Plasma fibrinogen and D-dimer in patients with acute myocardial infarction

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ABSTRACT

Objectives: To investigate the plasma fibrinogen level and D-dimer reaction in patients with acute myocardial infarction (AMI) together with other haematological parameters.
Design: A prospective clinico-haematological study.
Setting: Intensive coronary care unit in Ibn-Sina teaching hospital in Mosul during a period of 4 months from October 2004.
Participants: Forty patients with acute myocardial infarction together with a control group of 40 subjects.
Main outcome measures: Basic haematological parameters, plasma fibinogen level and plasma D-dimer reaction tests. Biochemical tests including cardiac enzymes measurement as creatine kinase (CK) and asparate transaminase (AST) were performed.
Results: Plasma fibrinogen level, white blood cell count and neutrophils count were significantly higher in patients compared to control group with P values (<0.05) (<0.01) and (<0.05) respectively. Positive plasma D-dimer reaction was significantly more frequent in patients than in control group (p<0.05). High plasma fibrinogen level and positive plasma D-dimer reaction were seen in those with worse outcome with p-value (<0.05), (<0.05) respectively. Plasma fibrinogen was significantly higher in those with extensive infarction compared to others (p<0.05).
Conclusion: High plasma fibrinogen and positive plasma D-dimer reaction were more frequently seen in patients with complicated course of myocardial infarction.

Key words: Fibrinogen, D-dimer, acute myocardial infarction.

الخلاصة

الأهداف: للتحري عن مستوى مولد الليفين واختبار د-المزدوج في بلازما الدم عند المرضى الذين يعانون من احتشاء عضلة القلب الحاد .
خطة العمل: دراسة سريرية مرضية مستقبلية .
مكان وزمان البحث: نفذت الدراسة في وحدة العناية القلبية المركزة في مستشفى ابن سينا التعليمي بالموصل ولمدة أربعة أشهر اعتبارا من تشرين الأول ٢٠٠٤م .
المشاركون: تتكون مجموعة المرضى الذين يعانون من احتشاء عضلة القلب الحاد من ٤٠ مريضا مع مجموعة ضابطة عددها ٤٠ شخصا .
القياسات المستخرجة: تم إجراء الاختبارات التالية:
اختبارات الدم الأساسية وقياس مقدار مولد الليفين مع اختبار د-المزدوج في بلازما الدم مع فحوصات لقياس أنزيمات القلب المعروفة AST., CK .
النتائج: لقد وجد هناك ارتفاع في مستوى مقدار مولد الليفين وعدد كريات الدم البيض وخاصة المتعادلة منها عند مجموعة المرضى مقارنة مع المجموعة الضابطة كما وجد أن تفاعل اختبار د-المزدوج كان موجبا بنسبة عالية عند المرضى . زيادة مستوى مولد الليفين في البلازما مع وجود تفاعل موجب لـ د-المزدوج عند المرضى الذين كانت لديهم مضاعفات .
الاستنتاج: زيادة مستوى مقدار مولد الليفين في البلازما مع تفاعل موجب لـ د-المزدوج في المرضى الذين لديهم مضاعفات مع احتشاء العضلة القلبية الحاد .

Acute coronary syndrome results from a ruptured plaque and intraluminal thrombus formation[1]. In addition to the hypercoagulable state, there is strong systemic imbalance of the haemostatic system with a shift to

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procoagulation than fibrinolysis. So the haemostatic system plays an important role during acute illness and development of atherosclerosis[2-4]. Fibrinogen might contribute to the formation and progression of atherosclerotic plaques[5-8]. Recently fibrin D-dimer the product of cross linked fibrin, has gained an increasing interest because it acts as marker of fibrin turnover and activation of haemostasis[9].

The aim of this study was to evaluate D-dimer reaction and plasma fibrinogen level in patients with acute myocardial infarction.

SUBJECTS AND METHODS

This study was conducted in the intensive coronary care unit (ICCU) in Ibn-Sina Teaching Hospital during a period of 4 months starting from october 2004. We included 40 patients diagnosed as cases with acute myocardial infarction according to the criteria of the World Health Organization[10]. There were 34 adult males (85%) and 6 females (15%) with ages ranging from 36-78 years with a mean of 57 years. The control group included 40 subjects who had no history of ischaemic heart disease, infection or malignant disease in the previous 6 weeks. Both control and patients groups were matched for their age and sex.

