

# STUDY OF EVALUATION OF RISK FACTORS OF ACUTE MYOCARDIAL INFARCTION WITH SPECIAL REFERENCE TO VITAMIN D STATUS- A CASE CONTROL STUDY, DONE AT A TERTIARY CARE HOSPITAL OF TRIPURA

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## ABSTRACT

### BACKGROUND

Acute Myocardial Infarction (AMI) is a leading cause of morbidity and mortality globally. Efforts are always there to identify predisposing risk factors associated with development of AMI so that preventive approaches can be adopted for therapeutic interventions or life style changes. This study was conceptualized to identify the responsible risk factors with AMI & to evaluate their power of association. An approach was also adopted to identify whether co-existence of deficiency of vitamin D (25(OH) D) along with the classic risk factors further endangers the population.

The objectives of the study were- 1) To identify risk factors of AMI & to evaluate their power of association. 2) To estimate vitamin D level in all cases and controls and to study statistical correlation of vitamin D with classic risk factors.

### MATERIALS AND METHODS

It is a case control study, where 130 cases of AMI & 130 healthy controls from patient's attendants were included. Patients were evaluated clinically, and investigations were done to identify the classic risk factors. Simultaneously vitamin D (25(OH) D) level was estimated in all cases and controls. Results obtained were analysed statistically to evaluate the power of association of the risk factors. The statistical package for social science version 16 IBM Corporation was used for statistical analysis and P Value of <0.05 was considered significant.

### RESULTS

The traditional risk factors responsible for predisposition of AMI were identified and it was studied that hyperlipidaemia is the most prevalent risk factor (62.3%) followed by hypertension (56.9%). Smoking was the next significant risk factor (52.3%). Diabetes mellitus was the fourth common risk factor (44.6%). Statistically no significant correlation was documented with alcoholism. Estimation of Odds ratio (OR) and its 95% Confidence Interval (CI) showed significant statistical correlation with the risk factors. The results showed the following: hyperlipidaemia (OR 4.1/CI 1.7-4.9), hypertension (OR 2.9/CI 1.7-4.9), smoking (OR 2.4/CI 1.4-2.0) & diabetes (OR 2.4/CI 1.4-4.1).

All cases and controls underwent vitamin D estimation and were analysed statistically to document any significant correlation with the classic risk factors. The study revealed significant association of deficiency of vitamin D among smokers (P= 0.0034) indicating that smokers with deficiency of vitamin D are having increased risk of developing AMI.

### CONCLUSION

This case control study was done to identify the risk factors associated with AMI and to study their role as a predisposing factor for development of AMI by studying their power of association. Statistically significant association was seen with hyperlipidaemia, hypertension, diabetes and smoking. There was always a search for new novel risk factors along with traditional ones and in this study, the role of deficiency of vitamin D was explored and it was seen that smokers have significantly deficient vitamin D levels which compounds further risk.

### KEYWORDS

Acute myocardial infarction, risk factors, hyperlipidaemia, hypertension, diabetes, smoking, vitamin D deficiency.

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### BACKGROUND

Cardiovascular disease is a global public health problem contributing to 30% of global mortality and 10% of the global disease burden.<sup>1</sup>

Myocardial infarction (MI) is one of the five main manifestation of coronary artery disease (CAD) and the other four being stable angina pectoris, unstable angina pectoris, heart failure and sudden cardiac death. The phrase

'acute coronary syndrome' includes unstable angina, non-ST elevation MI, ST elevation MI & Sudden cardiac death.<sup>2</sup>

The incidence of MI varies greatly in the world, in the United States approximately 650, 000 patients experience a new MI each year and 450, 000 patients of MI experience recurrent attacks of MI each year.<sup>3</sup>

The incidence of MI in India is 64.37/1000 people in men aged 29-69 years and death rate from MI is 31.7%. There has been a steady increase among Indian population the death rate due to MI, in 1970 it was 7% and it climbed to 32% in 2011.<sup>4</sup>

MI is defined in pathology as myocardial cell death due to ischemia. After the onset of myocardial ischemia, histological cell death is not immediate, but takes a finite time to develop as little as 20 mins. Complete necrosis of myocardial cells at risk requires at least 2-4 hrs or longer depending upon the presence of collateral circulation to the ischemic zone, persistent or intermittent coronary occlusion, the sensitivity of myocardial cells to ischemia & demand for oxygen and nutrients at that time.<sup>5</sup>

