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Original Research Article

Analysis of Iron and Lipid Profiles in Indian Male Acute Myocardial Infarction Patients

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Abstract: Body iron contributes to pathogenesis of coronary artery disease (CAD) through formation of free radicals by Fenton and Haber-Weiss reactions. Free radicals cause lipid peroxidation leading to formation of atherosclerotic plaques by deposition of modified low density lipoprotein (LDL). However, the relationship between body iron indices and acute myocardial infarction remains ambiguous. The present study intended to analyze alterations in body iron levels and correlate them with lipid profile in AMI patients in Indian population. The study enrolled 160 male subjects (40-60 years of age), 80 AMI patients with first MI incidence and 80 healthy controls (no history of angina/MI). Serum ferritin was measured by electro-chemiluminescence immunometric method by Roche Cobas e411 analyzer. Serum iron, TIBC, transferrin and lipid profile consisting of cholesterol (total, LDL, HDL), triglycerides were estimated by photometric and apolipoproteins, A1 and B, by immuno-turbidimetric methods on Roche Cobas c501 analyzer using commercially available kits from Roche. Iron and ferritin levels were found to be significantly increased ($p<0.001$) whereas, TIBC and transferrin levels were significantly decreased ($p<0.001$) in sera of AMI cases when compared to control. Patients with AMI had significantly high total cholesterol, LDL cholesterol, triglyceride and apolipoprotein B ($p<0.001$) and significantly low HDL cholesterol and apolipoprotein A1 levels than healthy subjects ($p<0.001$). Serum ferritin level for predicting AMI was found to be more than 196 ng/ml (Sensitivity 89 % and specificity 78%) in ROC curve analysis. In the present study, AMI patients demonstrate elevated serum ferritin levels along with concurrent dyslipidemic changes like raised LDL, total cholesterol, triglyceride and apolipoprotein B and decreased HDL apolipoprotein A1. Such association indicates that the body iron status coupled with the lipid profile might play a role in development and precipitation of acute myocardial infarction in Indian male population.
Keywords: AMI, Iron, Ferritin, Lipid profile, Apolipoprotein.

INTRODUCTION

Coronary artery disease (CAD) and its aftermath, myocardial infarction (MI), continue to be a cause of significant mortality and morbidity worldwide [1]. The Global Burden of Disease (GBD) study reported that in India, the disability-adjusted life years (DALYs) due to ischemic heart disease, were 26.2 million in the year 2010 [2]. The prevalence of CAD in India varies from 1%-2% and 2%-4% in rural and urban population respectively [3].

Body iron is involved in various metabolic processes, such as, synthesis of hemoglobin for transfer of oxygen from lungs to tissues [4], role in metabolism as a component of some proteins and enzymes [5, 6]. Iron is transported by the protein transferrin via blood to different tissues in the body for storage [7]. Iron is stored within a protein complex called ferritin in all the cells, but mainly in bone marrow, liver and spleen [8]. Serum ferritin concentrations correlate well with total body iron stores in steady state conditions [9], thus, serum ferritin is the most convenient laboratory test to estimate the body iron stores.

Free iron catalyzes the generation of hydroxyl radicals from superoxide and hydrogen peroxide by Fenton and Haber-Weiss reactions [10]. Free radicals cause lipid peroxidation leading to formation of atherosclerotic plaques by deposition of modified low density lipoprotein (LDL) [11]. Iron complexes are known to be involved in nitric oxide metabolism, which has a direct impact on the atherosclerosis process [12]. The regulatory role of iron in the activation of NF-κB was found to be crucial in TNF-α-induced inflammatory pathway in the atherosclerotic process [13]. However, the relationship between body iron indices and acute

myocardial infarction still remains ambiguous. Few studies have been carried out to investigate the relationship of serum iron profile and risk of acute myocardial infarction in Indian population. The present study intended to analyze alterations in body iron profile and correlate it with lipid profile in adult Indian male AMI patients.

METHOD AND MATERIAL

The case control study enrolled 160 male subjects (40-60 years of age), 80 AMI patients with first MI incidence and 80 healthy controls (no history of angina/MI). The study was conducted in the Department of Biochemistry of a tertiary care teaching hospital in North India over a period of one year from April 2016 to March 2017. The study was approved by Medical Ethics Committee of the Institution and written informed consent was obtained from all participants. Confirmation of diagnosis of AMI was based on WHO criteria of clinical history suggestive of myocardial ischemia, ECG findings and raised biochemical markers like CK-MB and hs-Troponin T. They had not taken B vitamins (B6, B12 and folic acid) and iron supplements for the last 5 months(self-administered questionnaire); had no history of smoking, hematological disorders (anemia, polycythemia, myeloproliferative disorders), severe bleeding that required a blood transfusion, malabsorption syndrome, liver disease, kidney disease, diabetes mellitus, hypertension and cancer. Fasting venous blood (10 ml) was collected within 24 hours of hospital admission. Serum ferritin was measured by electro-chemiluminescence immunometric method by Roche Cobas e411 analyzer. Serum iron, TIBC (total iron binding capacity), transferrin and lipid profile consisting of cholesterol (total, LDL, HDL), triglycerides were estimated by photometric and apolipoproteins, A1 and B, by immuno-turbidimetric methods on Roche Cobas c501 analyzer using commercially available kits from Roche. Unpaired student's t test was applied for statistical analysis. Normally distributed data is displayed as mean and 95% confidence interval (CI). The p value of <0.05 was considered significant. Receiver operating characteristic (ROC) curve analysis was done to determine the predictive value of serum ferritin for AMI.

