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Vitamin D Levels in Patients with Coronary Artery Disease

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Abstract

Introduction: Vitamin D deficiency is being suggested as a cardiovascular risk-factor. The present study was conducted to assess the association of vitamin D deficiency with the severity of coronary artery disease (CAD). *Methodology:* Vitamin D level was measured in patients who underwent coronary angiography in our department. CAD was defined as patients with angiography proven stenosis of ≥ 50% in at least one major coronary arteries. *Results:* Of 86 patients, 66% were diagnosed with CAD. The vitamin D level in these patients was significantly lower as compared to those with normal coronary. Vitamin D level was also found to be significantly associated with the severity of CAD in terms of the number of vessels involved. Among all patients with single vessel disease (n = 17), two patients had vitamin D level less than 20 ng/ml, 10 had vitamin D level 21 to 30 ng/ml and rest had vitamin D higher than 30 ng/ml. Among the 20 patients with double vessel disease, 9 had vitamin D level between 21 to 30 ng/ml and lower than 20 ng/ml each. Among the 20 patients with triple vessel disease, 11 patients had vitamin D levels below 20 ng/ml. This association was found to be statistically highly significant. *Conclusion:* Vitamin D deficiency was associated with angiographic severity of CAD. Low vitamin D level may be an emerging, independent and reversible cardiovascular risk-factor.

Keywords: Cardiovascular diseases; Coronary artery disease; 25-hydroxyvitamin D.

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Introduction

The World Health Organization predicts that the mortality from Cardiovascular Diseases (CVD) would increase from 17.1 million in 2004 to 23.4 million in 2030.[1] Coronary Artery Disease (CAD) is the foremost cause of disability and death the world over and is one of the top five causes of death in Indian population.[2] As a result, CAD has been gaining public health importance in India. Numerous risk-factors are known to be associated with CAD, older age, diabetes, hypertension, hyperlipidemia, obesity and smoking being some of them. However, many risk-factors are unknown as of now. Recent evidence has suggested the role of vitamin D in cardiovascular diseases. Vitamin D is a fat soluble vitamin and its receptors are expressed not only by cognate vitamin D targets but also by other cell types and tissues, implying that vitamin D has far a wider role in human physiology.[3] Several associative observations have suggested a wide expression of the vitamin D receptors in the cardiovascular system.[4] Systemic inflammation, impaired glucose metabolism and endothelial dysfunction are well-known risk-factors for atherosclerosis. Vitamin D has both an anti-inflammatory activity and a positive effect

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of endothelial function, which has led many investigators to hypothesize a potential detrimental effect of vitamin D deficiency on the development and the progression of atherosclerotic plaques *in vivo*. However, the evidence pertaining to the role of vitamin D as a potential risk-factor for CAD is not very robust. The present study, was therefore, conducted to assess the association of vitamin D deficiency with the severity of CAD.

Materials and Methods

Study Design and Sampling

This cross-sectional study was conducted in the Department of Cardiology, MGM Hospital, Navi Mumbai, in which patients aged 30 to 80 years of age of either gender underwent coronary angiography as per the ACC/AHA guide lines.[5] Patients with CKD (eGFR less than 60 mL/min per 1.73 m^2), hepatic impairment, known malignant disease, with evidence of infection, already taking vitamin D or calcium supplementation, hypo or hyper-parathyroidism or hypercalcemia and patients taking anticonvulsants, glucocorticoids or anti-HIV medications were excluded from the study. The patients were explained the purpose of the study and they had the right to withdraw from the study at any time. The study was approved by the Institutional Ethics Committee.

