Association of Adiponectin Levels with Coronary Artery Disease in Obese Patients

Nisreen A. Al-Fuqaha'a[1], Fayza A. Rahmatalla[2], Abdelbaqi A. Abdelbaqi[3], Atif A. Elagib[4]

[1]Health Ministry of Jordan, [2]Faculty of Medical Laboratory Sciences Omdurman Islamic University, [3]Faculty of Agriculture Omdurman Islamic University,[4] National Center for Research.
*Corresponding author: atifelagib@hotmail.com Tel: 00249912292399

Abstract

Background: Coronary artery disease (CAD) is one of many complication of obesity. Previously, they found that low serum adiponectin level associated with CAD. There for, adiponectin could be a predictive and clinical marker for CAD.

Objectives: To determine relation ship between the coronary artery disease (CAD) in obese patients and their adiponectin levels and measuring lipid profiles, FBS and adiponectin levels was also investigated in this work.

Materials and methods: Case control study of adipponectin levels Comparison between coronary artery patients and monitoring obese (control) for some blood serum parameters Lipid profiles, FBS and adiponectin levels for both obese coronary artery patients and control cases were measured by using Enzyme-Linked Immunoassay (ELISA) method. The study was carried – out during mid-March to mid-May of 2018 for CAD patients attending at Sudanese Heart Center, Khartoum State, Sudan.

Results: The findings of this study revealed that levels of Adiponectin were lower mean in both CAD obese patients and obese(*respectively*) than the normal value (0.9-2.45 µg/ml) adiponectin, but that was not statistically significant different between the CAD patients and control. On the other hand, CAD patients had a significantly higher mean levels of cholesterol , triglyceride and FBS than control cases, *respectively*), whereas the reverse was true for HDL. Furthermore, the findings indicated that the levels of LDL was not significantly different between the CAD patients and control. Regarding the demographic status of CAD patients, the level of adiponectin was not significantly

affected by gender, age of patients, BMI and duration of the disease. On the other hand, the correlation between the level of adiponectin in one hand and the demographic status and blood serum parameters in another hand indicated that there were positive, very weak ($r<0.200$) and insignificant ($P< 0.05$) correlation between adiponectin level and all gender, BMI, cholesterol, triglyceride, HDL and LDL, whereas the correlation between adiponectin level and age, duration and FBS were negative, very weak and insignificant.

Conclusion: CAD patients had a significantly higher mean levels of cholesterol , triglyceride and FBS than control cases but the level of adiponectin was statistically insignificantly defferent between CAD patients and control and Lipid .

Keywords: Obesity, Adiponectin, Coronary artery disease (CAD), Demographic status, Biochemical parameters, Correlation.

{**Citation:** Nisreen A. Al-Fuqaha'a, Fayza A. Rahmatalla, Abdelbaqi A. Abdelbaqi, Atif A. Elagib. Association of Adiponectin Levels with Coronary Artery Disease in Obese Patients. American Journal of Research Communication, 2019, 7(4): 1-13} www.usa-journals.com, ISSN: 2325-4076.

Introduction

Obesity is a major public health problem worldwide, with significant social and psychological dimensions which afflicted increasingly younger individuals and different socioeconomic groups In obesity the number and size of adipocytes increases with further increase of the total fat mass. Obesity is advancing along with its association with the risk of diseases such as dyslipidemia, insulin resistance, high blood pressure (HBP) and atherosclerosis or other cardiovascular diseases [1].

The prevalence of obesity (body mass index (BMI) >30 kg/m^2) has increased and more than 58% of adults worldwide will be overweight or obese by 2030. Obesity is an

independent risk factor for venous thromboembolism and ischemic heart disease, having a negative effect on public health. [2].

Adipose tissue is an active endocrine organ that secretes adiponectin [3], which is collagen-like protein that contain 247 amino acids in length [4].and was found to produce variety of adipo cytokines including liptin, adipsin, and tumor necrosis factor [5]. Adiponectin is the recently identified most abundant one which is a 30 kDa protein [6].

