Original Research Article

A comparative study to determine vitamin D status in type 2 diabetes and normal subjects in south India

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Abstract

Background: Vitamin D deficiency is common in general population in India in spite of adequate sunlight. We have decided to compare the prevalence of vitamin D deficiency in type 2 diabetes and normal individuals. **Methods:** 370 type 2 diabetes individuals attending Karnataka Institute of endocrinology and research outpatient department and 100 normal individuals were studied. Fasting plasma glucose, post prandial plasma glucose, lipid profile, vitamin D levels, BMI, waist circumference and BP of these subjects were measured. **Results:** Out of 370 type 2 diabetes subjects 67.3% were males and age group ranging from 21 to 80 years. Duration of diabetes vary from 0 to 20 years. Vitamin D deficiency was present in 83%, insufficiency in 13.8% and only 3.2% had normal vitamin D levels in type 2 diabetes. Vitamin D deficiency was common in individuals >50 years, males, BMI 25-30. Family history of diabetes was present in 60%. Hypertension was present in 47.6%. Total cholesterol, LDL, Triglycerides were lower and HDL levels were higher in type 2 diabetes individuals with vitamin D more than 20 nanograms per ml. In 100 normal individuals taken as controls 62% were males, age group ranging from 21 to 80 years. Vitamin D deficiency was present in 82% and insufficiency in 12% and 6% had normal vitamin D levels. **Conclusions:** Vitamin D deficiency was present in 83% of type 2 diabetes individuals and 82% of normal individuals. So both type 2 diabetes and normal controls from south India are equally deficient in vitamin D. Total cholesterol, LDL, Triglycerides were lower and HDL levels were higher in type 2 diabetes individuals with vitamin D more than 20 nanograms per ml.

Key words: Vitamin D, Type 2 diabetes,insulin sensitivity

Introduction

Vitamin D is a secosteroid which is converted into its active form via 1 α-hydroxylase enzyme. Though kidney is the classical site for 1 α-hydroxylase activity, it is also expressed in other tissues such as endothelial and vascular smooth muscle cells. [1]. Besides, vitamin D receptor (VDR) is present in more than 30 different tissues including pancreas, myocardium, lymphocytes, etc. The widespread distribution of VDR signifies important role of vitamin D in humans [2].

Prevalence of Vitamin D deficiency- Currently the prevalence of type 2 DM is high in urban as well as rural India [3,4] and by 2030, Asian Indian would bear the maximum burden of the disease in the world. [5]. Glycaemic control tends to worsen in winter months and is believed to be because of concomitant fall in 25(OH) D in this season. [6,7].

Pittaset al has systematically reviewed world literature related to [8].

1. association between VDD and prevalence/ incidence of type 2 DM in different population, and
2. randomized trials assessing role of vitamin D supplementation on glucose metabolism

The results of the above review, the evidence from the observational studies suggests an association between low vitamin D status and calcium intake (including low dairy intake) and risk of type 2DM

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or metabolic syndrome. However, definite conclusions from these studies are limited for a variety of reasons. In cross-sectional or case-control studies, vitamin D or calcium status was measured in patients with glucose intolerance or established diabetes, therefore these measures may not reflect vitamin D or calcium status prior to diagnosis and, as a result, the causative nature of the observed associations cannot be established. There is considerable variability in studied cohorts (normal glucose tolerance vs. diabetes [newly diagnosed vs. established], ethnicity, latitude etc). In most studies, there is lack of adjustment for important confounders, such as adiposity, physical activity, and importantly, vitamin D or calcium status.

Skin complexion, poor sun exposure, vegetarian food habits and lack of vitamin D food fortification program in the country explain the high prevalence of VDD in India despite its sunny climate.

Vitamin D and Type 2 DM: While vitamin D is critical for calcium homeostasis, current studies also highlight role of vitamin D deficiency (VDD) in diseases other than the metabolic bone disorders. The potential mechanisms of beneficial effect of vitamin D in type 2 DM include

(i) Improved β-cell function via direct effect of vitamin D or by increase in the intracellular ionized calcium which therefore would result in enhanced insulin release.

(ii) Increased insulin sensitivity related to expression of insulin receptor or via calcium dependent pathways in target cells leading to increase in the glucose utilization, and

(iii) Inhibition of β-cells apoptosis due to VDR transcription factor mediated inhibition of cytotoxic cytogene expression.

Research methods and statistical analysis- Study design and participants-370 South Indian type 2 diabetic individuals attending Karnataka Institute of endocrinology outpatient department were assessed for fasting and post-prandial plasma glucose, lipid profile, vitamin D levels, BMI, waist circumference and hypertension. 100 South Indian normal individuals were used as controls. Informed consent was obtained from all the participants. Inclusion criteria- All type 2 diabetes patients with age more than 20 and less than 80 years, duration of diabetes new to 20 years were included in the study.

Sample collection-venous blood sample collected under aseptic precautions and vitamin D was estimated by chemiluminescence.

Exclusion criteria-Patients taking vitamin D supplementation or having hepatic, renal or metabolic bone disorders (including parathyroid related problems) were excluded from the study.

