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To study correlation of Vitamin D deficiency in coronary artery disease

[1]Ankit Anand, PG Resident, Department of Medicine, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly

[2]Mahesh Kumar Mehrotra, Associate professor and Corresponding author, Department of Medicine, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly

[3]Smita Gupta, Professor and Head, Department of Medicine, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly

[4]Sharat Johri, Professor, Department of Medicine, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly

[5]Ankit Grover, Senior Resident, Department of Medicine, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly

Corresponding Author: Ankit Anand, PG Resident, Department of Medicine, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly

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Abstract

Introduction: Vitamin D is a fat-soluble vitamin which has various extraskeletal effects. Several human and animal studies have suggested that vitamin D deficiency might be a contributory factor in the pathogenesis of coronary artery disease (CAD). Recent studies demonstrated that vitamin D level deficiency (<30ng/ml) is associated with higher blood pressure and directly or indirectly with CAD due to vascular endothelial damage.

Aim: To find the association of vitamin D deficiency with CAD

Materials and Methods: In this cross-sectional observational study, serum vitamin D level was measured in 60 patients who underwent coronary angiography.

Result- As the severity of angiographic stenosis increases the mean vitamin D level was also decreasing . But this difference was statistically significant only when we compared it with mean vitamin D level of the patients with normal coronary artery (p= <0.0001). The mean (±SD) vitamin D was 21.67 ± 4.5 in normal individuals and it decreases as level of stenosis increases. The vitamin D level in patients with 50-70% stenosis was 13.39 ± 4.22 , in 70-90% stenosis was 9.83 ± 4.73 and in >90% stenosis was 8.5 ± 4.19.

There was no statistically significant difference in frequency of vitamin D deficiency when we compared it between patients with normal coronary artery and CAD with 50-70% stenosis , >70%-90% stenosis and >90% stenosis (p= 0.113).

conclusion: Prevalence of vitamin D deficiency is very high in CAD. However this does not co-relate with the severity of CAD.

Introduction

Coronary artery disease is one of the major life-threatening disease and it has emerged as a major cause of death worldwide. Like many high income countries during the last century, low and middle income countries are also witnessing an alarming increase in the rates of CAD. The World Health Organization estimated a rise in mortality from Cardiovascular Diseases (CVD) from 17.1 million in 2004 to 23.4 million in 2030[i]. CAD and hypertension are major contributors to global health problem. There are many risk factors for CAD in addition to hypertension. It is therefore important to find out newer preventable and modifiable risk factors for CAD and hypertension to decrease mortality related to CVD.

Vitamin D is a fat-soluble vitamin which is also known as sunshine vitamin and it is unique in the sense that it also functions as a hormone. Apart from its pivotal role in calcium homeostasis and bone mineral metabolism, vitamin D is now recognized to be involved in a wide range of fundamental biological functions in cell differentiation, inhibition of cell growth and immunomodulation. Vitamin D deficiency has been shown to result in cardiac hypertrophy and fibrosis by elevation of matrix metalloproteinase enzymes[ii,iii]. Its deficiency also predisposes to hypertension by upregulation of the renin-angiotensin system[iv].

Vitamin D inhibits the uptake of cholesterol by macrophages and in Vitamin D deficiency, cholesterol uptake by macrophages is increased and these cholesterol- laden macrophages, also known as foam cells, deposit in the endothelium forming atheromatous plaque and promote atherosclerosis[v]. Vitamin D deficiency has also been associated with decreased levels of high-density lipoprotein and apolipoprotein A-1, which further on promotes atherosclerosis[vi].

Vitamin D deficiency has also been associated with impaired endothelial function and vascular stiffness, which leads to cardiovascular morbidity and mortality[vii]. Furthermore, endothelial dysfunction has been shown to promote atherosclerosis via several processes including vasoconstriction, increased platelet aggregation, leukocyte adhesion and cytokine generation[viii] .

Framingham study proved that people with elevated plasma levels of MMP-9 had increased left ventricular end-diastolic dimensions and wall thickness with consequent increased risk of mortality and morbidity from cardiovascular (CV) diseases[ix].

