STUDY OF SERUM VITAMIN-D LEVELS IN YOUNG ADULTS WITH ST ELEVATION MYOCARDIAL INFARCTION

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Abstract

Background: Cardiovascular Diseases (CVD) is considered as the leading cause of health problems that influence the life of the people. Indians are more vulnerable to have coronary artery disease (CAD) in young age group with a prevalence of 5-10%. It is well known that vitamin D insufficiency, or deficiency, is highly prevalent in the general population. Peripheral arterial disorders are reported to be associated with low serum vitamin D levels. A growing amount of data has highlighted the potential link between vitamin D and major cardiovascular risk factors, such as diabetes, hypertension, and chronic kidney disease.

Aim: To assess the serum levels of 25(OH) vitamin D in patients with Acute ST Elevation Myocardial Infarction (STEMI) in young patients (aged ≤ 45 years).

Material and Methods: It was an observational age and sex matched case-control study conducted at PT. B.D. Sharma Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, in the Department of Cardiology for 12 months after the approval from ethical committee of PGIMS Rohtak. A total of 100 patients (50 case and 50 controls) were selected.

Results: A statistically significant correlation of hypovitaminosis D in the patients with age less than 45 years with acute myocardial infarction was observed. Most of patients who were admitted with acute MI had subnormal vitamin D levels. Statistically significant association was observed between vitamin D Level and case group ($p<0.001$). Participants in case group were having significantly higher vitamin D deficiency. There was significantly higher vitamin-D deficiency in age group of 36-45 years when compared to age group of 26-35 years among case group (p value < 0.001).

Conclusion: In present study, vitamin D insufficiency was found in most of the patients with acute myocardial infarction and was linked to many of its risk variables. Hypovitaminosis D is associated with other cardiovascular risk factors including hypertension, diabetes, obesity, metabolic syndrome and dyslipidaemia. The present study was proposed to assess the 25(OH) vitamin D status with acute ST elevation myocardial infarction in young patients of age less than 45 years and revealed that serum 25(OH) vitamin D levels were significantly lower in the cases of acute myocardial infarction when compared to the control population.

To prevent cardiovascular problems, this highly frequent vitamin D deficiency should be screened and treated adequately. The clinical analysis has shown that vitamin D deficiency is having a significant adverse impact on the cardiac function and blood pressure in AMI. Moreover, the vitamin D is exerting biological effects on cardiac myocytes, by stimulating calcium-ATPase activity and calcium uptake in cardiac myocytes.

Keywords: Cardiovascular Diseases (CVD), Vitamin-D, Acute ST Elevation Myocardial Infarction (STEMI), Acute ST Elevation Myocardial Infarction in young, STEMI in young, STEMI in Vitamin-D Deficiency.

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Introduction

Cardiovascular Diseases (CVD) is considered as the leading cause of health problems that influence the life of the people.[1] According to analysis, ischemic heart disease (IHD) is affecting the health of more than 126 million individuals(1,655 per 100,000), around the world which is approximately 1.72% of the world's population and is a cause of 9 million deaths in the world.[2]Indians are more vulnerable to have coronary artery disease (CAD) in young age group with a prevalence of 5-10%,[3] with over 50% of CAD mortality occurring in individuals aged less than 50 years, and one-fourth of all acute Myocardial Infarctions (MIs) are reported in patients below 40 years.

The major modifiable risk factors that account for over 90 percent of the population-attributable risk of a first MIare high blood pressure, abnormal blood cholesterol, tobacco use (chewing/ smoking), diabetes mellitus, obesity, physical inactivity, and unhealthy diets. Apart from this, factors such as low social economic status, alcohol use, mental ill-health and psychosocial stress, use of certain medications and left ventricular hypertrophy also contributes towards MI. Some non-modifiable risk factors are advancing age, heredity or family history, gender, and ethnicity.

Among all stated risk factors, hypovitaminosis D has been the focus of recent interest. It is well known that vitamin D insufficiency, or deficiency, is highly prevalent in the general population. Vitamin D receptors (VDRs) are present in most tissues including vascular smooth muscle, endothelium, and myocytes. The active form of vitamin D (1.25–dihydroxy vitamin D or calcitriol) inhibits renin secretion, proliferation of vascular smooth muscles and myocytes and regulates cell growth. Vitamin D receptor agonists (VDRAs) inhibit the development of atherosclerosis, calcification of the arteries, heart muscle hypertrophy, thrombosis, and suppress renin-angiotensin system by acting on these receptors. Peripheral arterial disorders are reported to be associated with low serum vitamin D levels. A growing amount of data has highlighted the potential link between vitamin D and major cardiovascular risk factors, such as diabetes, hypertension, and chronic kidney disease. The detection of nuclear vitamin D receptors (VDR) on vascular endothelial cells and cardiomyocytes has paved the way to studies for investigating the intriguing link between hypovitaminosis D and cardiac disease.[4]

Vitamin D deficiency was associated with a decrease of high-density lipoprotein (HDL) concentration and an increase of low-density lipoprotein (LDL) concentration.

