes among the study population was 5.9 years. The mean of fasting blood sugar, post prandial glucose, HbA1C and the Vitamin D3 levels are as follows 162mgs/dl, 254 mgs/dl, 6.05 gm% and 14.16 ng/dl. Pearson's correlation test was used to analyse the association between glucose parameters and the Vitamin D3 levels and it is proven that there was a strong negative correlation between Vitamin D3 and HbAIC (-0.037), fasting (-0.10)and postprandial blood glucose (-0.07).

Conclusion: In conclusion, the findings of our study had shown that the vitamin D3 level is negatively correlated to the blood sugar parameters among the patients with type 2 diabetes. Further prospective and multi-centric studies should be undertaken to clearly establish a causal association between vitamin D3 levels among the diabetes mellitus patients.

Keywords: Vitamin D3, Blood Sugar, type 2 Diabetes Mellitus

INTRODUCTION

Type-2 diabetes mellitus (T2DM) is a worldwide pandemic and India being the capital for it. World Health Organization (WHO) had predicted that the current rate of diabetic patients was 170 million and if the trend remains the same it would double to 370 million by the end of the year 2030.[1] The major complication of type 2 DM when left untreated are chronic microvascular and macrovascular conditions such as retinopathy, nephropathy, neuropathy and cardiovascular disease (CVD). The well-known factors contributing to the development of T2DM are physical inactivity, poor nutritional practices and obesity. Recently, vitamin D3 was a given some importance worldwide in the pathogenesis of diabetes.[2]

One of the most important hallmarks of T2DM is the occurrence of low-grade inflammation as a result of an increase in circulating cytokine such as TNF and IL-6 which contributes in the development of insulin resistance particularly in the muscles and adipose tissues.[3] Vitamin D3 being a potent immunosuppressant, tends to down-regulate the transcription of various proinflammatory cytokine genes like Interleukin-2, Interlukin-12, and TumorNecrosis Factor-α.[4,5] It also has a protective role on β cell mass and prevents it from apoptosis as the beta cell apoptosis would lead on to various pathological manifestations like excessive ROS production and cytokines (TNF-a, IL-6) production, glucotoxicityandlipotoxicity, which are the major features among the patients with T2DM.[6]

Few of the recent studies had shown the beneficiary role of vitamin D3 in cardiovascular disease prevention, cancer prevention, inhibiting parathyroid hormone secretion, promoting insulin secretion, inhibiting adaptive immunity while promoting innate immunity as well as inhibiting proliferation and stimulating differentiation of cells[7] and along with it Pittas et al in his study had documented that insulin sensitivity is improved by as much as 60% when levels of 25-hydroxy vitamin D3 are increased from 25 to 75 nmol/L,and this was also quoted by few of the studies done in India.[8,9]

Recent studies have shown association of 25-hydroxy vitamin D3 deficiency with an increased risk of stroke death and diabetes itself being one of the major risk factor for cerebro-vascular accidents, so with vitamin D3 deficiency it would further worsen the condition. Researchers had also shown the protective role of vitamin D3 on certain cancers like breast cancer and also on non-Alzheimers dementia.[10,11]

Concerned to diabetes vitamin D3 have a direct (via its role on the activation of pancreatic beta-cell and sensitive organs) as well as indirect (by regulation of calcium hemostasis) positive effect on insulin secretion and sensitivity.[12,13] Since as such very few studies had been conducted in India is assessing the association between vitamin D3 deficiency and diabetes mellitus this study was undertaken to assess the association between them which would help in preventing the further complications

[1]Assistant Professor, [2]Professor, Department of Internal Medicine, [3]Associate Professor, Department of Preventive Medicine, VMKVMCH, Salem 636308, Tamil Nadu, India

Corresponding author: Kirubhakaran Kanakaraju, Assistant Professor, Department of Internal Medicine,Vmkvmch, Salem 636308, Tamil Nadu, India

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Duration of diabetes (in years)	Frequency	Percentage	Mean ± SD (in years)	Min (in years)	Max (in years)
2 – 4	35	35	5.9±3.41	2	20
5 – 7	41	41			
8 – 10	17	17			
11 – 13	2	2			
14 – 16	4	4			
17 – 20	1	1			
Total	100	100			

