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A STUDY OF VITAMIN D LEVELS IN PATIENTS OF CORONARY ARTERY DISEASE

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ABSTRACT

Background: Coronary Artery Disease (CAD) is a major global health problem. Recent studies demonstrated that lower vitamin D level (<30ng/ml) is associated with higher blood pressure and directly or indirectly with CAD, due to vascular endothelial damage. However the results are inconsistent. **Aims and objectives:** To find the association between 25(OH) vitamin D serum levels and coronary artery disease risk. **Materials and Methods:** In this case control study, we compared Vitamin D levels in 120 subjects with angiographically proven coronary artery disease with those of 120 age and sex matched healthy controls. Serum 25(OH) vitamin D levels were estimated by ELISA. Data was collected and analysed by suitable statistical methods. **Result:** Levels of 25(OH) vitamin D were 11.7±1.06 ng/ml in cases as compared to 24.3±1.54 ng/ml in controls (p value <0.0001).

Conclusion: There is a strong inverse association between 25(OH) vitamin D serum levels and coronary artery disease risk.

KEYWORDS: Vitamin D, coronary artery disease.

INTRODUCTION

Coronary artery disease (CAD) is one of the common causes of death and disability in developed countries, responsible for about one in every five deaths.[1] It is rapidly becoming a pandemic within the developing world as well where it involves a relatively younger population.[2] Great reduction in mortality has been achieved by improvement in myocardial revascularization techniques however, the results are still unsatisfactory in high-risk patients.[3,4] Therefore, more interests have been focused on the identification of new risk factors for coronary artery disease (CAD) and its prevention.[5] Calcium metabolism disorders, and especially vitamin D (25-hydroxy -cholecalciferol, 25- OHD3) deficiency, represent a rising problem, whose social and economic impact is growing due to ageing of the population. Recently Vitamin D has received great interests for its multiple effects on inflammatory system and potential role in atherothrombosis. Vitamin D deficiency has been related to endothelial dysfunction and enhanced risk of CAD.[6-8]

In fact, vitamin D receptor has been identified on the surface of smooth muscle cells, endothelial cells and myocardial cells, inflammatory cells controlling their proliferation and differentiation, and even in platelets, thus potentially influencing thrombosis.[9-11] Furthermore, independent association has been observed between vitamin D deficiency and cardiovascular risk factors, such as hypertension, diabetes mellitus, obesity, metabolic syndrome, Subclinical atherosclerosis [intima-media thickness (IMT)], and coronary calcification.[12-18] Vitamin D deficiency has also been associated with cardiovascular events, such as MI, congestive heart failure, sudden cardiac death and total mortality.[19-21] Several studies have been done to find association of vitamin D level with coronary artery diseases in different part of world with varying result. No study has been done in rural population of central India. So this study was conducted to investigate association of coronary artery disease with vitamin D level.

MATERIALS AND METHODS

The study was conducted in the Department of Biochemistry in collaboration with Department of CTVS, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi. Clearance from institutional ethical committee was obtained before preceding the study. Cases included 120 newly diagnosed patients of CAD. Patients were considered to have confirmed coronary artery disease if they had previous episodes of ST elevation

myocardial infarction (MI) or angiographically proven CAD. All patients were clinically stable. Study was initiated after taking permission from institute ethical committee. Informed consent was taken from all participants before including in study. Exclusion criteria were the presence of neoplastic disease, heart failure, recent major surgical procedure, evidence of hypercalcemia and systemic inflammatory conditions, such as infection, liver, or kidney disease. The patients on vitamin D and calcium supplements were also excluded.

All the participant were queried for presence of cardiovascular risk factors such as age, sex, smoking status, physical activity, use of drugs, presence of diabetes and hypertension. The level of physical activity was assessed by a standard questionnaire (rapid assessment physical activity questionnaire) and the participants were divided to five categories according to the score they obtained by this questionnaire: without activity, low activity, light activity, moderate activity and appropriate activity.[22] Weight, height and the blood pressure of the participants were measured by the standard protocol. Body mass index (BMI) was calculated as weight/height2 (kg/m2). The blood pressure was measured two times with a five minute interval in sitting position from the right brachial artery. Then the mean blood pressure was calculated. Hypertension was considered as blood pressure ≥140/90 or the consumption of antihypertensive drugs.

All the participants were subjected to following investigation: complete blood count (CBC), fasting plasma sugar, post prandial plasma sugar (2 hour after 75gm of oral glucose), glycosylated haemoglobin (HbA1c), kidney function test (KFT) (serum urea and creatinine), liver function test (LFT) (serum bilirubin, albumin, SGOT, SGPT and alkaline phosphatase), 24 hour urinary protein, serum total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), very low density lipoprotein cholesterol (VLDL-C), fasting 25-hyroxyvitamin D (25(OH)D) and ultrasound whole abdomen, 12 lead electrocardiogram, treadmill test, echocardiography and coronary angiography (CAG) (if ECG and TMT were inconclusive). Vitamin D level were measured in the form of 25-hyroxyvitamin D (25(OH) D). 25-hyroxyvitamin D was estimated by ELISA method using ELISA kit by CALBIOTECH. CBC was estimated using analyser Sysmex xp-100 (Transasia). LFT, KFT, and plasma Sugar were estimated using fully automated Clinical Chemistry analyzer Siemens ADVIA 2400. Direct estimation of TC, HDL-C levels and TG were done using Clinical Chemistry analyzer Siemens ADVIA 2400. Low and very low

density lipoprotein cholesterols (LDL-C and VLDL-C) were calculated employing the Friedewald's formula.[23]

