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Research Article

Association of Adiponectin Levels with Coronary Artery Disease in Obese Patients

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Background:

Coronary artery disease (CAD) is one of many complicationof obesity. Previously, they found that low serum adiponectin level associated with CAD. There for , adiponectin could be apridictive and clinical marker for CAD. The study aimed to find association of adiponectin levels in opese (control) and in coronary artery disease patients.

The objectives of the present case control study were to determine whether any association between the coronary artery disease (CAD) in obese patients and their adiponectin levels. Comparison between coronary artery patients and monitoring obese (control) for some blood serum parameters (Cholesterol, Triglyceride, HDL, LDL, FBS and adeponectin levels) was also investigated in this work. Levels of adiponectin 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. The sample size of selected coronary artery disease (CAD) cases was 44 for characterized as follows: for CAD obese patients 37 (67.7%) cases were male and 7 (12.3%) were female, 2 (4.5%) cases were 22 – 35 year aged and 42 (45.5%) were > 35 year, 20 (45.5%) cases had body mass index (BMI) ranged between 22 – 35 and 24 (54.5%) cases had BMI > 35 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, 25 (56.8%) cases were male and 19 (43.2) were female, 22 (50.0%) aged 22 – 35 year and 22 (50.0%) aged > 35 year, 25 (56.8%) had body mass index (BMI) of 26 – 35 and 19 (43.2%) had BMI > 35.

The findings of this study revealed that CAD patients had a significantly higher mean levels of cholesterol (175.3±52.3), triglyceride (131.9±34.8) and FBS (130.0±50.9)

than control cases (137.9±39.2, 114.1±28.8 and 97.2±17.0, respectively), whereas the revese was true for HDL (32.5±9.3 for CAD patients corresponding to 40.1±10.0 for control). Furthermore, the findings indicated that the levels of both LDL and adoponectin were not significantly different between the CAD patients and control. Regarding the demographic status of CAD patients, the level of adoponectin was not significantly affected by gender (0.71±0.41 for male and 0.79±0.38 for female), age of patients (0.79±0.38 for 22 – 35 year and 0.79±0.38 for > 35 year), BMI (0.68±0.48 for 26 – 35 and 0.75±0.33 for > 35) and the duration of the disease (0.89±0.28 for ≤ 1 year and ≤ 1 year for > one year).On the other hand, the correlation between the level of adoponectin in one hand and the demographic status and blood serum parameters in anther hand indicated that there were +ve, very weak($r<0.200$) and insignificant ($P < 0.05$) correlation between adoponectin level and all gender (male = 1, female =2), BMI (26 – 35 = 1, > 35 = 2), cholesterol, triglyceride, HDL and LDL, whereas the correlation between adoponectin level and age (22 – 335 = 1, > 35 = 2), duration (≤ 1 year = 1, > 2 years = 2) and FBS were –ve, very weak and insignificant.

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

Introduction:

Obesity is a major public health problem world wide, with significant social and psychological dimensions which afflicted increasingly younger individuals and different socioeconomic groups. It is one of the most important determinants of many chronic non-communicable diseases (NCD) that significantly affect the mortality rate of many countries, including developing countries. Obesity is a condition in which the number and size of adipocytes increases with further increase of the total fat mass. With industrialization, obesity is advancing along with its association with the risk of diseases such as dyslipidemia, insulin resistance, high blood pressure (HBP), and eventually atherosclerosis or other cardiovascular diseases [1].

The prevalence of obesity (body mass index (BMI) >30 kg/m^2) has increased recently and forecasts suggest that if current trends continue, 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. Interactions between lifestyle factors (self-determined behaviors acquired socially or culturally, individually or as part of a group, and thus modifiable) and genetic factors (that modulate the body's response to changes in lifestyle factors)

are part of this perspective. Therefore, the combination of determinants of obesity and its complications include both lifestyle and genetic factors with different and important contributions [2].

