*Short Communication*

# DOES PLASMA FIBRINOGENS AND C-REACTIVE PROTIEN PREDICTS THE INCIDENCE OF MYOCARDIAL INFRACTION IN PATIENTS WITH NORMAL LIPIDS PROFILE?

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**ABSTRACT**

***Objectives*:** To evaluate plasma fibrinogen and C-reactive proteins in patients with acute myocardial infarction (AMI) and compare it with normal lipid profile in healthy controls.

***Methodology:*** Plasma fibrinogen and C-reactive proteins were determined in 165 patients and 165 age –sex matched control. The plasma fibrinogen was determined using kit, which was obtained from TECO GmbH, Dieselstr. 1, 84088 Neufahrn NB. The C-reactive protein were determined using high sensitivity enzyme Immunoassay kit manufactured by Life Diagnostics, inc. Also lipid profile was analysed enzymatically in these subjects. The values were expressed as means ± standard deviation (SD) and data from patients and controls was compared using student "t" test.

***Results:*** Serum CRP and Plasma Fibrinogen were increased significantly ($p<0.001$) in AMI subjects compared to controls. High fibrinogen concentration and C-Reactive proteins seem to be important contributory risk factor in Indian CAD patients.

***Conclusions:*** Thrombotic and inflammatory markers in combination may contribute to AMI with increased severity of the disease. Further larger studies on a nationwide basis recruiting a large number of AMI patients should be done to substantiate these findings.

**KEY WORDS:** Normal lipid profile, Plasma Fibrinogen, C-Reactive proteins and AMI.

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## INTRODUCTION

Although studies have demonstrated the role of fibrinogen and C-reactive protein as a coronary risk factor, there are controversial data on the correlation between plasma fibrinogen and c-reactive proteins and the ischemia process. Data regarding the role of fibrinogen and C-reactive proteins in patients of acute myocardial infarction with normal lipid profile is scanty. With the current understanding of the role of fibrinogen and C-reactive protein the present study was undertaken in normolipaedemic patients of acute myocardial infarction. Coronary Heart Disease (CHD) is associated with the greatest morbidity and mortality in industrialized countries.[1] The cost of management of CHD is a significant economic burden and so early detection and management is crucial. In the last decades a number of studies showed effective cost-benefit ratio of interventional approaches on the so-called "traditional" risk factors for coronary artery disease, with significant reductions in both cardiovascular morbidity and mortality.[2,3] The advancement in the understanding of pathophysiology of atherosclerotic vascular

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disease has given new insights regarding potential indicators of underlying atherosclerosis and cardiovascular risk. Thus, it has been recently tried world-wide to identify "new" possible atherosclerosis risk factors, including biochemical factors and genetic polymorphisms.[4] Several studies have suggested that high concentrations of fibrinogen may represent a strong risk factor for cardiovascular diseases[5-7] particularly Acute Myocardial Infarction.[8-10] Some of the newly emerged risk factors are called 'novel risk factors' which includes Lp(a), homocysteine, and hs CRP. Therefore, the aim of the present study was to evaluate, in a group of patients of AMI with normal lipid profile, the possible predictive role of plasma fibrinogen and C - reactive protein levels compared to normal healthy control. This study was undertaken due to lacunae of data on plasma fibrinogen and C-Reactive proteins in AMI patients with normal lipid profile.

## PATIENTS AND METHODS

*Setting Design and patients:* The study consisted of 165 patients (123 men and 42 women) with AMI, admitted to the Intensive Cardiac Care Unit, Faculty of Medicine, University of Peradeniya, Sri Lanka. The diagnosis of AMI was established according to diagnostic criteria: chest pain, which lasted for up to three hours, ECG changes (ST elevation of 2mm or more in at least two leads) and elevation of serum creatine phosphokinase (CPK-MB) and aspartate aminotransferase enzyme elevation. The study was conducted for a period of four and half years from April 2002 to September 2006. Informed consent was taken.

*Inclusion criteria:* Patients with diagnosis of AMI with normal lipid profile.

