

Assessment of Apolipoproteins A1, E, and Insulin Resistance in Iraqi Male Patients with Acute Myocardial Infarction

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Abstract:

Background: Insulin resistance is a risk factor for ischemic heart disease and myocardial infarction. It often manifests in myocardial infarction and is regarded as an independent predictor of in-hospital mortality, which can provide early risk stratification for recurrent acute coronary events.

Objective: The aim of this study was to assess the levels of apolipoproteins A1, E with insulin resistance in Iraqi male patients with acute myocardial infarction.

Patients and Methods: Forty five male patients with acute myocardial infarction were enrolled in this study. Their age range was (40-55) years and they are compared with 45 healthy male as control group. All patients with acute myocardial infarction were checked up by a cardiologist in Iraqi Centre for Cardiovascular Diseases/Al-Hariry Hospital/ Baghdad. Fasting venous blood samples were collected from all the subjects. Laboratory evaluations consisted of fasting serum glucose, glycated hemoglobin, serum insulin, and lipid profile. Furthermore, apolipoproteins A1 and E levels were determined in this study.

Results: There was a significant increase in fasting serum glucose and insulin levels in patients group as compared to the controls. Additionally, there was an elevation in glycated hemoglobin and homeostasis model assessment for insulin resistance in those patients, but they were not significant. There was a significant increase ($p= 0.001$) in serum total cholesterol, triglyceride, and low density lipoprotein cholesterol, while there was a significant decrease in serum high density lipoprotein cholesterol in patients group as compared to the controls. Moreover, there was a significant increase ($p= 0.001$) in apolipoprotein E, while a significant decrease ($p= 0.001$) in apolipoproteins A1 was found in patients group as compared to the controls.

Conclusions: Dyslipidemia, along with insulinemia and glycemia, is one of the most significant insulin resistance risk factors in the acute and early recovery phases of myocardial infarction

Keywords: Insulin resistance, Acute myocardial infarction, Apolipoproteins.

Introduction:

Acute Myocardial infarction (AMI) is well-known pathologically as myocardial cell death due to prolonged ischemia. Lessened cellular glycogen, and undisturbed myofibrils and sarcolemmal disruption, are the chief ultra-structural fluctuations and are seen as initial as 10–15 minutes after the onset of ischemia ⁽¹⁾.

Insulin resistance (IR) is a risk feature for cardiovascular disease (CVD) ⁽²⁾. The IR frequently exhibits in AMI and is considered as an liberated predictor of mortality, which may deliver initial risk stratification for frequent acute coronary proceedings ⁽³⁾.

Insulin resistance (IR) is defined as decreased sensitivity or responsiveness to the metabolic actions of insulin; consequently, a variety of restrictions, comprising traditional hyperinsulinemia and hyperglycemia, are deliberated to be IR markers. Nevertheless, some lipid metabolism factors are also supposed to be capable IR markers, with their effect in CVD being well-known. It is identified that free fatty acids (FFAs) block glucose carrying by preventing insulin's cooperation

with hepatocytes and monocytes, foremost to hyperglycemia and IR progress ⁽⁴⁾.

There is robust evidence that lipid abnormalities such as high plasma triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), and decreased high-density lipoprotein cholesterol (HDL-C) levels are associated with increased stroke risk ⁽⁵⁾.

Cholesterol can be complexed with apolipoproteins (apos). Besides its beneficial aspects in human physiology, an excess of cholesterol can also be harmful ⁽⁶⁾. Several observational studies consistently show an association between elevated LDL-C and high prevalence of CVD in adults, and, on the other hand, between high HDL-C and reduced prevalence of these diseases. Though this concept has been recently debated ^(7,8).

ApoA1 is a major apo of HDL-C and is involved in the regulation of reverse cholesterol transport and the metabolism of HDL particles. This transport process is regulated by a physical interaction of apoA1 with its molecular partner, the ATP-binding cassette transporter A1 (ABCA1), located in the plasma membrane ⁽⁹⁾.

ApoE, a major constituent of very low density lipoprotein (VLDL), has been shown to be an essential ligand for the uptake and clearance of atherogenic lipoproteins. Moreover, it has been demonstrated that apoE plays an important role in atherosclerosis by modifying inflammatory responses and facilitating cholesterol efflux from cells ⁽¹⁰⁾. Hence, the aim of this study was to assess the levels of apo A1, E with IR in Iraqi male patients with AMI.

Patients and Methods:

Forty five male patients with AMI were enrolled in this study. Their age range was (40-55) years and they are compared with 45 healthy male as control group. The questionnaire included duration of AMI, family history, height, weight, heart disease, and hypertension for patients and controls groups. All patients with AMI were checked up by a cardiologist in Iraqi Centre for Cardiovascular Diseases/Al-Hariry Hospital/ Baghdad. The diagnosis of AMI was dependent on the following criteria: 1- Typical history of acute chest pain. 2- Unequivocal changes of MI in the electrocardiogram (ECG) to confirm the diagnosis.

Patients with liver, renal, thyroid function disease, and hormonal abnormalities were excluded from this study.