Venous blood was drown during the first few hours from admission to ICCU(mean time 1.4 hour and a range of 1-3 hours). and complete blood counts including erythrocyte sedimentation rate (ESR) were done according to Dacie and Lewis[11]. Plasma D-dimer test was done by commercially available kit (Biomerieus/FDP slidex direct-73 -101/Francel kit). It is a rapid latex agglutination slide test for the qualitative determination of D-dimer reaction in plasma by agglutination of latex particles coated with anti-D-dimer monoclonal antibodies. Plasma fibrinogen measurement was done by using (Biomerieux/Fibrinomat-68 452/France kit) that depend on the clot based method of Clauss[12].

Cardiac enzymes assay (CK and AST) was done by routine enzymatic colorimetric methods of Randox (normal range of AST up to 22U/L and for CK up to 100U/L). All patients were followed for any evidence of complications as heart failure, arrhythmia or pericarditis until they are discharged or die.

The statistical analysis was based on all cases. Continuous variables were described by mean, value, standard deviation, range. Chi square and student's t-test were used.

RESULTS

Table (1) shows the laboratory characteristics of the study population.

The WBC count, neutrophil count and ESR level were significantly higher in patients compared to control group, ($P<0.05$), ($P<0.01$) and ($P<0.05$) respectively.

- High plasma fibrinogen was of significant values in patients who died or had complicated course during their admission in the ICCU ($p<0.05$), (Table 2).
- Positive D-dimer reaction was significantly higher in patients than in controls and in those with worse outcome than others, (Table 2). D-dimer reaction was negative in all controls. Significant positive correlation between ESR and AST level and between plasma fibrinogen and CK level with ($p<0.05$) and ($p<0.01$) in (Figure 1) and (Figure 2) there was no significant correlation between plasma fibrinogen and AST levels.