Atherosclerosis is the principal cause for myocardial infarction and cerebral infarction.<sup>6</sup>

Atherosclerosis is a smouldering immune-inflammatory disease fuelled by lipids where there is a plaque formation in the arterial intimal layer in medium and large sized arteries. Within the plaque lipid, inflammatory infiltrates smooth muscle cells and connective tissues accumulate.<sup>7</sup> Atherosclerosis begins in a hypercholesterolemic state where low density lipoproteins (LDL) infiltrate arterial endothelial wall and oxidation of LDL causes inflammatory response with infiltration of macrophages and T lymphocytes in the arterial wall and these inflammatory cells consume LDL & are now christened as foam cells.<sup>7</sup>

As a consequence, production of growth factors & cytokines, following inflammation takes place which regulate a variety of processes that affect the component makeup of the plaque.

Intra plaque inflammation with neo vascularisation is the key factor in a process of plaque destabilization with plaque erosion which is characterized by surface denudation and exposure of the immediate subendothelial tissues a process known as plaque rupture.<sup>8</sup>

It is a known fact that with atherosclerotic plaque rupture, ulceration of plaque and subsequent resultant formation of intraluminal thrombus by platelets & fibrin threads in one or more coronary arteries leading to decreased or complete stoppage of coronary blood flow ensues myocardial myocyte necrosis.<sup>9</sup>

Nearly three decades of intensive epidemiological investigations have identified a group of characteristics that predict an individual's probability of developing clinically manifest disease due to atherosclerosis and one of them is acute myocardial infarction. These characteristics are known as risk factors.<sup>10</sup>

Advances in our understanding of the ways in which traditional risk factors of atherosclerosis interact to initiate the pathology of atherosclerosis and promote the development of cardiovascular disease have enhanced our

ability to assess the risk in individual subjects.<sup>11</sup> The traditional risk factors include high level lipid profile and non lipid factors are hypertension, diabetes mellitus, obesity, sedentary life style, alcohol intake and smoking.<sup>12</sup>

In addition, the ongoing identification and understanding of novel new-found risk factors may further improve our knowledge to predict future risk when they are included along with classic risk factors. Some newer risk factors are impaired fasting glucose, triglycerides, lipoprotein A, homocysteine and high sensitive C reactive protein. All contribute to increased risk of coronary and cerebrovascular disease.<sup>13</sup>

Vitamin D deficiency is emerging as new-found risk factor for cardiovascular diseases, especially for atherosclerosis and hypovitaminosis D is a new interest of focus.<sup>14</sup>

Our state Tripura is a small, hilly, forested state in one of the remotest corner of the country with good Sunshine and the population consist of tribal and non-tribal population and both suffer from MI and have profound morbidity due to the incident.

The present study was designed to identify the traditional risk factors associated with atherosclerosis and MI and to study the power of association of these risk factors when compared with healthy controls of same age, gender and ethnicity.

Further vitamin D level was estimated in all cases and controls and its distribution among the risk factors was evaluated and statistical association of deficiency of vitamin D with traditional risk factors were studied.

### Aims and Objectives

1. To identify the risk factors associated with Acute Myocardial Infarction (AMI) cases.
2. To estimate vitamin D level in all cases and controls and to evaluate its association with the risk factors.

### MATERIALS AND METHODS

The study was carried out in the Dept. of Medicine at Agartala Government Medical College Agartala Tripura for a period of one and half years.

It's a case control study.

The study was done after taking permission from Institutional Research Committee and Institutional Ethics Committee

A total sample size of 130 cases of acute myocardial infarction (AMI) cases admitted at Medical Emergency both male and female and tribal and non-tribal were included according to the case definitions of AMI by the Third Universal MI Task Force.<sup>5</sup>

130 Controls were chosen from patient's party who were healthy matching to same age, sex and ethnicity. Subjects with any past history of Coronary Artery Disease (CAD) and hypovitaminosis D were not included.

Consent in written was taken from all 130 cases and 130 controls and were fully informed about the study protocol and pattern.

