Impact of adiponectin and oxidized low-density lipoprotein in acute coronary syndrome

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Objectives This study aimed to investigate and measure the relationships between the adiponectin levels and oxidized-low density lipoprotein (Ox-LDL) in acute coronary syndrome (ACS) patients in holy Kerbala city, Iraq.
Methods Fifty-eight patients included in the study. Patients admitted with a diagnosis of ACS and 30 control subjects. Circulating adiponectin and Ox-LDL were assessed; using enzyme-linked immunosorbent assays (ELISA).
Results Adiponectin serum concentrations were significantly lower ($p < 0.001$) in subjects with ACS compared with control subjects. Ox-LDL serum concentrations were significantly higher ($p < 0.001$) in subjects with ACS compared with controls subjects. The ACS patients showed a significantly higher ($p < 0.001$) result in total cholesterol and significantly lower ($p < 0.001$) level in HDL-C.
Conclusion Serum adiponectin negatively correlated with Ox-LDL level in patient group ACS and the healthy control group.
Keywords acute coronary syndrome, Ox - LDL, adiponectin

Introduction

Acute coronary syndrome (ACS) is one of the leading causes of morbidity and mortality globally.[1] ACS occurs because of the destabilization of atherosclerotic plaques, which may undergo rupture or erosion, with subsequent thrombosis and vessel occlusion. Many findings indicate that plaque destabilization correlates with the location and activation of inflammatory cells both within the plaque[2] and in the systemic circulation.[3] Although the identification of vulnerable patients remains a challenge.[4,5]

Adipose tissue is an active endocrine organ that secretes bioactive molecules known as adipokines.[6,7] These molecules play key roles in regulating energy, metabolic and inflammatory processes.[7] One of these classes of molecules, adiponectin, has drawn special attention due to its potential anti-inflammatory, insulin-sensitizing and anti-atherogenic properties.[8,9] Plasma adiponectin levels are lower in obese individuals and have a protective action against the development of type 2 diabetes.[10,11] Clinically, hypoadiponectinemia has been observed in patients with obesity, diabetes mellitus, and coronary artery disease (CAD).[12]

Among factors involved in the initiation, progression and destabilization of plaques, oxidized-low-density lipoproteins (ox-LDL) was thought to play a key role.[13] Excess circulating levels of ox-LDL has been shown to be associated with angiographically proven coronary artery disease (CAD).[14,15] Ox-LDL is a critical factor in the initiation and progression of atherosclerosis and contributes to endothelial dysfunction and plaque destabilization through multiple mechanisms. Ruptured plaques are rich in lipids.[16]

Methods

Study Design

The study group consisted of 58 patients age range (58.21), 38 males and 20 females with acute coronary syndrome (ACS), and 30 healthy control group age range (56.96), 17 males and 13 females. All 88 subjects who agreed to participate in the study were enrolled and all patients have undergone coronary angiography for clinical indications (mainly chest pain, dyspnea on exertion, or positive stress test). Patients in ACS subgroup had a last diagnosis of either unstable angina or acute myocardial infarction (MI), based on clinical feature, biochemical markers, and electrocardiographic changes. The patients were classified as having unstable angina if they had chest pain that was new in the starter. Patients were defined as having an acute MI if they had a cardiac marker rise in association with chest pain or ischemic electrocardiography changes. The exclusion criteria were a smoking history, history of previous coronary revascularization and prior chest radiation therapy.

Laboratory Methods

A volume of 5 ml venous blood was collected from all patients and control subjects. The serum samples were kept at -70°C for subsequent assay. The plasma concentration of adiponectin and Ox-LDL evaluated by a sandwich ELISA system (Adiponectin ELISA kit, Ox-LDL ELISA kit). Serum total cholesterol, triglyceride and HDL-C concentrations determined by an enzymatic mode. Body mass index (BMI) was calculated as weight divided by the square of height. Risk factors defined as follows, Diabetes mellitus was diagnosed according to World Health Organization criteria.[17] Dyslipidemia was defined as a total cholesterol concentration ≥ 200 mg/dL, a triglyceride concentration ≥ 150 mg /dL, an HDL-cholesterol focus < 40 mg/dL, and having received treatment for dyslipidemia.

Statistical Analysis

The data were analyzed by using SPSS. Continuous data were expressed as mean ± SD and difference of mean of two groups was set by unpaired Student's *t*-test. The level of significance was set at 0.05, and ANOVA test was used to investigate the difference among the means of more than two groups.

