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ORIGINAL ARTICLE

ASSOCIATION OF VITAMIN D LEVEL WITH FASTING PLASMA GLUCOSE IN TYPE 2 DIABETIC PATIENTS

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ABSTRACT: BACKGROUND: The prevalence of vitamin D deficiency has increased in India. Recently there have been plenty of research studies pointing to the essentiality of vitamin D beyond bone health. Type 2 diabetes is also found to be more prevalent in individuals with hypovitaminosis D. **AIM:** To evaluate the levels of vitamin D in type 2 diabetic patients and age matched healthy controls in South Indian population and also to correlate vitamin D level with fasting plasma glucose level and lipid profile in type 2 diabetic patients. **MATERIALS AND METHODS:** This cross-sectional study included 51 type2 diabetic patients and 51 healthy controls. Estimation of Fasting blood glucose and lipid profile was done in Beckmann-Coulter auto analyzer using standard kits. Vitamin D was estimated by Chemiluminescent Immuno Assay (C.L.I.A.) Statistical analysis was done using SPSS version 21 software. **RESULTS:** The vitamin D level was significantly lower in the diabetic patients. The fasting plasma glucose, total cholesterol, triglycerides, low density lipoproteins and very low density lipoproteins were increased in patients with vitamin D deficiency (i.e. vitamin D < 20 ng/ml) but the increase was statistically significant only in fasting blood glucose and triglycerides($p<0.01$). The level of high density lipoproteins was statistically significantly lower in the vitamin D deficient group ($p<0.01$). By Pearson's correlation vitamin D was found to be negatively correlated significantly (p value < 0.01) with fasting blood sugar and triglycerides and was found to be positively correlated significantly (p value <0.01) with HDL. **CONCLUSION:** There is high prevalence of Vitamin D deficiency in type 2 diabetic patients. These individuals have also been proved to have atherogenic dyslipidemia that may lead to vascular complications. Whether supplementing diabetic patients with vitamin D helps in reducing further complications is yet to be proved by interventional studies.

KEYWORDS: Vitamin D, Type 2 diabetes, Fasting plasma glucose, Dyslipidemia.

INTRODUCTION: Vitamin D deficiency is now a pandemic owing to the sophisticated lifestyle changes with practically nil exposure to sunlight in the modern world. Various factors like latitude, season and time of the day, pigmentation of the skin, ageing and the topical use of a sunscreen, influence the amount of synthesis of vitamin D in the skin.(1) Cholecalciferol (vitamin D3) is synthesized in skin from 7-dehydrocholesterol on exposure to sunlight. This is then hydroxylated in the liver to form 25-hydroxy Cholecalciferol which is again hydroxylated in the kidney by 1-α hydroxylase to form 1, 25-dihydroxy Cholecalciferol, the active form of vitamin D3. Most of the tissues having vitamin D receptors generate 1, 25-dihydroxy Cholecalciferol in a paracrine fashion from 25-hydroxy Cholecalciferol. This paracrine effect may be responsible for its role in cell growth regulation, the adaptive and innate immune system functioning, insulin secretion by pancreatic β cells, blood pressure regulation and normal neuromuscular functions.(2)

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It is a well-known fact that vitamin D is essential for proper skeletal development and its deficiency has been associated with calcium and bone homeostasis. Recently there have been many studies pointing to the essentiality of vitamin D beyond bone health. Many studies had shown that vitamin D deficiency was associated with increased risk for developing various types of cancers including cancers of the colon, prostate, breast and esophagus.[3-7] There are overwhelming scientific evidences for association of low vitamin D levels with tuberculosis[8] metabolic syndrome,[9,10] cardiovascular diseases[11,12] and stroke.[13] Many studies support the fact that Type 2 diabetes is also found to be more prevalent in individuals with hypovitaminosis D.[14-18] All these are evidences for the extra skeletal benefits of the so called sunshine hormone vitamin D.

Apart from the genetic predispositions of Indians to many diseases, westernized culture, urbanization and diet modifications like fast foods have led to the increase of a number of metabolic diseases like type 2 diabetes. In this context we propose to evaluate the levels of vitamin D in type 2 diabetic patients and age matched healthy controls in south Indian population and also to correlate vitamin D level with fasting blood glucose level and lipid profile in type 2 diabetic patients.

