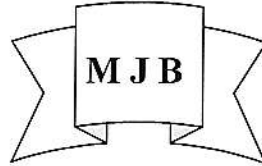# C-reactive protein and plasma fibrinogen in patients with stable angina pectoris

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Abstract

The study included 48 patients with stable angina pectoris and 41 control subjects to evaluate the association between inflammatory markers (C-reactive protein and plasma fibrinogen) and angina pectoris.

The study revealed that plasma fibrinogen ($P<0.001$), C-reactive protein ($P<0.01$), as well as lipid profile (total cholesterol ($P<0.001$), low-density lipoprotein cholesterol ($P<0.01$), triglycerides ($P<0.01$) and low-density lipoprotein cholesterol/high-density lipoprotein cholesterol ratio ($P<0.01$) were significantly higher among patients with stable angina pectoris compared to controls. While, there was no significant differences in high-density, lipoprotein cholesterol level between patients and controls ($P>0.05$).

The present study clearly demonstrated a strong association between inflammatory markers and angina pectoris, suggesting a role for these markers in the pathogenesis and the progression of coronary heart disease.

الخـــلاصــة

شملت الدراسة 48 مريضاً بالذبحة الصدرية المستقرة و 41 من الاصحاء وذلك لتقيــيم العلاقـــة بـــين دالات الالتهــاب (البروتين الفعال – سي وفايبرنوجين البلازما) والذبحة الصدرية.

اظهرت الدراسة بأن مستويات فايبرنوجين البلازما ($P<0.001$) والبـــروتين الفعــال ســي ($P<0.01$) وكـــذلك نمـــط الـــدهون (الكولسترول الكلي ($P<0.001$) ، كولسترول البروتينات الدهنية واطئة الكثافة ($P<0.01$) ، الدهون الثلاثيـــة ($P<0.01$) ونســبة كولسترول البروتينات الدهنية واطئة الكثافة/ البروتينات الدهنية عالية الكثافة ($P<0.01$)) كانت عالية بشكل معنوي عند مرضــى الذبحة الصدرية المستقرة مقارنة بالاصحاء.

بينما لم تكن هناك فروق احصائية فيما يتعلق بالبروتينات الدهنية عالية الكثافة بين المرضى والاصحاء ($P>0.05$).

أظهرت الدراسة بوضوح وجود علاقة قوية بين دالات الالتهاب والذبحة الصدرية وهذا يقود إلى الاحتمال بوجود دور لتلك الدالات في نشوء وتطور مرضى القلب التاجي.

Introduction

The suggestion that atheroscleososis is an inflammatory process is now increasingly accepted(1,2). Also, the list of inflammatory markers linked to atherosclerosis and coronary heart disease (CHD) is extending.

Beside the classical risk factors of CHD, several markers of inflammation have been implicated in the pathogenesis and progression of CHD such as fibrinogen, C-reactive protein, von Willebrand factor, serum amyloid A, and interleukin-6 (3-5).

It has been suggested that markers of inflammation particularly C-

reactive protein and fibrinogen, are independent predictors of CHD (6).

Also the levels of these markers are not only correlated with CHD severity, but also with the prognosis of CHD as well as subsequent cardiovascular events (7).

In an earlier study, we found that patients with acute myocardial infarction have significantly elevated plasma fibrinogen level and we suggested that the relationship of plasma fibrinogen with CHD may be as strong as that of lipid profile(8).

The aim of this study was to determine the level of plasma fibrinogen and C-reactive protein among patients with stable angina pectoris.

Patients and methods
Patients
This is a prospective study extended from September, 2001 throughout May, 2002 and included 48 patients with stable angina pectoris diagnosed by consultant physicians. They were 33 males and 15 females, their age ranged from 27-79 years (mean = 47.6). All were outpatients referred by their specialists for follow-up investigations.

Controls
Forty-one apparently healthy subjects were included as a control group. They were 27 males and 14 females, their age ranged from 30-69 years (mean= 49.2). There was no history of CHD , hypertension or diabetes mellitus among control individuals.

