

A Comparative Study on Plasma Fibrinogen and hs-CRP in Metabolic Syndrome

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ABSTRACT

Back ground & Objective: Metabolic syndrome (MS) comprises a group of various metabolic abnormalities related with high risk of cardiovascular disease. The relationship of plasma fibrinogen and hs-CRP levels with MS remains inconclusive. The aim of this study was to assess the correlation of fibrinogen and hs-CRP levels in metabolic syndrome.

Methods: It is a case control study. Detailed clinical, epidemiological and anthropometric characteristics were recorded using pro-forma. 5ml fasting venous blood collected from all the subjects after getting the informed consent. The blood samples thus obtained was used for studies including Lipid profile, hs-CRP, blood sugar and plasma fibrinogen.

Results: Fibrinogen and hs-CRP levels show significant increase in MS group. But there is no significant correlation between fibrinogen and hs-CRP levels.

Interpretation & Conclusion: Hyper fibrinogenemia and an increase in hs-CRP level in the test population explain the increased cardiovascular risk. Plasma determination of these inflammatory biomarkers might have a role in predicting the severity of metabolic syndrome.

Key words: Metabolic syndrome, Fibrinogen, hs-CRP

INTRODUCTION

Metabolic syndrome is a clinical condition characterized by the co-occurrence of abdominal obesity, impaired glucose tolerance, dyslipidemia and hypertension, associated with a high risk of coronary heart disease and mortality. The National Cholesterol Education Program's Adult Treatment Panel III report (ATP III)¹ identified the following components of the metabolic syndrome which relate to CVD:

1. Abdominal obesity
2. Dyslipidemia
3. Hypertension
4. Insulin resistance
5. Pro-inflammatory state
6. Pro-thrombotic state

These components of the metabolic syndrome are classified into *underlying*, *major*, and *emerging* risk factors. According to ATP III, underlying risk factors for CVD are abdominal obesity, physical inactivity, and an atherogenic diet. The major risk factors are cigarette smoking, raised blood pressure, high LDL cholesterol, low HDL cholesterol, family history of premature coronary heart disease (CHD), and aging. The emerging risk factors include elevated triglycerides, small LDL particles, insulin resistance, glucose intolerance, pro-inflammatory state, and pro-thrombotic state.

In the present study, we are evaluating the markers of pro-inflammatory and pro-thrombotic state. The pro-inflammatory state is recognized clinically by high C-reactive protein (CRP) level. A pro-thrombotic state is characterized by elevated plasma plasminogen activator inhibitor (PAI)-1 and

fibrinogen. Fibrinogen and CRP being acute phase reactants, rise in response to a high-cytokine state. Thus, pro-thrombotic and pro-inflammatory states might be metabolically interrelated.

FIBRINOGEN

Fibrinogen is a key plasma protein and cofactor in the final step of the coagulation cascade. It also plays an important role in plasma viscosity and erythrocyte aggregation². During an acute phase reaction, fibrinogen expression in the liver is up-regulated by interleukin-6. Chronic inflammatory processes can induce a persistent increase of interleukin-6 and thus turn the acute phase reaction into a perpetuating state with increased levels of fibrinogen³.

Elevations of fibrinogen and C-reactive protein have been identified in patients with unstable angina, as inflammation plays a major role in plaque rupture and thrombosis⁴. Thus, plasma fibrinogen is emerged as a risk factor for coronary heart disease. Plasma fibrinogen level has been correlated with BMI, systolic and diastolic blood pressure, total cholesterol, LDL, triglyceride, insulin and inversely with HDL cholesterol.

Moreover, subjects with diabetes mellitus have hyper-reactive platelets. This platelet hyper-reactivity in diabetes may result from increased fibrinogen levels, because fibrinogen act as across bridge between platelets.⁵ Poor diabetic control is also associated with higher levels of fibrinogen.

C - reactive protein (hs-CRP)

C-reactive protein (CRP) is the most widely studied pro-inflammatory molecule. In healthy individuals, CRP levels are only minimal. Under acute conditions, levels of CRP in the circulation increase during the first 6 to 8 hours and reach a peak value after approximately 48 hours⁶. CRP is an effective clinical marker because of its analytical stability, reproducible results, and commercial availability of high sensitivity assays with good precision.

