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Original Research Article

Study of vitamin D_3 level in patients with diabetes mellitus

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Abstract

Introduction: Glycated hemoglobin (HbA1c) is primarily measured to identify glycemic control in diabetic patients. According to The American Diabetes Association (ADA), and World Health Organization (WHO), HbA1c concentrations 6.5% or more is diagnostic of diabetes. Vitamin D_3 deficiency has high prevalence all over the India. It has been proposed that mild to moderate vitamin D_3 deficiency is a risk factor for type 2 diabetes and higher plasma vitamin D_3 is related to a lower risk for the development of diabetes mellitus in high-risk patients.

Aim and Objectives: The aim was to study the levels of vitamin D_3 and relationship between the levels of vitamin D_3 and HbA1c in diabetic patients.

Material and Method: HbA1c and vitamin D_3 were measured in 100 diabetic patients, and another 100 age and sex matched normal healthy individuals. HbA1c was measured by Immunoturbidimetry and vitamin D_3 was measured by Electrochemiluminescence.

Results: The mean vitamin D_3 level in diabetic patients (27.19 ± 6.03 nmol/L) was significantly lower than healthy individuals (61.13 ± 10.85 nmol/L) ($P < 0.001$). There was an inverse correlation between the levels of vitamin D_3 and HbA1c (Pearson's correlation coefficient, $r = -0.63$, $P < 0.001$).

Conclusion: Vitamin D_3 levels are deficient in diabetic patients, and there is an inverse correlation between the levels of vitamin D_3 and HbA1c. So, the level of vitamin D_3 is inversely associated with glycemic control in diabetic patients. Therefore, vitamin D_3 supplementation may be helpful in the treatment of Diabetes Mellitus.

Keywords: Vitamin D_3, Glycated Hemoglobin (HbA1c), Diabetes Mellitus

1. Introduction

Glycated hemoglobin (HbA1c) is a form of hemoglobin that is measured primarily to identify the average plasma glucose concentration over 2-3 months of time, and it is formed in a non-enzymatic glycation pathway by hemoglobin's exposure to plasma glucose. [1] According to the American Diabetes Association (ADA), and World Health Organization (WHO) have recently approved the use of HbA1c for screening and diagnosis of diabetes, and both the organizations have suggested that concentrations 6.5% or more be considered diabetes, and the ADA has recommended 5.7–6.4 % as diagnostic of pre-diabetes. [1-3]

Mild to moderate 25-Hydroxyvitamin D (vitamin D_3) insufficiency has been proposed as a risk factor for type 2 diabetes. [4] Higher plasma vitamin D_3 has been shown to be related to a lower risk for the development of diabetes mellitus in high-risk patients. [5] Vitamin D_3 deficiency appears to be related to the development of diabetes mellitus type 2. [4-6] Vitamin D_3 deficiency prevails in epidemic proportions all over the Indian subcontinent, with a prevalence of 70%–100% of the general population. [7] Vitamin D_3 is a hormone related to skeletal integrity. [8] Recently, the extra-skeletal effects of vitamin D_3 have raised considerable interest. [9,10] Vitamin D_3 deficiency has been shown to be associated with autoimmune diseases, including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), inflammatory bowel disease (IBD), multiple sclerosis (MS) and that vitamin D_3 supplementation prevents the onset and development of these autoimmune diseases. [11] Vitamin D_3 plays an essential role in calcium homeostasis and the development and maintenance of the skeleton. [12] It is recognized as the Sunshine fat soluble vitamin and exposure to beta ultraviolet light (290–320 nm) are the primary source of vitamin D_3. [13] Vitamin D has been shown to be related to glucose metabolism and the development of diabetes mellitus type 2 and the metabolic syndrome. [14] Gene

polymorphisms of vitamin D_3 receptor found to be related to components of the metabolic syndrome. [15] Moreover, vitamin D_3 seems to affect glucose homeostasis, vitamin D_3 levels having been found to be inversely related to glycosylated hemoglobin levels in gestational diabetes mellitus. [16] Also, vitamin D_3 deficiency seems to be related to an increased risk for the development of gestational diabetes mellitus. [17]

The aim was to study the levels of vitamin D_3 and to find the correlation between vitamin D_3 levels and glycemic control in the patients with diabetes mellitus type 2.

2. Material and Method

This study was a cross-sectional study, conducted in the Biochemistry Department at Pramukhswami Medical College, Karamsad. All the individuals attending the hospital were evaluated, from whom individuals were selected in the case and control groups after applying the inclusion and exclusion criteria.

2.1 Inclusion criteria

The case group included 100 diabetic patients, diagnosed by ADA guideline (Fasting Plasma Glucose ≥ 126 mg/dl (Fasting defined as no caloric intake for 8-10 hours) or HbA1c ≥ 6.5 %).

The control group included 100 age and sex matched healthy males and females.