Table-1: Distribution of study population based on the duration of diabetes

Blood parameters	Mean	SD	95% CI
Fasting blood sugar (mgs/dl)	162.26	60.24	133.26 – 196.45
Post-prandial blood sugar (mgs/dl)	254.7	54.27	227.48 – 278.54
HbA1C (gms%)	8.05	1.04	7.45 – 8.64

Table-2: Mean, SD and 95% CI of the various blood sugar parameters measured among the study population

Vitamin D3 3(ng/ml)	Frequency	Percentage	Mean ± SD	Min (ng/ml)	Max (ng/ml)
<8.5	37	37	14.16±10.61	1.25	57.67
8.5 – 30	58	58			
>30	5	5			
Total	100	100			

Table-3: Distribution of study population based on Vitamin D3 levels

S. No	Parameters	Pearson's correlation value (r value)	P value
1.	Duration of diabetes	-0.0239	<.001
2.	Fasting blood sugar levels	-0.1002	<.001
3.	Post – prandial sugar level	-0.0710	<.001
4.	HbA1C	-0.0378	<.001

Table-4: Pearson's correlation between Vitamin D3 levels and the blood sugar parameters

due to diabetes. Study aimed to assess the vitamin D3 levels among the type 2 diabetic patients and to correlate the vitamin D3 levels with the various blood sugar parameters.

MATERIAL AND METHODS

A cross sectional study was undertaken at our hospital in the medicine OPD. Around 100 diabetic mellitus patients were included in our study. The study was carried out after obtaining the clearance from the institutional ethical committee and getting the informed consent from all the patients. The patients who were taking vitamin D3 supplements were excluded from the study. After the patients had been at rest for at least 10 min in the supine position, blood samples for determination of plasma 25(OH)D$_3$ were collected in citrated tubes and centrifuged, and plasma was stored at −80°C. All samples were treated and stored under the same conditions. Levels of 25(OH) D3 were measured by radioimmunoassay (RIA) in a two-step procedure. The first step involved rapid extraction of 25(OH) D3 and other hydroxylated metabolites from serum or plasma with acetonitrile Following extraction, the treated samples were assayed by competitive RIA using an antibody with specificity to 25(OH)D3. The sample, antibody and tracer were incubated for 90 min at 20–25°C. It has been previously proposed that vitamin D3 deficiency should be defined as a serum 25OHD3 level <50 nmol/L (<20 ng/mL), however most endocrinologists

have a consensus that a serum 25OHD3 level of <75 nmol/L (<30 ng/mL) should be taken as abnormal/insufficient, and levels with less than 8.5 ng/mL was considered as severe vitamin D3 deficiency and in our study also we followed the same cut off levels.

Levels of HbA1c were measured by high-performance liquid chromatography (HPLC), with a within run coefficient of variation of 0.78%, a between run coefficient of variation of 0.52% and a total precision of 1.16%. Patients fasting blood sugar and post-prandial blood sugar were also recorded.

STATISTICAL ANALYSIS

All the data were entered and analyzed by using SPSS version 19 and for all the parametric variables mean and SD were calculated and the correlation was seen between the vitamin D3 levels and FBS, PPBS and HbA1C by using pearson's rank correlation.

RESULTS

The minimum age among the study subjects was 34 and the maximum age was 70 years. The male and female subjects were almost equal in number and the mean age among the males was 53.25 and among the females it was 55.15 years. Majority of the study subjects were between the age group of 50 – 70 years. The mean duration of diabetes among the study subjects was found to be 5.9 years with minimum duration of 2 years and a maximum duration of 20 years (table 1). Among the 100 study subjects 90 of them were taking only oral hypoglycaemic drugs (OHA) and the remaining 10 of them were taking both insulin and OHA's.

Mean, SD and 95% CI of the various blood sugar parameters which were measured among the study subjects were shown in table 2. The mean fasting blood sugar was 162.26 mgs/dl, and the mean post-prandial sugar was 254.7 mg/dl and the mean HbA1C was found to be 8.05 gms% and all the values were found to be above the normal level.

