Diagnostic Role of Fibrinogen alone and in Combination with Lipids among Cardiovascular Disease

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ABSTRACT

Inflammation plays an important role in the initiation, progression of atherosclerosis and subsequent development of atherosclerotic events. Elevated fibrinogen levels are considered as a risk factor for the development of atherosclerosis. The objectives of this study were first to evaluate the association between fibrinogen and cardiovascular disease and second to determine the role of combination of fibrinogen with lipid profile in the prognosis of cardiovascular disease. Two hundred patients were recruited for the study, of which hundred belongs to control and hundred were test group. For the entire study population fibrinogen and lipid profile were measured at the time of hospitalization. Among the patients with complication, there was a significant elevation in the levels of fibrinogen and lipid profile than the control. The results indicate that elevated plasma fibrinogen levels may be an independent risk factor for cardiovascular disease. It was found that a combination of measurement of fibrinogen with and total cholesterol or low-density lipoprotein cholesterol testing may prove to be even a better marker at risk response and this prognostic information may warrant closer monitoring and extra attention to modifiable cardiovascular risk factor.

Keywords: Fibrinogen, total cholesterol, inflammation, cardiovascular disease
INTRODUCTION

Cardiovascular disease (CVD) is prevalent in the general population, affecting the majority of adults, past the age of 50 years.\(^1\) In India the incidence of CVD is increased, which seems to be associated with the changes in lifestyle, diet, rapid urbanization, and possibly an underlying genetic component. According to the World Health Organization estimates, by 2010, 60 percent of the world's cardiac patients will be in India. Between 2000 and 2030, about 35 percent of all CVD deaths in India will occur among those aged 35 to 64, compared with only 12 percent in the United States and 22 percent in China.\(^2\) Two out of three cardiac deaths occur without any diagnosis of CVD.

Evidences support the role of inflammation in all phases of the atherosclerotic process, from lesion initiation through to progression and, eventually, the thrombotic complications of atherosclerosis.\(^3\) The growing appreciation of the role of inflammation in atherogenesis has focused attention on whether circulating levels of various inflammatory biomarkers which may help to identify those at risk of future cardiovascular events.\(^4\) Fibrinogen is generally considered to be an important mediator of clot formation. Therefore this study is aimed to investigate the fibrinogen and lipid profile of the patients with CVD in a variety of situations and to advocate greater use of their measurement in clinical practice.

MATERIALS AND METHODS

Patients: The total number of patients included in this study was two hundred. At the time of admission or entrance all patients responded to a standardized questionnaire covering many personal details (such as smoking habit, alcohol intake, physical activity, food habit, family history, and medical information) organised by trained interviewers. The study population consisted of one hundred patients (test group) with a mean age of 49.9±6.3 years; the control group included one hundred patients with mean age of 47.2±7.5 years.
Biochemical parameters and Assay: Samples for the analysis of fibrinogen and lipid profile were obtained in the fasting state. For determination of fibrinogen, blood samples were anticoagulated with 3.8% trisodium citrate. Plasma samples were quickly frozen and stored at −70°C for subsequent analysis. Fibrinogen levels were determined with the immunoprecipitation test and Clauss method. Total cholesterol (TC) and triglycerides (TG) were assayed by routine enzymatic methods using an auto analyser. High-density lipoprotein (HDL) cholesterol was measured using the same enzymatic method after precipitation of the plasma with phosphotungstic acid in the presence of magnesium ions. For cost reasons, low-density lipoprotein (LDL) cholesterol values have long been estimated using the Friedewald formula: \[ \text{[TC]} - [\text{total HDL cholesterol}] - 20\% \text{ of the TG value} = \text{estimated LDL cholesterol} \]. The very low-density lipoprotein (VLDL) cholesterol is estimated as one-fifth of the TG.