The increased release of proinflammatory cytokines in patients with vitamin D deficiency increases oxidative stress and enables release of immature and activated platelets from the bone marrow, with an increased mean platelet volume.[5]All these effects can lead to atherosclerosis of coronary arteries. Vitamin D receptor agonists (VDRAs) inhibit the development of atherosclerosis, calcification of the arteries, heart muscle hypertrophy, thrombosis, and suppress renin-angiotensin system by acting on these receptors. Thus, present paper aims to assess the serum levels of 25(OH) vitamin D in patients with Acute ST Elevation Myocardial Infarction (STEMI) in young patients (aged ≤ 45 years).

Objective of the paper

To compare the serum levels of 25(OH) vitamin D levels with age and sex matched healthy controls.

Material and Methods

It was an observational age and sex matched case-control study conducted at PT. B.D. Sharma Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, in the Department of Cardiology for 12 months after the approval from ethical committee of PGIMS Rohtak. A total of 100 patients (50 case and 50 controls) were selected based on following criteria:

Inclusion Criteria

1. Patients with acute ST Elevation Myocardial Infarction.
2. Patient's age >18 years but ≤45 years

Exclusion Criteria

1. Diabetes
2. Prior History of cardiovascular diseases
3. Renal disease
4. Hepatic disease
5. Prior history of vitamin D supplementation
6. Patients on drugs that affect vitamin D metabolism (antiepileptics, Steroids, Rifampicin)
7. History of tuberculosis
8. Pregnancy and lactation

Method

Seven mL venous blood was collected aseptically from antecubital vein in red capped vacutainer and serum was separated by centrifugation. The

parameters were preserved at -20^{o}C till analysis. Routine biochemistry investigations were done as per standard methods.

Statistical Analysis

Data was collected and analyzed statistically. The results were presented as percentages, mean, standard deviation. Quantitative data was analyzed by using Student t-test. Proportions were compared by using chi-square test. A 'p' value of less than 0.05 was considered statistically significant.

Results

There were two categories defined for age such as 26-35 years and 36-45 years. According to analysis, case group involve 28% participants aged between 26-35 years and 72% aged between 36-45 years. Control group involved 34% participants in 26-35 years of age and 66% between 36-45 years of age.

The mean age of case group was 38.34 (SD=4.0) and control group was 35.86 (SD=4.0). There were only male patients in both the groups and majority (64%) of them reported sudden onset of chest pain with mean duration of 6.67 (SD=2.58) hours.

Table 1: Age wise distribution of study participants

			Group		Total
			Case	Control	
Age Group (in years)	26-35	Count	14	17	31
		% within Group	28.0%	34.0%	31.0%
	36-45	Count	36	33	69
		% within Group	72.0%	66.0%	69.0%
Total		Count	50	50	100
		% within Group	100.0%	100.0%	100.0%

