Association of Fibrinogen as a Myocardial Infraction Risk Factor in Men

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Summary:

Background: Acute myocardial infarction (AMI) is an irreversible myocardial injury and necrosis caused by serious and long term ischemia. Fibrinogen is considered as one of the probable risk factors of myocardial infarction.

Patients and methods: 1.8-mL venous blood specimen from 40 patients with MI and 50 control subjects was obtained and put it into tubes containing 0.2 mol/L trisodium citrate. Plasma fibrinogen level was determined by the method of Clauss (Diagnostic Stago, France).

Results   The mean age of patients was (45.2 ± **6**)   years in patients with premature myocardial infarction and (45.06±**5**) years in the control group (p =0.07). There were no statistically significant relationships between the two groups in history of premature myocardial infarction in their first-degree relatives (p = 0.05), cigarette smoking (p = 0.06), diabetes (p = 0.08), or hypertension (p = 0.071). The mean plasma fibrinogen in patients (495 ±**10.2mg**/dL) was elevated markedly compared with the control group (465±**8.4 mg/dl**) (p = 0.01) . Hyperfibrinogenemia (>450 mg/dL) was detected in 87.5% of patients and 52.0% of controls.

Conclusion: This study introduced fibrinogen as a risk factor for premature coronary artery disease in Iraqi men.

Keywords: myocardial infarction, cigarette, hypertension, diabetes, fibrinogen

Introduction:

Acute myocardial infarction (AMI) is an irreversible myocardial injury and necrosis caused by serious and long term ischemia. It is generally seen in middle aged men with high risk factors for coronary artery disease. Only 4% of patients with AMI are under 40 years of age (1). Coronary anatomy is normal in 30% of young AMI patients (2). The presence of normal coronary anatomy is related to coronary vasospasm, embolism from endocardium or heart vessels, platelet aggregation or spontaneous lysis of thrombus (3). The notion that fibrinogen is related to cardiovascular diseases was first aired in the 1950s, when its level was found to be increased in patients with ischemic heart disease (4). Many prospective epidemiological studies have reported positive associations between the risk of coronary heart disease (CHD) and plasma fibrinogen levels (5,6,7,8,9) Fibrinogen is the major coagulation protein in blood by mass, the precursor of fibrin, and an important determinant of blood viscosity and platelet aggregation (10,11,12). Because fibrinogen levels can be reduced considerably by lifestyle interventions that also affect levels of established risk factors (such as regular exercise, smoking cessation, and moderate alcohol consumption), there is interest in the possibility that

measurement (or modification) of fibrinogen may help in disease prediction or prevention (10,11,13). Iraq is a developing country with a high and growing prevalence of coronary artery disease. The incidence of acute coronary syndromes during recent years has increased surprisingly, especially among young Iraqi men. In the present study we examined the relation between plasma total fibrinogen concentration and premature MI in Iraqi patients to further elucidate the role of fibrinogen as an independent risk factor for acute coronary heart disease (CHD) events.

Methods:
Study design
This study was conducted between January 2008 and December 2009 to investigate the association between plasma fibrinogen level and MI in men aged younger than 55 years admitted to the cardiac care units of Baghdad Teaching Hospitals. The diagnosis of acute myocardial infarction (AMI) was based on the presence of ischemic chest pain of at least 30 minutes' duration and creatine kinase (CK) elevation of at least twice the upper normal limit, with CK, muscle and brain (CK-MB) isoenzyme concentration of at least 6% of the peak CK value, accompanied by dynamic ST-segment elevation or depression of 1 mm or more in at least two adjacent leads. Premature AMI was

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defined as having the above-mentioned criteria in patients aged younger than 55 years.

Patients and controls that had hyperlipidemia were excluded from the study. Among 178 men with a first episode of AMI who were admitted within 12 hours of symptoms onset, 40 were enrolled as cases. None of these 40 patients had recurrent MI during their follow up and all of them completed the study.

Controls were 50 men aged under 55 years who survived to the end of the study period free from incident MI and stroke.

They were randomly selected with frequency matching to cases by the site of residence and by age group. They also were matched with case group regarding other CHD risk factors such as diabetes mellitus, hypertension, and cigarette smoking. Participating case and control subjects were asked to complete a questionnaire to obtain information on any history of known or suspected cardiovascular risk factors, including physician-diagnosed diabetes, hypertension, or high cholesterol, cigarette smoking, height and weight, alcohol consumption, physical activity, history of MI in first-degree relatives and demographic characteristics.

