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"CORRELATION OF VITAMIN D AND LIPID PROFILE IN CORONARY ARTERY DISEASE"

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Abstract

Background: Cardiovascular disease (CVD's) are the chief cause of mortality in country like India, were quarter of all mortality are due to CVD. Vitamin D inhibits inflammation through a variety of mechanisms. The aim of the study was to assess the influence of vitamin D level on the lipid profile of patients of coronary artery disease.

Material & Method: The present hospital based observational study was conducted among the patients who are more than 18 yrs with signs, symptoms and investigation (ECG) of coronary artery disease admitted to the AVMC hospital. Patients with chronic kidney disease, patients with elevated CRP, fever, patients with cancer and on supplementation of Vitamin D3 were excluded from the study. The lipid parameters and vitamin D3 were measured to assess the relation.

Results: In present study total of 160 patients included with mean age of patients was found to be 51.75±8.58yrs, 68.8% were male. Vitamin D deficiency was seen in 50%, insufficiency in 40.6% and sufficiency in 9.4% patients. We found a significant higher incidence of dyslipidemia among the patients with deficiency and insufficient vitamin D compared to sufficient vitamin D levels.($p<0.05$) Also there is significant negative correlation of total

cholesterol and LDL cholesterol with the vitamin D3 level and a significant positive correlation with the HDL cholesterol. ($p<0.05$)

Conclusion: There is higher incidence of presence of vitamin D deficiency and insufficiency among the patients with coronary artery disease in the present study

Keyword: Coronary Artery Disease, Vitamin D, Deficiency, Lipid parameters, Mortality

Introduction

The World Health Organization (WHO) estimates that 54% of deaths from non-communicable diseases are due to cardiovascular diseases (CVD), which involve various anomalies in the heart or the coronary arteries and other blood vessels.Inspite of important progress in medication and improvement in techniques of coronary intervention, the therapeutic outcome is still not satisfactory. So far, several risk factors of a cardiovascular event have been identified; however, much attention is still paid to finding new ones. Some people propose vitamin D deficiency, affecting 50% of the world population, which may increase occurrence of cardiovascular diseases.[1-2]

In spirit of humanity's continued quest of new armamentarium for improved quality of life, some promising test results showed an independent relation between low levels of vitamin D and documented risk factors of cardiovascular event such as hypertension,[3] atherogenic lipid profile,[4] diabetes,[5] and obesity.[6] Particularly noteworthy is the effect of vitamin D on the lipid profile. Many studies have found an inverse relationship of 25(OH)D in serum and different cholesterol fractions, what makes the study interesting is the role of Vitamin D in pathophysiology of coronary artery disease.[5,7,8] Inflammation found in the wall of large and medium arteries in the course of atherosclerosis is induced in response to destruction of endothelium. It was demonstrated that calcitriol is able to normalize endothelial cell function through decreased production of reactive oxygen species, increased activity of endothelial nitric oxide synthase, and protection of endothelial cells from end-products of glycosylation. Furthermore, it regulates proliferation, differentiation and function of immune system cells through inhibition of prostaglandin and cyclooxygenase-2 synthesis and induction of anti-inflammatory cytokines

A thin layer of connective tissue, large lipid nucleus, activity of inflammatory cells and increased neovascularisation are the main factors involved in destabilization of the

atherosclerotic plaque. Apart from its anti-inflammatory properties, calcitriol inhibits transformation of macrophages into foam cells, inhibits the activity of metalloproteinases , and negatively influences angiogenesis by inhibition of vascular endothelial growth factor (VEGF) and induction of apoptosis in epithelial cells .

After rupture of the atherosclerotic plaque, its lipid contents are released and the blood coagulation process is initiated. Calcitriol exerts its anticoagulant activity through down-regulation of tissue factor, increased production of thrombomodulin and inhibition of platelet adhesion to endothelium. The obtained results can contribute to enhancement of the strategy in prevention of coronary heart disease

Material & Method:

This hospital based observational study was conducted in AVMC HOSPITAL , Puducherry . Study participants included all cases above 18 yrs who had signs, symptoms and investigations (ECG) of coronary artery disease admitted to the hospital. Patients of CKD ,elevated markers of inflammation(CRP) or fever, with cancer (paraneoplastic syndromes and associated disorders of calcium-phosphate),on drugs or dietary supplements containing vitamin D or calcium were excluded from the study

Results:

The aim of the study was to assess the influence of vitamin D level on the lipid profile of patients of coronary artery disease. In present study total of 160 patients fulfilling inclusion criteria were included after obtaining the informed consent. The mean age of patients was found to be 51.75±8.58yrs. Among the included patients, 68.8% were male and 31.3% were female patients with male preponderance in the study. In present study, 57.5% were urban resident by location and 42.5% were rural. In present study, 46.9% were unemployed and 53.1% were employed. In present study, 71.3% were cigarette smokers and 28.8% were non-smokers. In present study, 60% were having history of alcohol consumption and 40% without

the alcohol consumption. In present study, dyslipidemia was seen in 73.8% and 26.3% without dyslipidemia .On assessment of vitamin D3 level, it was found that 50% were with vitamin D deficiency, 40.6% with insufficient vitamin D3 and 9.4% with sufficient vitamin D3.

