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Original Research Article

Is Vitamin D Deficiency & Increased BMI – An Independent Risk Factor of MI? - A Comparative Analysis among MI Patients

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Abstract: ***Background*:** Cardiovascular diseases (CVD) are the commonest cause of mortality and morbidity worldwide. Despite the rising proportions of CAD, only limited data are available on the relationship between Vitamin D. This study was aimed to assess the serum levels of 25(OH) Vitamin D and its causal association of Vitamin D deficiency as an independent risk factor in patients with Acute ST-Elevation Myocardial Infarction in National Institute of Medical Sciences and Research, Jaipur, Rajasthan. ***Material and Methods*:** Patients admitted with acute ST- Elevation and NON-ST- Elevation Myocardial Infarction in the CCU unit of the National Institute of Medical Science & Research, Jaipur were chosen as cases. Rest healthy same age and sex-match ambulatory subjects were kept as controls. The data entered in the MS EXCEL spreadsheet and analysis will be done using Statistical Package for Social Sciences (SPSS) version 23.0. Continuous variables were presented as mean ± SD. Categorical variables were expressed as frequencies and percentages. The Chi-square test of association or Fischer exact test has been used to determine if there is an association between two categorical variables. ***Results*:** Among 50 study cases, the prevalent age group where 50-60 years was 16(32%) followed by 40-50 years (28%) while in control the majority of the participants were in between 40-50 years, 16(32%) followed by 15 cases (30%) in 30-40 years. It was observed that the mean BMI of the study cases was 29.11 ± 3.1 and for controls was 24.41 ± 1.92. Fifty-four percent of cases were found overweight with a BMI range between 25-29.9 and 21(42%) were found obese. In considering the control group, 21(42%) subjects were found overweight with a BMI range between 25-29.9 while no subject was obese with above 30. Most of the cases with vitamin deficiency and vitamin insufficiency were either overweight or obese and had BMI above 25 and a statistically significant difference with p=0.02828. ***Conclusions*:** Vitamin D deficiency and overweight/obese were found significantly associated with myocardial infarction and found to be independent risk factors. We do recommend measuring the serum vitamin D levels for all patients especially overweight and obese substantially having cardiovascular risk.

Keywords: Cardiovascular diseases (CVD), Vitamin D, Vitamin D deficiency, BMI.

INTRODUCTION

Cardiovascular diseases are the commonest cause of mortality and morbidity worldwide [1]. The prevalence of the cardiovascular disease has rapidly increased in the past few years. Though there are many well-established risk factors for cardiovascular disease, emerging novel risk factors are being assessed by various epidemiological studies and continue to be an important aspect of debate regarding the nature of the association and the role they play in reducing death and disability due to cardiovascular disease [2].

Over the recent years, there has been much emphasis and research on 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

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function and its association with decreased risk of many chronic diseases. Hypovitaminosis D is a worldwide health problem. 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 as a positive correlation with hypertension, diabetes mellitus, metabolic syndrome, atherosclerosis, peripheral arterial disease, cancer, and many autoimmune disorders [3-5].

Several direct and indirect mechanisms have been proposed for the association of vitamin D with CHD. Vitamin D could be related to CHD via increased blood pressure, impaired glycaemic control, or secondary hyperparathyroidism. An excess of PTH levels is known to promote atherosclerosis. PTH promotes myocyte hypertrophy and vascular remodeling. Hypovitaminosis D is known to up-regulate Renin Angiotensin Aldosterone System (RAAS) and lead to hypertrophy of smooth muscles and the left ventricle, an adverse marker of a cardiovascular event. Consequently, low serum 25(OH) D has been associated with aberrant cardiac contractility, cardiomegaly, and increased ventricular mass due to myocardial collagen deposition [6, 7].

Vitamin D mainly acts through its role in maintaining calcium homeostasis and gene transcription to prevent cardiovascular diseases and their risk factors. Many data have shown that cardiovascular morbidity and mortality are 30- 50% more in the regions of less sun exposure due to season or latitude and that mortality from CAD is highest in winter. The prevalence of Vitamin D deficiency is even higher in dark-skinned people and elderly persons. Many studies worldwide have confirmed that myocardial infarction patients have lower Vitamin D levels than control subjects.