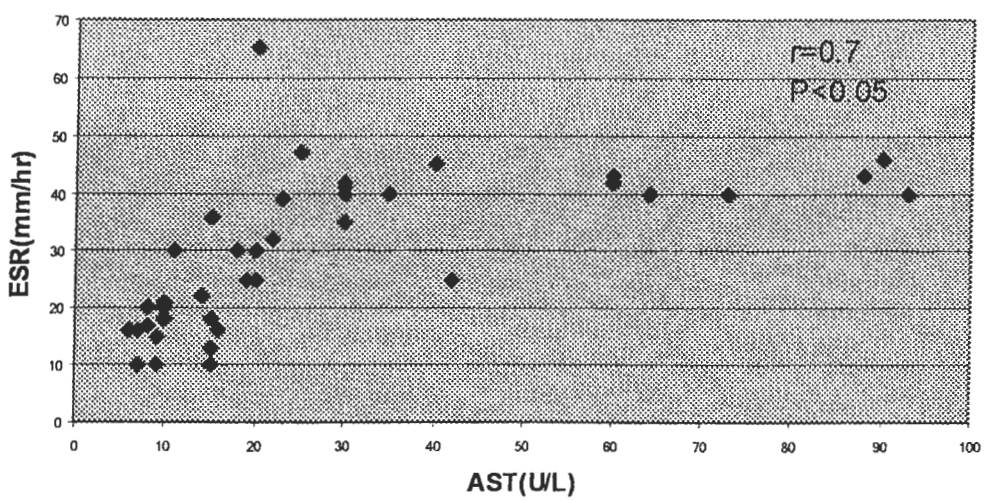

Figure (1): *Correlation between ESR and AST levels in AMI.*

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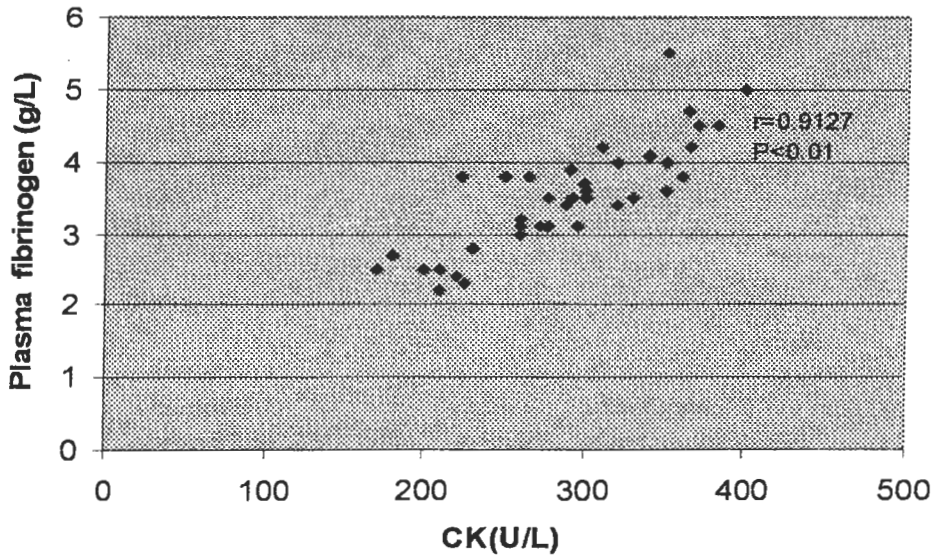

Figure (2): *Correlation between plasma Fibrinogen and CK levels in AMI.*

Table (1): *The laboratory parameters of the study population.*

	Patients (No=40)			Control(No=40)			P Value
	Mean ± SD		Range	Mean ± SD		Range	
Hb (g/l)	120	40	80-160	120	20	100-140	*NS
PCV (L/l)	0.38	0.08	0.29-0.47	0.38	0.07	0.31-0.45	NS
WBC x10^9/L	8	4	4-12	5.2	1.2	4.0-6.4	P<0.05
Neutrophil x 10^9/L	6	2	4-8.5	5	1.2	3.8-6.2	P<0.01
ESR (mm/hr)	26	20	6-46	8	2	6-10	P<0.05
Fibrinogen (g/L)	4	0.9	3.1-4.9	2.6	0.6	2-3.2	P<0.01
CK(U/L)	260	120	140-380	50	20	30-70	P<0.05
AST(U/L)	50	43	7-93	5.2	2	3.2-7.2	P<0.05

* Not significant

Table (2): *D-dimer and plasma fibrinogen in patients with acute myocardial infarction.*

	*Positive D-dimer	Negative D-dimer	**Patients with high Plasma Fibrinogen	Patients with low Plasma Fibrinogen
Patients with complicated course	24	11	25	10
Patients without complication	0	5	1	4

* $X(1)^2 = 5$ (P<0.05) **X(1) = 3 (P<0.05)

DISCUSSION

Leucocytosis may be observed within several hours after AMI and after 12 hours ESR increased above the references range values and remains elevated for several weeks[13]. These changes were also seen in our study and are most probably a response to the acute phase of the illness (Table 1).

High plasma fibrinogen was significant in those with complicated course in our study (Table 2). The increased level of plasma fibrinogen in AMI was noticed by "Kader et al" who mentioned elevated plasma fibrinogen level especially on days 3 and 4[14]. Also increased plasma fibrinogen level in complicated cases who died or had new myocardial infarction was discussed by others[15]. The incidence of MI and death predicted by plasma level of fibrinogen modified by its covariance with other inflammation sensitive proteins has been noticed[16]. Likewise, increased plasma fibrinogen levels have also been identified as an important risk factor for future cardiovascular events in several studies[5,6]. The increased plasma fibrinogen level reflects an acute phase response to the infarct tissue and this also may explain its high level in extensive infarction.

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Increased levels of fibrin D-dimer are indicative of hyper-coagulable state in acute coronary syndrome[18]. Nowadays, they consider fibrin D-dimer assays are more stable and more practical to measure and therefore more reliable in routine clinical purposes[9]. In our study we depended on the rapid latex agglutination slide test method for plasma D-dimer reaction which is the only available method in our laboratory and showed a high percentage of positive reaction in those with complicated course AMI indicating a hypercoagulable state. In our study both CK and AST enzymes were elevated significantly but CK was increased significantly in those with high plasma fibrinogen level (Figure 2). Adams et al mentioned that CK was more specific than AST and both reflect the presence of necrotic cardiac muscles. Also AST level had a significant positive correlation with ESR level which increased as a response to the acute phase of the illness.

Conclusion: Elevated plasma fibrinogen and positive plasma D-dimer reaction were more frequently seen in patients with complicated course myocardial infarction.

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