# Adiponectin and Lipid Profile Levels in Type-2 Diabetic Obese Patients in Kerbala Province

**Tariq H. Al-Kayatt[1] , Ph.D. ; Azher A. Ibraheem[1] , M.Sc. ; and Fadhil J. Al-Tu'ma[2] , Ph.D.**

[1]Department of Biochemistry – College of Medicine – University of Babylon / Hilla – Iraq.

[2]Department of Biochemistry – College of Medicine – University of Kerbala / Kerbala – Iraq.

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## Abstract

**Background:** The association between obesity and type-2 diabetes mellitus may be partly mediated by altered secretion of adipokines by adipose tissue. Adiponectin is an adipokines with anti-inflammatory and insulin sensitizing properties; it is secretion is down regulated in obesity. The correlation of plasma adiponectin with the risk of type-2 diabetes mellitus and hyperlipidemia is unclear.

**Objective:** To study the association between plasma adiponectin level with lipid profile in type-2 diabetic obese patients in Kerbala province: Iraq.

**Material and method:** A total number of 110 sample subjects with different age, and different gender were classified according to diabetes mellitus and obesity. Fasting serum adiponectin was measured by ELISA method. Measurements of fasting lipid profile also have been performed.

**Results and discussion:** It was obtained that adiponectin level was lowered significantly in diabetic group, obese group, and diabetic obese group as compared with control group. Serum adiponectin was correlate negatively with serum total cholesterol, serum TG, and with body fat percent (BF %), while it was correlated positively with HDL-C. Serum total cholesterol levels was correlated positively with each of serum TG, LDL-C levels and with BF%, while serum TG levels was negatively correlated with serum HDL-C and positively correlated with each of BMI and BF %. Serum LDL-C was positively correlated with BF %, while BF % correlates positively with age.

**Conclusion:** According to the presented data, adiponectin as hormone play an important role in the prevention of hyperlipidemia, and consequently atherosclerosis and its complications.

# مستويات الأديبونكتين وصورة الدهون في مرضى السكري – النوع الثاني البدناء في محافظة كربلاء

طارق حفظي الخياط , أزهر عبد المطلب إبراهيم و فاضل جواد آل طعمة


## الخلاصة:

من المعروف أن السمنة وداء البول السكري من النوع الثاني متلازمان في اغلب الاحيان, حيث ان السمنة وزيادة الخلايا الدهنية هي السبب الاساسي لمقاومة الانسجة للانسولين. اضافة الى ان الخلايا الدهنية تعمل كغدة صماء مسؤولة عن افراز العديد من الهرمونات التي لها دور كبير في تحول الشخص المصاب بالسمنة الى مريض بداء البول السكري, ومن بين هذه الهرمونات الهرمون البروتيني الاديبونيكتين المكتشف حديثا, حيث يتميز هذا الهرمون عن بقية الهرمونات التي تفرزها الخلايا الدهنية بان نسبتها تقل كلما ازدادت نسبة السمنة, وكذلك تشير بعض الدراسات السابقة ان مستوى الاديبونكتين يقل في المرضى المصابين بداء السكري النوع الثاني, اضافة الى خاصيته باعتباره مضاد للالتهابات وعلاقتها باضطرابات نسبة الدهون بالدم. بالرغم من ذلك فان المعلومات المتوفرة حول العلاقة بين السمنة ومستوى هرمون الاديبونكتين وداء السكري النوع الثاني في المرضى لاتزال قليلة في العراق.

**الهدف من البحث:** دراسة العلاقة بين هرمون الاديبونكتين وصورة الدهون في مرضى البول السكري – النوع الثاني البدناء.

**المواد و طرائق العمل:** تم اختيار 110 أشخاص لهذه الدراسة من المرضى المصابين بداء السكري النوع الثاني في العيادة الاستشارية لداء السكر في مستشفى الحسين التعليمي في مدينة كربلاء خلال الفترة الواقعة بين شهر تشرين الثاني من عام 2010 إلى شهر نيسان من عام 2011 وتم تقسيمهم الى ثلاث فئات وذلك حسب نوع الاصابة بمرض البول السكري من النوع الثاني مع/ او بدون السمنة ومن بينهم 43 شخصاغيرمصاب بالمرض كمجموعة ضابطة.وقد تم قياس تركيز الاديبونكتين وصورة الدهون في مصل الدم.

**النتائج:-** في الفئة الاولى اظهرت النتائج انخفاض معنوي لكل من الاديبونكتين والـ LDL-C والكوليستيرول وغير معنوي للدهون الثلاثية والـ HDL-C في مجموعة المرضى مقارنة مع المجموعة الضابطة. بينما اظهرت النتائج انخفاض معنوي لكل من الاديبونكتين والدهون الثلاثية وغير معنوي لكل من الكوليستيرول والـ LDL-C والـ HDL-C في المجموعة الاولى مقارنة مع المجموعة الثانية علما ان هناك زيادة معنوية واضحة لكل من منسب كتلة الجسم (BMI) ونسبة الشحوم في الجسم (BF %) بين المجموعتين في الفئة الثانية. أما بالنسبة للفئة الثالثة فقد اظهرت النتائج انخفاض معنوي لمستوى الاديبونكتين وزيادة معنوية لكل من الكوليستيرول, الدهون الثلاثية الجليسيرايد, والـ LDL-C والـ BMI ونسبة الشحوم BF% وغير معنوية للـ HDL-C في المجموعة الاولى مقارنة مع المجموعة الثانية. وبينت النتائج وجود علاقة معنوية سالبة بين الاديبونكتين و كل من الكوليستيرول و الدهون الثلاثية والـ BMI. وكذلك اظهرت الدراسة وجود علاقة معنوية موجبة بين مستوى الاديبونكتين والـ HDL-C.