It was postulated that those with low Vitamin D levels had almost 60% higher risk of myocardial infarction than those with the highest levels. Despite the rising proportions of CAD in Asians, only limited data are available on the relationship between Vitamin D, CAD, and endothelial dysfunction. Since Vitamin D deficiency can be easily measured and treated, trials to study the effect of hypovitaminosis D and its supplementation to prevent and treat cardiovascular diseases are currently considered important areas of research. The increasing rate of coronary artery disease and the associated morbidity and mortality make it necessary to develop further research in this study population.

Many studies have been done and many are going on to assess the Vitamin D status in these patients. A practical time to check for 25(OH) Vitamin D deficiency and to start treatment is at the time of acute myocardial infarction. Hence this study was designed to determine whether the presence of Hypovitaminosis D has a significant correlation with coronary artery disease. Our study aimed to assess the serum levels of 25(OH) Vitamin D in Patients with Acute ST-Elevation Myocardial Infarction and its causal association of Vitamin D deficiency as an independent risk factor for coronary artery disease patients conducted at the Department of General Medicine & Cardiology, National Institute of Medical Sciences and Research, Jaipur, Rajasthan. Keeping this background following objectives were framed;

i) To study the prevalence of Vitamin D deficiency in our study population and to assess the severity.
ii) To find an association between body mass index and serum levels of Vitamin D.

MATERIALS AND METHODS:

Study area and study population:

The present study was conducted in the Department of General Medicine & Cardiology, National Institute of Medical Sciences and Research, Jaipur, Rajasthan.

Ethical clearance: This research work was approved by our institutional ethical committee.

Duration of study: It was carried out for one and half years (Jan 2021- Jun 2022)

Study design: A comparative case-control study.

Inclusion criteria:

- All indoor patients of Acute Myocardial Infarction aged 18 years and above were included in the study.

Exclusion criteria:

- Chronic kidney diseases & Chronic liver diseases.
- Known endocrinal disorders, (hypoparathyroidism/hyperparathyroidism and others like Cystic fibrosis, celiac disease, Whipple's disease, Crohn's disease, hyperphosphatemia, rickets, tumor-induced osteomalacia, sarcoidosis, and tuberculosis.
- Refused consent

Methodology

All patients admitted with acute ST- Elevation and NON-ST- Elevation Myocardial Infarction in the CCU unit of the National Institute of Medical Science & Research, Jaipur were chosen as cases. Those cases that satisfied the inclusion and exclusion criteria were included in the study. Rest healthy same age and sex-match ambulatory subjects were kept as controls. A data collection form was prepared to record the name, age, sex, occupation, address, complaints, past medical history, smoking, alcoholism, drug intake, and another

relevant history. General examinations with an examination of vital signs, cardiac, respiratory, abdomen, and central nervous system were done. Each patient's clinical profile was noted. Following laboratory investigations were also recorded study subjects:

- Serum Vitamin –D (25-OH) level.
- Random Blood Sugar and Lipid profile.
- Renal Functions test and Liver Functions test, CBC, Uric acid & serum electrolytes.
- ECG & 2D –ECHO.

SAMPLE SIZE CALCULATION:
The formula used for the calculation of sample size is:

$$n = \frac{\left(z_{1-\frac{\alpha}{2}} + z_{1-\beta}\right)^2 \left(\sigma_1^2 + \sigma_2^2\right)}{\left(\mu_1 - \mu_2\right)^2}$$

α=Type I error=5%
β=Type II error=20%
σ_1=Standard Deviation for group 1=7
σ_2=Standard Deviation for group 2=8
μ_1=mean for group 1=25
μ_2=mean for group 2=22

z is the inverse normal value at a different level of alpha & beta. Sigma l & Sigma 2 are S.D of cases and control. µ1 and µ2 are the mean of cases and control. Alpha is the level of significance - 5% & 1-beta is the power of the test - 80%.

$$N = \frac{7.84 \times [(0.741)^2 + (0.62)^2]}{(9.09-8.92)^2}$$

N = 43 Sample Group
Z1 -ά/2 = 1.96 & Z1-B = 0.84

Calculations:
By this formula, we get a minimum Sample Size is 43.