Results

The clinical characteristics of ACS patients and healthy control subjects are shown in Table 1 and Figure 1. Serum adiponectin levels in the ACS patients was significantly lower mean = 21.888 than those in healthy control subjects mean = 36.09 ($p < 0.0001$) and serum ox-LDL levels in the ACS patients was significantly higher mean = 66.03 than those in healthy control subjects mean = 19.6 ($p < 0.001$). In Table 2, there were the mean BMI value and age was insignificant in the patient than healthy control ($p > 0.05$). The serum HDL-C was significantly lower mean = 35.33 in ACS patients ($p < 0.0001$) in comparison with a healthy control group, but there were a significant difference in the total cholesterol in the ACS patient group in comparison with a healthy control group ($p < 0.05$). Whereas no significant differences in the serum triglyceride, VLDL-C and LDL-C levels in comparison between ACS patient group and healthy control group ($p > 0.05$). Increased triglyceride mean = 199.49, LDL-C mean = 123.32 and VLDL-C mean = 39.899 associated with the presence in patients admitted to C.C.U.

Results obtained showed that serum ox-LDL was significantly higher mean = 83.008 in diabetic and non-diabetic mean = 52.26 acute coronary syndrome (ACS) patients group in comparison with healthy control group ($p < 0.001$), the results showed that there was a significantly lower levels mean = 18.7 of adiponectin in diabetic ACS patient group in comparison with healthy control group ($p < 0.001$) and no significant differences in the serum triglyceride, TC, VLDL-C and LDL-C levels in comparison between diabetic and non-diabetic ACS patients group in comparison with healthy control group ($p > 0.05$). While Serum HDL-C recorded a highly significant decreases in diabetic ACS patients mean = 31.48 in comparison with healthy control group ($p < 0.001$). On the other hand, the age and BMI showed no significant difference between patients and healthy control group ($p > 0.05$), as shown in Tables 3 and 4.

Table 1. **Comparison between acute coronary syndrome patients group and healthy control group in the measured adiponectin and Ox-LDL**

Parameters	Patients	Controls	*t*-test *p*-value
	Mean ± SD	Mean ± SD	
Number	58	30	
Adiponectin (ng/ml)	21.888 ± 6.531	36.09 ± 3.88	0.000*
Ox-LDL (U/ml)	66.03 ± 17.44	19.6 ± 3.15	0.000*

Student *t*-test between ACS patients and control group, *Highly significant; SD, standard deviation; Ox-IDL, oxidized-low-density lipoprotein; Student *t*-test between ACS patients and control group; Significant: $p < 0.05$; Highly significant: $p < 0.001$; No significant: $p > 0.05$.

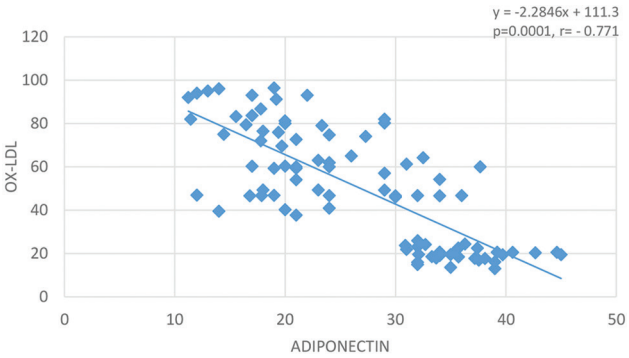

Fig 1. **Correlation between Ox-LDL and adiponectin in acute coronary syndrome patients and healthy control group.**

Discussion

Cardiovascular diseases are important medical and public health issues throughout the worldwide. The ACS becomes progressively more common with increasing age and as the average age of world population is increasing, this problem will also rise.[18] In the this study, hypoadiponectinemia was found to be highly associated with CAD prevalence after adjustment for well-known CAD factors such as diabetes mellitus, dyslipidemia, hypertension and smoking habit in human subjects. For translation into the clinical setting, it is very important to determine the abnormal range of serum adiponectin concentrations this agreement with Kumada et al.[17] Adiponectin levels decrease as the number of significantly narrowed coronary arteries increase. Similar observation was made by the number of previous study[19] that found the adiponectin levels decreased as a function of number of significantly narrowed coronary arteries and that, in patients with ACS, those with various complex lesions had significantly lower adiponectin than those with a single complex lesion. So the present study reinforce, the protective role of adiponectin in the

Table 2. **Comparison between acute coronary syndrome patients group and healthy control group in the measured parameters**