On comparison of the presence of dyslipidemia with vitamin D status, we found significant higher incidence of dyslipidemia among the patients with deficiency and insufficient vitamin D compared to sufficient vitamin D levels.($p<0.05$).On comparison of the mean levels of lipid parameters between the groups of vitamin D status, it was found that there is significant higher mean level of total cholesterol, triglycerides, and LDL cholesterol and significant lower HDL among the patients with insufficiency and deficiency levels compared to sufficiency level of vitamin D.($p<0.05$).On Pearson's correlation, there is significant negative correlation of total cholesterol and LDL cholesterol with the vitamin D3 level and a significant positive correlation with the HDL cholesterol. ($p<0.05$)

		Frequency	Percent
Dyslipidemia	Absent	42	26.3
	Present	118	73.8
	Total	160	100.0

Table1: Showing the presence of dyslipidemia among the included patients

		Frequency	Percent
Vitamin D3	Deficient	80	50.0
	Insufficient	65	40.6
	Sufficient	15	9.4
	Total	160	100.0

Table 2: Showing the vitamin D 3 status of included patients

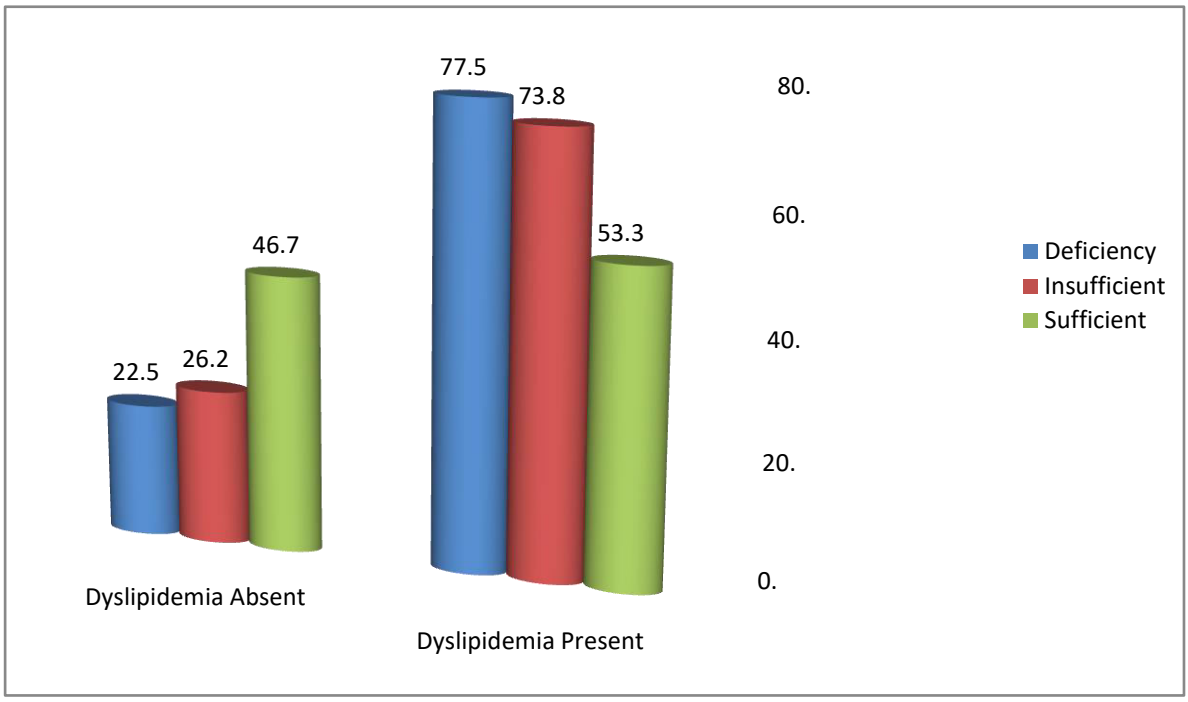

Figure 1: Comparison of dyslipidemia with the vitamin D status in patients

	Vitamin D3						p-value
	Sufficient		Insufficient		Deficient		
	Mean	SD	Mean	SD	Mean	SD	
T Cholesterol inmg/dL	201.1	28.4	210.0	32.3	215.6	39.2	0.01*
TG in mg/dL	150.1	41.4	167.2	44.1	160.8	48.3	0.01*
LDL in mg/dL	135	15.2	149.0	16.6	151.1	16.5	0.01*
HDL in mg/dL	26.8	3.3	21.6	3.3	23.4	4.3	0.01*

Table 3: Comparison of mean level of lipid profile with vitamin D status among patients

Discussion:

There are gaps in our understanding of vitamin D's involvement in the prevention of cardiovascular disease. Data from laboratory studies, ecological studies[9] and epidemiologic studies demonstrate that vitamin D has a protective impact against CVD[10] Vitamin D supplementation improved the severity of illness in individuals with rheumatoid arthritis, psoriasis, and scleroderma. In a number of studies,it was shown that a reduction in plasma levels of vitamin D was associated with the risk of ischemic heart disease, myocardial infarction, and sudden death.[11-14]

In the CACTI study by Young et al.[15] 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

It was observed in the Framingham heart study that those patients whose Vitamin D levels were <15ng/ml had a 60% greater incidence of cardiac events than those with higher levels. Though there are many meta analyses that have reported both positive and neutral correlations, some Indian studies have even reported that high levels of vitamin D may attribute to ischemic events.