Anthropometric parameters involved body mass index (BMI), systolic-, and diastolic- blood pressure (SBP, DBP) are estimated. Body mass index is calculated according to the following equation ⁽¹¹⁾:

$$BMI = \frac{\text{mass (kg)}}{(\text{height(m)})^2}$$

Laboratory evaluations consisted of fasting serum glucose (FSG), glycated hemoglobin (HbA1c), serum lipid profile including: [serum total cholesterol (TC), TG, HDL-C, VLDL, LDL-C], and serum insulin. Insulin resistance was estimated using the homeostasis model assessment for IR (HOMA-IR) index according to the following equation ⁽¹²⁾:-

$$HOMA-IR = G_0 \times I_0 / 405$$

Furthermore, serum apoA1 and E levels were determined by (Cusabio, China) kit.

Statistical Analysis:

Statistical package of social science (SPSS) version 17.0 was used for analysis of data. Results are expressed as means $\pm$ SD. Student-t test was used to compare between the groups. The *p* value of ≤ 0.05 was considered significant.

Results:

Anthropometric and clinical characteristics of patients and control are shown in table (1). There was a significant increase ($p \leq 0.05$) in BMI, SBP, and DBP in AMI patients as compared to the controls. There was no significant difference in age between the two groups.

There was a significant increase ($p = 0.01$) in FSG and insulin levels in AMI patients as compared to the controls, table (2). Additionally, there was an elevation in HbA1c and HOMA-IR in AMI patients, but they were not significant.

Table (1): Anthropometric and clinical characteristics of patients and control

Parameters	Means $\pm$ SD		<i>p</i> value
	AMI (n= 45)	Controls (n= 45)	
Age (Years)	50.67 $\pm$ 4.49	47.27 $\pm$ 6.88	0.06
BMI (Kg/m ²)	29.0 $\pm$ 0.76	22.70 $\pm$ 0.22	0.05
SBP (mmHg)	138.62 $\pm$ 6.43	120.33 $\pm$ 0.23	0.01
DBP (mmHg)	84.95 $\pm$ 2.81	79.50 $\pm$ 0.27	0.01
Duration of AMI (Years)	3.33 $\pm$ 1.44	-	-

* $p \leq 0.05$: Significant, ** $p \leq 0.01$: Highly significant

Table (2): Glycemic parameters of patients and control

Parameters	Means±SD		p value
	AMI (n= 45)	Controls (n= 45)	
FSG (mg/dl)	95.25±3.05	86.36±1.36	0.01
HbA1c (%)	5.42 ± 0.14	4.36 ± 0.09	0.08
Insulin (μIU/ml)	28.74 ± 2.12	12.05±1.11	0.001
HOMA-IR	7.04 ± 0.69	2.67 ± 0.28	0.06

* $p \leq 0.05$: Significant, ** $p \leq 0.01$: Highly significant

Lipid profile parameters are presented in table (3). There was a significant increase ($p=0.001$) in serum TC, TG, LDL-C, and VLDL in AMI group as compared to the controls. Also, there was an elevation in lipid ratios, but they were not significant. A significant increase in apoE, while a significant decrease ($p=0.001$) in apoA1 was found in AMI patients as compared to the controls, table (4).

There was a significant negative correlation between apoA1 and BMI, FSG, serum insulin, TC, TG, LDL-C, and apoE in AMI patients. While, there was a significant positive correlation between apoA1 and serum HDL-C in AMI patients as compared to the controls, table (5).

Table (3): Lipid profile parameters of patients and control

Parameters	Means±SD		p value
	AMI (n= 45)	Controls (n= 45)	
TC (mg/dl)	242.98±12.35	152.91±2.17	0.001
TG (mg/dl)	202.48±10.66	105.03±6.02	0.001
HDL-C (mg/dl)	34.88±1.44	65.17 ± 0.69	0.001
LDL-C (mg/dl)	169.23±9.74	66.10 ± 3.05	0.001
VLDL-C (mg/dl)	42.37±5.94	21.01 ± 1.20	0.001
TC/HDL-C ratio	0.96 ± 7.47	2.36 ± 0.06	0.08
TG/HDL-C ratio	6.30 ± 1.18	1.62 ± 0.09	0.09
LDL-C/HDL-C ratio	5.21 ± 0.71	1.03 ± 0.06	0.06

* $p \leq 0.05$: Significant, ** $p \leq 0.01$: Highly significant

Table (4): Apolipoproteins A-1 and E among patients and control

Parameters	Means±SD		p value
	AMI (n= 45)	Controls (n= 45)	
ApoA-1 (mg/dl)	136.43±1.49	175.37±2.15	0.001
ApoE (ng/ml)	52.08±3.46	28.30±2.37	0.001

** $p \leq 0.01$: Highly significant

Table (5): The correlation coefficient of apoA-1 with other parameters in AMI patients

ApoA-1 (mg/dl)	Correlation coefficient (r)	ApoA-1 (mg/dl)	Correlation coefficient (r)
BMI (Kg/m ²)	-0.67*	TC (mg/dl)	-0.92**
FSG (mg/dl)	-0.78**	TG (mg/dl)	-0.98**
HbA1c (%)	-0.35	LDL-C (mg/dl)	-0.90**
Insulin (μIU/ml)	-0.82**	HDL-C (mg/dl)	0.89**
HOMA-IR	-0.34	ApoE (ng/ml)	-0.81**

* $p \leq 0.05$: Significant, ** $p \leq 0.01$: Highly significant

Discussion:

In this study, It has been showed that an association existed between increased lipid-testing intervals of and elevated risk of AMI among Iraqi male patients, which is in agreement with the study of Jellinger et al., 2017⁽¹³⁾.