Recent studies suggest that CRP may have direct pro-inflammatory effects and contributes to the initiation and progression of atherosclerotic lesions. Functionally, CRP activates circulating monocytes and induces their recruitment to the arterial wall. It also mediate LDL uptake by macrophages and induce expression of cell adhesion molecules and tissue factor. Latest epidemiological studies have supported the significance of CRP level in predicting future CV risk.

Levels of plasma fibrinogen and hs-CRP add prognostic information to the severity of metabolic syndrome. In the present study, we are evaluating the correlation of fibrinogen and hs-CRP levels in metabolic syndrome

MATERIALS AND METHODS

The study was conducted at MES Medical College, Perinthalmanna, Kerala. Thirty clinically proved metabolic syndrome patients below the age of 70 years constitute the test group. Thirty subjects of control group are selected from the siblings, teaching and nonteaching staff of the Institute. Informed consent obtained from all the subjects as per the criteria laid down by the institutional Ethics Committee. Detailed clinical, epidemiological and anthropometric characteristics were recorded using pro-forma.

The subjects for the study were selected based on the following inclusion-exclusion criteria. All the subjects included in the study were in the age group of 31 to 70 years. Metabolic syndrome was diagnosed according to the NCEP-ATP III criteria (Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults –

Adult Treatment Panel III). They had no acute or chronic disease and were not suffering from any known cardiovascular, liver and renal diseases and had no autoimmune diseases. The control subjects did not have any illness and they were not on any medication.

Weight was measured with light clothes and without shoes to the nearest 0.1 Kg using a digital scale. Height measured without shoes to the nearest 0.1 cm with a measuring tape mounted on the wall. BMI calculated using the equation- $BMI = \text{weight [Kg]} / \text{height[m]}^2$. Systolic and diastolic blood pressure measured in a sitting position, after a 5- minute rest, using a mercurial sphygmomanometer. Waist circumference measured by a measuring tape to the nearest 0.1 cm at a point midway between the last rib and the iliac crest while the subject is in standing position and after expiration.

5 ml of fasting blood sample collected from all the subjects by venepuncture under sterile condition. 3ml transferred to a plain bottle and then centrifuged at 3000rpm for 10 minutes. The serum thus obtained was used for further studies including Lipid profile, hs-CRP and Blood sugar determination. 2ml transferred to vacuum tubes prefilled with EDTA. The tubes were centrifuged at room temperature for 15minutes. After separation, plasma aliquots for fibrinogen measurements were frozen at -70°C.

The blood samples collected were processed and analyzed at a fully automated central laboratory. Lipid profile and blood sugar estimated by a fully automated clinical chemistry analyzer (VITROS® 5600 Integrated System). Fibrinogen and hs-CRP estimated by turbidometric immunoassay (Quantamate). Results were expressed as mean \pm SD. Parametric correlation by Pearson done to compare hs CRP with serum fibrinogen levels. A p value < 0.05 were considered to be statistically significant.

RESULTS

The study was conducted to evaluate the significance of serum fibrinogen and hs- CRP levels in the assessment of metabolic syndrome and its usefulness in predicting the severity of metabolic syndrome.

Table 1: Test statistic of Blood Pressure

| | Category | Mean \pm SD (mmHG) | T test P value |
|-----|---------------|----------------------|----------------|
| SBP | Control(N=30) | 125.67 \pm 7.28 | <0.0001 |
| | Test (N=30) | 166.3 \pm 24.4 | |
| DBP | Control(N=30) | 82 \pm 4.07 | <0.0001 |
| | Test(N=30) | 90.1 \pm 6.45 | |

Table 2: Statistic of Fasting blood sugar

| Parameter | Category | Mean \pm SD (mg/dl) | T test P value |
|-----------|---------------|-----------------------|----------------|
| FBS | Control(N=30) | 96.7 \pm 10.63 | <0.0001 |
| | Test (N=30) | 206.93 \pm 70.37 | |