MATERIALS AND METHODS: This is a cross-sectional observational study including 51 type 2 diabetic patients and 51 healthy controls. Patients were selected from an outpatient diabetic clinic who were under treatment for type 2 diabetes. Patients with bone disorders, hepatic and renal diseases were excluded from the study. Controls were healthy volunteers who were not known diabetic. After getting informed consent from the patients and controls, 10 ml of venous blood was drawn after 8-10 hours of fasting. After clotting, the samples were centrifuged at 3000rpm for 10 minutes. Estimation of Fasting plasma glucose and lipid profile was done in Beckmann-Coulter auto analyzer using standard kits. Glucose was estimated by Glucose Oxidase-Peroxidase method. Lipid profile was done by the following methods: Total cholesterol by Cholesterol Oxidase-Peroxidase method, Triglycerides by enzyme hydrolysis, HDL by precipitating method. VLDL was calculated by the formula TGL/5. LDL was calculated using Friedwald's equation [LDL = TC – (VLDL + HDL)]. Vitamin D was estimated by fully automated Chemiluminescent Immuno Assay.

Statistical analysis was done using SPSS version 21 software. The means of all the parameters between the diabetic group and the healthy control group were compared using paired sample T test. Independent sample T test was used to compare the biochemical parameters of the diabetic patients when grouped by the vitamin D levels, (< 20ng/dl vs ≥ 20ng/dl). Pearson's correlation was used to correlate vitamin D level with other biochemical parameters. The p value < 0.05 was considered statistically significant.

RESULTS: The study population was 51 type 2 diabetic patients and 51 healthy controls. The means of blood pressure, fasting blood glucose, lipid profile and Body Mass Index (BMI) of the diabetic patients were very high compared to healthy controls and statistically highly significant. The descriptive statistics of the study group are given in Table-1 as mean±standard deviation and the p-value is also given.

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In the type 2 diabetic patients of the study population 27(53%) were found to be vitamin D deficient, 17(33%) insufficient and only 7(14%) of them were found to have sufficient vitamin D. But in controls only 3(6%) of them were found to be vitamin D deficient, 6(12%) insufficient, and 42(82%) were found to have sufficient vitamin D.

When the study population was grouped by vitamin D level the fasting blood glucose, total cholesterol, triglycerides, low density lipoproteins and very low density lipoproteins were higher in patients with vitamin D deficiency (i.e. vitamin D < 20 ng/ml) but the increase was statistically significant only in fasting plasma glucose and triglycerides ($p<0.01$). The level of high density lipoproteins was statistically significantly lower in the vitamin D deficient group ($p<0.01$). The biochemical parameters of patients with vitamin D < 20 ng/ml and ≥ 20ng/ml is given in Table 2. By Pearson's correlation vitamin D was found to be negatively correlated with fasting blood sugar and triglycerides. The correlation was statistically significant at p value < 0.01 level. Vitamin D was found to be positively correlated with HDL and the correlation was statistically significant at p value <0.01 level. The correlation is shown in the tables 3 and 4.

DISCUSSION: Vitamin D status of the study population is assessed by the level of 25-hydroxy vitamin D (25(OH) D). The Vitamin D deficient, insufficient and sufficient states are considered when the 25(OH) D level is < 20 ng/ml, 21–29 ng/mL and >30 ng/mL respectively. The preferred range is 40–60 ng/mL. Vitamin D intoxication occurs when 25(OH) D >150 ng/mL.[19]

The comparison of the biochemical parameters between the diabetic patients and healthy controls shows the atherogenic status of the diabetic group included in our study. The diabetic patients prone to atherogenicity is an established factor which is again proved by this study. The level of vitamin D in the diabetic group is much lower compared to healthy controls and is statistically significant. Hypovitaminosis D in type 2 diabetes is supported by many previous studies. The fasting blood sugar is much higher in vitamin D deficient type 2 diabetic patients i.e. <20ng/ml which has been proved by earlier studies.[20-26]

The role of vitamin D in the pathophysiology of type 2 diabetes is thought to be due to its extra skeletal effects on insulin secretion and insulin resistance. One of the mechanisms involved may be through its effect on calcium homeostasis. Calcium dependent insulin secretion and release has been proved by animal studies.[27,28] The endopeptidase essential for the human proinsulin conversion also needs calcium.[29] Studies have proved the presence of vitamin D receptors in pancreatic β cells[30] and also the expression of the enzyme 1–α hydroxylase that activates vitamin D in the β cells.[31] The association between the polymorphism of vitamin D receptors and type 2 diabetes was observed in some genetic studies.[32] It has also been shown that the vitamin D response element is present in the insulin gene.[33] All these evidences support the fact that vitamin D deficiency may lead to the development of type 2 diabetes. Our study which was done in South Indian population is an added evidence for the association of hypovitaminosis D and type 2 diabetes.