Data Collection and Data Analysis

Using a predesigned semi-structured proforma meticulous history was taken and findings of a detailed clinical examination were noted. Demographic data of the patients and their past medical and family history was obtained for their risk profiling. Interpretation of coronary angiogram was done by visual estimation in consultation with a senior cardiology consultant to assess the severity of coronary artery disease. CAD was defined as patients with angiography proven stenosis of ≥ 50% in at least one major coronary arteries.[6] These major arteries are left anterior descending artery, left main, left circumflex artery and right coronary artery with right dominant, balanced, or left dominant circulation. The angiography findings was reported as normal coronary artery (including insignificant CAD) or significant CAD with severity for coronary artery stenosis in the form of 50% to 100%. We considered angiographic normal and insignificant CAD as normal coronary artery for the purpose of this study. The severity of stenosis was graded as 50%–70%, > 70%–90% and > 90%. The number of vessels involved were noted as well. Serum 25-hydroxy vitamin D (vitamin D) levels were measured by Electrochemiluminescence immunoassay after overnight fasting, one day prior to the coronary angiography. Serum vitamin D level was graded as, normal (> 30 ng/ml), insufficiency (20–30 ng/ml) and deficiency (< 20 ng/ml).[7]

Data were compiled and analyzed in SPSS (version 23, IBM). Data were described as means and standard deviation or as frequency distribution. Means were compared ising student t test and proportions were compared using chi-square or Fisher's exact test. A p value of less than 0.05 was considered statistically significant.

Results

During the study period, we included 86 patients. Mean age of the patients was 57.83 years, 64% being males. The baseline characteristics of the patients are described in Table 1. There were 67% current smokers, 45% took alcohol, 60% were hypertensive, 57% were diabetics, 36% were overweight and 52% had a family history of ischemic heart disease. The mean vitamin D levels in all these patients have also been described and compared between different patient groups. Vitamin D level showed a decline with age but the difference was not statistically significant. Smokers had a significantly lower vitamin D as compared to nonsmokers (p - value = 0.04). Gender, alcohol, hypertension, diabetes, body mass index and family history of ischemic heart disease was not associated with vitamin D levels in our patients. After coronary angiography, 57/86 (66%) of the patients were diagnosed with CAD. The vitamin D level in these patients was significantly lower as compared to those with normal coronary (16.94 ± 3.03 *vs* 21.65 ± 4.58 ng/ml; p - value < 0.01). Among the 57 patients with an established CAD, 28% had 50 to 70% stenosis, 30% had > 70 to 90% and 42% had > 90% stenosis. The vitamin D level was significantly associated with the severity of stenosis as described in Table 2. Single vessel disease was found in 30% of the patients, while double and triple vessel disease was found in 35% of the patients each. Vitamin D levels were also found to be significantly associated with the severity of CAD in terms of the number of vessels involved. Among all patients with single vessel disease (n = 17), two patients had vitamin D level less than 20 ng/ml, 10 had vitamin D level 21 to 30 ng/ml and rest had vitamin D higher than 30 ng/ml as shown in Table 3. Among the 20 patients with double vessel disease, 9 had vitamin D level

between 21 and 30 ng/ml and lower than 20 ng/ml each. Among the 20 patients with triple vessel disease, 11 patients had vitamin D levels below 20 ng/ml. This association was found to be statistically highly significant.

Table 1: Baseline characteristics of the patients included in the study

Variables	*n*	%	Vitamin D (ng/ml)	*p* - value
Age (in years)				
< 45	27	31%	20.48 ± 3.75	0.88
≥ 45	59	69%	18.93 ± 4.21	
Gender				
Male	55	64%	18.62 ± 5.24	0.26
Female	31	36%	19.33 ± 4.61	
Current smoker				
Yes	58	67%	17.43 ± 4.02	0.04
No	28	33%	21.66 ± 3.95	
Alcohol				
Yes	39	45%	17.65 ± 4.14	0.68
No	47	55%	19.42 ± 3.76	
Hypertension				
Yes	52	60%	17.31 ± 2.51	0.25
No	34	40%	18.48 ± 3.64	
Diabetes mellitus				
Yes	49	57%	19.63 ± 4.23	0.06
No	37	43%	20.91 ± 3.02	
Body Mass Index				
Normal	55	64%	19.54 ± 5.31	0.11
Overweight	31	36%	18.6 ± 4.06	
Family history of IHD				
Yes	45	52%	19.76 ± 3.55	0.72
No	41	48%	18.02 ± 4.68	

Table 2: Comparing vitamin D levels among various patient groups according to their angiographic pattern

