

Iron Status in ST- and Non-ST-elevated Myocardial Infarction

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Abstract

Background: Myocardial infarction (MI) is the most common cause of death worldwide. The major risk factors for MI are family history, diabetes mellitus, smoking, hypertension, and lipid. Excess serum ferritin as a risk factor for MI is a relatively newer concept. High serum ferritin may increase the risk of MI in the presence of other risk factors that increase the formation of free radicals, thus accelerating atherogenesis through stimulation of low-density lipoprotein oxidation.

Aim: The aim of this study is to evaluate iron status in cases of acute MI (AMI) (ST-elevated MI [STEMI] and non-STEMI [NSTEMI]).

Materials and Methods: The study was conducted in Department of Biochemistry, Mamata Medical College, Khammam. The participants attending OP and IP Departments of General Medicine and Cardiology in Mamata General and Superspeciality Hospital were recruited for the study. Study group comprises 64 cases of AMI and was subdivided based on ST-segment elevation in electrocardiogram as STEMI and NSTEMI (33 and 31). 34 sex- and age-matched healthy participants were selected as controls. Serum ferritin was measured by ELISA. Serum iron was measured by FERROZINE method.

Results: Mean serum ferritin and iron levels were significantly increased in case of AMI when compared with healthy participants.

Conclusion: Serum ferritin and iron levels were increased in AMI and the increase was more pronounced in patients with STEMI.

Key words: Atherosclerosis, Ferritin, Iron, Myocardial infarction

INTRODUCTION

Myocardial infarction (MI) is the most common cause of death worldwide. The major risk factors for MI are family history, diabetes mellitus, smoking, hypertension, and lipids.¹ Excess serum ferritin as a risk factor for MI is a relatively newer concept.² Ferritin is a large protein shell having molecular weight 450 KDa comprised 24 subunits, covering an iron core containing up to 4000 atoms of iron. Ferritin acts as the soluble storage form of iron in tissue.³ High serum ferritin may increase the

risk of MI in the presence of other risk factors that increase the formation of free radicals, thus accelerating atherogenesis through stimulation of low-density lipoprotein (LDL) oxidation.⁴ A possible association between body iron status and the risk of coronary heart disease was bolstered from a 3-year Finnish study relating increased levels of both serum levels of ferritin and dietary iron to an increased risk of MI.⁵ The association of high iron stores and coronary heart disease was first suggested by Sullivan.⁶ Results of some studies have been in favor of ferritin being a risk factor for acute MI (AMI).⁷

A harmful biological effect of excessive iron loading in the human body has been recently suggested. In this regard, iron overloading especially in myocardial tissue has been proposed to be a potent risk factor for ischemic heart disease and occurring AMI.^{5,6,8,9} The cardiac iron deposition

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results in a decrease of heart function on a certain genetic background.¹⁰ Iron can also directly injure the myocardium. Iron can be accumulated in cells as hemosiderin, ferritin, and free iron named labile cellular iron that is the most toxic form stimulating the formation of free radicals.^{11,12} Since serum ferritin concentrations are directly proportional to intracellular ferritin concentration, it is considered the best clinical measure of body iron stores.¹³ Recently, some evidences have been provided linking the increased incidence of coronary artery disease and elevated level of stored iron concentration.⁵ In these, increased estimated body iron stores have been associated with increased risk of AMI in some,¹⁴⁻¹⁶ but some observations could not reveal this relationship.¹⁷⁻²²

MATERIALS AND METHODS

The study was conducted in Department of Biochemistry, Mamata Medical College, Khammam. The participants attending OP and IP Departments of General Medicine and Cardiology in Mamata General and Superspeciality Hospital were recruited for the study. The cases were diagnosed based on (a) typical chest pain, (b) electrocardiogram (c) creatine kinase (MB) levels d) troponin i levels. Study group comprises 64 cases of AMI, and 34 sex- and age-matched healthy participants were selected as control. The study group was subdivided based on ECG (33 and 31).