Parameters	Patients	Controls	*t*-test *p*-value
	Mean ± SD	Mean ± SD	
Number	58	30	
Age (years)	58.21 ± 8.57	56.96 ± 9.01	0.526
BMI (kg/m^2)	27.14 ± 2.82	27.01 ± 2.92	0.84
TG (mg/dl)	199.49 ± 99.42	165.18 ± 56.6668	0.084
T.C (mg/dl)	198.55 ± 62.034	173.951 ± 33.3128	0.046*
LDL (mg/dl)	123.32 ± 65.259	99.319 ± 32.904	0.063
HDL (mg/dl)	35.33 ± 6.166	41.59 ± 6.163	0.000**
VLDL (mg/dl)	39.899 ± 19.88	33.036 ± 11.333	0.084

Student *t*-test between ACS patients and control group: *Significant; **Highly significant; TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein-cholesterol; SD, standard deviation; LDL-C, low-density lipoprotein-cholesterol; VLDL-C, very low-density lipoprotein cholesterol; BMI, body mass index; *p* value derived from Student *t*-test; Significant: $p < 0.05$; Highly significant: $p < 0.001$; No significant: $p > 0.05$.

Table 3. **Comparison between diabetic and non-diabetic acute coronary syndrome patients group and healthy control group in the measured parameters using ANOVA test**

Parameters	Patient with ACS		Control (30) Mean ± SD	*p*-value
	D.M (26) Mean ± SD	Non D.M (32) Mean ± SD		
Number	26	32	30	
Adiponectin (ng/ml)	18.7 ± 4.9	24.4 ± 6.66	36.09 ± 3.88	0.000*
Ox-LDL (U/l)	83.008 ± 8.35	52.26 ± 8.08	19.6 ± 3.1	0.000*

*Highly significant; SD, standard deviation; Ox-LDL, oxidized low- density lipoprotein; *p* value derived from ANOVA test; Significant: $p < 0.05$; highly significant: $p < 0.001$.

Table 4. **Comparison between diabetic and non-diabetic acute coronary syndrome patients group and healthy control group in the measured parameters using ANOVA test**

Parameters	Patient with ACS		Control (30) Mean ± SD	*p*-value
	D.M (26) Mean ± SD	Non D.M (32) Mean ± SD		
Number	26	32	30	
Age	59.53 ± 8.72	57.12 ± 8.43	56.93 ± 9.018	0.480
BMI	27.8 ± 2.95	26.6 ± 2.6	27.01 ± 2.94	0.275
T.C	194.45 ± 76.15	201.4 ± 48.3	173.9 ± 33.313	0.125
TG	211.34 ± 102.12	189.93 ± 97.4	165.1 ± 56.666	0.149
LDL-C	121.32 ± 83.8	124.9 ± 47.3	99.319 ± 32.90	0.175
HDL-C	31.48 ± 6.98	38.5 ± 2.726	41.5 ± 6.163	0.000*
VLDL-C	42.2 ± 20.5	37.9 ± 19.47	33.036 ± 11.33	0.149

*Highly significant; TG, triglycerides; TC, total cholesterol; HDL-C, high density lipoprotein - cholesterol; SD, standard deviation; LDL-C, low-density lipoprotein-cholesterol; VLDL, very low-density lipoprotein cholesterol; BMI, body mass index; *p* value derived from ANOVA test; Significant: $p < 0.05$; Highly significant: $p < 0.001$; No significant: $p > 0.05$.

evolution of atherosclerotic plaque. The results of this study show that circulating levels of ox-LDL metric with an ELISA method are significantly higher in patients with ACS than in healthy control group, the ox-LDL levels correlate with the presence of angiographic complex plaques. These results support the key role that ox-LDL may have in plaque destabilization and tear.[20,21] Several studies have exact the relation between circulating levels of ox-LDL and clinical manifestations of CAD with conflicting results.[22,23] There is increasing evidence suggest that oxidative modification of LDL plays a pivotal role in the development of atherosclerosis.[24–27] This study found that the levels of ox-LDL were significantly higher in ACS cases than in healthy control group, which was similar to our previous findings.[26,27] These finding agree with the study mad by who found that Huiling Huang et al.[28] These findings indicate that serum ox-LDL levels are closely related with CAD.

Conclusion

It was found that a presence of significant association between the adiponectin and Ox-LDL in acute coronary syndrome (ACS). Level of serum adiponectin was significantly lower in patients with ACS compared with healthy control group and level of serum ox-LDL was significantly higher in patients with ACS compared with healthy control group. Serum Adiponectin was negatively correlated with Ox-LDL level in patients' group and healthy control group. Hypoadiponectinemia was significantly associated with the presence ACS.

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