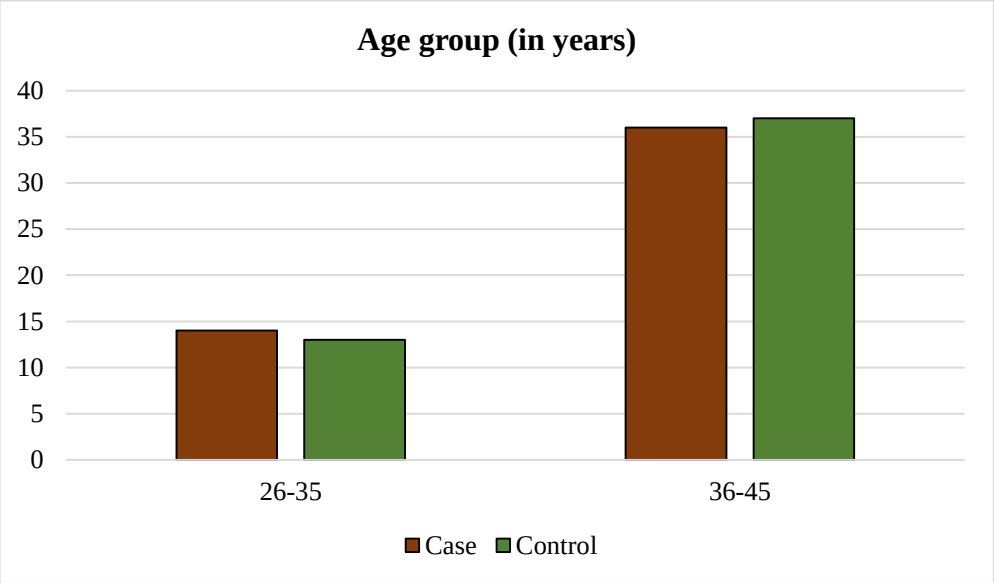

Figure 1: Age wise (in years) distribution of study participants

Table 2: Distribution of participants according to their alcohol and smoking habit

			Group		p-value
			Case	Control	
Alcohol	No	Count	17	38	<0.001
		% within Group	34.0%	76.0%	
	Yes	Count	33	12	
		% within Group	66.0%	24.0%	
Smoking habit	No	Count	10	37	<0.001
		% within Group	20.0%	74.0%	
	Yes	Count	40	13	
		% within Group	80.0%	26.0%	

As per table 2, statistically significant association was observed between habit of alcohol consumption and groups and smoking habit and group on applying chi square test of association (p-value < 0.001).

Case group have significantly higher number of alcoholics and smokers as compared to control.

Table 3: Comparing various parameters between groups.

Parameters	**Case**	**Control**	**P-value**
TLC/µL	9808.00 (3921.778)	6960.00 (2267.427)	<0.001
RBS (mg/dL)	103.72 (90.04)	90.04 (6.565)	<0.001
Serum creatinine (mg/dL)	0.930 (0.2082)	1.032 (0.1449)	0.005
Na^+ (mEq/L)	138.306 (3.7206)	139.800 (3.2135)	0.034
K^+ (mmol/L)	4.2442 (.50339)	4.4620 (.51938)	.036

As per table 3, there was statistically significant difference in all the parameters between case and controls (p>0.05).

Table 1: Distribution of participants according to Vitamin D level in both groups

		Group		**Total**	**p-value**
		Case	**Control**		
Vitamin D Level	**Deficiency (<20ng/ml)**	26 (52%)	10 (20%)	36	<0.001
	Insufficiency (20-30ng/ml)	20 (40%)	12 (24%)	32	
	Sufficiency (30-100ng/ml)	04 (8%)	28(56%)	32	
Total	**Count**	50	50	100	

Table 3 has analysed the level of vitamin D in both groups and found that among case group 52% of patients were having vitamin-D deficiency and 40%of patients were having vitamin-D insufficiency, 8%of patients were having vitamin-D sufficiency where as in control group, 20% of patients were having vitamin-D deficiency, 24%of patients were having vitamin-D insufficiency and 64%of patients were having vitamin-D sufficiency.

Statistically significant association was observed between vitamin D Level and case group (p<0.001) on applying chi square test of association (p value < 0.001). Participants in case group were having significantly higher vitamin D deficiency.

Table 2: Distribution of Vitamin D level as per age group (including both case and control group)

		Vitamin D Level (in ng/ml)				
Groups	**Age Group (in years)**	**Deficiency (<20 ng/ml)**	**Insufficiency (20-30 ng/ml)**	**Sufficiency (>30 ng/ml)**	**Total counts**	**p-Value**
Case	**26-35**	9 (18%)	4 (8%)	01 (2%)	14	<0.001
	36-45	17 (34%)	16 (32%)	03 (6%)	36	
Control	**26-35**	04 (8%)	04 (8%)	09 (18%)	17	
	36-45	06 (12%)	08 (16%)	19 (38%)	33	
Total		36 (72%)	32 (64%)	32 (64%)	100	

Table 4 has compared the Vitamin D level with age group including both case and control groups and found that from total 100 patients (including both case and control groups) 36% of patients were having vitamin-D deficiency, 32%of patients were having vitamin-D insufficiency and 32% of patients were having vitamin-D sufficiency when both case and control group considered together.

There was significant association between deficiency of vitamin D and case group on applying chi square test of association (p value < 0.001).

There is significantly higher vitamin-D deficiency in age group of 36-45 years when compared to age group of 26-35 years among case group on applying chi square test of association (p value < 0.001).

