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Study of pro-oxidant status in acute myocardial infarction

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ABSTRACT

Background: Apart from several well documented risk factors; oxidative stress may play an important role in the pathogenesis of myocardial infarction. Our study has been designed to investigate the pro-oxidant status in AMI patients who have no previous history of diabetes, hypertension and habit of smoking. **Aims and Objectives:** To measure the level of serum thiobarbituric acid reactive substances(TBARS) to assess the extent of oxidative damage in recently diagnosed cases of AMI and to look for any correlation between this stress marker and some of the lipid profile markers. **Materials and Methods:** A cross sectional study was conducted in a tertiary care hospital with 50 non-diabetic, non-hypertensive, non-smoker AMI patients of either sex as Cases and 50 age and sex matched healthy Controls. The biochemical parameters were measured by validated techniques. **Results:** Level of serum TBARS (4.78 ± 1.06 nmol/ml) has significantly increased ($p < 0.001$) in cases with respect to control group(2.19 ± 0.41 nmol/ml); a positive correlation between serum TBARS and LDL; a negative correlation between serum TBARS and HDL in cases. **Conclusion:** Our study indicates an increased oxidative stress in AMI patients even in absence of some high risk factors which are oxidative stress inducers by themselves. This evidence suggests that oxidative stress itself may play an important role in the pathogenesis of myocardial infarction. So, the oxidative stress marker may have the importance in early diagnosis of AMI. It also suggests the potential appropriateness of antioxidant therapy in the prevention of AMI.

Key words: AMI; Oxidative stress; Non-diabetic; Non-hypertensive; Non-smoker; TBARS; LDL; HDL

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INTRODUCTION

Cardiovascular disease (CVD) is one of the leading causes of death among people of both sexes in industrialized countries of the world. The incidence of CVD is showing increasing trend even in developing countries like India due to industrialization and changing life style.

Coronary heart disease (CHD); syn: ischaemic heart disease (IHD) is an important component of CVD. The WHO has drawn attention to the fact that CHD is our modern "epidemic" i.e. a disease that affects populations, not an unavoidable attribute of ageing.[1] Acute myocardial infarction (AMI) is specific and the important manifestation of coronary heart disease.

Coronary artery disease (CAD) is caused by additive and interactive effects of inherited and environmental factors. Coronary atherosclerosis is a complex inflammatory process characterized by accumulation of lipids, macrophages and smooth muscle cells resulting in the formation of intimal plaques in the large and medium size epicardial coronary arteries.

The etiopathogenesis leading to atherogenesis is still unknown. But a number of well documented risk factors have been identified. Modifiable risk factors are serum lipids, lipoproteins, hypertension (HTN), diabetes Mellitus (DM), smoking and tobacco chewing etc. Non modifiable risk factors are age, sex, genetics, and family history.[2] However, these factors explain only part of attributable

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cardiovascular disease. Evidence suggests that oxidative stress may play an important role in the pathogenesis of myocardial infarction.[3]

Oxidative stress is defined as a disturbance in the pro-oxidant and antioxidant balance in favor of the former, leading to potential damage and disruption of redox signaling and control. It has been shown that oxidative stress which is due to the disturbance in the balance between the production of reactive oxygen species (ROS) and antioxidant defense mechanisms of the body plays a vital role in the pathogenesis of coronary atherosclerosis and its complications. Enhanced formation of ROS may affect four fundamental mechanisms that contribute to atherogenesis namely: oxidation of low density lipoprotein (LDL), endothelial dysfunction, vascular smooth muscle cell growth and monocyte migration.[4]

Some systemic diseases like diabetes mellitus, hypertension themselves induce the oxidative stress as is the habit of smoking. In our study, we have excluded these contributory factors i.e. we have considered nondiabetic, nonhypertensive and nonsmoker AMI Patients. The primary objective of the current study was to evaluate the severity of oxidative stress in those previously apparently healthy patients and the secondary objective was to observe for any correlation between stress markers and some lipid profile markers.

With this background, the present study was designed to estimate the oxidative stress marker namely serum thiobarbituric acid reactive substances(TBARS) and serum lipid profile in previously apparently healthy AMI patients (free from high risk factors like diabetes mellitus, hypertension, smoking) admitted in a tertiary care hospital in north Kolkata,West Bengal.

MATERIALS AND METHODS

A total of 100 subjects, 50 patients (test) and 50 age/sex matched controls were selected for the study. The patients in the study group were diagnosed with AMI and were admitted in cardiology department. The study design was pre-approved by the ethical committee of the institute. All participants selected were counseled and were informed about the study with a written consent from them before embarking the study. Patients who were diagnosed to have AMI by clinical manifestations, ECG changes and by cardiac biomarkers like CPK, CPK-MB, Troponin T within 72 hrs of onset of chest pain; not received any thrombolytic therapy and willing to give valid consent were included. Control group was age and sex matched healthy people.