Blood collection and laboratory Methods

In this study, venous blood specimen from both case and control groups after a 12-hour fasting was obtained to eliminate the probable effect of diet on fibrinogen levels. To determine fibrinogen, we obtained a 1.8-mL venous blood specimen from 40 MI case subjects and 50 control subjects into vacuum tubes containing 0.2 mol/L trisodium citrate (9:1 blood/citrate, vol/vol). The blood was centrifuged immediately for about 15 minutes and the obtained plasma was then frozen at -20 C°. Plasma fibrinogen level was determined by the method of Clauss (Diagnostic Stago, France). A plasma fibrinogen level more than 450 mg/dL was considered high.

Statistical analysis

Statistical analysis was done using SPSS version 7.5 computer software (Statistical Package for Social Sciences). The mean value with the standard deviation (SD) for each value was determined .P- value less than the 0.05 level of significance was considered statistically significant.

Results:

The mean age of our case and control subjects was 45.2 ± **6** years and 45.6± 5 years, respectively (p = 0.07). Among patients with premature AMI, five (12.5%) had history of premature MI in their first-degree relatives whereas four (8.0%) control subjects had family history of premature AMI (p = 0.05). Both case and control groups were matched regarding other risk factors of coronary artery disease such as hypertension, diabetes mellitus, cigarette smoking and hyperlipidemia, table-1.

Table-1: Coronary heart disease risk factors in case and control groups

	Patients with CHD N0.=40	Control group N0.=50	P-value
Age (years)	45.2 ± **6**	45.06±**5**	0.07 (N S)
Cigarette smoking	20 (50%)	17 (34%)	0.06 (NS)
Diabetes mellitus	3 (7.5%)	1 (2.0%)	0.08 (NS)
Hypertension	7 (17.5%)	6 (12.0%)	0.07 (NS)
Family history of premature MI	five (10.0%)	four (8.0%)	(0.05)NS

Thirty five (87.5%) had elevated fibrinogen levels (>450 mg/dL). In 50 control group individuals, 26 (52 %) had elevated fibrinogen levels. The plasma fibrinogen level was significantly higher in case subject than in the control group (495 ±**10.2m**g/dL **Vs** 465±**8.4 mg/dl)** (p = 0.01), as in (table- 2).

Table-2: Level of fibrinogen in case and control groups

	Case		Control		P- value
	Number	%	Number	%	
Fibrinogen level < 450 mg/dl	5	12.5	24	48	0.01
Fibrinogen level > 450 mg/dl	35	87.5	26	52	0.01

Discussion:

The present study implies that high plasma fibrinogen levels are a risk factor for premature AMI..Several prospective and cross-sectional studies have revealed that plasma fibrinogen levels have a strong predictive value for CHD and stroke. In a large, population-based, prospective study, the Atherosclerosis Risk in Communities (ARIC) Study, plasma fibrinogen was found to be an important risk factor for CHD in women (14).In addition other scientist reported that , plasma fibrinogen levels were significantly higher in patients with AMI with ST-change (15,16). The physiological importance of elevated plasma fibrinogen levels is not fully understood. The mechanisms by which plasma fibrinogen may be involved in atherothrombosis are theological alterations, increased platelet aggregation tendency, increased fibrin formation, and stimulation of vascular cell proliferation and migration, with increasing plasma fibrinogen levels (17). Thus, elevated plasma fibrinogen levels, whatever their origin – genetic, as part of an inflammation reaction, or some other reason – may caused hypercoagulative state that could

influence the degree and duration of thrombus formation at the time of coronary injury. Elevated fibrinogen concentrations could be due to the disease (ie, MI) or to an underlying vascular disease (eg, atherosclerosis) rather than as a cause of MI or vascular

disease. This study was conducted among male patients and the sample size is relatively low. Further studies on the role of fibrinogen in acute coronary syndromes in other age groups and sexes are necessary. The role of plasma fibrinogen levels in premature coronary artery disease is less clear. The prevalence of cardiovascular disease especially among the youth is growing in Iraq and further investigations for finding risk factors in the Iraqi population seem to be of great importance. Our findings suggested that higher fibrinogen levels are associated with premature coronary artery disease in the Iraqi population.

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