

STUDY OF VITAMIN D LEVELS IN PATIENTS OF ACUTE MYOCARDIAL INFARCTION*Mrinal Debbarma¹, Arunabha Dasgupta², Chinmoy Biswas³*¹Senior Resident, Department of General Medicine, Tripura Medical College, Agartala, Tripura.²Associate Professor and I/C HOD, Department of General Medicine, Agartala Government College, Agartala.³Director of Medical Education, Government of Tripura.

ABSTRACT

BACKGROUND

Acute myocardial infarction (AMI) is a major concern globally and recent studies explored the role of vitamin D deficiency as one of the predisposing factors and documented its deleterious effect both in mortality and morbidity associated with the incident. Apart from its usual role of maintaining calcium homeostasis in humans new found role of vitamin D as a risk factor in cardiovascular incidents have gathered interest and it was proven by various studies available in literature that Vitamin D deficiency adversely affects post MI cardiac remodelling. So, hypovitaminosis D is also a major concern and needs therapeutic interventions. The present study was done with an aim to reveal any association existing between AMI cases & Vitamin D deficiency.

Aims and objectives- To study Vitamin D (25(OH)D) level in AMI cases and to study any significant statistical association existing between AMI cases & Vitamin D level.

MATERIALS AND METHODS

It is a case control study conducted at Agartala Government Medical College, Agartala, Tripura, at Department of Medicine, where 130 patients of AMI are included and they underwent necessary biochemical investigations including 25(OH) D. These values were compared with the values of 25(OH) D done on 130 healthy controls matched with same age and gender. The Statistical Package for Social Science version 16 IBM Corporation was used for analysis. P value of $P < 0.05$ was considered significant.

RESULTS

The mean value of 25(OH) D among the cases was 20.39 ± 6.96 and among the healthy controls was 24.08 ± 7.68 . Experts opine that the normal value of Vitamin D in humans is ≥ 30 ng/ml. With P Value < 0.05 , a significant association of Vitamin D level and occurrence of AMI was documented. The adjusted Odds Ratio was 3.034 and its 95% Confidence Interval was 1.119-8.225. It proves that subjects with deficient Vitamin D levels are having 3 times more chances of developing AMI than individuals with normal Vitamin D and this value is statistically significant. Low level of Vitamin D was found among those subjects who simultaneously were hypertensive, diabetic and hyperlipidaemic. Thus, it was inferred that low level of 25(OH) D is also an important risk factor of AMI and it adversely affects both mortality and morbidity of the disease.

CONCLUSION

This case control study was first of its kind done in our state to study the association of Vitamin D and occurrence of acute myocardial infarction. Patients were selected from medicine emergency and a total of 130 cases were studied along with 130 healthy controls matching same age and gender. All cases of AMI and their healthy controls were evaluated for 25 (OH) D levels and it was documented that the mean level of Vitamin D in cases was 20.39 ± 6.96 whereas in controls it was 24.08 ± 7.68 . The calculation of AOR was 3.034 & 95% CI was 1.119-8.225. This statistical data proves that vitamin D deficient individuals have 3 times more chance of developing AMI and similar findings were also documented by various studies available in literature globally.

KEYWORDS

Acute Myocardial Infarction, Vitamin D, deficiency, Risk Factor.

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**BACKGROUND**

Vitamin D is a fat-soluble vitamin resembling a steroid structure and functioning like a hormone; it was isolated in 1931 by Angus who named it calciferol.¹ It is synthesized by most of the vertebrates on adequate exposure of the skin to sunlight and it is critical that vertebrates obtain a sufficient amount of vitamin D either from exposure to sunlight or from diet which in humans includes fatty fish, fish liver oils and egg yolk.²

The active form of vitamin D is 1, 25(OH)₂D but its status in serum level is not clinically useful to judge vitamin D status; instead its precursor 25(OH)D is the major circulating form of vitamin D and its concentration reflect both vitamin D intake as well as endogenous production and hence an individual's overall vitamin D status.³

So, serum levels of 25(OH)D are used in clinical settings to assess vitamin D status & most experts define on optimal level is 30 ng/ml and deficiency below 20 ng/ml where as a level in between 21 ng/ml to 29 ng/ml is termed as vitamin D insufficiency.^{3,4}

Human studies indicate that 1, 25(OH)₂D inhibit rennin synthesis and thus may lower blood pressure and it is done by suppression of rennin gene expression.⁵ Hypertension plays a major role in development of left ventricular hypertrophy (LVH) and important contributor for development of coronary artery diseases (CAD). Vitamin D deficiency directly promotes development of hypertension and also leads to enhanced atherosclerosis with vascular smooth muscle proliferation with increased production of pro-inflammatory cytokines responsible for CAD.^{6,7} Further vitamin D deficiency triggers secondary hyperparathyroidism and parathyroid hormone promotes myocyte hypertrophy and too has a pro-inflammatory effect with release of cytokines.⁴

Weishaar RE et al found that cardiac myocyte lack 1 alfa-hydroxylase activity, the enzyme which converts inactive vitamin D to active form and hence depends on circulatory vitamin D and consequently its deficiency has been associated with cardiac contractility poor performance, cardiomegaly and LVH.^{8,9,10}

