

## Study of Serum Calcium as a Risk Factor In Patients of Acute Coronary Syndrome in Tertiary Care Hospital of Madhya Pradesh

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### Abstract

**Introduction:** The aim is to study whether increased serum calcium level is a risk factor in acute myocardial infarction or not.

**Material& Method:** Fifty (50) patients with acute myocardial infarction without taking treatment were included in the study. Twenty five (25) healthy controls were also included in the study for comparison.

**Results:** Calcium levels were increased in patients of myocardial infarction with  $11.3 \pm 0.59$  mg/dl (mean  $\pm$  SD) when compared to controls with  $9 \pm 0.23$  mg/dl (mean  $\pm$  SD) with a statistically significant 'p' value of  $<0.0001$ . CK-MB values were also increased in cases with  $68.38 \pm 5.52$  IU/L (mean  $\pm$  SD) compared to controls with  $16.68 \pm 1.93$  IU/L (mean  $\pm$  SD) with a statistically significant 'p' value of  $<0.0001$ .

**Conclusion:** Increased serum calcium level appears to be a risk factor for myocardial infarction.

**Keywords:** Myocardial infarction, calcium, CK-MB

### Introduction

Ischemic heart disease (IHD) is a condition in which there is an inadequate supply of blood and oxygen to a portion of the myocardium. It occurs when there is an imbalance between myocardial oxygen supply and demand. The most common cause of myocardial ischemia is atherosclerotic disease of a coronary artery causing reduction in the myocardial blood flow and inadequate perfusion of myocardium supplied by the involved coronary artery. Pathophysiology of myocardial infarction (MI) deals with the concept of myocardial supply and demand. It can occur if myocardial oxygen demands are markedly increased or when coronary blood flow is limited<sup>1</sup>.

The most common triggering event is the disruption of atherosclerotic plaque in the coronary artery, which leads to activation of the clotting cascade, sometimes resulting in complete occlusion of the artery<sup>2,3</sup>. An atherosclerotic plaque is formed due to gradual building up of cholesterol and fibrous tissue in the walls of coronary artery<sup>4</sup>, calcium deposition being an important factor<sup>5</sup>. Less commonly MI can also occur due to coronary artery spasm.

Myocardial infarction is the leading cause of death in both men and women all over the world. Acute myocardial infarction generally occurs when there is an abrupt decrease in coronary blood flow, following a rapid thrombotic occlusion of coronary artery which is previously narrowed by atherosclerosis. Myocardial infarction initially manifests as

coagulation necrosis that is ultimately followed by myocardial fibrosis. Myocardial infarction is caused by non-atherosclerotic causes like coronary occlusion secondary to vasculitis, ventriculitis and hypertrophy.

Since calcium is a ubiquitous ion involved in the regulation of a variety of physiological events, it might also be involved in other events leading to CHD such as coronary spasm, thrombosis formation and disruption of atherosclerotic plaque<sup>6,7</sup>. During MI, calcium handling between sarcoplasmic reticulum and myofilaments is disrupted and calcium is diverted to the mitochondria causing edema. Defective calcium handling causes reversible as well as irreversible myocardial injury. Under normal conditions the sarcoplasmic calcium concentration is low with gradient between intra and extracellular compartment. During an action potential, voltage gated  $\text{Na}^+$  channels are activated and inward  $\text{Na}^+$  current induces a rapid depolarization of sarcolemma that opens L type  $\text{Ca}^{++}$  channels. The  $\text{Ca}^{++}$  influx triggers opening of Ryanodine (RYR) receptor leading to release of calcium into the cytosol initiating contraction<sup>8</sup>. Cytosolic calcium accumulation plays a major role in initiation of programmed cell death.

Calcium is the most abundant mineral in the body. The average adult body contains 1kg. 99% is in the skeleton in the form of calcium phosphate salts. The extracellular fluid contains approximately 22.5 mmols of which 9 mmols is in the serum. The normal calcium level in plasma is 9-11mg/dl. Plasma calcium is of 3 types

1. Ionised calcium. 2. Protein(albumin) bound calcium. 3. Calcium complexes with organic acids. 40% of total is in the ionised form. The biological effect of calcium is determined by the amount of ionised calcium rather than the total calcium. The general mechanism of muscle contraction in the heart resembles that of skeletal muscle,

Cardiac muscle, like skeletal muscle is striated and uses actin-myosin-tropomyosin-troponin system. Cardiac muscle exhibits intrinsic rhythmicity and individual myocytes communicate with each other because of syncytial nature. Cardiac muscle thus relies on extracellular  $\text{Ca}^{++}$  for contraction. Isolated cardiac muscle deprived of calcium ceases to beat approximately within 1 minute. Cyclic AMP plays a more prominent role in cardiac than in skeletal

muscle. It modulates intracellular levels of  $\text{Ca}^{++}$  through the activation of protein kinase.

