VITAMIN D DEFICIENCY IN ACUTE CORONARY SYNDROME: A STUDY IN GOVT. ROYAPETTAH HOSPITAL

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ABSTRACT

BACKGROUND

Vitamin D deficiency has been linked to an increased risk of coronary artery disease and cardiovascular death. Vitamin D deficiency promotes endothelial dysfunction, which plays a vital role in the pathogenesis of coronary artery disease.

AIMS AND OBJECTIVES

1. To assess vitamin D levels and study the correlation of Vitamin D deficiency with acute coronary syndrome.
2. To analyse the vitamin D status of the study population.

METHODS

Serum 25 (OH) vitamin D levels were measured in 50 cases of Acute Myocardial Infarction and 50 matched controls. The association of vitamin D deficiency with other parameters such as age, gender, body mass index, lipid profile, serum albumin, and calcium were also analysed.

RESULTS

64% of the cases were deficient in Vitamin D (<15 ng/mL) and 36% of the cases had insufficient levels (15-30 ng/mL). The mean vitamin D level among the cases was 13.5 ng/mL and that among the controls was 24.3 ng/mL and this was indicative of a statistically significant difference. In the 100 subjects, 45% were deficient and 43% had insufficient levels. 70% of the patients with vitamin D deficiency had BMI > 25 kg/m^2.

CONCLUSION

Vitamin D deficiency may be an independent and potentially modifiable cardiovascular risk factor that can be easily diagnosed and corrected. The treatment is safe and cost effective. Hence, general awareness needs to be created on the early detection and management of this risk factor and guidelines need to be implemented.

KEYWORDS

Acute Myocardial Infarction, Coronary Artery Disease, Vitamin D Deficiency, Body Mass Index.

HOW TO CITE THIS ARTICLE: Iyadurai R, Sundararajan S, Selayan K, et al. Vitamin d deficiency in acute coronary syndrome: a study in govt. royapettah hospital. J. Evolution Med. Dent. Sci. 2016;5(55):3722-3726, DOI: 10.14260/jemds/2016/854

INTRODUCTION

Cardiovascular diseases are the commonest cause of mortality and morbidity worldwide. Though, there are many well established risk factors for coronary artery disease emerging novel risk factors are being assessed by various epidemiological studies and continue to be an important aspect of debate regarding their nature of association and the role they play in reducing death and disability due to cardiovascular disease.

Financial or Other, Competing Interest: None.
Submission 02-06-2016, Peer Review 28-06-2016,
Acceptance 04-07-2016, Published 08-07-2016.
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DOI: 10.14260/jemds/2016/854

Over the recent years, there has been much emphasis and research over one such risk factor i.e. vitamin D deficiency, which is now attracting importance from many medical and nutritional communities as knowledge emerges of its biological function and its association with decreased risk of many chronic diseases. It has been estimated that around 1 billion people worldwide suffer from vitamin D deficiency.[1] In addition to its well-defined role as a major regulator of bone and calcium metabolism several studies have found associations of poor vitamin D status with coronary artery calcification and heart failure as well positive correlation with hypertension.[2,3] diabetes mellitus.[4,5] metabolic syndrome, atherosclerosis, peripheral arterial disease, cancer, and many autoimmune disorders.

Vitamin D deficiency has been linked to an increased risk of Coronary Artery Disease (CAD) and cardiovascular (CV) death. In a large randomized trial by Wang et al[2], individuals with vitamin D deficiency showed hazard ratio of 1.62 for incident cardiovascular events. Many data have shown that

cardiovascular morbidity and mortality are 30-50% more in regions of less sun exposure due to season or latitude and that mortality from CAD is highest in winter.[6] It was postulated that those with low vitamin D levels had almost 60% higher risk of Myocardial Infarction.

Following the discovery of the expression of vitamin D receptors and 1α hydroxylase in the myocardium and endothelium.[7] several biological mechanisms that link vitamin D with CAD and its risk factors have been identified. Vitamin D exerts its protective effects on the endothelium directly by regulating calcium ion entry or indirectly by protecting against oxidant stress. Vitamin D deficiency leads to endothelial dysfunction by creating a proinflammatory and prothrombotic environment. This promotes atheroma formation and progression. Vitamin D mainly acts through its role in maintaining calcium homeostasis and gene transcription to prevent cardiovascular disease and its risk factors.

