

Original Research Article

A case control study to determine the role of vitamin D in the risk of coronary artery disease among type 2 diabetic individuals

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ABSTRACT

Background: Diabetes Mellitus comprises a group of metabolic disorder leading to hyperglycaemia. Vitamin D deficiency plays a role in Type 2 Diabetes Mellitus pathogenesis. Vitamin D appears to affect several metabolisms that have been associated with coronary artery disease. Vitamin D level has been recently considered as an adjustable risk factor of cardiovascular diseases, in individuals with type 2 Diabetes.

Methods: This case control study was conducted in the Department of Medicine, UPUMS. 100 diabetic individuals with low Vitamin D level were taken as cases and 100 diabetic individuals with normal vitamin D level as control. History and examination with necessary investigations were done. Patients with positive history were subjected to investigations to diagnose CAD.

Results: The proportion of case and controls had no significant difference in age distribution. The risk of coronary artery disease was 2.76 times higher among diabetes mellitus patients with vitamin D deficiency (1.36-5.59). The risk of CAD was adjusted for various risk factors (age, sex, hypertension, smoking, physical activity, and lipid profile) Odds ratio was found to be 2.8 (95% CI-1.19-6.94, p-0.018).

Conclusions: Vitamin D deficiency among diabetes patients was found to be an independent risk factor for CAD after adjusting other risk factors emphasizing that vitamin D can be a potential risk factor for development of coronary artery disease.

Keywords: Coronary artery disease, Diabetes mellitus, Hypovitaminosis

INTRODUCTION

Diabetes Mellitus comprises group of metabolic disorder leading to hyperglycaemia and underutilization of glucose. Non-Insulin Dependent Diabetes mellitus has emerged as a leading public health problem. In 2013, the prevalence of diabetes was 382 million and by 2035, this figure is estimated to grow to 592 million. Developing countries pose maximum burden of the disease worldwide.¹ Vitamin D deficiency, an environmental factor which may play a role in T2DM pathogenesis.²

Vitamin D was discovered in 1922 by McCollum. It is a fat soluble vitamin and its main source is endogenous vitamin D synthesized in the skin.³ Vitamin D is not only an important element for mineral metabolism and bone integrity but it also has several pleiotropic effects, including the endocrine system.⁴ Vitamin D deficiency in diabetes patients is a newer research evidence which has brought focus on vitamins in diabetic patients.⁵

Researchers have confirmed that vitamin D plays an important role in endothelial function, blood pressure

control, and calcification of the coronary vasculature, increased vascular resistance and prevention of cardiovascular disease (CVD).⁶ The effect of vitamin D on regulation of the lipid profile is one of the proposed mechanisms for the link between vitamin D deficiency and coronary artery disease.⁷

Vitamin D deficiency may be a overlooked cardiovascular risk factor in the among type 2 diabetes mellitus patients. Vitamin D appears to affect several metabolisms that have been associated with coronary artery disease, such as inflammation, vascular calcification, myocyte hypertrophy, proliferation of smooth muscle cells in blood vessels, arteriosclerosis, rennin-angiotensin system, blood pressure control and insulin resistance.^{8,9}

The incidence of coronary artery disease and other atherosclerotic disease manifestations are often seen in individuals with Diabetes mellitus. Type 2 diabetes mellitus is also associated with increased risk for mortality from coronary artery disease than in age matched non- diabetic.¹⁰

Vitamin D level has been recently considered as an adjustable risk factor of cardiovascular diseases, in individuals with type 2 diabetes.¹¹ The aim of the study is to determine the role of Vitamin D as a risk factor of coronary artery disease in type 2 diabetes mellitus and association with other risk factors of CAD.

METHODS

Study design

This is an observational case control study. Patients were recruited between January 2017 and June 2018 conducted at Medicine department of UPUMS, Saifai, Etawah.

Sample size

About 100 diabetic individuals with low Vitamin D level was included in the study as cases and 100 diabetic individuals with normal vitamin D level was included as control.

Inclusion criteria

- Adult patients with type 2 diabetes mellitus living in rural area of central India.

Exclusion criteria

- Current use of vitamin D, Pregnant women, Patients with chronic kidney disease or liver disease, Patients having any infection or malignancy, Patients with malabsorptive intestinal diseases or status post bariatric surgery, Patients taking anticonvulsants, drugs for the treatment of HIV/ AIDS, steroids,

rifampicin, cholestyramine, orlistat or other drugs affecting vitamin D metabolism and absorption.

