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The Impact of Fetuin-A Level on Patients with Acute Myocardial Infarction.

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ABSTRACT

Acute myocardial infarction is one of the commonest disease with serious complications and increasing morbidity and mortality. Coronary atherosclerosis plays a crucial role in the underlying pathophysiology. Fetuin-A is a protein which is closely linked with increased risk of cardiovascular disease, and secreted mainly by the liver, induces insulin resistance and subclinical inflammation in rodents. The aims of this study was an attempt to evaluate the involvement of fetuin-A in the pathogenesis of acute myocardial infarction. Moreover, we aimed to assess fetuin-A with some of the known risk markers such as HbA1c, total serum cholesterol and serum creatinine. This is a case–control study included 88 subjects divided into two groups; 44 patients with acute myocardial infarction and the other 44 were apparently healthy individuals taken as a control. Serum fetuin-A levels were measured by using ELISA technique. HbA1c was determined by high performance liquid chromatography and serum cholesterol and serum creatinine by colorimetric method. There was significant differences in serum fetuin-A levels between patients and control, (p value ≤ 0.05).However, The output estimated by logistic regression model indicates that fetuin A studying among other studied risk markers is not significantly associated with the probability of using as a risk marker (odds ratio=0.818) .This study concluded that a decreased level of fetuin-A in myocardial infarction might play a role in its etiology.

Keywords: Fetuin-A, Acute myocardial infarction, ELISA technique, Risk marker. pathogenesis

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INTRODUCTION

Acute myocardial infarction(AMI) is one of the commonest disease with serious complications and increasing morbidity and mortality. Annually, about three and four million people are estimated to have an acute ST-elevation MI (STEMI) and non-ST-elevation MI (NSTEMI) respectively. The disease is seen predominantly in developed countries, however it becomes increasingly more common in developing countries [1].

The critical risk factors of AMI are preexisting cardiovascular disease (CVD), old age, smoking, hypercholesterolemia , diabetes mellitus , hypertension, physical inactivity, obesity, and chronic high stress levels.[2,3]

Depending on ECG finding, MI is classified as STEMI and NSTEMI. Existence of a ST segment elevation on ECG or Q-wave are associated with poor prognosis [4].

Human FA is a glycoprotein mainly formed and secreted by liver , kidneys and many organ of human being. It exerts its effect throughout toll like receptors which are widely distributed in different tissues. It is thought that FA has pro inflammatory and anti inflammatory effects [5].

The function of fetuin A is a mediating signal for antagonizing growth factor and inhibition of skeletal matrix mineralization. FA can inhibit calcification depending on a property of binding with cationic ions like Ca^{2+} preventing its deposition in soft tissues.[6,7]

The relationship between circulating FA and CVD risk appears to be complicated , the risk of MI is increased with the increased FA level. However, subclinical and clinical CVD are associated with Low plasma FA levels. In patients with insulin resistance syndrome, FA levels have shown to be elevated and the incident type 2 diabetes can be predicted by high FA concentrations. [8, 9].

Aim of the Study

The aims of this study was an attempt to evaluate the involvement of fetuin-A in the pathogenesis of acute myocardial infarction. Moreover, we aimed to assess fetuin-A with some of the known risk markers such as HbA1c, total serum cholesterol and serum creatinine.

MATERIALS AND METHOD

Subjects:

This is a case–control study performed between the first of December 2015 and first of March 2016 included 88 subjects divided into two groups; 44 patients with AMI and the other 44 were apparently healthy individuals taken as a control. Patients were diagnosed by consultant physician at Marjan Medical City /Hilla. The patients´ Mean age ±SD was 61.29±10.85 which matched with control group (Mean age ±SD was 56.72±9.86) , furthermore the socio-demographic status between two groups was matched also. The practical part of the study was achieved at the laboratories of Department of Pathology and Clinical Biochemistry / Babylon College of Medicine.

Ethical considerations:

Legal agreements from research related offices had been taken , in addition , verbal acceptance from all participants involved in this study was undertaken.

Sample collection:

From each subject enrolled in the study. about 5 ml of blood was obtained by vein puncture. However, The patient diagnosed with AMI, the blood was aspirated within 24 hours to avoid changes in

parameters results. The aspirated blood was put in gel separating tube, centrifuged at 6000 X g for 10 minutes. The obtained serum was stored in eppendorf and kept freezing until time of analysis.

Methods:

Fetuin-A level in serum was measured by sandwich enzyme-linked immune-sorbent assay (ELISA) using a kit provided by Biorbyt / USA . HbA1c was determined by high performance liquid chromatography(HPLC) using D-10 instrument /USA, Serum cholesterol and creatinine were measured by colorimetric method using a kit supplied by Biolabo/France .

Statistical analysis:

The obtained data were analyzed by computer using SPSS program ,version 19th . Descriptive data were expressed as (mean ± SD),while level of significance between variables was determined by Chi square (X2) test. Logistic regression was used to describe the relationship between one dependent and independent variables. were The selected level of significant for *P* values was less than (0.05)

RESULTS

Table 1 showed differences of patients and control by age, marital status, residence, educational levels and occupational status .There was no significant difference between patients and control group (p value>0.05) .

Table 1: Age and Socio-Demographic Distribution of Studied Groups.