Vitamin D supplementation lowers blood levels of MMP-9 and MMP-2. Similarly, reversal of cardiomegaly by calcium and Vitamin D supplementation has been described in children with rickets and in an adult with congestive heart failure[x].

Materials And Methods

Study Design and Study Population: It was a cross-sectional observational study. A total of 60 patients were selected consecutively and underwent coronary angiography as per ACC/AHC guideline. Study was performed in Department of General Medicine, at SRMS - IMS Bareilly, Uttar Pradesh for duration of (1st January 2020 to 31th March 2020) . Patients were recruited as per medical ethics and informed consent was taken from each participant. Patients with 40-70 years of age, irrespective of gender were included in the study. Patients who were haemodynamically unstable, in shock or heart failure were excluded. Patients, who were already taking vitamin D, had known cardiac disease, chronic kidney disease, liver disease, hypo or hyperparathyroidism, pregnancy, evidence of infection and fever were also excluded from the study. Patients with anaemia (serum haemoglobin level <13g/dl for male and <12g/dl for female) were also

excluded as low haemoglobin is associated with increased risk and greater severity of CAD.

CAD was defined as patients with angiography proven stenosis of ≥50% in one or more major coronary arteries. These major arteries are left anterior descending artery, left main, left circumflex artery and right coronary artery. The angiography findings was reported as normal coronary artery, insignificant CAD, significant CAD with severity for coronary artery stenosis in the form of 50% to 100% or complete cut-off. In this study angiographic normal and insignificant CAD were included in the normal coronary artery group. The severity of stenosis was graded as 50%-70%, >70%-90% and >90%. Serum 25-hydroxyvitamin D (vitamin D) was measured in overnight fasting blood sample, 1-2 days prior to the coronary angiography. Serum vitamin D level was graded as, normal (>30ng/ml), insufficiency (20-30ng/ml) and deficiency (<20ng/ml). The severity of vitamin D deficiency was further graded as, moderate deficiency (>10-<20ng/ml), severe deficiency (>3-10ng/ml) and very severe deficiency (≤ 3ng/ml).

Statistical Analysis

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD. Quantitative variables were compared using Independent t Test between the two groups and ANOVA between more than two groups. Qualitative variables were compared using Chi-Square test/Fisher's Exact test. A p value of <0.05 was considered statistically significant. The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

Observation

Table 1: Baseline data

Baseline data	Population(n=60)	Vitamin D(ng/mL)	P value
Gender			
Female(%)	25(41.67)	13.64 ± 6.34	0.518
Male(%)	35(58.33)	12.54 ± 6.51	
Age(years)			
<=50(%)	5(8.33)	16.8 ± 7.05	
51-60(%)	24(40%)	13.17 ± 6.34	0.34
61-70(%)	31(51.67)	12.26 ± 6.36	
Smoker(%)	20(33.33)	12.15 ± 8.19	0.533
Diabetic(%)	28(46.67)	13.96 ± 5.58	0.280
Hypertension(%)	29(48.33)	13.79 ± 6.69	0.358
Coronary			
Normal(%)	12(20)	21.67 ± 4.5	
50-70% stenosis(%)	18(30)	13.39 ± 4.22	<.0001
70-90% stenosis(%)	18(30)	9.83 ± 4.73	
>90% stenosis(%)	12(20)	8.5 ± 4.19	

In this study total of 60 patients were included, out of which 25 were female and 35 were male and age group was grouped as <50 years , 51-60 years and 61-70 years. Co morbities - smoking , diabetes and hypertension is included. CAD stenosis is based on angiographic findings.

Table 2: Comparison of vitamin D level between coronary artery disease.