Adiponectin is an insulin-sensitizing hormone with anti-inflammatory and anti atherogenic effect [7]. In accordance, plasma adiponectin is decreased in metabolic disorders including type II diabetes mellitus (T2DM) and coronary artery disease also it predict insulin resistance (IR)[8].In addition, higher levels of adiponectin were associated with a lower incidence of DM2. [9]. Additionally, individuals with lower plasma levels of adiponectin have LDL cholesterol molecules of smaller size, lower lipoprotein lipase activity, lower HDL-cholesterol levels, and higher triglyceride levels [9].. Studies have suggested an effect of adiponectin on blood pressure homeostasis , and controlling energy metabolism [10].

Coronary artery disease (CAD) is a significant contributor to global health burden [11] It plays a predominant role accounting for one third of all cases in public health problem that increase range of mortality at the world and one of many complication of obesity. Previously, they found that low serum adiponectin level associated with CAD [12]. Therefore, adiponectin could be a predictive and clinical marker for CAD.

Adiponectin may affect regulation of insulin sensitivity with energy metabolism and serve to link obesity with insulin resistance. [13].The effects of lifestyle modifications and cardiovascular drugs on adiponectin levels suggest plausible mechanisms that may be important for treating atherosclerosis and coronary heart disease [14].

Materials and Methods

This is a case control study. The study was conducted on patients attending Center of Sudanese Heart Center in Khartoum State, The study was approved ethically by research board of faculty of Medical Laboratory Sciences - Omdurman Islamic University and a written informed consent was obtained from all participants. A

structured questionnaire was designed to obtain demographic data (Gender, Age, BMI and Duration for CAD patients). The laboratory investigation data (Cholesterol, Triglyceride, HDL, LDL, and FBS) were also reported in the same form .

The study sample was performed on obese and overweight patients suspected with Coronary Artery Disease (CAD). Of the 88 voluntaries, 62 were male (aged 22to 61 years) and 26 were female (aged 22 to 49 years). The study cases were divided into two groups: Control group (44 cases), Test group (44 cases). The diagnosis of control group was based on obesity without coronary artery disease, whereas the diagnosis of test group was based on obesity with coronary artery diseases. All voluntaries were subjected to assessment of history, thorough clinical examination and routine laboratory test such as serum (Cholesterol, Triglyceride HDL, LDL, FBS and level of adiponectin level) using ELISA method.

Patients with obesity and coronary artery disease were included in this study (both sex) with Body Mass Index (BMI) above 25 kg/m^2who underwent elective coronary angiography for the investigation of the existence of chronic stable CAD. Patient with 50% or greater diameter stenosis in at least one major coronary artery was considered as CAD positive patients, and was classified into two groups. The first group was obese patients suffering from CAD and the second group was obese patients free from CAD. Patients without coronary artery and obesity were excluded from the study. And patient with un stable angina or acute myocardial infarction, un stable condition included infection , heart failure, malignancies, menopause female, renal disease (creatinine level >1.5mg/dl) were excluded.

Venous blood samples (10 ml) were collected from patients with Coronary Artery Disease and obese healthy controls. Of these, 5 ml blood samples were collected in plane tube for measuring adiponectin level the samples were centrifuged for 10 min at 13000 rpm. Serum and plasma were stored at - 20 ºC until analysis.

Semi automation method was used by the apparatus (Bio Base EL-10, Fabricated by DRG Instruments Gmbh. Germany). A buffered solution of the antigen to be tested for is added to each well of a micro titer plate, where it is given time to adhere to the plastic through charge interactions. A solution of non-reacting protein, such as bovine serum albumin (BSA) case in, was added to the wells in order to cover any plastic surface in the well which remains uncoated by the antigen. The enzyme-conjugated primary

antibody is added, which binds specifically to the test antigen coating the well. A substrate for this enzyme was then added. Often, this substrate changes color upon reaction with the enzyme. The higher the concentration of the primary antibody present in the serum, the stronger the color change. A spectrometer was used to give quantitative values for color strength.