Shanker et al.[16] 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.[17] Sanjeev kumar Syal et al. 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 was also more frequently observed in those with 25(OH)D levels.[18]

High mortality rates associated with CAD in people living far away from the equator was studied by Fleck et al.[19] and Rostand et al.[20] Grimes et al.[21] showed that mortality was inversely proportional to the number of 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.[22] reported a strong seasonal variation with higher mortality rates in winter when Vitamin D levels are lowest. Many large prospective studies such as The Framingham Offspring Study, The Health Professionals Follow up Study, The Third National

Health and Nutrition Examination Survey (NHANES III) have proved a positive association between low Vitamin D levels and the risk of adverse cardiac events.[23] Hence, many studies suggest that poor Vitamin D status is associated with poor cardiovascular outcomes.

Many reports argue that the 25(OH)D acts as a acute phase reactant and its levels reduce significantly during disease processes, similar to other vitamins. Moreover, there isn't substantial evidence to state that a single hormone can be a harbinger of such severe and diverse disease processes[24].

In spite of these controversies, there are multiple studies worldwide reporting positive correlation between low vitamin D levels and adverse cardiac events. Various studies have also claimed that Vitamin D supplementation has reduced the incidence of cardiovascular disease and its complications with a significant decrease in all-cause mortality.[25]

In concordance to present study, Dziedic EA et al., documented 25(OH)D level had a statistically significant negative connection with TC ($p = 0.0057$), LDL-C ($p = 0.00037$), and TG ($p = 0.00017$) throughout the whole research group.Women and men over the age of 70 had an inverse relationship between their 25(OH)D levels and the stage of coronary atherosclerosis. The levels of TC, LDL-C, and TG are affected by 25(OH)D deficiency.[26]

Some studies documented the vitamin D level linked to the blood pressure changes and the atherosclerosis severity among the patient. There by improvement in vitamin D level may reduce the cardiovascular related morbidity and mortality.[27] The relationship between baseline vitamin D status, vitamin D supplement dose, and cardiovascular events is still being studied in ongoing randomised trials; however, growing evidence suggests that providing a simple, well-tolerated, and low-cost correction of vitamin D deficiency favourably affects the

morbidity and mortality of cardiovascular disease, as well as the prevention of the most common chronic degenerative diseases.[28]

.Studies conducted on adolescents, revealed that the low level of vitamin D is obviously accompanied by abdominal obesity, elevated hypertension, and high fasting blood sugar (FBS) and metabolic syndrome.[29] Previous studies also showed that vitamin D deficiency is associated with cardiovascular risk factors such as hypertension, hypercholesterolemia, obesity and diabetes mellitus.[29-31]

Another study that divided 2910 patients with coronary artery disease history (acute myocardial infarction-unstable angina- stable angina) to three groups on the basis of their angiography results showed that although vitamin D deficiency is prevalent in all groups, it is more prevalent in patients with stable angina and also it is indicative of a worse prognosis (such as death, MI, cerebral stroke, or the need to revascularization) in them.[32]

However, how vitamin D influences lipid profile is not clear yet. Previous data has suggested that increasing intestinal calcium absorption could reduce synthesis and secretion of hepatic TG.[33] Vitamin D could inhibit synthesis and secretion of TG through stimulating intestinal calcium absorption. It has also been suggested that increased level of intestinal calcium could reduce intestinal absorption of fatty acid due to the formation of insoluble calcium-fatty complexes.Serum levels of LDL-C would be reduced by the decreased absorption of fat, particularly saturated fatty acids.[34] In addition, calcium could promote the conversion of cholesterol into bile acids and thereby reduce the level of cholesterol.[35]. In addition, previous studies have provided a strong evidence that vitamin D deficiency may be associated with impaired b-cell function and insulin resistance which could affect lipoprotein metabolism and lead to an increase in TG level and a decrease in HDL-C level.[36] In addition, vitamin D has been suggested to be involved in lipid metabolism such as the

synthesis of bile acid in the liver[37], suggesting that vitamin D may affect the regulation of lipids directly.

Hence, to conclude, our study showed a positive correlation of low Serum 25(OH) Vitamin D < 15ng/ml as a risk factor for Coronary Heart Disease. There was also a positive correlation of Hypovitaminosis D with high Body Mass Index > 25 kg/m2

Conclusion

There is higher incidence of presence of vitamin D deficiency and insufficiency among the patients with coronary artery disease in the present study. Also there is significant higher incidence of the dyslipidemia among the patients with lower vitamin D levels compared to normal vitamin D levels. There was significant strength of association was documented between the lipid parameters with the serum vitamin D levels showing the role of vitamin D deficiency in the pathophysiology in coronary artery disease

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