The increasing rate of coronary artery disease and the associated morbidity and mortality make it necessary to develop further research in this study population. Hence, this study was designed to determine whether the presence of Hypovitaminosis D has significant correlation with coronary artery disease.

OBJECTIVES OF THE STUDY

1. To assess the serum levels of 25(OH) vitamin D in patients with Acute Myocardial Infarction and compare their levels with controls.
2. To study the prevalence of vitamin D deficiency in our study population and to assess the severity.
3. To identify any association between age, gender, BMI, lipid profile, calcium, and albumin with serum vitamin D.

MATERIALS AND METHODS

Study Design

Observation case control study.

Sample Size

100 (50 cases; 50 controls).

METHODOLOGY

Patients admitted with Acute Myocardial Infarction were chosen as cases in the study for a period of 6 months. 50 age and sex matched subjects were kept as controls.

Blood samples were drawn at the time of admission to measure the serum 25(OH) vitamin D, blood sugar, lipid profile, renal and hepatic function. A data collection form was prepared and each patient's clinical profile was noted.

Serum levels of 25(OH) vitamin D were measured using Chemiluminescence Immunoassay Technique.

Inclusion Criteria

Patients with Acute Myocardial Infarction admitted in the intensive coronary care unit at our hospital.

Exclusion Criteria

1. Age <18 years.
2. Diabetes.
3. Hypertension.
4. Prior history of cardiovascular disease.
5. Prior history of cerebrovascular or peripheral vascular disease.
6. Renal impairment.
7. Chronic liver disease.
8. Prior history of vitamin D supplementation.
9. Patients on drugs that affect vitamin D metabolism (Anti epileptics, steroids, rifampin).
10. Pregnancy and lactation.

Ethical Clearance

Obtained from the Institutional Ethical Committee.

Informed Consent

Patients who were willing to participate were included after getting their written informed consent.

Statistical Analysis

Data was entered in Microsoft Spreadsheet. Data analysis was done with the use of standard SPSS (Statistics Products Services Solutions) 16.0 Software Package. Descriptive statistics were used to calculate the frequency, mean, and Standard Deviation. Student 't' values were applied for significance. Significance was considered if the P value was below 0.05.

RESULTS

Both men and women between ages 25 to 80 years were included and their baseline characters are shown in Table 1.

	Cases (50)	Controls (50)	P value
Age (Years)	51.72±12.99	51.8±10.63	0.586
Sex (M:F)	45:5	44:6	1.000
BMI (Kg/m^2)	27.14±3.88	24.5±2.84	0.070
Smoking	39 (78%)	34 (68%)	0.368
Total Cholesterol (mg/dL)	209.02±31.95	182.38±20.33	0.126
Triglycerides (mg/dL)	170.94±48.77	122.74±23.57	0.147
Calcium (mg/dL)	8.92±0.74	9.09±0.62	1.000
25(OH) Vitamin D (ng/mL)	13.49±5.35	23.43±12.52	0.001

Table 1: Baseline Characteristics of Study Population

Vitamin D and Acute MI

We found a statistically significant correlation of Hypovitaminosis D in the patients with Acute Coronary Syndrome (Table 2 and 3).

Cases

All the patients who were admitted with the acute MI had subnormal vitamin D levels. 64% of the cases were deficient in vitamin D (<15 ng/mL) and 36% of the cases had insufficient levels (15-30 ng/mL).

Controls

26% had deficient levels and 50% had insufficient levels whereas only 24% of the control group had normal 25(OH) vitamin D levels.

On assessing the overall vitamin D status in our study population of 100 subjects, we found that only 12% had normal levels. Remaining 88% had low levels, out of which 45% were deficient and 43% were insufficient in vitamin D (Table 2).

	Cases (50)	Controls (50)	Total (100)
Deficiency (<15 ng/mL)	32 (64%)	13 (26%)	45%
Insufficiency (15-30 ng/mL)	18 (36%)	25 (50%)	43%
Normal (>30 ng/mL)	0	12 (24%)	12%

Table 2: Vitamin D Status in the Study Population

The mean vitamin D level among cases was 13.5 ng/mL and that among the controls was 24.3 ng/mL and this was indicative of a statistically significant difference (P value 0.001) as shown in Table 3.

	Cases (50)	Controls (50)	P value
25 (OH) Vitamin D (ng/mL)	13.49±5.35	23.43±12.52	0.001

Table 3: Mean Vitamin D Levels in the Study Population

Patients with low serum vitamin D were further divided into 3 categories based on the severity of vitamin D deficiency. Out of the 50 cases, 16 patients had mild deficiency and 16 had moderate deficiency. Among the controls, 8 patients had mild deficiency and 5 had moderate deficiency (Table 4).