*Exclusion criteria:* Patients with diabetes mellitus, renal insufficiency, current and past smokers, hepatic disease or taking lipid lowering drugs or antioxidant vitamin supplements.

*Selection of Controls:* Age-, sex-matched subjects healthy volunteers consisting of 165 subjects, 123 men and 42 women were studied as control.

*Collection of Samples:* Blood collection and biochemical methods used: 10ml of blood was collected after overnight fasting in different containers.

1. EDTA vial: 5.0ml of blood was taken which was used for Plasma Fibrinogen assay.
2. Plain vial: Remaining blood was taken and serum was separated. Serum was used for determination of lipid profile, C-reactive proteins.

*Lipid profile:* Total cholesterol, triglycerides, and HDL-cholesterol) were analyzed enzymatically using kit obtained from (Randox Laboratories Limited, Crumlin, UK). Plasma LDL-cholesterol was determined from the values of total cholesterol and HDL-cholesterol using the following formulae:

$$\text{LDL-cholesterol} = \text{Total cholesterol} - \frac{\text{Triglycerides}}{5} - \text{HDL-cholesterol (mg/dl)}$$

*C-reactive protein:* The C-reactive protein were determined using high sensitivity enzyme Immunoassay kit[11] manufactured by Life Diagnostics,inc., Catalog Number: 2210. The principle of the assay was based on a solid phase enzyme-linked immunosorbent assay.

*Plasma Fibrinogen:* The plasma fibrinogen was determined using kit[12] which was obtained from TEClot Fib Kit 10 Catalog No: 050-500, manufactured by TECO GmbH, Dieselstr. 1, 84088 Neufahrn NB Germany.

*Statistical Analysis:* The data from patients and controls were compared using Student's 't'-test. Values were expressed as mean ± standard deviation (SD). Microft excel for windows 2000 was used for statistical analysis. 'P' value of less than 0.05 was considered to indicate statistical significance.

## RESULTS AND OBSERVATIONS

Baseline variable of control and AMI patients are shown in Table-I. The differences in age, height and body mass index (BMI) in control and AMI patient are insignificant. The weight, waist circumference, mid arm circumference, biceps and triceps skin fold thickness were higher in AMI subjects as compared to control ($p<0.001$) (Table-I) and (Table-II). Systolic and

Table-I: Baseline variables in Control and AMI patients (mean ±SD)

| *Variables* | *Control (n=165)* | *Case (n=165)* |
|---|---|---|
| Age | 60.55 ± 3.98 | 61.84 ± 3.80† |
| Height (cm) | 1.63 ± 0.04 | 1.64 ± 0.05 ‡ |
| Weight ( kg) | 68.34 ± 3.97 | 72.01 ± 5.37 § |
| BMI ( $kg/m^2$) | 25.40 ± 1.20 | 26.16 ± 1.45 \|\| |
| Waist Circumference (cm) | 93.70 ± 3.63 | 100.77 ± 6.06 § |
| Hip Circumference (cm) | 100.01 ± 3.16 | 105.72 ± 5.23 § |
| Waist: Hip* | 0.93 ± 0.01 | 0.95 ± 0.01 ¶ |
| Mid Arm Circumference(cm) | 29.70 ± 1.47 | 30.63 ± 1.87** |
| Biceps skin fold thickness (mm) | 6.95 ± 1.05 | 7.5 ± 1.38 § |
| Triceps skin fold thickness (mm) | 11.97 ± 1.27 | 12.89 ± 1.69 § |
| Systolic blood pressure(mm of Hg) | 113 ± 8 | 136 ± 23 ** |
| Diastolic blood pressure(mm of Hg) | 85 ± 7 | 95 ± 10 ** |

* ratio † (p=0.0037) ‡ (p=0.2919) § (p<0.001) || (p<0.01) ¶ (p<0.02)** (p<0.05) degree of freedom 328

diastolic blood pressure was significantly higher in AMI patient compared with controls (p<0.05) (Table-I).