Adipos tissue is an active endocrine organ that secretes adiponectin[3], which is acollagen-like protein that contain 247 amino acids in length[4].and was found to produce variety of adipocytokines including liptin,adipsin,and tumer necrosis factor[5-10]. Adiponectin is the recently identified most aboundant of them which is a 30 kDaprotein [11-12].

Adiponectin is viewed as an insulin-sensitizing hormone with anti-inflammatory and anti atherogenic effect [13-15]. 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). [16].In addition, higher levels of adiponectin were associated with a lower incidence of DM2. Individuals in the lowest tertile of adiponectin levels developed approximately nine times more DM2 than those individuals belonging to the highest tertile(17). 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[17]. Regarding blood pressure, lower levels of circulating adiponectin were observed in hypertensive compared to non-hypertensive patients, even after adjusting for obesity, insulin resistance, and DM2. Studies have suggested an effect of adiponectin on blood pressure homeostasis[18],and controlling energy metabolism[19].

Heart diseases are an important cause of morbidity and mortality in Sudan. The tetrad of hypertension, RHD, IHD and cardiomyopathy constitute the bulk of CVD. Hypertension is prevalent, with poor control rates. The SHHS reported a prevalence of 2.5% for heart disease. According to the latest WHO data published in may 2014 Coronary Heart Disease Deaths in Sudan reached 9,491 or 3.64% of total deaths. The age adjusted Death Rate is 56.31 per 100,000 of population ranks Sudan 146 in the world[20].

Coronary artery disease (CAD) is a significant contributor to global health burden [21] it plays apredominant role accounting for one third of all cases in public health problem that increase range of mortality at the wold [22] and one of many complication of

obesity.previously, They found that low serum adiponectin level associated with CAD. 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. Obesity-related disorders including the metabolic syndrome, diabetes, atherosclerosis, hypertension, and coronary artery disease are associated with decreased plasma levels of adiponectin, insulin resistance, and endothelial dysfunction. Lifestyle modifications and some drug therapies to treat atherosclerosis, hypertension, and coronary heart disease have important effects to simultaneously increase adiponectin levels, decrease insulin resistance, and improve endothelial dysfunction.[23]. 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[24]. Furthermore, the lowest concentration of adiponectin is associated more strongly with quantification of visceral abdominal fat than with subcutaneous abdominal fat, suggesting a possible relationship with MS[25]. The inverse relation between adiponectin levels and criteria for MS is well demonstrated that overweight individuals have lower levels of adiponectin compared to lean individuals, and that levels of this hormone decrease as BMI increases in men and women[26].

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, (Appendix 2) 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, FBS) were also reported in the same form (Appendix 1).

The study sample was performed on obese and overweight patients suspected with Coronary Artery Disease (CAD). Of the 88 patients, 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 adeponectin level) using ELISA method.

Patients with obesity and/or coronary artery disease were included in this study(both sex) with Body Mass Index (BMI) above 25 Kg/m who 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 (creatinin level>1.5mg/dl) were excluded.