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The vitamin D3 levels among the study subjects was given in table 3. Vitamin D3 levels were measured in ngm/dl. Values of less than 8.5 ngm/dl were considered to be severe vitamin D3 deficiency and the values between 8.5 – 30 ngm/dl were considered as vitamin D3 insufficiency. In our study the prevalence of severe vitamin D3 deficiency was found to be 37% and 58% of the subjects had insufficient levels of vitamin D3 and only 5% of them had normal levels of vitamin D3 and the mean vitamin D3 level was 14.16 ngm/dl.

Correlation between the vitamin D3 levels and the blood sugar parameters was shown in table 4. It was proved that there was a strong negative correlation between the vitamin D3 levels and the duration of diabetes also with the fasting blood sugar, post prandial blood sugar and the HbA1C values, which means that as the blood sugar values increases the vitamin D3 level decreases and the decrease was found to be statistically significant (P<.05).

DISCUSSIONS

The present study had shown that the overall prevalence of vitamin D3 deficiency was found to be 95% with 58% having insufficient levels of vitamin D3 and 37% of them had severe vitamin D3 deficiency. The results of our study was almost in par with the study done by Daga et al[14] in the North of India in which he had quoted that 91.1% of diabetic patients had vit D insufficiency and in another study done by Mohammed Ali Bayani etal[15] among the diabetic patients in Iran had shown that the overall prevalence of vitamin D3 deficiency was 90%. In a multi-centric study in Iran, Heshmat et al. reported that the prevalence of moderate to severe vit D deficiency was 47.2, 45.7 and 44.2% in age group of <50, 50-60 and >60 years old, respectively.[16]

India is a tropical country and is sunny all around the year. Vitamin D3 deficiency is found to be an epidemic inspite of plenty of sunlight.[17-19] This is mainly due to darker skin pigmentation, reduced physical activity, pollution, inadequate sun exposure (purdah system), low consumption of vitamin D3 rich foods, absence of fortification, old age, female sex, higher latitudes and winter season. The third NHANES reported an inverse association between vitamin D3 and metabolic risk factors.[20,21] Vitamin D3 deficiency per se producing many of the systemic complications and when this is combined along with type 2 diabetes mellitus it further leads on to various systemic manifestations like coronary artery diseases and cerebro-vascular diseases.

Vitamin D3 is related to bone metabolism, being a steroid synthesized in the skin by the action of ultraviolet irradiation from the sun. The extra-skeletal effects of vitamin D3 are now being the current focus of research. There is a strong relationship between the vitamin D3 and the immune system and already many studies had proven it and it had also been shown that vitamin D3 induces immune tolerance.[22] Reports have told vitamin D3 deficiency is related to the development of autoimmune diseases, such as multiple sclerosis.[23,24]

Although we found a significant negative correlation of both FPG and HbA1c with 25(OH)D3 deficiency, similar findings have been reported inconsistently in previous work. While an inverse association of 25(OH)D3 and FPG has been observed several times in different populations[25] inverse associations

with HbA1c were not detected in younger Americans[26] but detected in older Germans.[25] There are several lines of evidence to support that vitamin D3 influences impaired β-cell function, insulin resistance and systematic inflammation.[27] It has been demonstrated that vitamin D3 receptors exist in many tissues including pancreatic β-cells, allowing vitamin D3 to potentially modulate the insulin response to elevated blood glucose. In another study conducted by Dalgard and associates among Faroese residents found that increasing concentration of HbA1c was associated with decreasing levels of vitamin D3 levels and that was independent of sex, smoking status and body habitus.[28]

CONCLUSION

In conclusion, the findings of our study had shown that the vitamin D3 level is inversely proportionate to the blood sugar parameters associated with type 2 diabetes. Further prospective and multi-centric studies should be undertaken to clearly establish a causal association between vitamin D3 levels among the diabetes mellitus patients

Studies like randomized controlled trials will have a major role in examining whether vitamin supplementation is a useful intervention in preventing or delaying the onset of type 2 diabetes. Vitamin D3 screening among the healthy adults may not be warranted at present but people at risk for type 2 diabetes will possibly get benefited by conducting a screening for vitamin D3 levels.

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