The study conducted by Cigolini et al showed increased level of triglycerides in type 2 diabetic patients with hypovitaminosis D.[34] Further in the study done by Jaydip Ray Chaudhuri vitamin D deficiency was shown to be independently associated with elevated triglycerides and decreased HDL levels in Indian subjects.[35] Similarly in our study we found a positive association

of vitamin D with HDL and negative association with triglycerides. This shows that vitamin D deficiency in diabetes may potentially increase the risk of atherogenic dyslipidemia, thus enhancing cardiovascular morbidity and mortality.

CONCLUSION: Our study is an added evidence for the high prevalence of Vitamin D deficiency in type 2 diabetic patients. These individuals have also been proved to have atherogenic dyslipidemia, which may further lead to vascular complications. Whether supplementing diabetic patients with vitamin D helps in reducing further complications is yet to be proved by interventional studies. Many such projects are already underway. From a clinical perspective these studies may help to determine the dosage schedule of vitamin D in diabetes.

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Variables	Cases (N=51) (Mean±SD)	Controls (N=51) (Mean±SD)	p value
Systolic BP (mm/Hg)	131.24±19.74	117.49±7.67	<0.0001
Diastolic BP (mm/Hg)	79.67±15.54	74.67±8.14	0.024
FBS (mg/dl)	205.12±72.44	99.04±7.36	<0.0001
TC (mg/dl)	206.63±55.92	165.33±16.35	<0.0001
TGL (mg/dl)	258.24±122.50	130.65±19.81	<0.0001
LDL (mg/dl)	126.24±44.32	89.55±14.32	<0.0001
VLDL (mg/dl)	40.52±25.68	26.20±4.05	<0.0001
HDL (mg/dl)	30.58±7.41	50.37±5.64	<0.0001
VITAMIN D (ng/ml)	20.71±9.72	41.00±11.32	<0.0001
BMI	26.64±4.44	23.43±2.33	<0.0001

Table 1: Mean and standard deviation (SD) of all the descriptive variables of cases and controls

FBS=Fasting Blood Sugar, TC=Total cholesterol, TGL=Triglycerides, LDL=Low density lipoproteins, VLDL= Very Low density lipoproteins, HDL=High density lipoproteins, BMT=Body Mass Index

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variables	Vit D ≥ 20ng/ml (N=24)		Vit D < 20ng/ml (N=27)		p value
	Mean	Std. Deviation	Mean	Std. Deviation	
Age in years	52.79	10.06	55.81	12.94	0.354
Systolic BP (mm/Hg)	133.33	20.17	129.37	19.54	0.481
Diastolic BP (mm/Hg)	82.58	12.90	77.07	17.39	0.202
FBS (mg/dl)	153.46	47.14	251.04	58.94	0.000
TC (mg/dl)	193.79	52.01	218.04	57.73	0.121
TGL (mg/dl)	205.29	73.20	305.30	138.68	0.002
LDL (mg/dl)	121.59	42.42	130.37	46.34	0.483
VLDL (mg/dl)	34.28	13.72	46.07	32.16	0.091
HDL (mg/dl)	33.72	9.04	27.80	4.02	0.006
BMI	26.81	4.07	26.48	4.81	0.793

Table 2: Biochemical parameters of the study population when grouped by vitamin D level

Variables		Systolic BP	Diastolic BP	FBS	BMI
Vitamin D	Correlation coefficient (r)	.198	.098	-.790	-.021
	p value	.164	.495	.000	.884

Table 3: Pearson's correlation of vitamin D with blood pressure, fasting blood sugar and BMI

BP=Blood Pressure, FBS=Fasting blood sugar, BMI=Body Mass Index.

Variables		TC	TGL	LDL	VLDL	HDL
Vitamin D	Correlation coefficient (r)	-.016	-.435	.128	-.194	.697
	p value	.911	.001	.370	.173	.000

Table 4: Pearson's correlation of vitamin D with Lipid profile

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