Informed consent and clearance from the Ethical Committee was taken. Under aseptic precautions, 5 ml fasting blood sample was collected, and serum was separated after clot retraction. Serum ferritin was measured by ELISA. Serum iron was measured by FERROZINE method.

Study Design

This was a cross-sectional comparative study.

Inclusive Criteria

All the patients in the age group of 30-50 were included in the study.

Exclusive Criteria

1. Patients above 50 years
2. Patients on iron and antioxidant supplements.

Statistical Analysis

Mean \pm standard deviation values of all biochemical parameters were calculated in the study and control groups, and the mean difference was compared using *t*-test.

RESULTS

Mean serum ferritin and iron levels are increased in cases of MI compared to controls (Table 1). Among the cases,

there is a significant increase in the levels of mean serum ferritin and iron in cases of STEMI when compared to NSTEMI (Table 2).

DISCUSSION

In our study, serum ferritin and iron are significantly increased in MI, and the rise was more pronounced in STEMI. Serum ferritin more than 200 $\mu\text{g/L}$ has been introduced as a major predictor for occurrence of AMI and the higher rate of this marker led to 5-fold increased risk of MI.²³ Our findings are consistent with previous studies by Klipstein-Grobusch *et al.*²⁴ and Dominguez-Rodriguez *et al.*²⁵ Another evidence of an association between increased risk of MI and elevated serum ferritin concentrations came from the prospective Monica AMI project in middle-aged eastern Finnish men.¹⁰ Frey and Krider did not support the hypothesis that high serum ferritin levels could be associated with myocardial infarct.²⁶

A variety of the underlying reasons has been proposed to explain association between increased ferritin level and occurrence of AMI. First considering the key role of stress on triggering AMI, it was shown that peripheral blood monocytes derived from healthy individuals incubated with hydrocortisone showed a significant enhancement of their ferritin content, a finding suggesting that these cells activated by steroids during stress could be a source of the increased serum ferritin level leading to MI.²⁷ Basic research has provided strong evidence that LDL oxidation plays an important role in the pathogenesis of atherosclerosis and cardiovascular disease.²⁸ LDL oxidation can be enhanced by metal-catalyzed reaction, resulting in highly reactive hydroxyl radicals. Superoxide anions produced by oxidative stress and reducing agents have been found to be capable of mobilizing iron from ferritin. We observed that the elevated serum ferritin concentrations to be associated with increased risk of MI in the Indian population, and ferritin

Table 1: Normal cases and controls

| Parameters | Cases mean \pm SD (n=64) | Controls mean \pm SD (n=34) | P |
|------------------------------|-------------------------------|----------------------------------|---------|
| Ferritin ($\mu\text{g/L}$) | 213.94 \pm 40.2 | 92.24 \pm 19.21 | <0.001* |
| Iron ($\mu\text{g/dL}$) | 110.01 \pm 27.18 | 81.11 \pm 17.33 | <0.001* |

*Statistically significant

Table 2: STEMI and NSTEMI

| Parameters | STEMI mean \pm SD (n=33) | NSTEMI mean \pm SD (n=31) | P |
|------------------------------|-------------------------------|--------------------------------|--------|
| Ferritin ($\mu\text{g/L}$) | 238.52 \pm 43.6 | 187.81 \pm 36.22 | <0.01* |
| Iron ($\mu\text{g/dL}$) | 118.26 \pm 28.7 | 101.24 \pm 26.31 | <0.01* |

*Statistically significant. STEMI: ST-elevated myocardial infarction, NSTEMI: Non-ST-elevated myocardial infarction

may adversely affect MI risk in the presence of other risk factors. It may be possible that these factors in interaction with elevated body iron stores may accelerate atherogenesis by stimulating oxidation of LDL.²⁹

CONCLUSION

Increased serum ferritin and iron levels are seen in MI. The increase is more pronounced in STEMI. Although there are some pathophysiological mechanisms for the role of serum iron and ferritin levels to predict occurrence of AMI, the underlying mechanism remained to be elucidated in further studies. Therefore, screening for iron status and supplementation of antioxidants may be beneficial in the management of MI.

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