2.2 Exclusion criteria

Individuals were having liver diseases (diagnosed by Liver Function Test), kidney diseases (diagnosed by Renal Function Test) and individuals on vitamin D_3 supplements (decided by drug and history) were excluded from both the case and the control groups.

Written informed consents were obtained from all the participants, and then full history was taken. Both serum and whole blood samples were taken from the participants, and all the tests were done in Biochemistry Laboratory by fully automated instruments. Fasting Plasma Glucose was measured by Enzymatic reference method with hexokinase and HbA1c was measured by Immunoturbidimetry method standardized according to IFCC in Cobas Integra 400 Plus clinical chemistry analyzer, while vitamin D_3 was measured by the competitive principle of Electrochemiluminescence (ECL) method in Cobas e-411 immunoassay analyzer. Ethical clearance was obtained from Institutional Ethics Committee.

2.3 Statistical Analysis

All the data required for this study were collected and analyzed statistically to determine the significance of different parameters by using the commercially available statistical software MedCalc version 14.8.1 and Microsoft Office 2016. All the values were given as mean ± SD. Comparison between the case and the control groups were made using Student's t-test (unpaired), and the P value of less than 0.05 was considered statistically significant.

3. Result

3.1 Demographic data of age and sex

In this study total, 200 participants were included (93 men and 107 women) out of which 100 participants with diabetes mellitus were included in the case group, and another 100 healthy individuals were included in the control group. Table 1 shows the details of demographic data of the study.

3.2 Comparison of variables by Student's t-test

The mean age of the participants in the case group was 52.05 ± 10.49 years, and that of the control group was 51.55 ± 10.04 years. Both the groups were statistically similar in the age with the P value of 0.731. Details of various characteristics of the case and the control groups are given in Table 2. The mean of fasting plasma glucose and HbA1c levels in the case group (166.62 ± 32.93 mg/dl, 7.64 ± 1.22 % respectively) were statistically significantly higher than the control group (97.2 ± 6.39 mg/dl, 5.58 ± 0.32 % respectively) with the P value of <0.0001 and the mean value of vitamin D_3 for diabetic patients and healthy individuals were 27.19 ± 6.03 and 61.13 ± 10.85 nmol/L respectively, which is statistically significantly different. Figure 1 shows that the level of vitamin D_3 was significantly low in the case group with diabetic patients than healthy individuals.

3.3 Correlation of vitamin D_3 and HbA1c

We also found that there was an inverse correlation between vitamin D_3 (nmol/L) and HbA1c (%) in all the participants of the study by Pearson's correlation coefficient ($r = -0.63$, $P<0.001$, 95% confidence interval for $r = -0.70$ to -0.54) (Figure 2).

Table 1: Age and Gender Distribution of the Case and the Control Groups

Age (years)	Case			Control			Total
	Men	Women	Total	Men	Women	Total	
21-30	1	1	2	1	2	3	5
31-40	5	9	14	8	7	15	29
41-50	13	16	29	11	15	26	55
51-60	20	11	31	12	18	30	61
61-70	12	12	24	10	16	26	50
Total	51	49	100	42	58	100	200

Table 2: Comparison of the Various Parameters in the Case and the Control Groups (The Independent t-tests)

Parameter	Cases (Mean ± SD)	Controls (Mean ± SD)	P value*
Age (years)	52.05 ± 10.49	51.55 ± 10.04	0.731
Fasting Plasma Glucose (mg/dl)	166.62 ± 32.93	97.2 ± 6.39	< 0.0001
Glycated Hemoglobin (HbA1c) (%)	7.64 ± 1.22	5.58 ± 0.32	< 0.0001
Vitamin D_3 (nmol/L)	27.19 ± 6.03	61.13 ± 10.85	< 0.0001

*P < 0.05 = Statistically Significant

Figure 1: Showing Vitamin D_3 (nmol/L) Level in the Case and the Control Groups with Box and Whisker Plot.