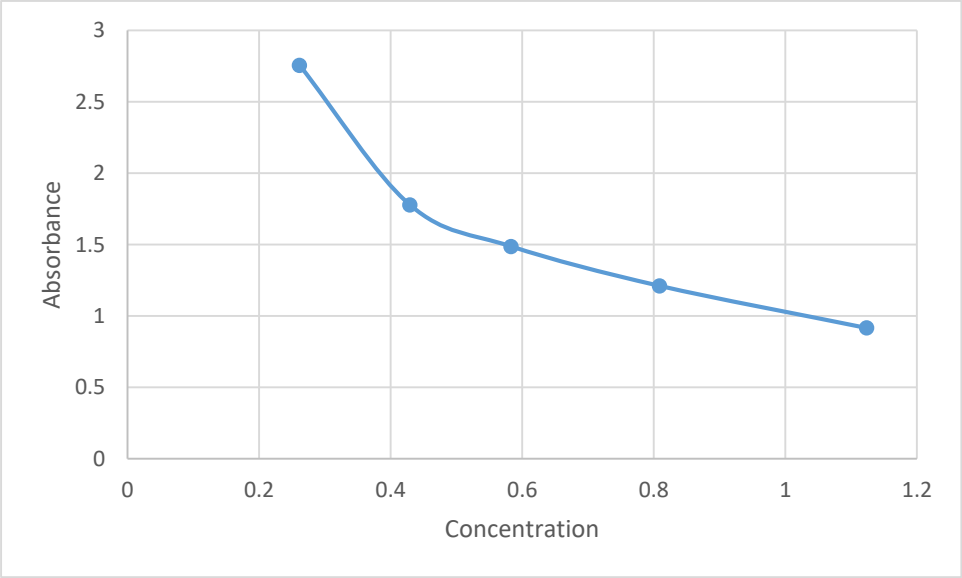
Venous blood samples (5 ml) were collected from patients with Coronary Artery Disease and obese healthy controls. Of these, 5 ml blood samples were collected in plane tube for measuring adiponectin level The samples were centrifuged for 10 min at 13000 rpm. Serum and plasma were stored at -20 ºC until 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 microtiter 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) casein, 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 colour upon reaction with the enzyme. The higher the concentration of the primary antibody present in the serum, the stronger the colour change. A spectrometer was used to give quantitative values for colour 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^{o}C) for 2 hours, shacked at ca. 300 rpm

on an orbital microplate 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 colour development. The absorbance of each well was determined using a microplate reader set to 450 nm.(Marinoni E *et al*.,2008).

Figure (1) Human Adiponectin ELISA Calibration Curve



Statistical analysis:

Descriptive statistics, Student t Test and correlation between adiponectin level and demographic status (Sperman'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 patiens were male and 7 (12.3%) were female, 2 (4.5%) cases were 22 – 35 year aged and 42 (45.5%) were > 35 year, 20 (45.5%) cases had body mass index (BMI) ranged between 22 – 35 and 24 (54.5%) cases had BMI > 35, 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 year and 22 (50.0%) aged > 35 year, 25 (56.8%) had body mass index (BMI) of 26 – 35 and 19 (43.2%) had BMI > 35.

Table (1): Descriptive statistics showed 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 (year)	22 - 35	22	50.0	2	4.5
	>35	22	50.0	42	95.6
	Total	44	100.o	44	100.0
BMI	26 - 35	25	56.8	20	45.5
	> 35	19	43.2	24	54.5
	Total	44	100.0	44	100.0
Duration	≤ 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), triglyceride (131.9±34.8) and FBS (130.0±50.9) than control (137.9±39.2, 114.1±28.8 and 97.2±17.0, respectively), whereas the reverse was true for HDL (32.5±9.3 for CAD patients corresponding to 40.1±10.0 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 tested by using ELISA method.

Blood serum parameters	Case comparison		Statistics		
	Control	CAD patients	df (N-2)	P – value	Sig. level
Cholesterol	137.9±39.2	175.3±52.3	86	0.000	**
Triglyceride	114.1±28.8	131.9±34.8	86	0.010	**
HDL	40.1±10.0	32.5±9.3	86	0.000	**
LDL	105.5±28.2	109.8±33.1	86	0.521	Ns
FBS	97.2±17.0	130.0±50.9	86	0.000	**
Adoponectin	0.73±0.33	0.72±0.40	86	0.893	Ns

ns: No significant difference

**: Significant difference at 1%

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

Table3 demonstrated that adiponectin level of CAD patients was not significantly affected by gender (male and female), age of patients (22 – 35 and > 35 year aged), BMI (26 – 35 and > 35) and the duration of the disease (≤ one year and > one year), although the level of this parameter was slightly elevated in female, old aged (> 35 year) and higher BMI (> 35) patients, while it was lower in patients of > 35 years history of duration