A pipette was used to take 50 µl of diluted standards, samples, quality controls and dilution buffer, then 50 µl of conjugate solution was added into each well, and Incubated the plate at room temperature (ca. 25°C) for 2 hours, shacked at ca. 300 rpm on an orbital micro plate shaker. The wells was washed 3 times with wash solution (0.35 mL per well). After final wash, the plate was inverted and tapped strongly. 200 µl of Substrate Solution added into each well. The plate was covered with aluminum foil. Then the plate incubated for 15 minutes at room temperature. 50 µl of stop solution was added to stop the color development. The absorbance of each well was determined using a micro plate reader set to 450 nm [15].

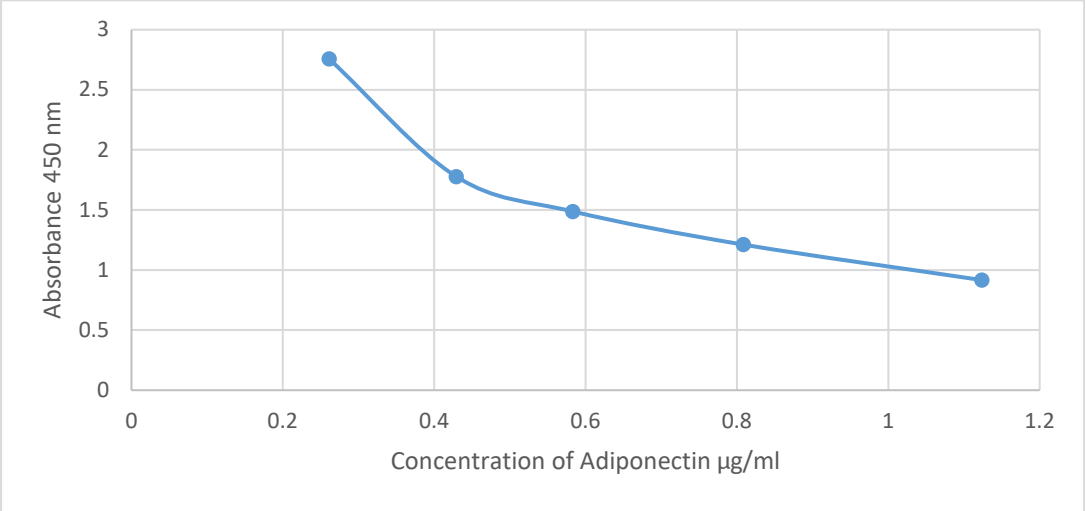

Figure (1) Human Adiponectin ELISA Calibration Curve.

Statistical analysis

Descriptive statistics, Student t test and correlation between adiponectin level and demographic status (Spearman's correlation) as well as blood serum biochemical parameters (Pearson's correlation) were done by using SPSS (Statistical Package for Social sciences), version 16 for windows.

Results

Descriptive statistics. Means comparison and correlation statistics for collected data were presented in tables 1, 2, 3 and 4.

1. Descriptive statistics: The frequency and percentage for demographic measures were presented in table1. As shown from the table that 37 (67.7%) of selected CAD patients were male and 7 (12.3%) were female, 2 (4.5%) cases were 22 - 35 years aged and 42 (95.5%) were > 35 years, 20 (45.5%) cases had body mass index (BMI) ranged between 22- 35 kg/m^2 and 24 (54.5%) cases had BMI > 35 kg/m^2, and 5 (11.4%) cases showed one year disease history corresponding to 39 (88.6%) cases showed disease history of more than one year. On the other hand, for obese free CAD (control), 25 (56.8%) cases were male and 19 (43.2%) were female, 22 (50.0%) aged 22- 35 years and 22 (50.0%) aged > 35 years, 25 (56.8%) had body mass index (BMI) of 26 - 35 kg/m^2 and 19 (43.2%) had BMI > 35kg/m^2.