### Inclusion Criteria

A patient was considered as a case of AMI if two of the three criteria were positive on admission; satisfying the definition of AMI by the Third Universal MI task force<sup>5</sup> and above the age of 18 and consented for participation for the study.

### Exclusion Criteria

All cases refused to give consent for the study, previously known case of chronic renal and liver diseases, known case of hypovitaminosis D and patients on vitamin D supplements also patients with known malignancies were excluded from the study.

### Methodology

Detailed histories with through general and systemic examination were done. The socio demographic data of age, sex, marital status, education and life style history were documented. Data pertaining to clinical variables like smoking, alcohol consumption, lack of physical activity, obesity, hypertension, diabetes mellitus, hyperlipidaemia, previous history of cerebrovascular accident & CAD, chronic renal, liver and lung diseases were also noted. Previous history of any PTCA and CABG were also collected.

Hypertension was defined as systemic BP  $\geq 140$  Systolic and BP  $\geq 90$  Diastolic OR on any hypertensive medications.<sup>15</sup> Diabetes Mellitus was documented if Fasting Blood Glucose  $\geq 126$  mg/dl OR on insulin therapy or hypoglycaemic oral medications.<sup>16</sup>

Hyperlipidaemia was defined when total cholesterol  $>200$  mg/dl, LDL  $>100$  mg/dl & triglycerides  $>150$  mg/dl.<sup>17</sup>

Vitamin D deficiency was defined when vitamin D  $\leq 20$  ng/ml.<sup>18</sup>

Regular alcohol consumption for 3 times a week for one year was considered as alcoholic.<sup>11</sup>

Smoker was defined as a person smoking ten cigarettes per day for last one year regularly.<sup>19</sup>

12 Lead ECG was done in all patients and cases with ST segment elevation were included in the study

Serum samples were obtained as the patients were admitted and before initiation of any treatment. Laboratory investigations included complete haemogram, random blood sugar, HbA<sub>1c</sub>, renal function test, liver function test, lipid profile, cardiac enzymes like troponin and creatinine kinase MB & Vitamin D 25(OH)D.

Blood glucose was measured by glucose oxidase method by automated analyser.

Lipid profile was measured by enzymatic method by automated analyser.

25(OH) D was measured using ELFA technique by Vidas analyser from Biomerieux.

The statistical package for social science version 16 IBM Corporation was used for statistical analysis and P Value of  $<0.05$  was considered significant. Collected data were analysed by frequency, percentage, mean and standard deviation.

### RESULTS

A total of 130 cases of acute myocardial infarction (AMI) and 130 healthy controls matching with same age, gender & ethnicity were included in the study.

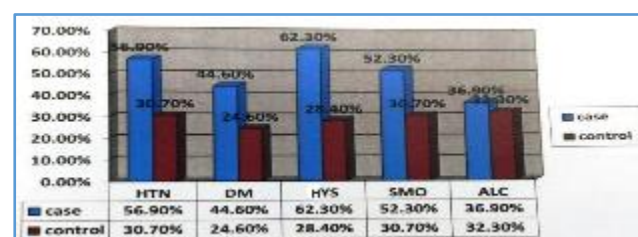
Among them 60% were males and 40% were female.

The minimum and maximum age documented was 38 yrs. and 92 yrs. respectively and maximum of the cases are documented in between 53 to 62 yrs. amounting to 49.2%.

The classic risk factors associated with AMI occurrence studied are hypertension, diabetes mellitus, hyperlipidaemia, smoking and alcoholism.

Our observations of the risk factors are-

1. 56.9% of cases & 30.7% of controls are hypertensive.
2. 44.6% of cases & 24.6% of controls are diabetic.
3. 62.3% of cases & 28.4% of controls are hyperlipidaemic.
4. 52.3% of cases & 30.7% of controls are smokers.
5. 36.9% of cases & 32.3% of controls are alcoholic.



**Figure 1. Distribution of Cardiovascular Risk Factors among Subjects**

(HTN- Hypertension, DM- Diabetes Mellitus, HYS- Hyperlipidemia, SMO- Smoking, ALC- Alcohol)

Risk Factor	Cases n= 130	Controls n= 130	P Value
Hypertension	74	40	0.000*
Diabetes	58	32	0.008*
Hyperlipidaemia	81	37	0.000*
Smoking	68	40	0.000*
Alcoholism	48	42	0.43

**Table 1. Distribution of Risk Factors Studied in Cases & Controls**

\*Significant.