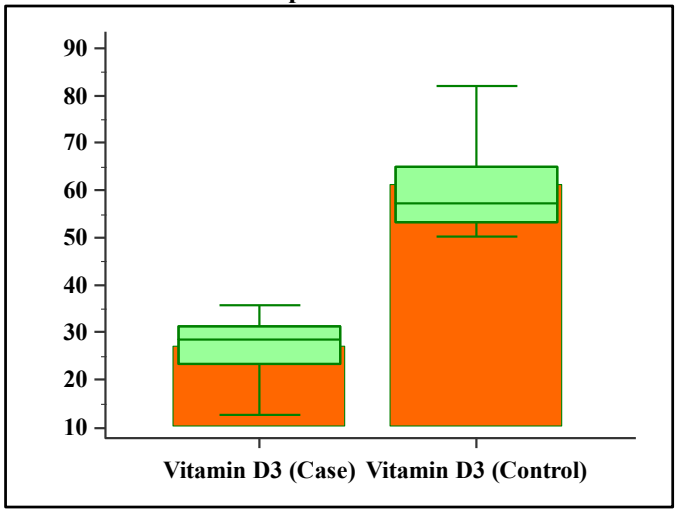
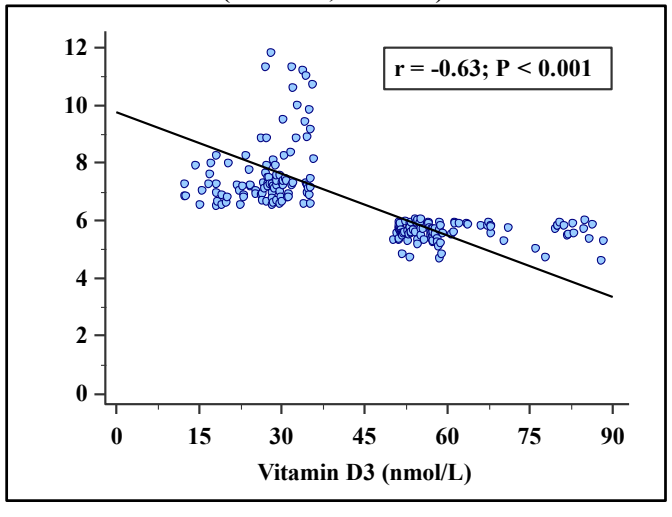


Figure 2: The Inverse Correlation between Vitamin D_3 (nmol/L) and HbA1c (%) in All the Participants of the Study by Parson's Correlation Coefficient (r = -0.63, P<0.001).



4. Discussion

In this present study, we found significantly low levels of vitamin D_3 in diabetic patients than healthy individuals and also an inverse correlation was found between vitamin D_3 levels and HbA1c levels in all the participants of the study. Vitamin D_3 levels were deficient in the patients with diabetes mellitus. (The vitamin D_3 level <50 nmol/L is considered as deficient). [7]

In a recent study, Heaney *et al.* 2013 found that the vitamin D_3 inversely associated with insulin responsiveness. It was localized to the serum vitamin D_3 range extending from 16–36 µg/L, and there was no association at vitamin D_3>32–36 µg/L, indicating that the vitamin D_3 association applied principally to values below that level. [18] Kostoglou-Athanassiou *et al* stated that vitamin D_3 levels appeared to be lower in the diabetes mellitus type 2 patients than in the control group of healthy people and the vitamin D_3 levels being related to the glycemic control in the people with diabetes mellitus type 2. [19]

A case-control study Pittas *et al* for middle-aged women found that vitamin D_3 concentration was inversely associated with the development of type 2 diabetes as an independent risk factor and also stated that raising vitamin D_3 level may be an effective strategy for reducing the risk of incident type 2 diabetes in women. [4] Another prospective observational study Pittas AG *et al* found that higher plasma vitamin D_3, assessed repeatedly was associated with lower risk of incident diabetes in high-risk patients, after adjusting for lifestyle interventions (dietary changes, increased physical activity, and weight loss) known to decrease diabetes risk. [5]

In a longitudinal study of the determinants of insulin resistance and the metabolic syndrome, a significant inverse association of baseline vitamin D_3 with incident Metabolic Syndrome, which may be partly association with glucose homeostasis. [14] In a study involving 8421 participants from the National Health and Nutrition Examination Survey III (NHANES III) of the noninstitutionalized civilian U.S. population, was observed significantly lower levels of vitamin D_3 in the subjects with metabolic syndrome than in those without it. [20] Vitamin D_3 facilitates the secretion of insulin from pancreatic beta cells, thus appearing to regulate insulin secretion and therefore vitamin D_3 deficiency may be related to impaired insulin secretion in the diabetes mellitus type 2. [21]

Osei *et al* studies recommend vitamin D_3 supplementation to improve glucose control in type 2 diabetes mellitus patients. [22] In a randomized controlled trial, the administration of 2000 international units (IU) cholecalciferol daily for 16 weeks was found to improve beta cell function in adults at high risk for diabetes, and there was a trend toward attenuating the rise in HbA1c. [23]

Because of the cross-sectional design, the present study has several limitations. Also, the study was based on a single measurement of vitamin D_3 so, no conclusion can be made for cause and effect relationship between vitamin D_3 and HbA1c and also there was no data on pancreatic beta cell function or insulin resistance. More studies are needed with vitamin D_3 supplementation and long-term observation of glucose control in the diabetes mellitus type 2.

5. Conclusion

The study shows that the vitamin D_3 levels appeared to be deficient in the diabetic patients than the normal healthy individuals, and there is an inverse correlation between the levels of vitamin D_3 and HbA1c. It seems that the level of vitamin D_3 is inversely associated with glycemic control in the diabetic patients. Therefore, vitamin D_3 supplementation may be recommended along with the treatments of the patients with diabetes mellitus.

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