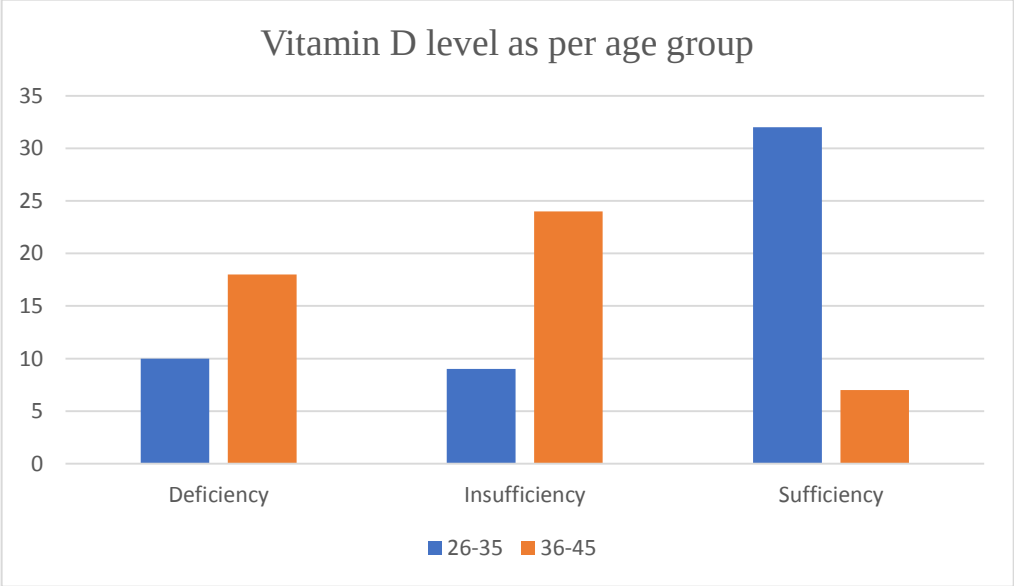

Figure 21: Distribution of Vitamin D level (ng/ml) as per age group (in years) in both groups.

Table 5: Distribution of Vitamin D deficiency level (ng/ml) as per age group in cases.

			Age Group(in years)		Total
			26-35	36-45	
Vitamin D deficiency (ng/ml)	Severe (<5ng/ml)	Count	1	0	1
		% within Age Group	11.1%	0.0%	3.8%
	Moderate (5-10 ng/ml)	Count	3	4	7
		% within Age Group	33.3%	23.5%	26.9%
	Mild (11-20 ng/ml)	Count	5	13	18
		% within Age Group	55.6%	76.5%	69.2%
Total		Count	9	17	26
		% within Age Group	100.0%	100.0%	100.0%

Table 5 has provided the information related to age and deficiency of vitamin D in case group and found that 1 patient (11.1%) from the age group of 26-35 years was having severe vitamin-D deficiency; 3 patients (33.3%) from the age group of 26-35 years and 4 patients (23.5%) from age group of 36-45 years were having moderate vitamin-D deficiency. Moreover, 5 patients (55.6%) from the age group of 26-35 years and 13 patients (76.5%) from age group of 36-45 years were having mild vitamin-D deficiency.