Statistically significant association was seen with AMI and hypertension, diabetes, hyperlipidaemia and smoking.

Calculation of Odds ratio (OR) and 95% Confidence Interval (CI) to establish the power of association of the risk factors with AMI occurrence showed the following results-

Risk Factors	Odds Ratio	95% Confidence Interval	P Value
Hypertension	2.9732	1.7869-4.9471	P <0.0001*
Diabetes	2.4670	1.4549-4.1831	P = 0.0008*
Hyperlipidaemia	4.1550	2.4689-6.9926	P <0.0001*
Smoking	2.4677	1.4861-4.0977	P = 0.0005*
Alcoholism	1.2265	0.7351-2.0463	P = 0.4344

**Table 2. Calculation of Odds Ratio and its 95% CI of the Risk Factors**

\*significant.

Our study revealed hypertensive subjects are having 2.9 times more chances of developing AMI when compared with normotensive subjects.

The diabetics are 2.4 times more prone to develop AMI than non-diabetics.

Hyperlipidaemic subjects are highly susceptible to develop AMI and they are 4 times more prone to develop AMI than persons with normal lipid parameters.

Smokers are having 2.4 times more chances of developing AMI than non-smokers.

All these results are statistically significant.

However, we did not have any significant association in between alcoholism and AMI occurrence as no significant statistical co relation was documented.

Vitamin D level was estimated in all cases of AMI and controls. There is always a constant search for new risk factors along with the traditional risk factors and deficiency of Vitamin D is one of them. Level of Vitamin D was measured in all hypertensive, diabetics, hyperlipidaemic, smokers and alcoholic subjects of the cases and controls who were found to have these risk factors and also with the individuals who were not having those risk factors.

The results obtained are analysed statistically to establish any association existing between vitamin D deficiency and traditional risk factors.

Risk factors	Vitamin D status in Cases (n= 130)				Vitamin D status in Controls (n=130)				
	Deficient	Insufficient	Sufficient	Total	Deficient	Insufficient	Sufficient	Total	P Value
Hypertension	34	33	7	74	14	21	5	40	P = 0.519
Diabetic	28	24	6	58	8	17	7	32	P = 0.070
Hyperlipidaemia	42	33	6	81	12	23	2	37	P = 0.095
Smoker	35	27	6	68	8	23	9	40	P = 0.0034*
Alcoholism	25	17	4	48	13	24	5	42	P=0.0920

**Table 3. Evaluation of Vitamin D among Cases & Controls**

\*significant.

Though Vitamin D level was found to be low in all the risk factors, statistically significant association of Vitamin D deficiency was documented in the smokers (P= 0.0034).

## DISCUSSION

This is a case control study done at Agartala Government Medical College Agartala Tripura to identify the risk factors present amongst the population of Tripura with development of acute myocardial infarction.

130 cases of acute myocardial infarction were enrolled in the study and they were matched with 130 controls of same age, gender and ethnicity selected from the patient's attendants.

Of the cases 60% were males and 40% were females with maximum number of cases 49.2% in between 53 to 62 yrs.

The prevalence of risk factors studied are hypertension, diabetes mellitus, hyperlipidaemia, smoking and alcoholism.

The most prevalent risk factor documented among the cases was hyperlipidaemia (62.3%) followed by hypertension (56.9%) and then smoking (52.3%). Diabetes as a risk factor was seen in 44.6% cases.

Calculation of Odds ratio and 95% Confidence Interval were done to establish statistically the power of association of the risk factors and AMI occurrence.

It revealed that hyperlipidaemia is the prominent risk factors and hyperlipidaemic subjects are 4 times more prone to develop AMI than subjects with normal lipid profile.

The next important risk factor was hypertension and hypertensives are having 2.9 times the risk of developing AMI than normotensive individuals whereas diabetics are having a risk of 2.4 times.

Smoking is also a strong risk factor and smokers run a risk of 2.4 times of developing AMI than non-smokers.