There was a significant increase in BMI between the patients and the controls,. Also, there was an increase in FSG, HbA1c, insulin, and HOMA-IR in AMI patients. Thus, any method to predict insulin sensitivity in normoglycemic individuals should first be compared with fasting insulin.

Mahato et al., 2011 reported that estimated risk of CVD has shown to be increased by 18% for each 1% increase in absolute HbA1c value. Positive relationship between HbA1c and CVD has been demonstrated in non-diabetic cases even within normal range of HbA1c. It has been estimated that reducing the HbA1c level by 0.2% could lower the mortality by 10% according to that study⁽¹⁴⁾.

In addition, it has been reported that a number of clinical and metabolic abnormalities have been associated with IR. The metabolic disorders classified included hyperglycemia, dyslipidemia, and hypertension. However, they did confirm that the best method was dependent on glucose status⁽¹⁵⁾.

Levels of fasting insulin in AMI patients were above 25 μIU/ml, which is the upper limit of normal insulin reference range. Thus all patients in this study were hyperinsulinemic.

This study reveals increased levels of TC, TG, LDL-C, and decreased levels of HDL-C. The main disorders of lipid metabolism in this study are hypercholesterolemia, and hypertriglyceridemia. This finding is in concord with a previous study on hypertriglyceridemia⁽¹⁶⁾.

Dyslipidemia characterized by elevated TC, LDL-C, and lowered HDL-C, is a conventional risk factor observed in AMI patients, and is the major cause of atherosclerosis are suggested to act synergistically with non-lipid risk factors to increase atherogenesis. On the other hand, a characteristic dyslipidemia is also associated with IR. Insulin affects the liver apos production. It

regulates the enzymatic activity of lipoprotein lipase (LPL) and cholesterol ester transport protein. All these factors are likely cause of dyslipidemia in CVD. Moreover, insulin deficiency reduces the activity of hepatic lipase and several steps in the production of biologically active LPL may be altered in AMI⁽¹⁷⁾.

Kimm et al., 2010 demonstrated that the lipid ratios of TC/HDL-C, TG/HDL-C, and LDL-C/HDL-C as well as TG and HDL-C, were each consistently associated with the number of metabolic syndrome components, IR based on homeostatic model assessment. The lipids ratios that include information on at least two measures might have a more integrated explanation than single lipid measures such as TG or LDL-C with HDL-C. They were useful makers for both men and women, especially TG/HDL-C ratio in men. Based on the present results, this r-atio consider as a simple means to estimate atherogenic dyslipidemia⁽¹⁸⁾.

Serum HDL-C has been used to predict a person's risk of developing atherosclerosis. Like high LDL-C and low HDL-C < 40 mg/dl are associated with a higher risk of developing CVD. Increased TG and decreased HDL-C are considered to be a major risk factor for the development of IR and MS. The TG/HDL-C ratio is also widely used to assess the lipid atherogenesis⁽¹⁹⁾.

Abnormalities in lipoprotein metabolism are important in atherogenesis, obesity, insulin resistance and diabetes; all being major areas of concern for public health, individual wellbeing and research.

Holmes et al., 2018 recently confirmed these results in a nested case-control study showing that apoA1 was strongly associated with risk of MI. Serum apoA1 of, 120 mg/dl for men and, 140 mg/dl for women approximately correspond to what is considered as low for HDL-C⁽²⁰⁾, which is in agreement with the present data.

Total number of apoE is increased in metabolic abnormalities are better reflected by TG/HDL-C ratio than LDL-C alone. Once these lipid complexes begin to circulate through the blood, LPL bound to the capillary endothelium of muscles and adipose tissue converts their TG to FA and glycerol. These

molecules are then used for energy by most cells or reassembled into TG for storage in adipose tissue⁽²¹⁾.

Generally, patients in this study had low levels of HDL-C and apoA1 while high levels of LDL-C, apoE, and TG levels, which typically coexist in people with IR⁽²²⁾.

Low HDL-C concentrations among people with DM may indicate a specific reduction in large HDL particles as well as a possible increase in small HDL particles, which may not necessarily significantly reduce apoA1 levels. Moreover, the multiplex apo test can be performed in the non-fasting state⁽²³⁾.

Conclusions:

Dyslipidemia, along with insulinemia and glycaemia, is one of the most significant IR risk factors in the acute and early recovery phases of MI. Dyslipidemia is characterized by a high lipid level; an imbalance in apos metabolism; and a deficiency of apoA1 in the acute and early recovery periods of MI. ApoA1 and E can be used as promising molecular markers to stratify the risk of recurrent acute coronary events in MI patients.

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