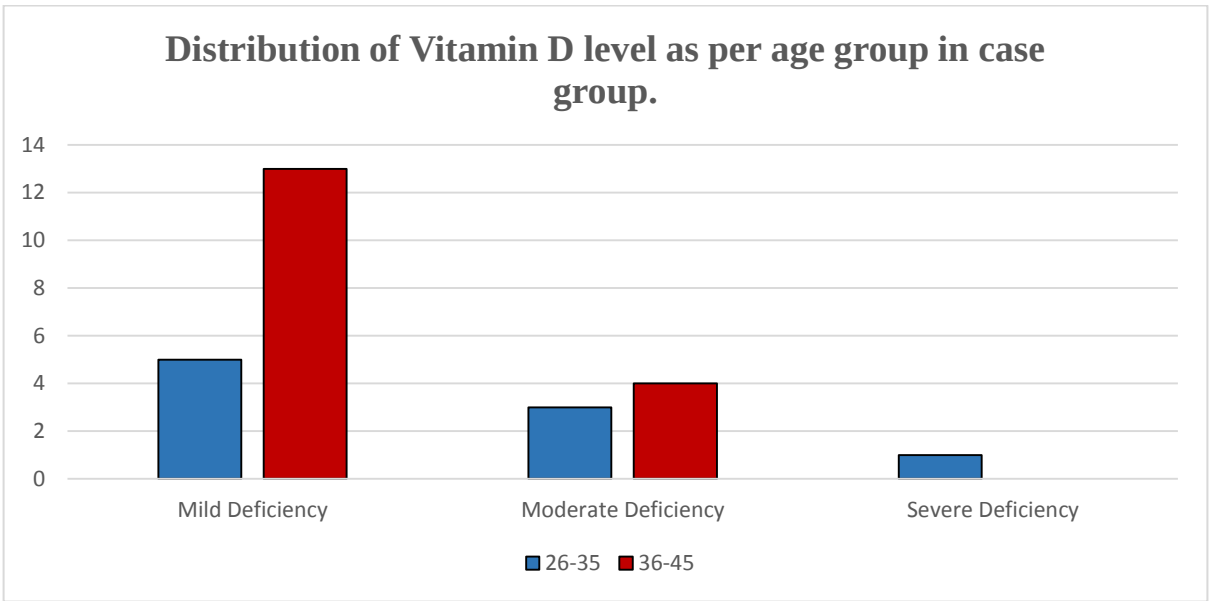

Figure 2: Distribution of Vitamin D level (ng/ml) as per age group (in years) in case group.

Discussion

According to the findings of current study, the mean of TLC/µL for case group was 9808.00 (SD=3921.77) and control group was 6960.00 (SD=2267.42). Moreover, the mean value in cases was 2.41 (SD=0.81) and in control, it was 2.93 (SD=0.85). Although the TLC was in the normal range (4000-11,000/µL) in both the groups, there was significant difference found in TLC as value of $p<0.05$.

TLC was significantly higher in case group. Highlighting the participation of leukocytes in the pathogenesis of the ischemic damage that occurred during an acute coronary event, in particularly during the acute myocardial infarction (MI). Blood sugar was found to be higher in case group.

Moreover, there was significant difference found in RBS as value of $p<0.001$. RBS was significantly higher for case group when compared to control group. This is reflecting the fact that hyperglycemia can also occur when normal hormonal control of blood glucose concentration is disturbed by the stress associated with acute myocardial infarction.

The blood glucose is raised in the immediate period following acute myocardial infarction irrespective of diabetes status. A statistically significant correlation of hypovitaminosis D in the patients with age less than 45 years with acute myocardial infarction was observed. According to present analysis, the level of vitamin D were studied and among case group 52% of patients were having vitamin-D deficiency and 40% of patients were having vitamin-D insufficiency, 8%of patients were having sufficiency where as in control group, 20%of patients were having deficiency, 24% of patients were having insufficiency and 64%of patients were having vitamin-D sufficiency.

It revealed that vitamin D level is even lower in the study case group as compared to controlgroup. Vitamin D deficiency is associated with risk of acute MI even after adjusting for the known risk factors of acute MI.

Our study has also analysed the association of age and deficiency of vitamin D and found that one patient from the age group of 26-35 years was having severe deficiency and 3 patients of age between 26-35 years followed by 4 patients from age group of 36-45 years were having moderate deficiency. Moreover, 5 patients from age group of 26-35 years and 13 patients from age group of 36-45 years were having mild deficiency. There was a significant association between deficiency of vitamin D Level and case group ($p<0.05$).

The high prevalence of vitamin D deficiency found in our study is consistent with previous studies published in India. A rural prevalence study in North Indians showed that though vitamin D levels in rural subjects were significantly higher than in urban Indians, the prevalence of vitamin D deficiency [serum 25(OH) vitamin D < 20 ng/ml] in them was as high as 70%.[6]

Another study from Delhi, in healthy individuals near 50 years of age, revealed deficiency [serum 25(OH) vitamin D < 20 ng/ml] in 91.2% including severe deficiency [serum 25(OH) vitamin D < 10 ng/ml] in 62% and vitamin D insufficiency [serum 25(OH) vitamin D levels 20-30ng/ml] in additional 6.8% of the population.[7] A study from Andhra Pradesh similarly reported a very high prevalence of vitamin D deficiency.[8]

The levels of vitamin D deficiency (<30ng/ml) was 88% and 94% in urban males and females respectively. In rural areas the numbers were 84% and 99% in males and females respectively. The causes for high prevalence of Vitamin D deficiency in Indians is attributed to dark-skin, lack of adequate direct skin exposure to sunlight and lack of vitamin D in predominant Indian diet.