Methodology

Diabetic patient were selected according to inclusion and exclusion criteria. Informed consent was taken from all participants. All diabetic patients were asked about demographic parameter like age, sex, residence and religion. Anthropometric parameter like height, weight, hip circumference, waist circumference and BMI will be recorded.

The study participants were asked about conventional cardiovascular risk factor like smoking, family history of premature CAD, sedentary lifestyle. All participants clinically examined and any patient with history suggestive of CAD was subjected to ECG, 2D ECHO, TMT and angiography to diagnose CAD.

Statistical analysis

All statistical analyses performed by using IBM SPSS version 23.0 (SPSS Inc., Chicago, IL). Unpaired t test and Chi-square test were used for comparison. Association of vitamin D deficiency with coronary artery disease had been done by univariate and multivariate logistic regression method. Risk of coronary artery disease in participant with low vitamin D level was expressed in terms of odds ratio with 95% confidence interval. A p value of <0.05 will be considered statistically significant.

Assessment of vitamin D

Serum 25 (OH) D levels were measured by commercially available assay (EDITM total 25-OH vitamin D EIA Kit). The analytical sensitivity of this assay for 25 (OH) D is 0.9557 ng/mL, 37.0 ng/mL and 40.0 ng/mL with CV of 3.1%, 4.3% and 2.5% respectively.

RESULTS

The study enrolled 100 cases and controls in the department of Medicine, UPUMS Saifai. The age distribution of case and control had no significant difference. The average age of the study sample was 60.02±11.16 years. Majority of the patients were between 51 to 65 years of age in both groups among cases and controls. Statistically this association was found not significant. The sex ratio in our study population was 60.5% male and 39.5% female. The proportion of females was more among case compared to controls, i.e. 47% and 32% respectively.

Statistically this association was found significant. Majority of patients were found in lower middle class in both groups i.e.40% and 52% respectively. Statistically this association was found not significant.

Table 1: Distribution of demographic profile of study participants.

	Case	Control	Total	P value
Age (Years)				
35 to 50	16 (16.0%)	28 (28.0%)	44 (22.0%)	Chi=9.897; P-value=0.070
51 to 65	45 (45.0%)	52 (52.0%)	97 (48.5%)	
> 65	39 (39.0%)	20 (20.0%)	59 (29.5%)	
Gender				
Male	53 (53.0%)	68 (68.0%)	121 (60.5%)	Chi=0.708; P-value=0.033
Female	47 (47.0%)	32 (32.0%)	79 (39.5%)	
Socioeconomic status				
Upper class & Upper middle	2 (2.0%)	2 (2.0%)		Chi=2.953; P-value=0.399
Middle	35 (35.0%)	28 (28.0%)		
Lower middle	40 (40.0%)	52 (52.0%)		
Lower	23 (23.0%)	18 (18.0%)		

Table 2: Distribution of risk factors among case and control.

	Case	Control	Total	P value
Smoker	24 (24.0%)	15 (15.0%)	39 (19.5%)	Chi=2.580; P-value=0.108
Non smoker	76 (76.0%)	85 (85.0%)	161 (80.5%)	
BMI				
18.5 to 24.9	25 (25.0%)	44 (44.0%)	69 (34.5%)	Chi=8.156; P-value=0.017
25 to 29.9	56 (56.0%)	40 (40.0%)	96 (48.0%)	
Above 29.9	19 (19.0%)	16 (16.0%)	35 (17.5%)	
Blood Pressure				
Hypertensive	48 (48.0%)	29 (29.0%)	77 (38.5%)	Chi=7.623; P-value=0.006
Normal	52 (52.0%)	71 (71.0%)	123 (61.5%)	
Waist Hip Ratio	1.10 ±0.38	1.07 ±0.37	--	0.563
Blood Glucose				
FBS	227.83 ±65.19	223.90 ±64.49	--	0.669
PPBS	283.74 ±91.89	272.84 ±86.17	--	0.38
HBA1c	11.11±2.75	9.34±1.51	--	0.034

Table 3: Lipid profile among case and control.