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

Demographic Variables	Cases	Adoponectin level	Statistics		
			df	P – value	Sig. level
Gender	Male	0.71±0.41	42	0.620	Ns
	Female	0.79±0.38			
Age (year)	22 - 35	0.71±0.41		0.620	Ns
	> 35	0.79±0.38			
BMI	26 - 35	0.68±0.48	42	0.560	Ns
	> 35	0.75±0.33			
Duration	One yeay	0.89±0.28	42	0.312	Ns
	> one year	0.70±0.41			

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

Table4 shows that the correlation between the level of adoponectin in one hand and the demographic status and blood serum parameters in anther hand indicated that there were +ve, very weak ($r<0.200$) and insignificant ($P < 0.05$) correlation between adoponectin level and all gender (male = 1, female =2), BMI (26 – 35 = 1, > 35 = 2), cholesterol, triglyceride, HDL and LDL, whereas the correlation between adoponectin level and age (22 – 335 = 1, > 35 = 2), duration (≤ 1 year = 1, > 2 years = 2) and FBS were –ve, very weak and insignificant. The +ve correlation means that as one variable increases, another variable will also icrease, whereas the –ve correlation means as one variable increases, another variable will decrease. The weak correlation ($r \leq 0.2$) means that the effect of variable on the change of another variable is small. The insignificant correlation means that the relationship between the two variable is lickely

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

Variable	Demographic status				
	Gender	Age	BMI	Duration	-

S	0.077 ns	-0.149 ns	0.023 ns	-0.156 ns	-
Adoponectin	**Blood serum parameters**				
	Cholesterol	**Triglyceride**	**HDL**	**LDL**	**FBS**
	0.024 ns	0.002 ns	0.139 ns	0.033 ns	-0.140 ns

Discussion:

The level of adiponectin in the present study was statistically insignificant between CAD patients and obese free CAD (control). This result may be attributed to high levels of adipocytes among obese CAD patients wich increase the total fat mass . This result was in agreement of that reported by (Nasser., *et al* 2012). while it was in contrast to the findings of (Shui *et al.*, 2016) and (Abdalla *et al*., 2016). 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).

In present work, adiponectin level in CAD patients was not significantly affected their gender, age, BMI and duration of disease. Same result obtained by (Nasser., *et al* 2012). 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 (+ve) correlation between adiponectin level of CAD patients and their gender and BMI means that it was increased among female direction (Female = 2), and with increasing of BMI the same result was in agreement with (Von, et al, 2014)[27] . On the other hand, the negative (–ve) correlation of adiponectin level and their both age and disease duration means that it is level was reduced with age and disease duration this result was in agreement with (Sefa *et al*., 2017)[28] while it was contrast to the findings of (Chung-Hu Hsu, et al, 2012)[29] the reason for this contrast may be the sample of the previous study contained diabete mellitus patients with CA patients. 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 this result was in agreement with (Nur Firdaus Isa, et al, 2017)[30] . 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 +ve and –ve (direction), weak (strength) and insignificant correlation between adiponectin level and the biochemical parameters (cholesterol, triglyceride, HDL, LDL and FBS) of CAD patients could be interpreted as similar as mentioned above. The determination coefficient of (cholesterol, triglyceride, HDL, LDL and FBS were 0.1, 0.0, 1.9%, 0.1% and 2.0%, respectively. This result was in agreement with findings of (Nasser., *et al* 2012) and (Chung-Hu Hsu, et al, 2012), while it was in contrast to the findings obtained by (Sefa *et al*., 2017).

Conclusion:

Based on the findings of the present study, it could be concluded that:

1.The level of adiponectin (regarding the selected sample cases) was statistically insignificant between CAD patients and control.
2. The levels of cholesterol, triglyceride and BFS were significantly higher in CAD patients than in control, whereas the reverse was true for HDL.
3. The level of adiponectin in CAD patients were not significantly affected their demographic status.
4. The correlation between the level of adiponectin and all gender, BMI, cholesterol, triglyceride, HDL and LDL was +ve, very weak nad insignificant, while it was –ve, very weak and insignificant with age, duration and FBS variables.