Vitamin D level	Normal (n=12)	50-70% (n=18)	70-90% (n=18)	>90% (n=12)	Total	P value	Test performed
Deficient{<20}	7 (58.33%)	18 (100%)	18 (100%)	12 (100%)	55 (91.67%)		
Insufficient{20-30}	5 (41.67%)	0 (0%)	0 (0%)	0 (0%)	5 (8.33%)	0.0003	Fisher Exact Test
Total	12 (100%)	18 (100%)	18 (100%)	12 (100%)	60 (100%)		

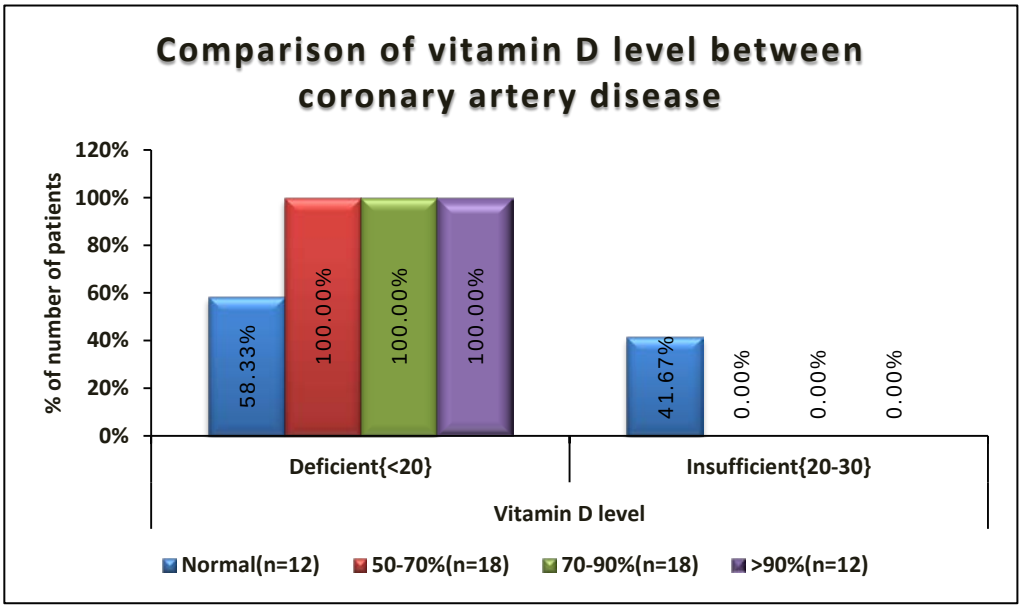

Figure 1:-Comparison of vitamin D level between coronary artery disease.

This figure signify that level of vitamin D was low (<20ng/dl) in patients with CAD as compared with patients with vitamin D insufficiency (20-30 ng/dl)

Table 3: Comparison of severity of Vitamin D deficiency between severity of coronary artery disease.

Severity of Vitamin D deficiency	Normal (n=12)	50-70% (n=18)	70-90% (n=18)	>90% (n=12)	Total	P value	Test performed
Moderate deficiency{>10 to <20}	7 (100%)	12 66.67%)	11(61.11%)	7 (58.33%)	37(67.27%)		
Severe deficiency{>3 to <=10}	0 (0%)	6 (33.33%)	3 (16.67%)	2 (16.67%)	11 (20%)	0.113	Fisher Exact Test
Very severe deficiency{<=3}	0 (0%)	0 (0%)	4 (22.22%)	3 (25%)	7 (12.73%)		
Total	7 (100%)	18 (100%)	18 (100%)	12 (100%)	55 (100%)		