Also, those patients with use of glucocorticoids or anti-seizure medications in the previous 6 months; or those patients having history of malabsorption syndromes such as celiac disease or active malignancy or with active infection were excluded from the study. Patients were also excluded if they had any severe medical illness, such as sepsis, severe infection, malignancy, liver cirrhosis, heart failure, or renal failure.

Statistical methods-Descriptive statistical analysis was carried out in the present study. Results on continuous measurements were presented on Mean ± SD (Min-Max) and results on categorical measurements were presented in Number (%). Significance was assessed at 5% level of significance. Analysis of variance (ANOVA) was used to find the significance of study parameters between three or more groups of patients. Chi-square/ Fisher Exact test was used to find the significance of study parameters on categorical scale between two or more groups. The Statistical software namely SAS 9.1.3, SPSS 10.0 was used for the analysis of the data.

Results

370 type 2 diabetes subjects were studied. 67·3% were males and age group ranging from 21 to 80 years. Duration of diabetes vary from 0 to 20 years. Vitamin D deficiency was present in 83%, insufficiency in 13·8% and only 3·2% had normal vitamin D levels.In 100 South Indian normal individuals taken as controls 62% were males, age group ranging from 21 to 80 years. Vitamin D deficiency was present in 82% and insufficiency in 12% and 6% had normal vitamin D levels.(Table1). Family history of diabetes was present in 60%. Hypertension was present in 47·6%.

Table- 1: Prevalence of Vitamin D deficiency in type 2 diabetes and normal subjects.

Vitamin D (ng/ml)	Number of type 2 diabetes subjects	Percentage	Number of normal subjects	Percentage
Deficient (<20 ng/ml)	307	83	82	82
Insufficiency (>20-30 ng/ml)	51	13.8	12	12
Normal (>30 ng/ml)	12	3.2	6	6
Total	**370**	**100.0**	**100**	**100**

Vitamin D deficiency was common in individuals >50 years, males, BMI 25-30, duration of diabetes ranging from less than one year to more than 10 years. (Table2)

Table- 2: Correlation of Clinical variables with levels of Vitamin D levels in type 2 diabetes individuals.

Clinical variables	Levels of Vitamin D				P value
	Deficient (<10 ng/ml) (n=166)	Insufficiency (10-20 ng/ml) (n=141)	Insufficiency (21-30 ng/ml) (n=51)	Normal (>30 ng/ml) (n=12)	
Age in years					
• <50 years	57(34.3%)	50(35.5%)	21(41.2%)	1(8.3%)	0.199
• >50 years	109(65.7%)	91(64.5%)	30(58.8%)	11(91.7%)	
Gender					
• Male	105(63.3%)	98(69.5%)	38(74.5%)	8(66.7%)	0.431
• Female	61(36.7%)	43(30.5%)	13(25.5%)	4(33.3%)	
BMI (kg/m^2)					
• <18.5	1(0.6%)	0(0%)	1(2%)	0(0%)	0.232
• 18.5-25.0	61(36.7%)	56(39.7%)	26(51%)	3(25%)	
• 25.0-30.0	73(44%)	54(38.3%)	18(35.3%)	8(66.7%)	
• >30.0	31(18.7%)	31(22%)	6(11.8%)	1(8.3%)	
Duration of DM					
• New cases	8(4.8%)	8(5.7%)	1(2%)	0(0%)	<0.001**
• <1 years	8(4.8%)	12(8.5%)	3(5.9%)	0(0%)	
• 1-2 years	19(11.4%)	28(19.9%)	7(13.7%)	1(8.3%)	
• 2-5 years	31(18.7%)	24(17%)	12(23.5%)	1(8.3%)	
• 5-10 years	48(28.9%)	33(23.4%)	12(23.5%)	3(25%)	
• >10	52(31.3%)	36(25.5%)	16(31.4%)	7(58.3%)	
Hypertension					
• No	86(51.8%)	67(47.5%)	20(39.2%)	3(25%)	0.167
• Yes	80(48.2%)	74(52.5%)	31(60.8%)	9(75%)	

HDL levels were higher in those with vitamin D levels more than 20 and 30 mg/dl when compared to patients with vitamin D levels less than 20 mg/dl. We can assume that correction of vitamin D deficiency may help in increasing HDL levels which reduces atherosclerosis. But this has to be further confirmedby larger studies. (Table 3)

Table-3: Comparison of T.C, TG HDL, LDL & VLDL with Vitamin D in four groups studied.