References

(1) Pelajo CF, Lopez-Benitez JM, Miller LC.(2015). Obesity and disease activity in juvenile idiopathic arthritis.PediatrRheumatol Online J; 10(1):3.

(2) Tsai WC, Lin CC, Chen JY, HuangY Y, Lee CH, Li WT, et al. Association of adiponectin with procollagen type I carboxy terminal propeptide in non-diabetic essential hypertension. Blood Press. 2008;17(4):233-8.

(3) Jai Prakash, Balraj Mittal, ShallyAwasthi, NeenaSrivastava. Association of adiponectin gene polymorphismlevels and risk for insulin with adiponectinrisistance syndrome.(2015); 6:31.

(4)JianminWu, GuoyanXu, WenqinCai, Yun Huang, NingyaXie, YihuaShen, LiangdiXie. The association of tow olymorhisminadiponectin-encodinggene with hyertention risk and the changes of circulating adionectin and blood pressure: Ameta – analysis. 2017:8(9).

(5) Maeda K,Okobo K, Shimomura I, Funahashi T, Mtsuzawa Y, Matsubara K: cDNAcloning and expression of novel adipose specific collagen-like factor, apM1 (Adipose most abundant gene transcript 1). BiochemBiophys Res commun 1996,221(2):286-289.

(6) Friedman JM, Halaas JL: Leptin and regulationof body weight in mammals. Nature 1998, 395:763-770.

(7) Ahima RS, Flier JS: adipose tissue as an endocrine organ. Trends EndocrinalMetab 2000,11:327-332.

(8) Hotamisligil GS: The role of TNF-a and TNF receptors in obecity and insulin resistance. J Int Med 1999, 245:621-625.

(9) Mohamed Ali V, Pinkney JH, Coppak SW: Adipos tissue as an indocrine and paracrine organ. Int J Obes Relate MetabDisord 1998,22:1145_1158.

(10) Scherer PE, Williams S ,FoglianoM,Baldini G, LodishHF:Anovel serum protein similar to C1q, produced exclusively in adipocyte. J BiolChem 1995, 270(45):26746-26749.

(11) Hu E, Liang P, Spiegelman BM: AdipoQ is anoveladpose-spesific gene dysregulatedinobesity.JBiol Chem1996, 271(18):10697-10703.

(12) Fasshauer M, Klein J, Neumann S, Eslzlinger M, Paschke R, Hormonal regulation of adiponectin gene expression in 3 T3-L1adipocyte. BiochemBiophys Res common 2002,290(3):1084-1089.

(13) Yokota T, Oritani K, Takahashi I, Ishikawa J, Matsuyama A, Ouchii N, Kihara S, Funahashi T, Tenner AJ, Tomiyama Y, Matsuzawa Y:Adiponectin anew memberof the family of soluble defens collagens, negatively regulates the growth of myelomonocytic progenitors and the functions ofmacrophages. Blood2000 96(5):1723-1732.

(14) Ouchi N, Kihara S, Arita Y, Okamoto Y, Maeda K, Kuriyama H, Hotta K, Nishida M, Takahashi M, Muraguchi M, Ohmoto Y, Nkamura T, Yamashita S, Funahashi T, Matsuzawa Y: Adiponectine,anadipocyte-derived plasma protein, inhibit indothelial NK-kappa B signaling hrough a cAMP-dependent pathway. Circulation 2000, 102(11):1296-1301.

(15) Ouchi N, Kihara S, Arita Y, Okamoto Y, Matsuzawa Y, Matsuzawa , Ishigami M, Kuriyama H, Hotta K, Nishida M, Muraguchi M, Ohmoto Y, Nkamura T, Yamashita S, Funahashi T, Matsuzawa Y:Adipocyte-derived plasma protein, adiponectin, suppresses lipid accumulation and class A scavenger receptor expression in human monocyte-derived macrophages. Circulation 2001, 103(8):1057-1063.