Angiographic findings	*n*	%	Vitamin D (ng/ml)	*p* - value
Final impression				
Normal coronary	29	34%	21.65 ± 4.58	< 0.01
Coronary artery disease	57	66%	16.94 ± 3.03	
Severity of stenosis (*n* = 57)				
50 to 70%	16	28%	20.44 ± 3.74	
> 70 to 90%	17	30%	16.38 ± 5.21	< 0.05
> 90%	24	42%	14.22 ± 4.82	
Vessel involvement (*n* = 57)				
Single	17	30%	17.49 ± 2.09	
Double	20	35%	15.26 ± 3.64	< 0.05
Triple	20	35%	12.76 ± 3.55	

Table 3: Association of vitamin D levels with the severity of coronary artery disease

Vessel involvement	*n*	Vitamin D (ng/ml)			*p* - value
		< 20	21 to 30	> 30	
None	29	2	9	18	
Single	17	2	10	5	< 0.001
Double	20	9	9	2	
Triple	20	11	6	3	
		27	54	34	

Discussion

A general increase in the burden of cardiovascular diseases among Asian-Indian population as been demonstrated.[8] Recent review of Indian population has found hypovitaminosis D ranging from 42 to 74% among pregnant women, 70 to 81.1% among lactating mothers and 30 to 91.2% among adults.[9] We conducted a cross-sectional study to assess the association of vitamin D deficiency with CAD. We found that lower vitamin D levels were significantly associated with smoking, which is an important risk-factor for the development of CAD. There has been evidence which suggested that cigarette smoking led to lower vitamin D levels.[10] Cigarette smoke decreases the production of the active form of vitamin D (1, 25-dihydroxyvitamin D) in lung epithelial cells.[11] Cigarette smoke may also affect expression levels of the vitamin D receptor.[12]

In addition, lower vitamin D levels were almost statistical significantly associated with the presence of diabetes mellitus (*p* - value = 0.06) in our patient population.This is supported by the finding that polymorphisms of the Vitamin D Receptor (VDR) have been linked to diabetes.[13] It has been suggested that vitamin D acts to control many of the processes that initiate the onset of diabetes such as the formation of Ca^{2+} and Reactive Oxygen Species (ROS). The low levels of Vitamin D in obese patients may contribute to the onset of diabetes, because it functions to regulate many of the processes that are altered during the onset of both insulin resistance and the subsequent decline in β-cells that results in diabetes.[14] Ours being a smaller sample might have missed statistical association and should be investigated in future studies with larger samples.

We observed that the CAD patients had a significantly lower vitamin D levels and the severity of CAD in terms of percentage stenosis and number of vessels involved as also significantly associated with development of CAD. Two Indian studies had similar conclusions that low vitamin D was associated with increased risk for CAD[15,16]

and endothelial dysfunction and the patients with lower vitamin D had higher prevalence of double or triple vessel and diffuse CAD. Syal et al. found that those with lower 25 (OH) D levels had significantly lower brachial artery flow-mediated dilation (FMD; 4.57% *vs* 10.68%: $p < 001$) and significantly higher prevalence of impaired FMD (values < 4.5%; 50.6% *vs* 7%; $p < .002$). A graded relationship between 25 (OH) D levels and FMD was observed; impaired FMD was noted in 62.2%, 38.6%, and 13.3% in those with 25 (OH) D levels < 10 ng/mL, 10–20 ng/mL, and > 20 ng/mL, respectively. Salla et al. also found low Vitamin D levels in higher proportions in patients with single, double or triple vessel involvement.[17] This is in contrast to the results by Dhibar et al., who found that patients with normal coronary artery had much lower mean vitamin D (11.30 ng/ml ± 9.50) as compared to the patients with CAD (14.10 ng/ml ± 10.70).[18] Though the frequency of vitamin D deficiency was higher in patients with normal coronary artery as compared to the patients with CAD, it was statistically insignificant. There are a few limitations of this study. First, we could not follow the patients for survival analysis as this was a cross-sectional study. Second, our being a single center study, the results of this study might not be generalizable to other geographical locations, which might have varying patterns of vitamin D deficiency.

Conclusion

The result of the present study, add to the emerging body of evidence that vitamin D deficiency might be an independent risk-factor in cardiovascular diseases. Longitudinal multi-centric trials are needed to support the results of our study.

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Conflict of interest: None

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