Calcium enters myocytes via the calcium channels, which allow entry of only  $\text{Ca}^{++}$  ions. The major portal of entry is the L type or slow  $\text{Ca}^{++}$  channel, which is voltage-gated, open during depolarization induced by spread of the cardiac action potential and close when the action potential declines. Slow  $\text{Ca}^{++}$  channels are regulated by cAMP dependent protein kinases and cGMP protein kinases and are blocked by calcium-channel blockers<sup>9</sup>. The resultant increase of  $\text{Ca}^{++}$  in the myoplasm acts on the  $\text{Ca}^{++}$  release channel of the sarcoplasmic reticulum to open it. This is called  $\text{Ca}^{++}$  induced  $\text{Ca}^{++}$  release. It is stimulated that approximately 10% of the  $\text{Ca}^{++}$  involved in contraction enters the cytosol from extracellular fluid and 90% from sarcoplasmic reticulum. Stretch of the myocardium is known to modulate the electrical activity of cardiac muscle.

CK-MB isoenzyme is found mainly in the cardiac muscle and also in tongue, diaphragm, uterus, prostate and skeletal muscle. After myocardial infarction the serum CK-MB increases within 3-8 hours, peaks at 9-24 hrs and returns to normal by 48-72 hrs. An elevated serum CK-MB is usually specific for an acute MI<sup>7</sup>.

## Material And Methods

The present study was conducted on 50 individuals diagnosed with myocardial infarction in the Department of Medicine PCMS&RC Bhopal, Madhya Pradesh, India. Their age varies from 40 to 70 years. Age and sex matched 25 healthy individuals taken as control groups.

## Inclusion Criteria

1. Ischemic myocardial pain of more than 30 minutes duration but less than 24 hours.
2. ECG changes– Evidence of Transmural infarction.

## Exclusion Criteria

1. ECG of patients showing left ventricular hypertrophy, bundle branch block, fascicular block.
2. All patients who received IV streptokinase and on oral antiplatelet medication.

Estimation of serum calcium levels was done by Orthocresolphthalein complexone method.

Principle: At alkaline pH, calcium binds with orthocresolphthaleincomplexone to form a bluish purple complex. The intensity of the colour formed is proportional to the concentration of calcium. The optical density is recorded at 578 nm and interference from Mg is overcome by presence of 8-hydroxyquinoline in reagent which binds free magnesium.

**Procedure:** 5ml of blood is taken in a test tube, serum is separated by centrifugation. Test was done by orthocresolphthaleincomplexone method. Optical densities were measured colorimetrically. Values were obtained by standard curve. Normal range:9-11 mgs /dl

The assay for CK-MB activity is performed on serum sample using an automated Mindray BS 300 analyzer. Normal Range of serum CK-MB is 0-24 U/L.

### Results And Observation

The present study comprises of 50 cases of MI patients and 25 healthy controls.

Serum calcium levels increased significantly in patients of myocardial infarction than in healthy controls. In the present study the mean value of calcium among cases is 11.3+0.59 mg/dl (mean +SD) and that of controls is 9.0+0.23mg/dl(mean +SD). The increase of serum calcium in cases compared to controls is significant with „p“ value of <0.0001.

Following acute myocardial infarction CK-MB activity increases significantly and this elevation is highly specific for the diagnosis of MI. Mean value of CK-MB in cases is 68.38+ 5.52 IU/L( mean+ SD) that of controls is 16.68+ 1.93 IU/L ( mean+SD).The increase of CK-MB in cases compared to controls is significant with a „p“ value of <0.0001.

### Discussion

50 MI patients were studied for serum calcium and CK-MB levels. 25 age matched healthy controls were taken for comparison. As per the results obtained it was found that patients with MI had increased levels of calcium compared to healthy controls and they are statistically significant with „p“ value <0.0001.This study correlates with Tromso study<sup>10</sup>,1999 May having a „p“ value <0.001. The possible reason of increased calcium in patients with MI could be due to strong relation of total calcium to blood pressure.

Increased serum calcium is the risk factor in MI. Thus the increased total serum calcium appears to be a marker of cardio vascular disease. Cardiac muscles require calcium to contract and squeeze blood out of the heart into the arteries. At the end of the contraction calcium flows out of the channels to allow the muscle to relax. Increased calcium can cause abnormality in heart muscle leading to tight contraction of myocardium causing arrhythmias. Calcium overload can cause high blood pressure. Calcium is critical in triggering timely and strong enough contractions in cardiac muscle to circulate blood throughout the body. A positive association between serum calcium levels and vascular calcifications were observed in several studies<sup>11</sup>.Increased serum calcium might cause these pathological changes by influencing this calcification modulations such as pyrophosphate and binding to calcium-sensing receptors on vascular smooth muscle cells<sup>12</sup>.

CK-MB levels were significantly increased in MI patients compared to healthy controls, serving as early, relatively easy and widely available tool to diagnose acute MI.

### Conclusion

High serum calcium is found to have correlation with myocardial infarction. Serum calcium was found to be an independent prospective risk factor for MI suggesting that extracellular calcium plays a role in the atherosclerotic process.

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