The patients with previous history of known Lipid disorders; on drugs (e.g. statin group) affecting lipid metabolism; with previous history of MI; with Diabetes mellitus or Hypertension; having smoking habit; with thyroid hormone disorders; receiving any antioxidant (Allopurinol, Probucol) or vitamin supplements; suffering from cancer, dermatological disorders, psychiatric disorders, CNS disorders; suffering from any acute or chronic inflammatory illnesses were excluded.

The study was a Cross sectional, descriptive, observational one. Total Cholesterol (TC) was measured by cholesterol oxidase phenol amino phenazone (CHOD-PAP) method,[5] triglyceride (TG) by glycerol-3-phosphate oxidase phenol amino phenazone (GPO-PAP) method,[5] high density lipoprotein (HDL) cholesterol by Accelerator Selective Detergent method[6] and low density lipoprotein (LDL) cholesterol was calculated by Friedewald Equation.[7] Serum thiobarbituric acid reactive substances (TBARS) was measured by Photometric Method (Method of Yagi).[8]

Statistical Analysis

Statistical analysis was performed using Statistical Package for the Social Sciences, SPSS 20. The quantitative data were evaluated whether they followed the normal distribution. The basis to declare a certain parameter as normally distributed was SD < ½ MEAN. Results were expressed as mean ± SD as well as median (confidence interval) according to distribution of the data. The differences of mean values between groups were established by Independent samples t - test. Pearson correlation coefficients were used to test correlation between two parameters. A p-value less than 0.05 (2-tailed) was considered statistically significant.

RESULTS

Comparative analysis of serum Lipid Profile i.e Total cholesterol, Triglycerides, HDL and LDL in controls and cases is shown in Table 1. Mean levels of serum Total cholesterol, Triglycerides & LDL have increased in cases compared to controls and are statistically highly significant. At the same time, mean serum level of HDL has decreased in cases compared to controls which is also statistically highly significant ($p<0.001$).

Comparative analysis of TBARS in controls and cases is shown in Table 2. Mean level of serum TBARS has increased in the case group compared to the control group and it is statistically highly significant ($p<0.001$). The pearson correlation coefficient between serum TBARS and serum HDL and LDL is shown in Table 3 and Table 4 respectively.

Scatter diagram showing distribution of serum HDL values according to serum TBARS values in cases of

Table 1: Comparison of lipid profile in controls and cases

Parameter	Mean±SD		p value
	Controls	Cases	
Triglycerides (mg/dl)	112.02±14.74	154.88±13.68	<0.001
Total Cholesterol (mg/dl)	156.34±10.54	214.56±23.63	<0.001
HDLc (mg/dl)	50.62±3.43	44.52±2.52	<0.001
LDLc (mg/dl)	83.26±10.17	140.40±21.46	<0.001

Table 2: Comparison of serum TBARS in controls and cases

Parameter	Mean±SD		p value
	Controls	Cases	
TBARS (nmol/ml)	2.19±0.41	4.78±1.06	<0.001

Table 3: Statistical correlation between serum TBARS and serum HDL in Acute Myocardial Infarction patients

Parameter	Pearson correlation coefficient (r)	p value
serum TBARS vs serum HDL	–0.737	<0.001

Table 4: Statistical correlation between serum TBARS and serum LDL in Acute Myocardial Infarction patients

Parameter	Pearson correlation coefficient (r)	p value
serum TBARS vs serum LDL	0.907	<0.001

Acute Myocardial Infarction as shown in Figure 1. There is significant negative correlation between these two parameters.

Scatter diagram showing distribution of serum LDL values according to serum TBARS values in cases of Acute Myocardial Infarction (Figure 2). There is significant positive correlation between these two parameters.

