Review Article

Serum fibrinogen level in patients with ST-segment elevation myocardial infarction admitted to the coronary care unit in Shaab Teaching Hospital, Khartoum, Sudan

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Abstract

Introduction

Elevated serum fibrinogen level (SFL) is associated with increased risk of stroke and myocardial infarction. During ST-segment elevation myocardial infarction (STEMI), SFL rises and appears to be influenced by several factors. This is a study of SFL in Sudanese patients with STEMI and its relationship to patient factors and hospital outcomes.

Methods

The study was a prospective observational hospital-based conducted at Shaab Teaching Hospital in Khartoum, Sudan. Eighty consecutive patients with STEMI from July to September 2017 were enrolled. SFL was measured 72 hours post STEMI. Other recorded variables included demographic data, hypertension (HTN), diabetes mellitus (DM), smoking status, thrombolysis use, hemodynamic instability and hospital mortality.

Results

Eighty STEMI patients were enrolled with mean age of 54.9±10.6 years and M:F ratio of 3:1. Comorbidities prevalence: DM (43.8%), HTN (35%), smoking (46.3%), use of thrombolysis (78.8%) and hemodynamic instability (75%) . No in-hospital mortality was recorded in the cohort.

The mean SFL was 393.8 ± 100.1 mg/dl. 62 (77.5%) patients had SFL ≥ 350 mg/dl.

Elevated SFL of ≥ 350 mg/dl had statistically significant relationship with age 40-60 years, female gender and smoking (P value ≤ 0.05), while P values were > 0.05 for DM, HTN, thrombolysis use and hemodynamic instability

Conclusion

SFL in a cohort of Sudanese patients with STEMI was elevated but similar to reported levels and showed significant relationship with age 40-60 years, female gender, and smoking. No significant correlation was seen with HTN, DM, thrombolytic therapy or hospital outcomes.

Keywords: Coronary Artery Disease, Ischemic Heart Disease, Stable

Introduction

Ischemic heart disease (IHD) , including ST segment elevation myocardial infarction (STEMI), is the leading cause of death and loss of disability-adjusted life years (DALYs) worldwide, including low and middle income countries (1,2). Most of the cases of acute myocardial infarction can be attributed to traditional risk factors for atherosclerosis. However, less than 10% of cases are not associated with any of these factors (3).

Fibrinogen, a complex acute phase reactant glycoprotein, with pivotal roles in coagulation and platelet aggregation is produced primarily in the liver and has a half-life of about 100 hours with normal levels of 150-350 mg/dl (4). It has emerged both as a risk factor and a possible prognostic tool in acute myocardial infarction.

Several epidemiological studies have linked elevated SFL with increased risk for acute myocardial infarction (5,6,7).

In the setting of acute myocardial infarction, fibrinogen rises within the first 24 hours, peaks 3-5 days later and remains elevated for several month (8,9).

To our best knowledge, this is the first study in Sudan that looked at SFL in STEMI and its association with age, gender, risk factors for atherosclerosis, thrombolysis and hospital outcomes.

Objectives

- To study serum fibrinogen levels in patients with STEMI in a cohort of Sudanese patients admitted to Shaab Teaching Hospital
- To study the relationship between serum fibrinogen levels and patients' age, gender, DM, HTN and smoking.
- To study relationship serum fibrinogen levels and use of thrombolysis and hospital outcomes.

Methods

This is a prospective observational hospital-based study conducted at Shaab Teaching Hospital in Khartoum, Sudan from July to Sep 2017. Eighty consecutive patients with STEMI admitted to the coronary care unit (CCU) were included. Patients who refused to participate, died or transferred before 72 hours were excluded.

Blood samples were taken 72 hours after admission to the CCU. To determine SFL, 1.8 ml of venous blood specimens were collected into vacuum tubes containing 0.2 mol/L trisodium citrate (9:1 /blood: citrate). The blood samples were centrifuged immediately for about 15 minutes and the obtained plasma specimens were frozen at -10°C to -15 °C. Plasma fibrinogen level was measured with full automation using MINDRAY BS 800 automated analysis system.

Variables studied were age, gender, smoking status, DM, HTN, troponin level, thrombolysis usage, hemodynamic stability and hospital mortality. Hemodynamic stability was defined as SBP < 90 mmHg requiring inotropes or acute heart failure. Entered data were analyzed by Statistical Package for Social Science program (SPSS; version 21.0). The analyzed data were represented in tables and figures. ANOVA test was used to determine significance, and the P value was considered as significant at level ≤ 0.05.

Results:

A total of 80 STE-ACS patients were enrolled in this study with M:F ratio of 3:1. The mean age was 54.9±10.6 years. Age distribution show 3 patients were below 40 years, 56 were between 40-60 and 21 were above 60 years.

Variable	Value
Age	54.9±10.6 years
Male: Female ratio	3:1
Diabetes Mellitus	35%
Hypertension	43.8%
Smoking	44%
Hemodynamic instability	25%
Elevated troponin	100%
Thrombolysis	78.8%
Mean serum fibrinogen level	393.8±100.1 mg/dl
% of patients with elevated fibrinogen level (≥350 mg/dl)	77.5%

Table 1: Baseline clinical characteristics

28 (35%) of the patients were hypertensive, 35 (43.8%) were diabetics and 37 (44%) were smokers. All of the participants were troponin positive. Of the total cohort, 63 (78.8%) received thrombolysis and 60 (75%) were hemodynamically stable. No in-hospital mortality was recorded in the cohort. Table 1 summarizes baseline characteristics of the study sample.