Statistical analysis:
The data entered in the MS EXCEL spreadsheet and analysis will be done using Statistical Package for Social Sciences (SPSS) version 23.0. Continuous variables were presented as mean ± SD. Categorical variables were expressed as frequencies and percentages. The Chi-square test of association or Fischer exact test has been used to determine if there is an association between two categorical variables. In inferential statistics, the use of a t-test to compare groups and comparison of p-value with alpha 5%.

P<0.05 has considered statistically significant. Difference between means has been observed by the T-test. P < 0.05 has considered a significant level.

RESULTS

In this study, we have observed in patients admitted with acute ST- ELEVATION and NON-ST ELEVATION Myocardial Infarction and compared them with healthy subjects with same age and sex match ambulatory patients as controls. The observational findings of the study are as follows;

Table 1 shows the age distribution of study cases the prevalent age groups were 50-60 years, 16(32%) followed by 40-50 years (28%) while in controls the majority of the participants were in between 40-50 years, 16(32%) followed by 15 cases (30%) in 30-40 years. 12% of cases were found below the age of 30 years while 10% of controls were found below the age of 30 years. Rest 3 cases (6%) and 4 (8%) controls were found more than age 60 years. The mean age of the study cases was 45.9 ± 10.4 and the controls was 44.16 ± 10.42.

Table 1: Frequency distribution of age of patients

Age interval (In years)	Control (n=50)	Case (n=50)
20 – 30	5 (10%)	6 (12%)
30 – 40	15 (30%)	11 (22%)
40 – 50	16 (32%)	14 (28%)
50 – 60	10 (20%)	16 (32%)
> 60	4 (8%)	3 (6%)

There was male predominance than female among cases, 28(56%) as well as 31(62%) in control subjects (Figure 1).

Table 2 shows the BMI distribution among study cases and controls. It was observed that 27(54%) of cases were found overweight with BMI range between 25-29.9 and 21(42%) was obese with above 30. On considering control group, 21(42%) subjects were found overweight with BMI range between 25-29.9 while no subject was obese with above 30. Two (4%) cases were found with normal BMI with 18.5-24.9 while 29(58%) subjects among control group. The mean BMI of the study cases was 29.11 ± 3.1 and controls was 24.41 ± 1.92.

Table 2: Distribution of BMI distribution of patients

BMI	**Control**	**Case**
18.5 - 24.9	29 (58%)	2 (4%)
25 - 29.9	21 (42%)	27 (54%)
30 - 34.9	0	21 (42%)