Table (1): The frequency and percentage of gender, age and BMI for control and CAD obese patients

Variable	Cases	Control		CAD obese patients	
		Frequency	Percent	Frequency	Percent
Gender	Male	25	56.8	37	67.7
	Female	19	43.2	7	12.3
	Total	44	100.0	44	100.0
Age (years)	22 - 35	22	50.0	2	4.5
	>35	22	50.0	42	95.6
	Total	44	100.o	44	100.0
BMI (kg/m^2)	26 - 35	25	56.8	20	45.5
	> 35	19	43.2	24	54.5
	Total	44	100.0	44	100.0
Duration (years)	≤ one year	-	-	5	11.4
	> one year	-	-	39	88.6
	Total	-	-	44	100.0

2. Comparison between CAD patients and control in respect to demographic status:

Table2 shows that CAD patients reported a significantly higher mean level of cholesterol (175.3±52.3 mg/dl), triglyceride (131.9±34.8 mg/dl) and FBS (130.0±50.9 mg/dl) than control (137.9±39.2, 114.1±28.8 and 97.2±17.0, mg/dl *respectively*), whereas the reverse was true for HDL (32.5±9.3 mg/dl for CAD patients corresponding to 40.1±10.0 mg/dl for control). On the other hand, the difference between CAD patients and control for LDL and adiponectin levels was statistically insignificant.

Table (2): Comparison between control and CAD obese patients for the level of blood serum parameters

Blood serum parameters mean ± SD	Case comparison		
	Control (n=44)	CAD patients (n=44)	P – value
Cholesterol (mg/dl)	137.9±39.2	175.3±52.3	0.000**
Triglyceride (mg/dl)	114.1±28.8	131.9±34.8	0.010**
HDL (mg/dl)	40.1±10.0	32.5±9.3	0.000**
LDL (mg/dl)	105.5±28.2	109.8±33.1	0.521 Ns
FBS (mg/dl)	97.2±17.0	130.0±50.9	0.000**
Adiponectin (µg/ml)	0.73±0.33	0.72±0.40	0.893 Ns

ns: No significant difference , **: Significant difference at 1%

3. Level of adiponectin in CAD patients as affected by their demographic status:

Table 3 demonstrated that adiponectin level of CAD patients was not significantly affected by gender, age of, BMI and the duration of the disease, although the level of this parameter was slightly elevated in female, old aged (> 35 year) and higher BMI (> 35 kg/m^2) patients, while it was lower in patients of > 35 years history of duration.

Table (3): Level of adiponectin for CAD patients as affected by the demographic variables

Demographic Variables	Cases	Adiponectin level (µg/ml)	P- value
Gender	Male (n=37)	0.71±0.41	0.620 Ns
	Female (n=7)	0.79±0.38	
Age (years)	22 - 35	0.70±0.28	0.041 Ns
	> 35	0.72±0.41	
BMI (kg/m^2)	26 - 35	0.68±0.48	0.560 Ns
	> 35	0.75±0.33	
Duration (years)	One	0.89±0.28	0.312 Ns
	> One	0.70±0.41	

3.3. Correlation between adiponectin level and demographic and biochemical parameters:

Table 4 shows that the correlation between the level of adiponectin in one hand and the demographic status and blood serum parameters in anther hand indicated that there were positive, very weak ($r<0.200$) and insignificant ($P < 0.05$) correlation between adiponectin level and all gender, cholesterol, triglyceride, HDL and LDL, whereas the correlation between adiponectin level and age, duration and FBS were negative, very weak and insignificant.