	Group	N	Mean	Standard Deviation	P value
Total cholesterol	Cases	100	188.65	68.59	0.038*
	Controls	100	170.64	52.33	
TGS	Cases	100	158.42	81.04	0.028*
	Controls	100	138.67	46.85	
HDL	Cases	100	54.65	5.71	0.050
	Controls	100	52.41	6.42	
LDL	Cases	100	138.29	27.42	0.230
	Controls	100	134.00	22.73	
VLDL	Cases	100	28.44	2.14	0.081
	Controls	100	27.19	2.89	

Table 2 reveals that, the prevalence of smoking was more (24%) among diabetic patients with vitamin d deficiency compared controls (15%), but the association was not statistically significant. The prevalence of risk of obesity, hypertension and HbA1c was more among diabetics with vitamin D deficiency compared to their counterparts, and

this association was found to be statistically significant. Patients with vitamin D deficiency revealed increased values of lipid profile compared to controls. Total cholesterol and triglycerides were significantly increased among cases (p = 0.03 and 0.028 respectively).

Table 4 out of 200 subject 22.5% patient has CAD and absent in 77.5% patient. Out of 45 cad patient 31% and 14% CAD patient present in cases and controls group respectively. Statistically this difference was found significant. Table 5 reveals the independent effect of risk factors on patients with vitamin d deficiency. Diabetic patients with vitamin d deficiency were 2.76 times higher

risk for coronary artery disease compared to diabetics with normal vitamin d level. The risk was found to be increased to 2.88 (95% CI - 1.19-6.94) by adjusting other risk factors in multivariate analysis. Hypercholesterolemia and hypertriglyceridemia were also shown to independent risk factors for CAD (adjusted or - 6.3 and 14.3 respectively).

Table 4: Association of CAD characteristics between groups (N=200).

CAD	Case	Control	Total	Odds ratio (95% CI) P-value
Present	31 (31.0%)	14 (14.0%)	45 (22.5%)	2.76 (1.36-5.59)
Absent	69 (69.0%)	86 (86.0%)	155 (77.5%)	0.004*

Table 5: Multivariate logistic regression analysis of CAD with various risk factors among diabetic patients.

Parameters	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Case (vitamin D deficient)	2.76 (1.36-5.59)	0.004	2.88 (1.19-6.94)	0.018
Age (>=45yr)	1.43 (0.52-3.94)	0.481	-	-
Sex (Male)	1.46 (0.74 – 2.86)	0.264	-	-
Hypertensive (present)	0.96 (0.48-1.90)	0.91	-	-
Smoking (yes)	1.14 (0.577 – 3.45)	0.44	-	-
Physical activity (sedentary)	1.11 (0.54 – 2.28)	0.76	-	-
Obese (Present)	1.025 (0.43-2.44)	0.95	-	-
Hypercholesterolemia (Present)	18.14 (6.62-49.7)	<0.0001	6.325 (1.78- 22.44)	0.004
Hypertriglyceridemia (Present)	25.96 (9.51-70.84)	<0.0001	14.30 (4.54 – 45.01)	<0.001

DISCUSSION

The prevalence of vitamin D deficiency was seen to be increasing with increase in the age. The prevalence of diabetes was more among males, but the deficiency of vitamin D was nearly same in both males and females. The findings of our study were in line with Subramanian et al which revealed increased vitamin D deficiency among females.¹²

The proportion of smokers were more among diabetics with vitamin D deficiency revealing that Vitamin D levels were significantly lower in smokers than in non-smokers. Ren W et al also cited this effect of smoking on vitamin D.¹³ The prevalence of vitamin D deficiency was increasing with increase in body mass index, similar findings were found by Cimbek et al.¹⁴ and Hypönen et al.¹⁵ The vitamin D deficiency was associated with hypertension similar to findings of Jeong et al, revealed that low serum levels of vitamin D showed more risk to develop hypertension.¹⁶

Van Ballegooijen et al also showed association of vitamin D and hypertension.¹⁷ Diabetics with vitamin D deficiency showed increased serum levels of total cholesterol and triglycerides. The inverse correlation of

vitamin D and serum cholesterol was also seen in the studies conducted by Roilim et al.¹⁸

Coronary artery disease was significantly associated with vitamin d deficiency among diabetic patients. Diabetics with vitamin d deficiency were 2.88 times higher chance of coronary artery disease compared to diabetics with normal vitamin d level. Kumar M et al, also showed similar findings with odds ratio of 2.9 times increased risk.¹⁹ Similar findings were observed among Syal et al.²⁰

CONCLUSION

Diabetic patients with vitamin d deficiency had higher risk of coronary artery disease. Vitamin d deficiency among diabetes patients was found to be an independent risk factor for cad after adjusting other risk factors emphasizing that vitamin d can be a potential risk factor for development of coronary artery disease. However, in present study sample was small. So further study is needed on large sample so that the result may extrapolated to general population.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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