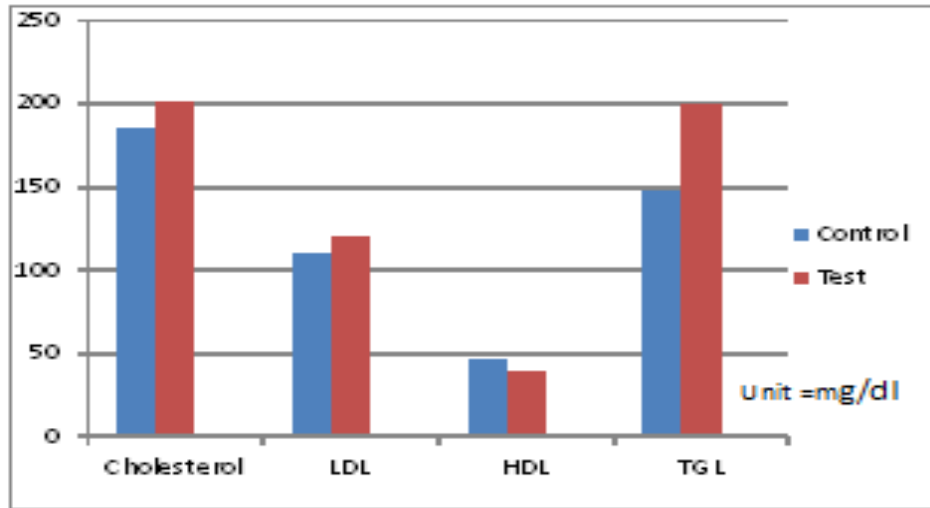


Figure 1: Graphical representation of lipid profile

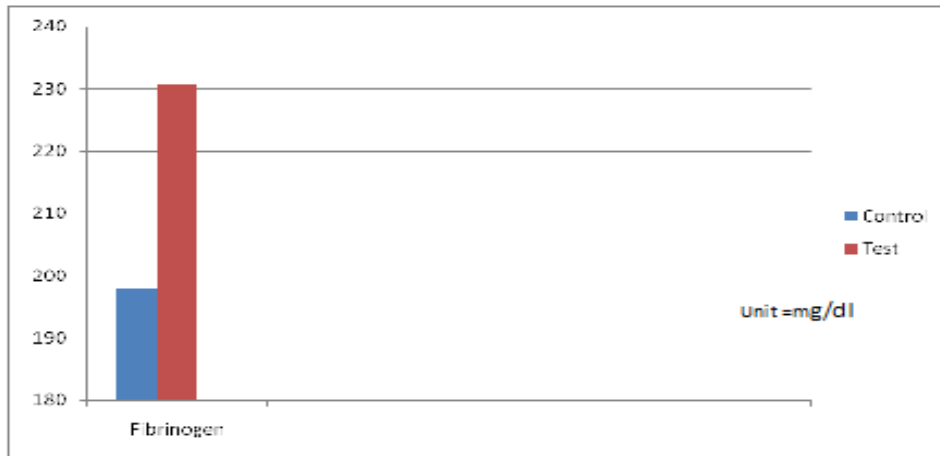


Figure 2: Graph showing mean fibrinogen values



Figure 3: Mean hs-CRP values

Table 3: Correlation of Fibrinogen vshs-CRP

| Fibrinogen | Pearson Correlation | Hs-CRP |
|------------|---------------------|--------|
| | Sig.(2-tailed) | 0.048* |
| | | 0.717 |

*Correlation is not significant.

DISCUSSION

For Systolic BP, the mean \pm SD of control is 125.67mmHg and of test is 166.3mmHg. When compared to the mean \pm SD for DBP there is a significant increase in the mean SBP. Table 2 shows mean \pm SD for glycemic values. For FBS, the mean \pm SD of control was 96.7mg/dl and of test 206.93mg/dl. Among the lipid parameters, total cholesterol, LDL and TGL values were higher in the test group compared to that of control, while mean HDL lower. Serum fibrinogen levels were significantly high in metabolic syndrome group compared to the control group. Mean \pm SD for CRP for control was 0.31 ± 0.13 and for test it was 2.36 ± 2.23 .

These results are consistent with earlier studies in diabetic⁷ and non diabetic people.⁸ Some studies have suggested that the inflammatory biomarkers, C-RP and fibrinogen, play a role in the initiation, aggravation and progression of atherosclerosis in diabetic patients^{9,10}. These biomarkers are more closely related with the metabolic syndrome and insulin resistance compared to cytokines, and they influence the onset of potential cardiovascular events. However, the relationship between the number of Met S components and hs CRP appeared to be largely due to obesity. This observation supports the fact that CRP in diabetic subjects primarily reflects the magnitude of obesity.

CONCLUSION

Both fibrinogen and hs-CRP levels are significantly associated with metabolic syndrome. But there is no significant correlation between fibrinogen and hs-CRP levels. Plasma determination of these inflammatory biomarkers might have an implication in predicting the severity of metabolic syndrome.

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