Vitamin D (ng/ml)	Deficient (<10 ng/ml)	Insufficiency (10-20 ng/ml)	Insufficiency (21-30 ng/ml)	Normal (>30 ng/ml)	P value
Total cholesterol (mg/dl)	173.12±42.06	172.61±45.41	162.96±33.81	161.08±39.14	0.375
TG	158.22±115.68	161.33±135.04	140.98±59.11	119.58±54.72	0.500
HDL	39.87±9.79	38.58±9.43	40.56±8.50	43.67±8.42	0.211
LDL	101.50±34.66	102.06±33.61	93.07±31.91	93.83±32.71	0.344
VLDL	31.20±23.43	30.43±22.99	28.14±12.04	23.67±11.19	0.593

Discussion

Type 2 Diabetes Mellitus (T2DM) is the commonly seen endocrine disorder characterized by hyper-glycemia. The International Diabetes Federation (IDF 2015) estimates around 69.2 million diabetic individuals in India with a global estimate of 415 million diabetics. There are several factors that seem to play a role in its development including genetic, lifestyle, environmental and nutritional conditions. Amongst nutritional factors, vitamin D is likely to have an important role either in glycemic control or in attenuating diabetic complications.The probable mechanisms indicating the role of vitamin D in glucose homeostasis is likely to be through beta cell dysfunction and insulin resistance in cases with vitamin D deficiency.

Vitamin D deficiency is now regarded as pandemic in all age groups in humans. The cross-sectional study involving largest cohort of non diabetic Americans (n = 6288) reported an inverse relationship between serum 25(OH) D concen-tration and fasting or post glucose load values. [8,9]. In nine of 13 case-control studies reviewed by the authors, patients with type 2 diabetes showed a lower mean 25(OH) D concentrations than the non diabetic controls. Association between vitamin D intake and incidence of type 2 DM was examined in Women's Health Study. [8,10]. Subjects with daily vitamin D intake >511 IU had lower risk of incidence of DM when compared to a cohort with daily vitamin D intake of <159 IU per day (2·7% vs. 5·6%). Pittas et alalso examined association between combined vitamin D and calcium intake and incidence of type 2 DM among 83,806 women in Nurses Health Study. After adjusting for age, BMI, and non dietary covariates, a significant inverse association was observed between vitamin D intake and calcium intake on one hand and risk of type 2 DM on the other [11]. There is a paucity of interventional trials assessing effect of vitamin D supplementation on glycaemic control over long term period. Pittas et al studied 92 diabetic subjects and reported decrease in fasting plasma glucose after 3 yr in group receiving daily supplementation of 700 IU of vitamin D and 500 mg of calcium citrate. [12].

David*et al* has shown that 63.5% of type 2 diabetes individuals compared to 36% of type 1 diabetes were deficient in vitamin D. [13]. Goswami*et al*of AIIMS in 2000 measured vitamin D levels in apparently healthy subjects in Delhi and showed that significant vitamin D deficiency was present in 90% of them [14]. Rajesh *et al* in their pilot study showed that 96·7% of Asian Indian patients with fragility hip fracture were deficient in vitamin D [15]. Harinarayanan*et al*reported vitamin D deficiency in 62% and 72% in urban males and females, 44% and 77% rural males and females in south India[16]. Marwaha *et al*reported prevalence of vitamin D deficiency in 91·2% of healthy Indians aged above 50 years [17].

There are no studies regarding prevalence of vitamin D deficiency in type 2 diabetics in south India. Our study shows the prevalence of vitamin D deficiency in 83% and insufficiency in 13·8% of south Indian type 2 diabetes individuals. South Indian normal individuals taken as controls had vitamin D deficiency in 82% and insufficiency in 12%. The present study has also shown a higher incidence of vitamin D deficiency in overall recruited subjects indicating that both T2DM (83%) subjects and non-diabetic control subjects (82.0%) were equally deficient. This is in accordance with other studies demonstrating low serum vitamin D levels in 70% to 100% populations across India.

The high percentage of VDD in this study was explained by decreased sunshine exposure, limited outdoor activities, dark complexion and decreased awareness about fortification with vitamin D. Although sunshine exposure is good in India, it is limited to only few months, and fortification of food with vitamin D is not routine in the country.

Whether vitamin D status in patients with diabetes has a role in the pathogenesis *of* diabetes mellitus in patients needs to be elucidated in future studies. It has been argued by Lo *et al.* that to meet an adequate requirement of vitamin D, people in India require sun exposure almost double than Caucasians due to increased skin pigmentation. [18,19]. Life style factors like in-door working or working in close environment with minimum sun exposure is also likely for high prevalence of vitamin D deficiency in our population. Normal office hours in India are usually from 10 am to 6 pm while maximum sun exposure and absorption is between 11 am to 2 pm with an UV index of 7-9 required for conversion of 7-dehydrocholesterol to pre-vitamin D_3 [20]. But this seems to be unrealistic as being a tropical country summers in India are very hot, forcing most of its people to stay indoor during this time. This results in low exposure to the sunlight contributing for very low vitamin D status in our population.

Conclusions

Vitamin D deficiency was present in 83% of type 2 diabetes individuals and 82% of normal individuals. So both south Indian type 2 and normal persons are equally deficient in vitamin D. HDL levels were higher in type 2 diabetes individuals with vitamin D more than 20 nanograms per ml.

We can assume that correction of vitamin D deficiency may help in increasing HDL levels which reduces atherosclerosis but this has to be further validated by larger studies. Correction of vitamin D deficiency in type 2 diabetes may help in improving glycemic control. This has to be further validated by further studies in India.

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