RESULTS

The mean age of the enrolled AMI patients and control subjects was 49.2 ± 8.7 years and 48.4 ± 7.2 years respectively; the range being 40–60 years for both. The mean hemoglobin level was almost same for the AMI cases (15.49 g/dl) and the controls (15.63g/dl). The different lipid profile parameters studied in the sera samples of AMI patients and healthy controls are listed in the Table 1.

Table 1: Comparative analysis of lipid profile parameters in sera of AMI patients and healthy subjects

PARAMETER (in serum)	CASES (n= 80) *	CONTROLS(n= 80) *	p value
Total Cholesterol (mg/dl)	223.2±29.64	145.9±20.74	< 0.001
LDL Cholesterol (mg/dl)	150.0 ±25.88	87.84 ± 19.71	< 0.001
HDL Cholesterol (mg/dl)	29.59± 7.306	42.08± 9.153	< 0.001
Triglycerides (mg/dl)	198.9 ±32.33	137.6 ±19.21	< 0.001
Apolipoprotein B (mg/dl)	160.2 ±17.73	100.0 ± 20.65	< 0.001
Apolipoprotein A1(mg/dl)	95.87 ±11.48	136.6 ± 18.78	< 0.001

*Parameter values are mean ± S.D for n = 80 subjects in each group.

In this study, total cholesterol, LDL cholesterol, triglycerides and Apo B levels were found to be raised in the sera of AMI patients than the controls. On the contrary, HDL cholesterol and Apo A1 levels were significantly reduced in sera of the AMI patients as compared to the serum levels of the control subjects.

Our results demonstrated significantly high levels of serum iron and ferritin in the AMI patients in comparison to the healthy individuals. However, serum TIBC and transferrin concentration were considerably low in the AMI patients as compared to the controls (Table 2).

Table 2: Comparison of iron profile in serum samples of AMI patients and controls

PARAMETER	CASES (n= 80) *	CONTROLS (n= 80) *	p value
Serum Iron (µg/dl)	173.9 ±36.05	124.1 ±27.61	< 0.001
Serum TIBC (µg/dl)	211.82 ± 24.32	336.2 ± 21.17	< 0.001
Serum Transferrin (mg/dl)	180.9 ± 28.77	244.1± 24.27	< 0.001
Serum Ferritin (ng/ml)	227.7 ± 30.36	153.0±25.86	< 0.001

*Parameter values are mean ± S.D for n = 80 subjects in each group.

In ROC curve of serum ferritin level, the area under curve (AUC) was found to be 0.943 (95% confidence interval l=0.911 to 0.975). The optimal cut off value of serum ferritin level for predicting AMI was 196 ng/ml (Sensitivity 89 % and specificity 78%).

DISCUSSION

Although the pathogenesis of acute myocardial infarction (AMI) is multi-factorial, impaired lipid metabolism seems central to its development [14, 15]. Our results showed significant increase in the levels of total cholesterol, triglyceride, LDL and Apo B in the sera of the AMI patients in comparison to the healthy controls ($p < 0.001$). At the same time, HDL cholesterol and Apo A1 levels were found to be significantly lower in sera of the AMI patients than the control group subjects ($p < 0.001$). Several lines of evidence indicate that the oxidative modification of LDL plays a key role in atherosclerosis [16-18], as the oxidized LDL is ingested by macrophages to form foam cells [19, 20]. On the other hand, HDL particles are believed to retard atherosclerosis via the reverse cholesterol transport pathway [21]. Thus, our findings suggest that decreased serum HDL along with increased serum LDL levels seem to be strong indicators of AMI risk. Similarly, high Apo B and low Apo A1 serum levels in AMI patients as compared to healthy controls indicate that an elevated Apo B/Apo A1 ratio is associated with AMI risk [22-24].

In this study, we found increased body iron stores in AMI patients as serum ferritin levels were significantly raised in comparison to healthy controls. Serum ferritin level >196 ng/ml was significantly associated with AMI. At the same time, we observed raised iron and reduced TIBC and transferrin in sera of AMI cases. These findings are in agreement with the findings of previous studies [25-30].

As we know that, iron is tightly bound to transferrin and ferritin proteins to prevent its involvement in free radical formation. High body iron can catalyze free radical formation through Haber-Weiss and Fenton reactions generating highly reactive hydroxyl radical due to its ability to get reversibly oxidized and reduced [31]. The free radicals, thus generated promote lipid peroxidation, followed by reaction of products of lipid hydro peroxides, mostly aldehydes with LDL-apolipoprotein B leading to oxidative modification of LDL particles [18, 19, 32], oxidized LDL induces inflammation in blood vessels, including the progression of atherosclerosis [20, 33] and increased risk of death from AMI [34].

CONCLUSION

Indian male with high body iron stores are at an increased risk of first acute myocardial infarction. Therefore, in our view, changes in iron status in conjunction with alterations in lipid levels can precipitate AMI in Indian male population.

Conflict of Interest: None

Acknowledgment: None

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