Variable	Study groups		*P* Values
	Patients	Control	
Age	Mean±SD	Mean±SD	0,627
	61.2954±10.85	56.72±9.86	
Residence Urban area Rural area	28 (63.6 %) 16 (36.4%)	30 (68.2%) 14 (31.8%)	0.653
Educational levels Illiterate Primary school Secondary school Higher education	 13 (29.5%) 11 (25.0%) 11 (25.0%) 9 (20.5%)	 12 (27.3%) 14 (31.8%) 14 (31.8%) 4 (9.1%)	0.443
Marital status Married Non-Married	 37 (84.1%) 7 (15.1)	 33 (75.0%) 11 (25.0%)	0.290
Occupational status Employed Non-Employed	 22 (50.0%) 22 (50.0%)	 29 (65.9%) 15 (34.1%)	0.131

Table 2 showed the model of logistic regression for study groups by FA, total cholesterol, HbA_{1C}, waist circumference. The odds ratio for FA 0.818 less than 1, indicated that patients were 0.818 times less than control to have high FA. The odds ratio for HbA1C, total cholesterol, were 3 and 2 respectively, which indicated that patients were 3 and 2 times to have high HbA1C and total cholesterol, respectively. However, the odds ratios for S.creatinine were protective (near 1).

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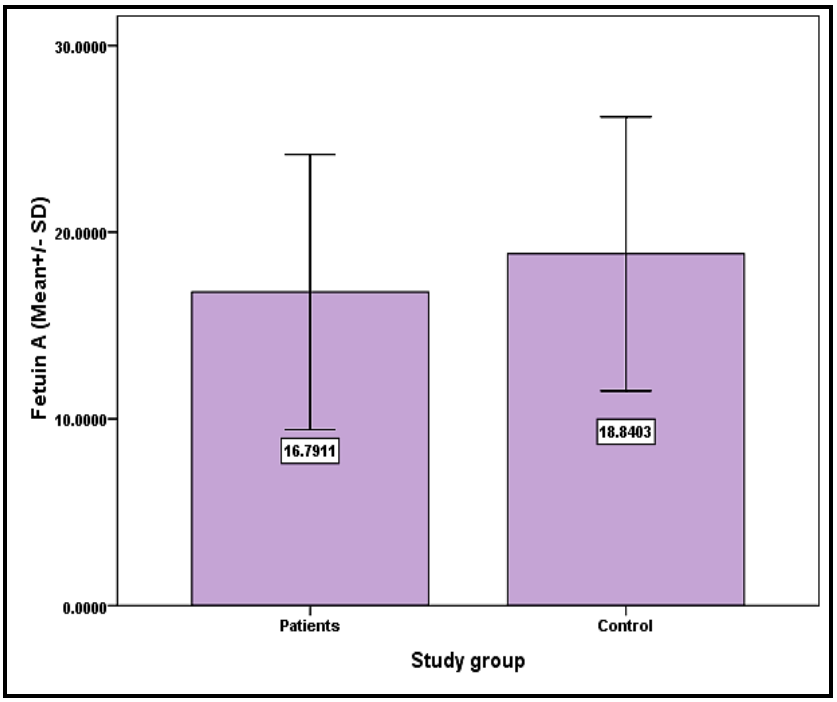
Table 2: Logistic Regression Model for Study Groups by Study Parameters

Parameters	Wald	P value	Odds Ratio	95% C.I.for Odds Ratio	
				Lower	Upper
FetuinA	5.212	0.022	0.818	0.688	0.972
T.Cholesterol	5.367	0.021	2.185	1.128	4.234
HbA1c	7.992	0.005	3.071	1.411	6.686
S.creatinine	5.181	0.023	1.046	1.006	1.087
Constant	10.015	0.002	0.000		

*** p value < 0.05 is significant**

Figure 1 showed comparison of patients and control by FA level. The mean ± SD was 16.9 ±3.6 ng/ml and 18.3± 4.41 ng/ml respectively. There was a significant difference in the level of FA between patients and control group (*p* value<0.05) .



*** p value ≤ 0.05 is significant**

Figure 1: Comparison of patients and control by Fetuin-A

DISCUSSION

Age and sex are important risk factor in AMI. In general, Men are at higher risk than women at any age, become equal after menopause [10] , however, AMI causes slightly more total deaths in women because in general women live longer than men [2]. In the present study, there was no significant mean difference between the mean age and other socio-demographic criteria between patients and control. This age matching aids elimination the differences in studied parameters results.

MI results as consequence of atherosclerotic process [11]. Deposition of Ca^{+2} in large vessels is one part of atherosclerotic plaque formation. Ca^{+2} deposits in the coronary arteries can be identified by CT scans. Several studies have shown that coronary Ca^{+2} can give predictive knowledge beyond that of well known risk factors.[12.13]. High FA levels may provide protection against CV events by keeping Ca+2 and phosphorus solubilised in serum[7].In the current study the FA level was low in patient with AMI compared to controls which in turn causes loss of this solubilisation process and Ca +2 deposition in coronary arteries.

Inflammation is another important part in the process of atherosclerotic plaque formation

[14]. Fetuin-A appears to participate in both inflammatory process and calcification of vascular system. Literally, FA is declined during systemic inflammatory process that is to say it is a negative acute phase reactant [7].A low FA concentration will promote the continuous inflammatory process and may impair directly functions of heart and producing cardiac calcification and fibrosis and hence enhance progression of CVD. So the present study concluded that decreased level of fetuin-A in MI might play a role in the formation of atherosclerotic plaque.

In the current study, logistic regression model demonstrated that FA had the least power among selected risk marker where HbA_{1c} and total serum cholesterol were the powerful risk markers for development of AMI.

CONCLUSION

The evidence of decreased level of fetuin-A in myocardial infarction might play a role in the pathogenesis of this disease .

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