Statistical Analysis: Data was analysed using Graph Pad Prism 5.0 version. The data is presented as Mean ± SEM. A p value of <0.0001 is considered significant. The difference in vitamin D levels in subjects with CAD compared to age and sex matched healthy controls was evaluated by the unpaired ***t***-test. The association between vitamin D level and CAD risk was evaluated by calculating odd ratios (OR) and 95% confidence intervals (CI).

RESULTS

The levels of serum vitamin D in patients of CAD were very low as compared to that in healthy controls (Table 1). The level in CAD patients (11.7±1.06 ng/ml) when compared to that in healthy controls (24.3±1.54 ng/ml) show statistically significant association (p < 0.0001).

Table 1: Serum 25(OH) Vitamin D mean levels among cases and controls.

	Mean ± SEM (ng/ml)	p value
CAD patients (n=120)	11.7±1.06	<0.0001*
Controls (n=120)	24.3±1.54	

*statistically significant

Vitamin D deficiency is defined as 25(OH)D < 20 ng/mL, insufficiency as 20–30 ng/mL and sufficiency as ≥30 ng/mL.[17] By evaluating association between 25(OH) D level and CAD risk, it was observed that 66.7% of CAD patients were deficient as compared to 41.7% of healthy controls (Table 2).

Table 2: Serum 25(OH) vitamin D levels and CAD Patient.

25(OH)D Level (ng/ml)	Cases (n=120)	Controls (n=120)	OR	95% CI
Less than 20	80 (66.7%)	50 (41.7%)	2.80	1.66-4.73
20-30	28 (23.3%)	22 (18.3%)	1.36	0.72-2.53
More than 30	12 (10%)	48 (40%)	0.17	0.08-0.33

DISCUSSION

Vitamin D deficiency is on the verge to become a major public health problem in India. There is widespread prevalence of varying degrees (50- 90%) of Vitamin D deficiency in Indian population.[18] Incidence of CAD is increasing in India.

Multiple studies showed that, vitamin D deficiency is directly or indirectly associated with CAD. Most of these studies were retrospective type and included patients with already diagnosed CAD. In addition it showed that, the prevalence of vitamin D deficiency is also very high in patients with normal coronary artery. So far none of the previous studies compared the serum vitamin D level and severity of vitamin D deficiency with the angiographic severity of CAD, according to the percentage of stenosis as well as the number of vessels involved.[5]

Data regarding association of vitamin D deficiency with CAD are also very less in South-east Asian and Indian population, where prevalence of vitamin D deficiency is very high. Two recent studies in Indian population concluded that low vitamin D was associated with increased risk for CAD and endothelial dysfunction and the patients with lower vitamin D had higher prevalence of double or triple vessel and diffuse CAD. But the sample size was small, vitamin D was graded as deficiency (<20ng/ml) or non-deficiency (≥20ng/ml) only and the angiographic severity was not graded as percentage of stenosis.[6-10]

According to our study vitamin D deficiency and severity of vitamin D deficiency was not associated with angiographic severity of CAD according to percentage of stenosis and as well as the number of vessel involved. Recently published studies, conducted upon the population of Australia and Israel also found that vitamin D deficiency was significantly associated with CAD but the sample size was small. The only Indian study that showed association of vitamin D deficiency with CAD did not reveal the mean vitamin D of patients with normal coronary artery; neither compared it with other severity groups. The data regarding vitamin D status in normal healthy Indian population is still lacking. So far one study showed mean vitamin D level of 52.9ng/ml in summer and 31.8ng/ml in winter which was quite higher in comparison to our study population.[18-21]

In our study almost whole population had vitamin D deficiency. According to our study, the patients with angiography proven normal coronary artery and CAD, both had high frequency of vitamin D deficiency, however the patients with normal coronary artery had much lower mean vitamin D (11.30ng/ml) as compared to the patients with CAD (14.10ng/ml). It may appear that lower vitamin D level may have protective role in developing CAD or patients with higher vitamin D level are more prone to have CAD, but it is not correct, as very high percentage (83.50%) of study population had vitamin D deficiency and very low percentage (4.40%) of study population had normal vitamin D level. These may be the cause that the

patients with normal vitamin D showed higher frequency of CAD, as the patients who were suspected to have CAD underwent coronary angiography.[22]

According to our study, there was no significant difference of vitamin D deficiency and severity of vitamin D deficiency, between the patients with normal coronary artery and the different severity of CAD. But this cannot deny the association of vitamin D deficiency with CAD as the patients with angiographic normal coronary artery or insignificant CAD may not be the true representative of healthy population as they all had some symptom and sign for CAD and they all underwent coronary angiography as per indications and guide line.[23-25]

CONCLUSION

There is a strong inverse association between 25(OH) vitamin D serum levels and coronary artery disease risk

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