New found evidences suggest that vitamin D has a role in development of other risk factors of CAD, and they include not only hypertension but also diabetes mellitus and metabolic syndrome.^{11,12}

The incidence of Acute Myocardial Infarction (AMI) in India is 64.37/1000 people in men aged 29-69 years and death is 31.7%.¹³ It is a known fact that atherosclerotic plaque rupture, ulceration of plaque with the resultant formation of intraluminal thrombus in one or more coronary arteries leading to decreased or stoppage of coronary blood flow ensues myocardial myocyte necrosis.¹⁴

Apart from its known role in human body, such as in bone & calcium metabolism; vitamin D is now increasingly seen as an important risk marker in myocardial infarction and CAD, not only in causation but also in morbidity and mortality associated with this incident.¹⁵

Vitamin D deficiency is known to cause adverse cardiovascular events in a post-MI setting and adversely affects post-MI cardiac remodelling.

Hence besides the known traditional risk factors associated with CAD, new risk factors are like Vitamin D deficiency are now recognised which requires therapeutic interventions and in the present-day scenario hypovitaminosis D is a new-found interest of focus.¹⁵

In this study the new-found evidences supporting the relationship between vitamin D and acute myocardial infarction and prognostic relevance are documented as

found in our state, which is a hilly place and having deep vegetations with diverse ethnic food habits. And all these environmental diversities might influence vitamin D status.

Aims and Objectives

1. To estimate the Vitamin D levels in patients with acute myocardial infarction
2. To study the association between Vitamin D level and acute myocardial infarction.

MATERIALS AND METHODS

This is a case control study done at Agartala Government Medical College, Agartala, Tripura over a period of one year and half years.

Total sample sizes of 130 patients of acute myocardial infarction were included in the study and 130 controls were also included.

Inclusion criteria:

A patient was considered as a case of AMI if two of the three criteria were positive on admission fulfilling the definition of AMI by the third Universal MI Task Force.¹⁴ (Clinical symptoms, ECG changes & raised enzymes levels) and those patients who have given consent for the study.

Controls were healthy subjects from patient's party matching to the cases for age and gender.

Exclusion Criteria

Known case of vitamin D deficiency, patients on vitamin D supplements, known case of Chronic Renal Failure, known case of chronic liver disease, patients with underlying malignancies and those individuals not willing to be a part of the study are excluded.

The study was performed after getting clearance from Institutional Research Committee and Institutional Ethics Committee.

Study subjects were male and female patients admitted with AMI & controls were age and sex matched subjects, a normal individual, without AMI, & informed consent was taken from both study subjects and controls.

A detailed history, general and physical examination were done along with all required investigations, including ECG and cases with ST segment elevation in ECG were included for study.

Socio-demographic data of each individual and data pertaining to clinical variables like pre-disposing factors of smoking, diabetes mellitus, hypertension, hyperlipidaemia along with chronic renal failure, chronic liver diseases and past history of CAD with history of any percutaneous coronary angioplasty and coronary by-pass grafting were collected.

Serum samples were obtained and before initiation of any treatment. The laboratory investigation included complete haemogram, blood sugar, HbA_{1c}, renal function tests, liver function tests, lipid profile, cardiac enzymes – troponin & creatinine kinase MB, calcium, phosphorus and 25(OH)D estimation.

25(OH) D levels were estimated by ELFA technique by Vidus analyser from Biomerieux.

Comparison of means and status of vitamin D and risk factors were conducted after matching each case with next control subjects recruited of the same age and gender.

The Statistical Package for Social Science version 16 IBM Corporation was used for analysis. P value of $P < 0.05$ was considered significant.

RESULTS

A total of 130 patients of AMI and 130 healthy controls were worked up in this study.

The minimum age documented was 38 yrs. & maximum age was 92 yrs. and maximum number of cases in between 53 to 62 yrs. constituted 49.2% of cases.

Among the subjects 60% were male and 40% were females.

The mean value of vitamin D studied showed that the study cases had 20.39 ± 6.96 of vitamin D level in comparison to the control groups who had a mean level of vitamin D of 24.08 ± 7.68 with an estimated P value = 0.000 which is highly significant and suggested that vitamin D level is different in both the groups.

The study of distribution of Vitamin D levels showed that deficiency of vitamin D (≤ 20 ng/ml) amongst cases was 48.4% and in controls it is 28.4%

The insufficiency of vitamin D (21-29 ng/ml) amongst cases is 43% and controls it is 55.3%.

Sufficient level of vitamin D (≥ 30 ng/ml) was found in 8.4% of cases and in controls it was 16.1%.

With a P value =0.003 a significant association was studied between vitamin D levels and AMI incidents. Deficiency of vitamin D was found in patients of AMI.