(16) Jai Prakash, Balraj Mittal, ShallyAwasthi, NeenaSrivastava. Association of adiponectin gene polymorphismlevels and risk for insulin with adiponectinrisistance syndrome. (2015); 6:31

(17) Daimon M, Oizumi T, Saitoh T, Kameda W, Hirata A, Yamaguchi H, et al. Decreased serum levels of adiponectin are a risk factor for the progression to type 2 diabetes in the Japanese Population: the Funagata study. Diabetes Care. 2003;26(7):2015-20.

(18) Iwashima Y, Katsya T, Ishikawa K, Oushi N, Oushi M, Sugimoto K, et al. Hypoadionectimia is an independent risk factor for hypertention 2004;34(6);1318-23.

(19) Muna H. Al Sheikh. The determinant of litin levels in diabetic and non diabetic Saudi males. 2017(7):3506871.

(20) World health Organization. Cardiovascular disease Fact sheet No.317.Geneva. Setember 2014. Accessed on 10 April 2018 at:http//www.who.int/mediacener/factsheet/fs317/en /index.html, 30 october 2015.

(21) HouHaifeng, GeSiqi, Zhao Linlin, WangChinglin, Wang Wei, ZhhaoXuezhen, and Sun Zhing. An updated systematic Review and meta analysis of association between adpionectin gene polymorphism and coronary artery disease 2017:21,6,0007.

(22) R.A. Souza, C. M. R. Alves, C. S. V. de Olivera, A. F. Reis and A. C. Carvalho.Circulating levels of adiponectin and extent of coronary artery disease in patients undergoing elective coronary angiography.2018:51(2).

(23) Tsai WC, Lin CC, Chen JY, HuangY Y, Lee CH, Li WT, et al. Association of adiponectin with procollagen type I carboxyterminalpropeptide in non-diabetic essential hypertension. Blood Press. 2008;17(4):233-8.

(24) Kern PA, Di Gregorio GB, Lu T, Rassouli N, Ranganathan G. Adiponectin

expression from human adipose tissue: relation to obesity, insulin resistance, and tumor necrosis factor-alpha expression. Diabetes. 2003;52(7):1779-85.

(25) Cnop M, Havel PJ, Utzschneider K M, Carr DB, SinhaMKBoyko EJ, et al. Relation ship of adiponectineto body fat distribytion ,insulin sensitivity and plasma lipo proteins: evidence for independent roles of age and sex. Diabetologia. 2003:46(4):459-69.

(26) Arita Y., Kihara S., Oushi N., T. akahashi M, Maeda K, Miagawa J, et al. paradoxical decrease of an adiose tissue-sesificprotein,adionectin, in obesity BiochemBiophys Res Commun. 1999;257(1):79-83.

(27)Von Frankenberg AD, Silva FM, de Almeida JC, Piccoli V, do Nascimento FV, Sost MM, et al. Effect of dietary lipids on circulating adiponectin: a systematic review with meta-analysis of randomised controlled trials. Br J Nutr. 2014;112(8):1235-50.

(28) Sefa Şenol.(2017). Adiponectin and leptin polymorphisms in patients with coronary artery disease, Turk Gogus Kalp Dama; 23(4):637-642

(29) Chung-Hu Hsu, Adiponectin Level Predicts HDL-Cholesterol Level in Type 2 Diabetes, The Open Atherosclerosis & Thrombosis Journal, 2012, 5, 1-5

(30) Nur Firdaus Isa, ASSOCIATION OF SERUM ADIPONECTIN LEVELS WITH METABOLIC SYNDROME RISK FACTORS IN MALAY ADULTS, World Nutrition Journal vol.1 No. 1 July 2017 | http://dx.doi.org/10.25220/WNJ.V01i1.0005