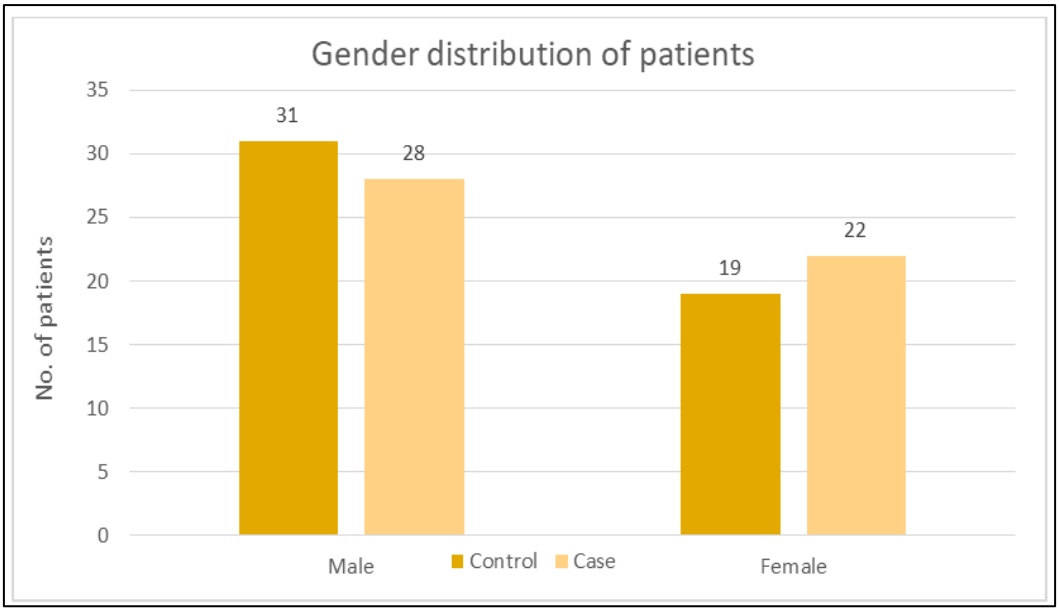

Figure-1: Bar diagram showing gender distribution

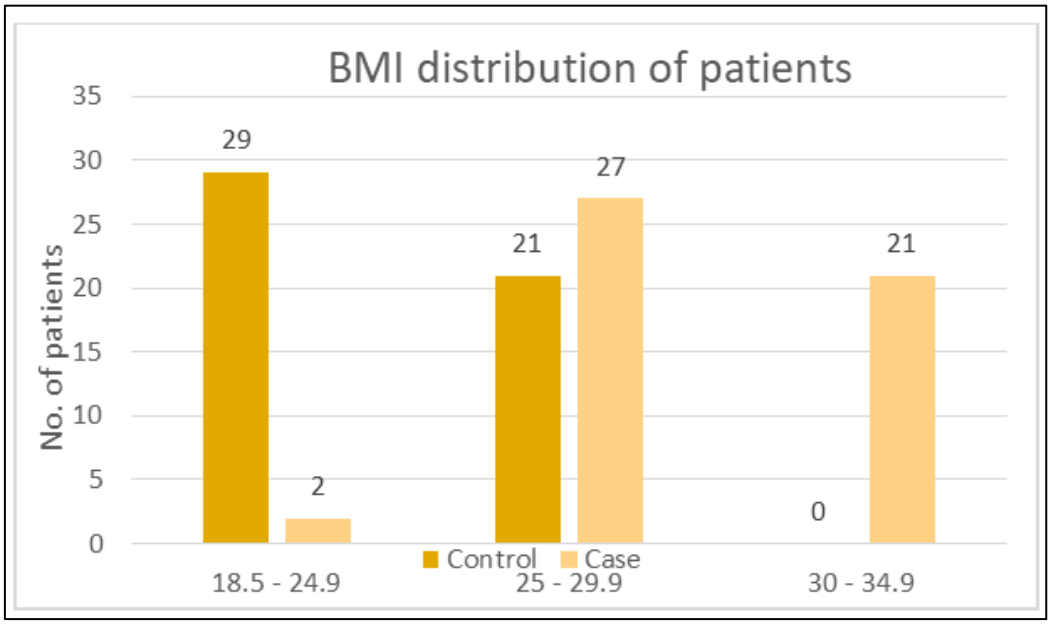

Figure 2: Bar diagram showing the Distribution of BMI

On assessing the serum level of Vitamin –D (25-OH) among the study groups, it was observed that 21(42%) of cases were found vitamin D deficiency and 7(14%) control subjects were vitamin D deficient. There was vitamin D insufficiency among 17 (34%) cases while 15 (30%) controls. Twelve (24%) cases were found with sufficiency of vitamin D levels and 28(56%) subjects among control group.

Table 3: Distribution of vitamin D level among patients

Vitamin D Level	Control	Case
Deficiency	7 (14%)	21 (42%)
Insufficiency	15 (30%)	17 (34%)
Sufficiency	28 (56%)	12 (24%)

In the present study the association between vitamin D deficiency and various anthropometric and vital parameters has been carried out among study cases and controls and the following observations were recorded.

On considering the association of vitamin D deficiency and BMI, most of the cases with vitamin deficiency and vitamin insufficiency were either overweight or obese and had BMI above 25. There is a statistically significant difference with p=0.02828. Most of the controls have vitamin D sufficiency and have BMI of either normal or overweight. there is a statistically insignificant association (p=0.72781).