Methods
Blood sample were collected after 10-12 hour fasting. Each blood sample was divided into 2 parts: The first part, anticoagulated with sodium citrate for the determination of plasma fibrinogen level (9). Serum was separated from the second part for the

determination of C-reactive protein concentration and lipid and lipoprotein profile. C-reactive protein was determined using kit from Biomaghreb, Tunis. Lipid and lipoprotein profile (total cholesterol (TC), high density lipoprotein cholesterol (HDL-C) and triglycerides (TG)) levels were determined using kits from bioMerieux, France. All procedures were performed according to the instructions of the manufacturer. The level of low density lipoprotein cholesterol (LDL-C) was calculated using friedewald equation (10).

$$LDL-C = TC-(HDL-C + TG/5)$$

Statistical analysis. Chi-square and t-tests were used (P<0.05) was considered to be statistically significant.

Results
Table 1 summarizes the basic characteristics of patients with stable angina pectoris and control subjects. Systolic and diastolic blood pressure were significantly elevated among angina pectoris patients in comparison to controls (P<0.001). On the other hand, there were no significant differences between patients and controls with regard to age, body mass index, frequency of cigarette smokers and family history of CHD (P>0.05).

As shown in **Table 2**, the levels of inflammatory markers (fibrinogen (P<0.001) and C-reactive protein (P<0.01) as well as lipid and lipoprotein profile (TC (P<0.001), TG (P<0.01), LDL-C (P<0.01) and LDL-C/HDL-C ratio (P<0.01) were significantly higher among angina pectoris patients compared to controls, while there was no significant differences in HDL-C level between patients with stable angina patients and controls (P>0.05).

Discussion
CHD is one of the leading cause of morbidity and mortality both in developed and developing countries(11).

Plasma fibrinogen and C-reactive protein are the most frequent markers of inflammation implicated in CHD(3,12). The independent association of elevated plasma fibrinogen with cardiovascular death was at least as strong as that of elevated blood cholesterol1(3).

The present study clearly demonstrated significantly elevated plasma fibrinogen and C-reactive protein in patients with stable angina pectoris. This is in agreement with several reports(2,7,14). It implies a substantial role of these inflammatory markers in the pathophysiology of CHD.

Plasma fibrinogen is an independent correlate of prognostically relevant cardiovascular target organ damage(15), and also, predicted cardiac death in patients suffered from myocardial infarction(16). On the other hand, causal, association has been demonstrated between C-reactive protein and the pathogenesis of coronary atherosclerosis(12). In addition, C-reactive protein can serve as a marker of prevalent CHD risk in populations with low cholesterol, levels(17).

C-reactive protein levels aggravate the risk due to classical CHD risk factors (18).

The role of infection in the initiation and/or progression of atherosclerosis and CHD has attracted considerable attention in recent years.

The important pathogens implicated in the pathogenesis of atherosclerosis are Chlamydia pneumoniae and helicobacter pylori (19,20). Stille and Dittmann (21) suggested that an increased inflammatory markers in association with myocardial infarction are not risk factors, but signs of an active chronic infection. It is possible that elevated levels of inflammatory markers may be secondary to a pre-existing infective process and not primary risk factors.

In conclusion, the association between plasma fibrinogen and C-reactive protein level and CHD risk is strong, and the inclusion of the measurement of these markers in patients with CHD may have valuable prognostic significance.

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Table 1 Characteristics of patients with angina pectoris and control subjects.

Characteristic	Patients (n = 48)	Controls (n=41)
Age (years)	47.6±10.8	49.2±9.8
Body mass index (kg/m^2)	30.5±5.3	29.1±3.4
Systolic blood pressure (mmHg)	154.1±14.9***	141.7±10.6
Diastolic blood pressure (mmHg)	92.9±5.1***	87.8±4.9
Cigarette smoking (%)	45.8	39.0
Family history of CHD (%)	25.0	14.6

Values are given as mean±standard deviation
*** : P<0.001

Table 2 Plasma fibrinogen, C-reactive protein and lipid profile among patients with stable angina pectoris and control subjects.

Parameters	Patients (n = 48)	Controls (n=41)
Fibrinogen (mg/dl)	331.6±128.0***	234.0±50.1
C-reactive protein (mg/l)	8.3±5.6**	6.3±1.3
TC (mg/dl)	228.8±46.9***	197.8±27.8
TG (mg/dl)	211.1±98.9**	160.2±41.6
HDL-C (mg/dl)	44.5±6.1	46.8±8.4
LDL-C (mg/dl)	140.8±43.1**	119.1±25.9
LDL-C/HDL-C ratio	3.2±1.1**	2.6±0.7

Values are given as mean±standard deviation
** : P<0.01
*** : P<0.001