In present study we found that participants in case group had significant vitamin D deficiency when compared with control group. It was found that 52%of patients were having vitamin-D deficiency, 40% of patients were having vitamin-D insufficiency and only 8%of patients were having vitamin-D sufficiency. There was significant association between deficiency of vitamin D and case groups ($p<0.05$).

There were significantly higher chances of age group of 36-45 years to have vitamin D deficiency as compared to age group 26-35 years. The mean Vitamin D level in the casegroup was lower than the controlgroup in each age group. There was significant decrease in vitamin D levels in the young CAD patients <45yrs. Their mean vitamin D level was only 19.30 ng/ml when compared to the control group whose mean vitamin D level was 30.14 ng/ml suggesting a significant role of hypovitaminosis D as an independent risk factor for myocardial infarction in the absence of other conventional risk factors.

These findings are similar to previous study for example as per the Saeed et al., (2022),[9] where they have measured serum vitamin D level in STEMI and found that Vitamin D deficiency is present in over half of patients with ST elevated myocardial infarction. Only 20% of patients with acute myocardial infarction had normal vitamin D values, while remaining having insufficient levels.

As per the Dziedzic et al., (2022),[10]vitamin D concentrations affect the levels and function of platelets, which are the crucial mediator of atherothrombosis and plaque rupture. The main aim of their study was to examine the relationship of serum 25-hydroxyvitamin D (25(OH)D) levels with the platelet activity in patients with a history of an acute coronary syndrome (ACS).

This study found that a significantly lower level of 25(OH)D was demonstrated in patients who had acute MI compared to those with Chronic Stable Angina (CSA) ($p < 0.05$).

Another case-control study in patients of acute MI performed in the United State of America Scragg Ret al.,[11]reported similar inverse association between 25(OH) vitamin D levels and risk of acute MI. A more recent study by Iqbal MPet al.,[12]from Pakistan revealed that individuals with normal levels of 25(OH)vitamin (>30ng/ml) had lower risk of MIas compared to those with vitamin D deficiency even after adjusting for known co-variates with an adjusted odds ratio of 0.82 ($p < 0.01$).Similarly, a study by Syal et al.,[13] from North India found that 100 patients undergoing coronary angiography revealed more severe coronary artery disease and greater endothelial dysfunction among individuals with low vitamin D.

Another interesting finding of our study was that alcohol use was associated with increased risk of acute MI. This association corroborated with the findings of the Indian arm of the INTERHEART study[14], a case control study of acute MI, and another case control study of industrial population from India.[15]

Conclusion

In present study, vitamin D insufficiency was found in most of the patients with acute myocardial infarction and was linked to many of its risk variables. Various epidemiologic data and observational studies have shown that serum vitamin D concentrations are lower in patients with coronary artery disease compared with healthy controls. However, hypovitaminosis D was also associated with other cardiovascular risk factors including hypertension, diabetes, obesity, metabolic syndrome and dyslipidaemia.

The present study was proposed to assess the 25(OH) vitamin D status with acute ST elevation myocardial infarction in young patients of age less than 45 years. The study included 50 cases of acute myocardial infarction and 50 healthy age and sex matched controls.

Present analysis revealed that serum 25(OH) vitamin D levels were significantly lower in the cases of acute myocardial infarction when compared to the control population.

To prevent cardiovascular problems, this highly frequent vitamin D deficiency should be screened and treated adequately. The clinical analysis has shown that vitamin D deficiency is having a significant adverse impact on the cardiac function and blood pressure in AMI.

Moreover, the vitamin D is exerting biological effects on cardiac myocytes, by stimulating calcium-ATPase activity and calcium uptake in cardiac myocytes. Although smoking and other forms of tobacco, dyslipidemia and hypertension are major modifiable risk factors in the young.

There are number of other emerging modifiable risk factors which are now being investigated. More than 100 new emerging risk factors have been discovered for their ability to improve global cardiac risk assessment. All these new risk factors are emerging with potential relevant therapeutic implications.

Among them, hypovitaminosis D has been the focus of recent interest. Large randomized controlled trials are required to firmly establish the relevance of vitamin D status on cardiovascular health.

Monitoring serum 25- hydroxyvitamin D levels and correction of vitamin D deficiency is indicated for optimization of general health. Vitamin D deficiency can be diagnosed by blood testing and treated easily; therefore it is crucial to solidify knowledge of its association and contribution to cardiovascular disease.

Conflict of interest-None

Source of funding – None

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