Table (4): Correlation between level of adiponectin and both demographic status and biochemical parameters of CAD patients

Variable	Demographic status				
	Gender	**Age**	**BMI**	**Duration**	**-**
Adiponectin (µg/ml)	0.077 ns	-0.149 ns	0.023 ns	-0.156 ns	-
	Blood serum parameters				
	Cholesterol	**Triglyceride**	**HDL**	**LDL**	**FBS**
	0.024 ns	0.002 ns	0.139 ns	0.033 ns	-0.140 ns

Discussion

Adiponectin is an insulin-sensitizing hormone with anti-inflammatory and anti atherogenic effect [7]. In accordance, plasma adiponectin is decreased in metabolic disorders including type II diabetes mellitus (T2DM) and coronary artery disease also it predict insulin resistance (IR)[8]. The current study aims to determine the association between the coronary artery disease (CAD) in obese patients and their adiponectin levels. The level of adiponectin in the present study were lower mean in both CAD obese free CAD (control),although the deference between patients and controls was statistically insignificant. This result support the suggestion that the lower adiponectin levels are strongly associated with overweight, obesity metabolic syndrome, type 2 diabetes mellitus and cardiovascular risk factors in adulthood. The reason for the reduction in adiponectin in obese subjects remains unclear, but it may be due to either transcriptional suppression or decreased secretion caused by inflammatory cytokines such as IL-6[30]. These findings were in agreement with the findings reported by Nasser *et al.,* 2012[17]. While it was in contrast to the findings of Shui *et al.*, 2016 [18] and Abdalla *et al*., 2016 [19]. On the other hand, the significant elevation in levels of cholesterol, triglyceride and FBS among CAD patients than in control may be due to imbalance in lipid profile can increases levels of cholesterol, triglyceride and FBS among CAD patient. Similar results were also reported by Marina *et al*., 2014 [20]. In present work, adiponectin level in CAD patients was not

significantly affected their gender, age, BMI and duration of disease. All participants in the study are free of diabetes mellitus, this may be behind the reason of similarity in adiponectin level in gender and/ or age and/or BMI. The positive correlation between adiponectin level of CAD patients and their gender and BMI means that it was increased among female direction, and with increasing of BMI . On the other hand, the negative correlation of adiponectin level and their both age and disease duration means that it is level was reduced with age and disease duration. Furthermore, the weak correlation between adiponectin level and gender, age, BMI and duration indicated the low effect of these variables on changes of adiponectin level (strength of correlation). The determination coefficients (r^2) (which estimates the contribution of each demographic variable on changes of adiponectin level as percentage) for gender, age, BMI and disease duration were 0.6%, 2.2%, o.1% and 2.4%, *respectively*. This means that these variables contributed in changes of adiponectin level by their corresponding percentage values. The observed insignificant correlation between adiponectin level of CAD patients and demographic variables indicates that the relationship between the variables and adiponectin level is likely to be by chance. Similarly, the positive correlation between adiponectin level and the lipid profile (cholesterol, triglyceride, HDL and LDL) of CAD patients could be interpreted as similar as mentioned above. The determination coefficient of (cholesterol, triglyceride, HDL and LDL were 0.1, 0.0, 1.9%, 0.1%, *respectively*. Several studies have also reported a positive correlation between plasma adiponectin and HDL levels. These results suggest a possible direct link between adiponectin and HDL[21]

Conclusion

Based on the findings of the present study, it could be concluded that: The levels of cholesterol, triglyceride and BFS were significantly higher in CAD patients than in control, whereas the reverse was true for HDL. The correlation between the level of adiponectin and all gender, BMI, cholesterol, triglyceride, HDL and LDL was positive, very weak and insignificant, while it was negative, very weak and insignificant with age, duration and FBS variables.

The level of adiponectin (regarding the selected sample cases) was statistically insignificant defer between obese with CAD and obese control, while the level of adiponectin in CAD patients were insignificantly affected their demographic status.

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