Table 4: Association between Vitamin-D deficiency and BMI

Variable		Deficiency	insufficiency	Sufficiency	Chi-Square test	P - Value
Control	**18.5 - 24.9**	2 (4%)	4 (8%)	23 (46%)	0.635	0.72781
	25 - 29.9	5 (10%)	7 (14%)	9 (18%)		
	30 - 34.9	0	0	0		
Case	**18.5 - 24.9**	1 (2%)	1 (2%)	0	7.132	**0.02828***
	25 - 29.9	11 (22%)	10 (20%)	6 (12%)		
	30 - 34.9	9 (18%)	6 (12%)	6 (12%)		

DISCUSSION

In the present study, 50 inpatients admitted with acute ST- Elevation and NON-ST Elevation Myocardial Infarction were enrolled as cases and compared with healthy subjects with the same age and sex match 50 ambulatory patients as controls. The most prevalent age groups among cases were 50-60 years (32%) while in controls 40-50 years (32%). The mean age of the study cases was 45.9 ± 10.4 and the controls were 44.16 ± 10.42. The p-value was 0.410648 which shows it is statistically insignificant.

Ameen M. Mohammad (2018) [8] the patients' mean age was 60.12 ± 12.22 ranging from 28 to 84 years. In all, 78 (75%) patients had STEMI and 26 (25%) patients had NSTEMI. Vitamin D deficient and insufficient numbers were 60 (57.7%) in cases and 53 (51%) in controls.

In the present study, male predominance was noticed among cases, (56%) as well as (62%) in controls. However, Verdoia, M *et al*., (2015) [9] reported that females were associated with increased severity of coronary artery disease and independently associated with significant Vit D deficiency. Various studies have reported that variations in men and women may be due to variations in the presentation of coronary artery disease in women, frequently with atypical symptoms, or with asymptomatic myocardial ischemia. In Islam M. E *et al*., (2017) [10] study vitamin D was found to be significantly reduced in AMI patients when compared with that of controls which were 28.50±16.68 ng/ml in cases and 38.32±16.47 ng/ml in controls, P=0.011.20 Karur and colleagues [11] has included AMI patient from all ages and found 83.5% vitamin D deficiency or insufficiency.

In our study, 54% of cases were found overweight with a BMI range between 25-29.9 and 42% were obese with above 30. In considering the control group, 42% of subjects were found overweight with a BMI range between 25-29.9. The mean BMI of the study cases was 29.11 ± 3.1 and the control was 24.41 ± 1.92. Shanker *et al*., (2011) [12] found that low vitamin D levels were associated with increased risk for CAD, contrary to which, Rajasree *et al*., (2001) [13] reported a paradoxical increase in coronary heart disease with 25(OH)D levels >89 ng/mL compared to those with lower levels.

In our study, it was observed that 42% of cases found vitamin D deficiency and 14% of control subjects were vitamin D deficient. There was vitamin D insufficiency among 34% of cases and 30% of controls. Similarly, in a study conducted by Hosen I *et al*., (2019) [14], 86.7% of cases were deficient (moderate/severe) in vitamin D which is significantly more compared to controls (46.7%, P<0.001). Vitamin D deficiency is widespread, the lowest vitamin D levels are commonly found in regions such as the Middle East and South Asia and the main risk factors were attributed to elderly women, higher latitude, winter season, less sunlight exposure, skin pigmentation, dietary intake, and low vitamin D fortified foods.

On considering the association of vitamin D deficiency and BMI, most of the cases with vitamin deficiency and vitamin insufficiency were either overweight or obese and had BMI above 25. There is a statistically significant difference with p=0.02828. Most of the controls have vitamin D sufficiency and have a BMI of either normal or overweight. there is a statistically insignificant association. (p=0.72781) The patients had a higher prevalence of obesity and smoking status in the study by Ameen M. Mohammad (2018) [8]. There was a significant difference in terms of the cardiovascular risk factors between the two groups (P < 0.001).

The main limitation of our study was a hospital-based study with a small number of subjects that were included. Very few female patients were studied. Further studies need to be done with a larger study population including more women. The Parathormone levels were not measured and hence its role as a confounding factor could not be analyzed. The cause for hypovitaminosis D in the study subjects was not evaluated. The patients were not followed up after Vitamin D supplementation and hence we could not assess the prognosis. The etiology of MI in young patients was not studied and so we could not rule out other confounding factors.

CONCLUSION

Vitamin D deficiency and overweight/obese were found significantly associated with myocardial infarction and found to be independent risk factors. Similar studies should be conducted in the future and are needed to find the causal relationship. We do recommend measuring the serum vitamin D levels for

all patients especially overweight and obese substantially having cardiovascular risk and treating it if it was deficient to decrease the relative risk of acute MI.

Conflict of interest: None to declare

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