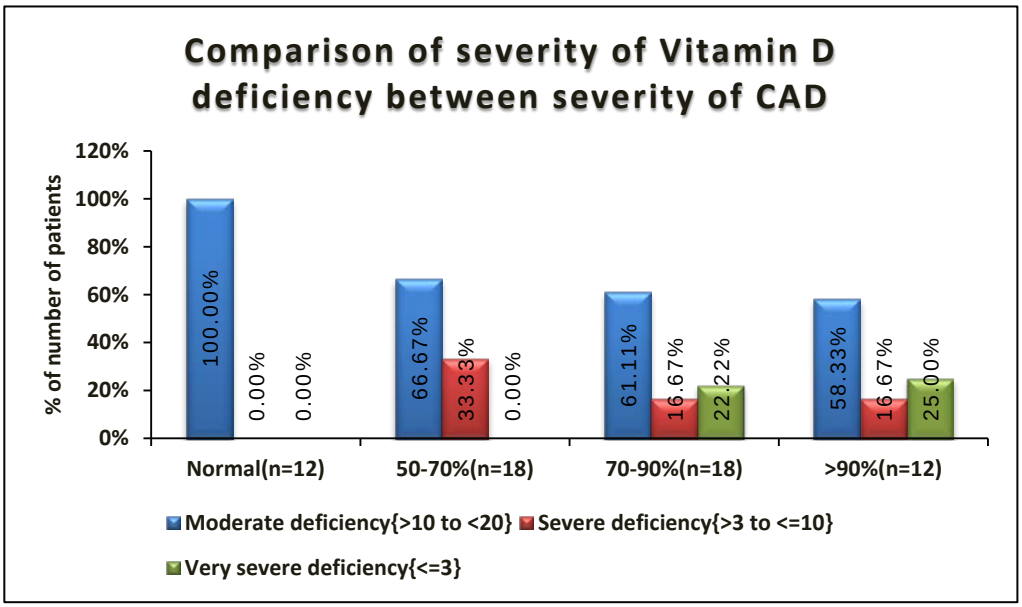

Figure 2:-Comparison of vitamin D level between severity of coronary artery disease.

This table signifies that level of vitamin D does not correlate with the angiographic severity of CAD although low level of vitamin D was present in all groups. As in very severe deficiency that is <3ng/dl , moderate deficiency is found in 58.33 % cases , severe deficiency in 16.67% and very severe deficiency in 25% cases. Hence there is no positive co-relation in level of vitamin D deficiency with severity of CAD.

Discussion

Vitamin D has been regarded as a key player in the development and regulation of skeletal system function but in the recent decade, it was speculated to be involved in the pathogenesis of several other diseases. Serum 25(OH)Vitamin D level was shown to be associated with the incidence of autoimmune diseases, malignancies, Alzheimer's disease and dementia[xi,xii] . Vitamin D

deficiency is more prevalent among patients with hypertension compared with general population[xiii].

The association between vitamin D deficiency and adverse cardiovascular outcomes has been investigated in multiple observational studies. Vitamin D deficiency was shown to be associated with fatal or non-fatal myocardial infarction[xiv].

In Multi-Ethnic Study of Atherosclerosis (MESA), an inverse association between serum 25(OH)VitD level and incident CHD risk was reported in white and Chinese participants after 8.5 years of follow-up, but not in blacks and Hispanics[xv]. Wang et al[xvi] observed a relation between low 25(OH)VitD level and incident cardiovascular diseases in patients with hypertension. SK et al[xvii] in a study of 100 Indian patients undergoing coronary angiography, the mean 25-OHD level was 14.8±9.1 ng/mL (36.9±22.7 nmol/L). Vitamin D deficiency was present in 80% and only 7% had optimal 25-OHD levels (>30 ng/ml or 75 nmol/L). Double or triple-vessel CAD (53% vs. 38%) and diffuse CAD (56% vs. 34%) were more prevalent in those with low vitamin D levels (<20 ng/ml or 50 nmol/L).

H Khalili et al[xviii] in a prospective study of 139 patients concluded that vitamin D deficiency (25-OHD) levels of <14 ng/ml (35 nmol/L) was present in 72.7% of the patients who presented with myocardial infarction. Similarly , JH et al[xix] in a cross-sectional population multicentre study demonstrated that vitamin D levels <30 ng/ml (75 nmol/ml) were present in almost all patients with AMI. Out of the 239 enrolled patients (mean age 57.6 years), 179 (75%) had low 25-OHD levels (≤20 ng/ml) and 50 (21%) had 25-OHD levels in the range of 20 to <30 ng/ml.

Syal et al[xx] reported a higher prevalence of vitamin D deficiency in angiographically proven CAD patients and noted a positive association with severity of CAD and endothelial dysfunction with vitamin D deficiency. Dhibar et al[xxi] concluded that vitamin D deficiency is also prevalent in subjects with angiography-proven normal coronary artery, and vitamin D deficiency and severity of deficiency does not correlate with angiographic severity of the disease. Karur et al[xxii] in their study noted that vitamin D deficiency is widely prevalent in newly diagnosed CAD patients presenting with myocardial infarction.

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