The mean fibrinogen level was 393.8±100.1 mg/dl. 62 (77.5%) patients had SFL ≥ 350 mg/dl.

Elevated fibrinogen levels of ≥ 350 mg/dl had statistically significant relationship with age 40-60 years, female gender and smoking. There was no significant relationship with DM, HTN, administration of thrombolysis or hemodynamic instability (Table 2).

Discussion

The mean age of our study sample was 55 years with majority (70%) in the 40 – 60 years age group, reflecting the relatively young age of patients with STEMI in our setting. This is seen in other low and middle-income countries with high prevalence of traditional risk factors of DM, HTN and smoking (10).

Our mean fibrinogen level in this study though quite elevated is comparable to other studies which measured fibrinogen level during the course of an acute myocardial infarction (9,11,12, 13,14). Our study showed significant correlation between elevated SFL and female gender, smoking and age between 40-60 years but not DM, HTN, thrombolysis administration and hospital outcomes.

Variable	Fibrinogen level		P. value
	≤ 345 mg/dl	>345 mg/dl	
Age (Years)			
<40	2 (66.7%)	1 (33.3%)	0.72
40 – 60	7 (12.5%)	49 (87.5%)	0.004
> 60	9 (42.8%)	12 (57.2%)	0.43
Gender			
• Male	16 (26.7%)	44 (73.3%)	0.361
• Female	2 (10%)	18 (90%)	0.002
Smoking	4(10.8%)	33(89.2%)	0.018
Hypertension	6 (21.4%)	22 (78.6%)	0.551
Diabetes	7 (20%)	28 (80%)	0.442
Thrombolysis	12(19%)	51(81%)	0.137
Hemodynamic instability	5(25%)	15(75%)	0.488

Table 2: Relationship between fibrinogen to patient factors, thrombolysis and hospital outcomes

Studies into the relationship between fibrinogen levels during myocardial infarction, patient characteristics and hospital outcomes had variable outcomes. An early study by Hashmi et al did not find any relationship between peak fibrinogen level and patient age or hospital outcomes (8). A later study by Cristal et al, showed that peak fibrinogen levels are not related to hospital outcomes. However, elevated initial fibrinogen levels of ≥ 400 mg/dl correlated well with hospital outcomes including re-infarction, cardiogenic shock and death (9).

In a subsequent study by Bennermo et al, 225 patients with STEMI who received thrombolysis fibrinogen level at 48 hours was 340 mg/dl. Patients younger than 55 years had higher fibrinogen but no difference with DM. Fibrinogen concentrations measured at 48 hours were associated with cardiovascular death or a new myocardial infarction during follow-up in univariate analysis, but not on multivariate analysis when age, DM and ejection fraction were taken into account (11).

Shi eta al studied 136 patients with acute coronary syndrome (ACS) including STEMI. Their mean fibrinogen level was 302 +/- 90 mg/dl on admission and before institution of therapy. No significant differences in fibrinogen levels were found with respect to age, gender, and other cardiovascular risk factors including HTN and DM. Fibrinogen levels were higher in ACS patients compared to stable angina pectoris and control patients, and was associated with a statistically significant increase in clinical events for up to 2 years irrespective of age, gender and traditional risk factors (12). However, in this fibrinogen levels were taken on admission and hence represent baseline levels rather than peak levels.

In a study by Peppes et al in Greece including 123 patients, 65 of whom had acute myocardial infarction, showed mean fibrinogen level of 464+/-161 mg/dl in the first 48 hours. Significant association was found between serum fibrinogen and severity of angiographic coronary artery disease using the Gensisni score (14).

Smoking has been shown in several studies to correlate with elevated baseline serum fibrinogen levels (15,16). Our values seem to agree with prior studies on the relationship of smoking and elevated SFL.

Our study did not show significant relationship between elevated fibrinogen levels and thrombolytic therapy. We used Streptokinase, which was previously shown to reduce SFL in the early hours after administration to rise to baseline levels at 24 hours (17). Our samples taken at 72 hours is a possible explanation.

Interestingly, no mortality was recorded in this cohort. This may be explained partly by the fact that a large proportion of mortality due to STEMI occurs in the first 72 hours (18). Another explanation is that critical patients may have been transferred elsewhere for invasive coronary angiography.

Study Limitations

Beside the small number of patients, other limitations include sampling at peak levels only without baseline or admission fibrinogen levels, exclusion of cases within the first 72 hours when most acute complications of STEMI are expected, and exclusion of cases which were referred for coronary angiography in other hospitals since cardiac catheterization services were not available at the hospital during the study period.

Conclusion

Peak fibrinogen levels in a small cohort of Sudanese patients with acute myocardial infarction were elevated after 72 hours of admission and showed significant correlation with age of 40-60 years, female gender and smoking. No significant correlation was seen with DM, HTN, thrombolytic therapy or hospital outcomes. The above limitations must be taken into account when interpreting the results. For better understanding of the correlation between SFL and hospital outcomes, a larger study is needed wherein SFL levels are tested on admission, at 72 hours and on discharge, and wherein all STEMI comers are enrolled, including those who get transferred or die within 72 hours.

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