72% of the cases and 29% of the controls had vitamin D deficiency. This showed a statistically significant correlation between subnormal vitamin D levels and Acute Coronary Syndrome.

Vitamin D Deficiency	Cases (50)	Controls (50)	Total (100)
Mild (10-15 ng/mL)	16 (36%)	8 (18%)	24%
Moderate (5-10 ng/mL)	16 (36%)	5 (11%)	21%
Severe (<5 ng/mL)	0	0	0
Total	**32 (72%)**	**13 (29%)**	**45%**

Table 4: Severity of Vitamin D Deficiency in Cases and Controls

Vitamin D and other Biochemical Parameters Studied

There was no significant correlation between 25(OH) vitamin D and serum cholesterol, triglycerides, calcium, and albumin (Table 5 and 6).

25 (OH) Vitamin D (ng/mL)	Total Cholesterol (mg/dL)		Triglyceride	
	<240	<240	<200	>200
Deficiency (<15 ng/mL)	43 (95.6%)	43 (95.6%)	32 (71.1%)	13 (29.9%)
Insufficiency (15-30 ng/mL)	41 (95.3%)	41 (95.3%)	31 (72.1%)	12 (27.9%)
Normal (>30 ng/mL)	12 (100%)	12 (100%)	8 (66.6%)	4 (33.3%)
P value	0.752		0.400	

Table 5: Correlation of Vitamin D with Total Cholesterol and Triglycerides

25 (OH) Vitamin D (ng/mL)	Serum Calcium		Serum Albumin	
	9-11 mg%	<9 mg%	<3.5 g%	> 3.5 g%
Deficiency (<15 ng/mL)	42 (93.3%)	3 (6.7%)	6 (13.3%)	39 (86.7%)
Insufficiency (15-30ng/mL)	37 (86.0%)	6 (14.0%)	4 (9.3%)	39 (90.7%)
Normal (>30ng/mL)	11 (91.7%)	1 (8.3%)	2 (16.7%)	10 (83.3%)
P value	0.512		0.734	

Table 6: Correlation of Vitamin D with Serum Calcium and Serum Albumin

Vitamin D and Body Mass Index

Out of 45 patients with vitamin D deficiency, 31 patients had BMI >25 kg/m^2 and in the 43 patients with vitamin D insufficiency, 15 patients had BMI >25 kg/m^2 (Table 7). This is in concurrence with many studies that link Vitamin D Deficiency to high BMI, Obesity, and Metabolic Syndrome.

25 (OH) D (ng/mL)	Body Mass Index			Total	P value
	Normal	Over Weight >25 kg/m^2	Obese > 30 kg/m^2		
Deficiency (<15 ng/mL)	14 (31.1%)	18 (40.0%)	13 (28.9%)	45	0.070
Insufficiency (15-30 ng/mL)	28 (65.1%)	11 (25.6%)	4 (9.3%)	43	
Normal (>30 ng/mL)	8 (66.7%)	4 (33.3%)	0	12	

Table 7: Correlation of VITAMIN D Status and BMI

Age and Gender Distribution of Vitamin D Levels

The study participants were divided into three age groups. There was significant decrease in vitamin D levels in the young CAD patients <40 yrs. Their mean vitamin D level was only 9.58 ng/mL when compared to the control group whose mean level was 26.52 ng/mL (Table 8).

Age Group	N	Mean 25 (OH) D (ng/mL)	
		Cases	Controls
20 - 39 years	12	9.58	26.52
40 - 59 years	62	15.08	24.15
> 60 years	26	13.54	20.83

Table 8: Vitamin D Status in Each Age Group

Among the cases, vitamin D deficiency was seen in 28 men and 4 women whereas insufficiency was seen in 17 men and 1 woman. In the control group, deficiency was seen in 12 men and 1 woman and insufficiency seen in 23 men and 4 women (Table 9).

Gender	N	Mean 25 (OH) D (ng/mL)	P value
Male	89	18.69±10.99	0.536
Female	11	16.54±9.28	

Table 9: Gender Wise Distribution of Vitamin D Levels

DISCUSSION

In our study of 100 patients, we included 50 cases of acute Myocardial Infarction and 50 age and sex matched controls. We had selected our cases on the basis that they had no

previous history of Diabetes, Hypertension, Dyslipidaemia, or prior cardiovascular disease because we wanted to study the association of low vitamin D levels as an independent risk factor for the occurrence of first cardiovascular event in the patient.