Alcoholism however though known as an important contributor as a risk factor for AMI, in our study we did not had significant statistical association but found nearly same number of cases (36%) & controls (32%) are alcoholics which indeed is a matter of concern, looking into all deleterious effect of alcoholism.

The Interheart Latin American study done to evaluate the risk factors for acute myocardial infarction in Latin American population by Lanus F, Avezum A et.al published in Circulation 2007 calculated Odds ratio and 95% Confidence Interval for several traditional risk factors associated with AMI and documented the following Odds ratio/ 95% Confidence Interval of different risk factors and are statistically significant results. They found strong association with hypertension (OR 2.81/ CI 2.39-3.31); persistent psychological stress (OR 2.81/2.07-3.82); diabetes mellitus (OR 2.59/CI2.09-3.22); current smoking (OR 2.31/CI1.97-2.71) and increased hip to waist ratio (OR 2.49/1.97-3.14). All these risk factors are associated with higher risk of acute myocardial infarction.<sup>11</sup>

These results were similar to the Odds ratio that we achieved for power of association of the risk factors.

In one Indian study published in Indian Journal of Community Medicine 2015 and conducted by Sanjay P Zodpey, Sunanda N Srikanth et al., a case control study, done in Central India also revealed strong association of hypertension, diabetes, smoking, raised serum cholesterol level, financial stress and family history of ischemic heart disease with development of myocardial infarction. The calculation of odd ratio and its 95% Confidence Interval

showed the following statistically significant results: hypertension (OR 2.96/CI1.70-4.98), raised serum cholesterol (OR 3.70/CI2.31-5.94), smoking (OR 1.3/CI 1.04-1.61) and a new risk factor C - reactive protein (OR 3.4/CI 2.10-5.49)<sup>20</sup>

Our study which has been conducted in the Northeast part of the country too showed similar significant results and is concordant with the results done globally and also in the country.

In search of new found risk factors we evaluated Vitamin D deficiency, the co-existence of which with classic risk factors might compound the existing risk. The level of Vitamin D was estimated in all subjects with the classic risk factors. This study showed a significant deficiency of vitamin D level among smokers and seriously compounding risk (P=0.0034). Pais<sup>21</sup> et.al has shown similar results in their study and also in studies performed by Mulligan et al.<sup>22</sup>

Our study found hyperlipidaemia as the most prevalent risk factor and statistically significant association with development of AMI (P=0.000) and if it is further associated with Vitamin D deficiency than the risk increases. This study showed hyperlipidaemia is associated with 32.3% of cases with deficient vitamin D levels and 25.3% of cases with insufficient Vitamin D levels. These results are concordant with the results of Jaydip et.al<sup>23</sup> and the results showed co-existence of low level of vitamin D with hyperlipidaemia endangers population with early onset of cardiovascular and cerebrovascular diseases.

Further studies are needed for confirmation of therapeutic benefits with vitamin D supplementation along with statins.

## CONCLUSION

This is a case control study done in a north-eastern state of India to identify the risk factors associated with development of myocardial infarction and to evaluate the power of association of these risk factors with AMI occurrence and to compare the results with the studies available in the literatures.

130 cases of AMI admitted in Medicine Emergency with ST elevation in ECG were included in the study and 130 controls included healthy individuals from patient's attendants matching with same age, gender and ethnicity.

The most prevalent risk factor identified was hyperlipidaemia followed by hypertension. Smoking and association with diabetes mellitus were next common risk factors.

Estimation of odds ratio and its 95% Confidence Interval showed significant statistical correlation with the risk factors. The results showed the following: hyperlipidaemia (OR 4.1/CI 1.7-4.9), hypertension (OR 2.9/CI 1.7-4.9), smoking (OR 2.4/CI 1.4-2.0) & diabetes (OR 2.4/CI 1.4-4.1). All these associations of risk factors found in our study are statistically significant (P<0.05) and the results of our study are concordant with the studies done elsewhere globally as found in the existing literatures.

We too studied the level of Vitamin D in all cases and controls to reveal if coexisting vitamin D deficiency with the

traditional risk factors further compound the existing risk. Though vitamin D deficiency and vitamin D insufficiency was found in cases and controls with these risk factors, significant statistical association was documented with smoking (P=0.0034) showing that smokers with vitamin D deficiency are having increased risk of development of AMI.

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