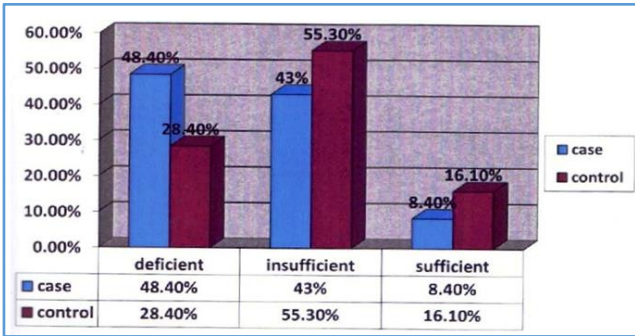


Figure 1. Distributions of Vitamin D Status Among Cases and Controls

Logistic regression model documented the following association of vitamin D level & AMI.

Status of Vitamin D Level (ng/ml)	Adjusted Odds ratio(AOR)	95% Confidence Interval(CI)	P Value
Deficient (≤ 20)	3.034	1.119-8.225	0.029
Insufficient (21-29)	1.371	0.524-3.586	0.521
Sufficient	1	-	-

Table 1

Thus, it was documented that subjects with deficient vitamin D level has 3.034 times more chances of developing AMI and it is statistically significant, $P=0.029$.

Therefore, deficiency of vitamin D constitutes an important risk for development of AMI.

The association of vitamin D with other cardiovascular risk factors known to be responsible predisposing factors for development of AMI was studied and results were analysed.

The Results Showed the Following-

1. 26.1% of AMI cases who were hypertensive had deficient Vitamin D level
2. 25.3% of AMI cases who were diabetics had deficient Vitamin D level
3. 32.5% of AMI cases who were dyslipidemic had deficient Vitamin D level.
4. 26.9% of AMI cases who were smokers had deficient Vitamin D level.

Both cases and controls with sufficient Vitamin D levels had least number of other cardiovascular risk factors.

DISCUSSION

This case control study was done at Agartala Government Medical College, Agartala Tripura to recognise any significant association existing between Acute Myocardial Infarction and Vitamin D levels along with other established risk factors for CAD.

Literatures showed not many studies were done to establish any relationship existing between Vitamin D level and AMI and this study is first of this kind of our state where various tribal and non-tribal populations are residing with diverse food habits and mostly they are fish consuming population.

Vitamin D levels were done in both the case study and control groups and Vitamin D level was significantly lower among cases compared to their age and gender matched controls with a $P<0.05$. This result is concurrent with the findings of Scragg et al where age and sex matched controls of 179 pairs obtained by random sampling of general population in Auckland area of New Zealand were analysed and they too found significantly low mean Vitamin D level in patients with AMI.¹⁶

Lund et al compared Vitamin D level along with seasonal variations and found low level of vitamin D level in winter season amongst patients of both angina and AMI in contrast to the timings in between July–August, indicating that Vitamin D level changes with sun exposure and seasons.¹⁷

In Indian scenario, studies done by Satish Karur et al have found the prevalence of Vitamin D deficiency was higher in patients of CAD and as well as established AMI cases. In this study $P<0.05$ was found demonstrating significant association of Vitamin D levels and AMI.¹⁸

Taking Vitamin D level ≤ 20 ng/ml as deficient, Odds ratio of vitamin D was calculated in cases compared to controls and adjusted with other risk factors as co varieties. The adjusted odd ratio (AOR) was 3.034 & its 95% Confidence Interval (CI) was 1.119-8.225.

It proves that subjects with deficient Vitamin D levels has 3.034 times more chance of developing AMI & this value

being statistically significant it can be assumed that Vitamin D deficiency constitute a risk factor for development of AMI. In a review article published by Pittas et al, the authors analysed the role of Vitamin D on different cardiovascular outcomes & effect of vitamin D supplementation. They identified seven longitudinal studies and all studies measured 25(OH) D concentration and found low levels are associated with increased risk of cardiovascular disorders.¹⁹

In Framingham Offspring study found similar results with low levels of vitamin D, showing increased risk for all types of cardiovascular events but the association was strongly significant with subjects with hypertension at baseline.²⁰

So this study is concordant with most of the study available in the literature and point towards maintaining of a normal level of Vitamin D to prevent cardiovascular events.

This study also showed that controls have statistically significantly more number of subjects with insufficient Vitamin D levels which is a matter of concern. The lack of adequate sunshine, inadequate intake of vitamin D and sedentary life styles are possible reasons even though this area is a fish consuming population.

CONCLUSION

This case control study was first of its kind done in our state to study the association of Vitamin D and occurrence of acute myocardial infarction. Patients were selected from medicine emergency and a total of 130 cases were studied along with 130 healthy controls matching same age and gender. All cases of AMI and their healthy controls were evaluated for 25 (OH) D levels and it was documented that the mean level of Vitamin D in cases was 20.39 ± 6.96 whereas in controls it was 24.08 ± 7.68 . The calculation of AOR was 3.034 & 95% CI was 1.119-8.225. This statistical data proves that vitamin D deficient individuals have 3 times more chance of developing AMI and similar findings were also documented by various studies available in literature globally.

So along with other established risk factors of AMI like hyperlipidaemia and hypertension, Vitamin D deficiency too is an important risk factor and further multicentre interventional trials are needed for prognostic therapeutic conclusions.

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