Our study showed significant correlation of serum 25(OH) vitamin D <30 ng/mL with Coronary Heart Disease. There was also a positive correlation of Hypovitaminosis D with high BMI.

Vitamin D levels were significantly low in the young patients (<40 yrs.) with acute MI.

In the CACTI study by Young et al,[8] the association of vitamin D deficiency with prevalent Coronary Artery Calcification was independent of known CAD risk factors including confounders such as BMI and mediators such as lipids. This adds proof to the fact that vitamin D is related to CAD through unique biologic mechanisms.

The Framingham Heart Study.[2] showed that patients whose vitamin D levels were <15 ng/mL had 60% greater incidence of cardiac events than those with higher levels. Shanker et al[9] found that low vitamin D levels were associated with increased risk for CAD in contrary to which Rajasree et al reported a paradoxical increase in coronary heart disease with 25 (OH) D levels >89 ng/mL compared to those with lower levels.[10] Sanjeev Kumar Sayl et al[11] observed a high prevalence of Hypovitaminosis D in Indian patients with angiographically documented CAD. They demonstrated that patients with lower levels of vitamin D had higher prevalence of severe (Double and triple-vessel CAD) and diffuse disease on coronary angiography, independent of established CV risk factors. In their study, endothelial dysfunction as assessed by brachial artery FMD (Flow mediated dilation) was also more frequently observed in those with low 25 (OH) D levels.[12]

The high rates of vitamin D deficiency in our study group is reflective of the high prevalence of Hypovitaminosis D in the Indian population as demonstrated in a study by Harinarayan et al, which showed that 50-90% of the people living in India are deficient vitamin D.[12] The mean vitamin D level in our control group was found to be 24.3 ng/mL. This is similar to the NHANES 2005-2006 survey that showed a mean vitamin D level of 24 ng/mL among apparently healthy subjects.

High mortality rates associated with CAD in people living far away from the equator was studied by Fleck et al[13] and Rosand et al[14] Grimes et al[15] showed that mortality was inversely proportional to the hours exposed to sunlight. He also proposed vitamin D as a protective factor by regulating serum cholesterol levels and by inhibiting Chlamydia pneumonia. Douglas et al[16] reported strong seasonal variation with higher mortality rates in winter when vitamin D levels are lowest. Many large prospective studies such as Framingham Offspring Study, The Health Professionals Follow up Study, The Third National Health and Nutrition Examination Survey (NHANES III) have proved association between low vitamin D levels and the risk of adverse cardiac events.[17]

Various studies have also claimed that vitamin D supplementation has reduced the incidence of CAD and its complications with a significant decrease, all cause mortality.[18]

Limitations of our study include a small sample size, the parathormone levels and the aetiology for low serum vitamin D was not evaluated. The patients were not followed up after vitamin D supplementation and hence we could not assess the prognosis.

Future Implications

- Routine estimation of serum vitamin D levels need to be done in those with CAD, diabetes, hypertension, and other risk factors because early detection and treatment of deficiency states have proven beneficial effects on mortality and morbidity.
- Diabetic and hypertensive patients with low vitamin D levels should be carefully monitored for CAD and other vascular events.
- Obese individuals and those with dyslipidaemia should also have routine estimations of serum vitamin D.
- India is a developing country with high prevalence of CAD in both urban and rural populations where poverty and illiteracy dominate. It is necessary to implement public health awareness programs and food fortification programs to overcome this deficit.

CONCLUSION

- Various epidemiologic data and observational studies show that serum vitamin D concentrations are lower in patients with coronary heart disease and other cardiovascular risk factors.
- Our analysis revealed that serum 25(OH) vitamin D was significantly lower in cases of Acute Myocardial Infarction. High BMI significantly correlated with Hypovitaminosis D.
- These findings may have potentially broad public health implications given the high prevalence of vitamin D deficiency in our country and the contribution of lifestyle and geography to vitamin D status.
- Large scale prospective randomized controlled trials are needed to firmly establish the role of vitamin D deficiency in cardiovascular health and to study the effects of vitamin D supplementation on the prognosis and prevention of coronary artery disease.
- In the meanwhile, monitoring and correction of vitamin D deficiency is indicated for optimization of general health.

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