DISCUSSION

In the current study, the case group comprised of 50 recently diagnosed AMI patients. They were apparently healthy as they had no known previous history of diabetes, hypertension and smoking. When their lipid profile status was assessed, only 5 AMI patients i.e. 10% of the case group were normolipidemic and the rest 90% were dyslipidemic and all of them had increased serum TBARS in comparison to their age and sex matched healthy controls. So, it is quite apparent that they have increased oxidative stress. But the impact of the incidental finding of dyslipidemia on oxidative stress related status in these cases

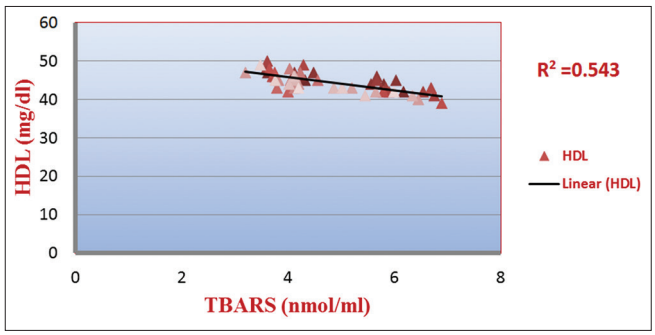

Figure 1: Correlation between serum TBARS and serum HDL in Acute Myocardial Infarction

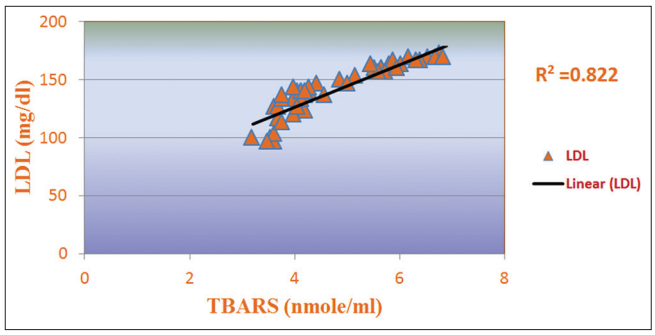

Figure 2: Correlation between serum TBARS and serum LDL in Acute Myocardial Infarction

cannot be ascertained as derangement of lipid regulation is associated with the MI event itself.

We found significant increase in triglyceride levels in patients compared to controls ($p<0.001$); significant increase in total Cholesterol levels compared to controls ($p<0.001$); significant decrease in HDL levels compared to controls ($p<0.001$); significant increase in LDL levels compared to controls ($p<0.001$).

Meisinger C et al[9] in a prospective, nested, case control population based MONICA study showed significant raised concentrations of LDL, predictive of future CHD events in apparently healthy men. Thus they showed, ox-LDL may represent a promising risk marker for clinical CHD complications and should be evaluated in further studies. HDL is regarded as one of the most important protective factors against atherosclerosis. HDL's protective function has been attributed to its active participation in the reverse transport of cholesterol and its paraoxonase activity which protects LDL from oxidation.[10]

Triglyceride brings significant change in LDL particle size, density, distribution and composition producing small dense LDL which is more atherogenic; oxidation of LDL plays important role in atherogenesis. Since most of the cholesterol is carried by LDL, increase in LDL level may directly lead to increase in total cholesterol levels.

In our study, there was significant increase in serum TBARS levels in patients compared to controls ($p<0.001$). Our findings are in accordance with K. Kaur et al[11] who attributed increased level of lipid peroxidation occur as a result of the fact that naturally occurring scavenging mechanisms are suppressed and free radical generating processes are enhanced.

We found positive correlation between serum TBARS and LDL; negative correlation between serum TBARS and HDL. It clearly indicates that hypercholesterolemia and lipid peroxidations are independent risk factors for Myocardial Infarction. Changes in the concentration of plasma lipids including cholesterol are complications frequently observed in patients with MI and certainly contribute to the development of vascular disease. Cholesterol has been singled out as the primary factor in the development of atherosclerosis.

CONCLUSION

So, it is evident that our study group of AMI patients have increased oxidative stress even in the absence of previous exposure to some known oxidative stress inducing conditions like DM, HTN, smoking. Also, 90% of our AMI patients have incidental finding of dyslipidemia. From our study findings, we can assume that oxidative stress itself may play an important role in the pathogenesis of myocardial infarction. In conclusion, this study suggests that if we can assess the pro-oxidant status of the population who are apparently healthy; it will significantly contribute to the risk assessment of CHD and its prophylaxis at an early stage.

WHAT THIS STUDY ADDS

Our study has excluded three most well established stress inducing risk factors of AMI from the case group when designed to study the pro-oxidant status in the recently diagnosed AMI patients; thus has helped to establish the evidence that oxidative stress itself is a contributing factor of CHD.

LIMITATIONS OF THE STUDY

We could not exclude dyslipidemia from the case group which is itself an inducer of oxidative stress; for that a study of much longer duration is needed.

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Authors Contribution:
TK-Concept and design of the study, collected sample and data, statistically analyzed and interpreted, literature search, manuscript preparation; **CS**–Concept and design of the study, method standardization, critical revision of the manuscript; **SD**–Reviewed the literature, helped in preparing first draft of manuscript; **BM** – Helped in sample collection, review of the study.

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