Statistical Analysis: Statistical analysis was performed with SPSS 13 statistical software package. Data were recorded on a pre-designed proforma and managed on spreadsheet. Descriptive statistics for quantitative variables were computed by mean and standard deviation. Means in the two groups were compared by Student’s t-test. In this study, p<0.05 has been considered as statistically significant.
Table 1 Clinical and biochemical characteristics of the study subjects

<table>
<thead>
<tr>
<th></th>
<th>Control (n=100)</th>
<th>Test group (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-modifiable risk factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>47.2±7.5</td>
<td>49.9±6.3</td>
</tr>
<tr>
<td>Sex M/F</td>
<td>19/11</td>
<td>40/35</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>8</td>
<td>22</td>
</tr>
<tr>
<td>Obesity</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Physical inactivity</td>
<td>4</td>
<td>42</td>
</tr>
<tr>
<td><strong>Modifiable risk factor</strong></td>
<td></td>
<td></td>
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<tr>
<td>Fibrinogen</td>
<td>305.6±66.7</td>
<td>416.6±25.2</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>179.1±24.1</td>
<td>211.8±9.1</td>
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<tr>
<td>Triglycerides</td>
<td>170.1±34.5</td>
<td>210.1±81.0</td>
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<tr>
<td>High-density lipoprotein cholesterol</td>
<td>45.2±4.8</td>
<td>44.6±5.3</td>
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<tr>
<td>Low-density lipoprotein cholesterol</td>
<td>99.7±25.1</td>
<td>125.1±19.1</td>
</tr>
<tr>
<td>Very low-density lipoprotein cholesterol</td>
<td>34.0±6.9</td>
<td>39.1±4.9</td>
</tr>
</tbody>
</table>

RESULTS

Baseline characteristic of the patients were shown in the Table 1. The present study demonstrates that considerable variability is observed between control and test group. Among the patients with complication the baseline mean fibrinogen concentration increased significantly (p<0.001) than the control. The mean level of fibrinogen in control is found to be 305.6±66.7, in test group 416.6±25.2. The mean level of TC in control is found to be 179.1±24.1 and in test
group 211.8±9.1. The mean level of TG in control is found to be 170.1±34.5 and in test group 210.1±81.0. From the results, there is a significant increase of TC and TG levels (p<0.001) in test group than the control.

The mean level of HDL cholesterol in control is found to be 45.2±4.8, in the test group 44.6±5.3. There was no significant in HDL cholesterol was found in test group when compare to control. The mean level of LDL cholesterol in control is found to be 99.7±25.1, in the test group 125.1±19.1. Significant increases (p<0.001) were noted in the mean levels of LDL cholesterol in test group. The mean level of VLDL cholesterol in control is found to be 34.0±6.9, in the test group 39.1±4.9. There was a significant elevation in VLDL cholesterol was observed in test group (p<0.001). The elevated level of fibrinogen and lipid profile seems to be a strong indicator of CVD risk.

**DISCUSSION**

In the present study the elevated levels of TC and LDL cholesterol provides a valuable tool for identifying patients at risk for cardiovascular events and a strong indicator of seriousness in CVD. The present study also showed that fibrinogen was positively associated with CVD. The results obtained from this study are consistent with and extend those of other studies linking fibrinogen to prevalent CVD \[^6,7\] and to traditional cardiovascular risk factors. \[^8\]

There are several mechanisms by which fibrinogen may increase cardiovascular risk. First, it binds specifically to activated platelets via glycoprotein IIb/IIIa, contributing to platelet aggregation. Second, increased fibrinogen levels promote fibrin formation. Third, it is a major contributor to plasma viscosity. Finally, it is an acute-phase reactant that is increased in inflammatory states. \[^9\]
It has been identified that the elevations of fibrinogen and C-reactive protein is observed in patients with unstable angina, thus, supporting the hypothesis that inflammation may play an important role in plaque rupture and thrombosis. [10] C-reactive protein has been shown to be predictive of future myocardial infarction. [11]

The strong relationship between fibrinogen and LDL cholesterol level suggests that the increased risk of CVD associated with elevated LDL levels may be mediated in part through fibrinogen. The Prospective Cardiovascular Munster (PROCAM), study found that individuals who had LDL and fibrinogen levels in the highest tertile had a 6.1-fold increase in coronary risk compared with those in the lowest tertile. [12]

**CONCLUSION**

In conclusion, the results indicate that elevated plasma fibrinogen levels may be an independent risk factor for CVD. Elevated levels of fibrinogen should be given consideration while assessing cardiovascular risk in order to better evaluate the risk of atherosclerotic vascular disease especially in patients with a hyperlipidemia.

**REFERENCES**