The lipid profile are shown in Table-II. Total cholesterol, TC: HDL-C ratio, triglycerides, LDL-cholesterol, LDL: HDL-C ratio were higher in AMI subjects as compared to control (Table-II) (p<0.001). Also, significant differences were seen in HDL-C levels between AMI and controls (p<0.001). LDL-cholesterol, LDL: HDL-C ratio were higher in male AMI subjects compared to control (Table-IV) (p<0.001).

The C-reactive protein and plasma fibrinogen concentrations are shown in Table-II. Both parameters were significantly increased (p<0.001) in AMI patients compared to controls.

## DISCUSSION

The present study investigated fibrinogen and C-reactive protein in acute myocardial infarct patients since there is a paucity of data in Indian patients. There have also been reports

Table-II: Lipid profile and plasma fibrinogen and C-reactive proteins in control and AMI patients (mean ± SD)

| *Variables* | *Controls (n=165)* | *Patients (n=165)* |
|---|---|---|
| *Total Cholesterol* § | 168.58 ± 12.16 | 186.44 ± 13.95 † |
| *HDL-Cholesterol* § | 50.51 ± 6.78 | 41.27 ± 4.62 † |
| *TC: HDL-C** | 3.39 ± 0.36 | 4.57 ± 0.58 † |
| *Triglycerides* § | 107.84 ± 11.51 | 128.96 ± 12.19 † |
| *LDL-Cholesterol* § | 83.59 ± 11.95 | 119.37 ± 14.05 † |
| *LDL:HDL-C** | 1.90 ± 0.31 | 2.93 ± 0.51 † |
| *TG: HDL-C** | 2.17 ± 0.35 | 3.16 ± 0.49 ‡ |
| *Plasma Fibrinogen (mg/dl)* | 237.55 ± 17.40 | 357.88 ± 23.18† |
| *C-Reactive Proteins (mg/L)* | 1.12 ± 0.33 | 2.97 ± 1.11 \|\| |

* ratio † (p<0.001) ‡ (p= 1.0008) § (mg%) || (p<0.05) degree of freedom=328 Plasma fibrinogen CI= 23.18 ± 5.937 C-reactive protein CI = 1.11 ± 0.284

which show that cardiovascular disease has reached alarming proportions in India and it cannot be neglected.[13,14] The present study found higher levels of plasma fibrinogen and C-reactive protein (CRP) in patients with AMI compared to control (p<0.001). Fibrinogen levels were significantly elevated in MI patients in agreement with previous Indian studies.[15-17]

Various studies have[18] suggested that the genesis of atherosclerotic plaque is dependent on the interplay of cellular components of the immune system like cytokines, adhesion molecules, lipids, platelets and endothelial cells, and the role of inflammatory markers like C-reactive protein cannot be ignored.[19] It is an acute phase reactant considered as a classical marker for inflammation. Acute inflammation, infection, or tissue injury induces a marked increase in CRP. As atherosclerosis involves inflammation of the vascular endothelium, CRP levels tend to be raised.[20] The notion that fibrinogen is strongly, consistently, and independently related to coronary risk has been widely accepted. The evidence is based on numerous prospective epidemiological studies and clinical observations. However, the reasons why fibrinogen is elevated in coronary disease and in atherosclerosis are not fully understood. All cells involved in the atherogenetic process

are able to produce cytokines which induce an acute phase reaction. The potential pathophysiologic mechanisms by which elevated fibrinogen levels mediate coronary risk are manifold: It forms the substrate for thrombin and represents the final step in the coagulation cascade; it is essential for platelet aggregation; it modulates endothelial function; it promotes smooth muscle cell proliferation and migration; it interacts with the binding of plasminogen with its receptor; and finally it represents a major acute phase protein. Whether or not fibrinogen is causally involved in atherothrombogenesis still remains to be determined and even though other unsolved issues await conclusive answers, fibrinogen has emerged as an important additional marker of coronary risk.

## CONCLUSIONS

High fibrinogen concentration and C-Reactive proteins seem to be important in Indian CAD patients. Thus, it can be said that thrombotic and inflammatory markers in combination may contribute to AMI with increased severity of the disease. Further larger studies on a nationwide basis recruiting a large number of AMI patients should be done to substantiate these findings.

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