## الاستنتاج:-

1. حدوث انخفاض واضح في مستوى هرمون الاديبونكتين في المرضى الذين يعانون من السمنة وداء السكري من النوع الثاني مقارنة بالاشخاص الاصحاء.
2. حدوث انخفاض مستوى هرمون الاديبونكتين في الدم يصاحبه عدم انتظام صورة الدهون في المرضى الذين يعانون من داء السكري - النوع الثاني البدناء.

## Introduction

Adiponectin is a 244 – amino acid-long polypeptide, collagen like protein that is exclusively secreted by adipocytes and acts as a hormone with anti-inflammatory and insulin sensitizing properties by several mechanisms through which adiponectin may decrease the risk of type-2 diabetes mellitus, including suppression of hepatic gluconeogenesis, stimulation of fatty acid oxidation in the liver, stimulation of fatty acid oxidation and glucose uptake in skeletal muscle, and stimulation of insulin secretion [(1)]. These effects may be partly mediated by stimulatory effects of adiponectin on signaling pathways for 5'-adenosine monophosphate activated protein kinase (5'-AMPK), and peroxisome proliferator-activated receptor gamma (PPAR-γ) [(2)]. Adiponectin secretion, in contrast to secretion of other adipokines, is paradoxically decreased in obesity. These may be attributable to inhibition of adiponectin gene transcription by inflammatory and angiogenic factors secreted by hypertrophic adipocytes [(3)].A number of studies have shown that obesity, insulin resistance and atherosclerosis are accompanied by decreased adiponectin levels and that adiponectin replacement under experimental settings is able to diminish both insulin resistance and atherosclerosis [(4)].

The aim of the presented work is to study the association between plasma adiponectin levels and lipid profile in type-2 diabetic obese patients in Kerbala province of Iraq.

## Materials and Methods

Sample was recruited at the Al-Husain Teaching Hospital / Kerbala, during Nov. 2010 - April , 2011. A total number of 110 subjects with age ranged between (22 - 75) years and different gender were stratified according to obesity and/or diabetes mellitus into three categories:

1. In the first category, study subjects were divided according to diabetes mellitus into two groups: (Diabetic, n =67 and Non-diabetic n =43).
2. In the second category, study subjects were divided according to obesity into two groups: (Obese with BMI $\geq$ 30 kg/m$^2$, n =65 and non-obese with normal BMI < 25 kg/m$^2$, n =45).
3. According to both obesity and diabetes mellitus, study subjects in the third category were divided into two groups: (diabetic obese patients with body mass index $\geq$ 30 kg/m$^2$ , n =42 and controls non-diabetic non-obese with BMI < 25 kg/m$^2$ , n =20).

BMI was measured according to World Health Organization (WHO) procedure [(5)]. Body fat percentage can be estimated from a person's BMI by the following formula [(6)]:

**Body Fat% = (1.2 x BMI) + (0.23 x age) − 5.4 − (10.8 x gender)**

Where gender is equal to 0 if female and to 1 if male.

Seven milliliters of fasting venous blood was aspirated using disposable syringes and needles. The blood was allowed to clot in plain tubes for 30-45 minutes at room temperature and serum was recovered by centrifugation at 2000 rpm for 10 minutes and transferred into plain plastic tubes and kept frozen at -18 $^{o}$C until the time of assay.

Adiponectin hormone was determined by ELISA method. Available kit for adiponectin was supplied from DRG Company / Germany[(7)].

Lipid profiles (Total cholesterol, Triacylglycerol, and HDL-C) were measured quantitatively in serum by various procedures [(8-10)]. Serum level of LDL-C was calculated by Friedewald formula, which was based on the assumption that VLDL is present in serum at a concentration equal to 1/5 of triglyceride concentration [(11)].

Therefore:

**LDL-C = TC - [HDL-C + TG / 5 ]**

The formula is only valid when all concentrations are given in (mg/dl), and at serum triglyceride concentration of less than 400mg/100ml [(12)].

Statistical analysis was used to show the mean and standard deviation of variables. The significance of difference between mean values was estimated by Student T-Test. The probability P< 0.05 = significant, P> 0.05 = non-significant. Correlation analysis was used to test the linear relationship between parameters.

## Results and Discussion

Adiponectin is a hormone of adipocyte origin that is involved in the homeostatic control of circulating glucose and lipid levels, so the level of adiponectin was reduced in type-2 diabetic patients in association with insulin resistance. These data demonstrate a significant reduction in adiponectin level in type-2 diabetic as compared with control (p <0.001) as shown in (**Table-1)**. Previous study performed by Weyer *et. al*. in (2001) demonstrated a hypo-adiponectinemia in obesity and type-2 diabetes mellitus and a close association with insulin resistance and hyperinsulinemia[13].

Serum lipid profile levels show significant elevation in total cholesterol (p< 0.01), LDL-C (p< 0.05) , while TG level was not significantly elevated as compared with that found in control group (p> 0.05) as shown in the **(Table-1)**, while there was not significant differences in HDL-C level.

Elevation in serum level of total cholesterol, and LDL-C in type-2 diabetic patients as compare with control group (although it's mean within borderline high) may predict the association of diabetes mellitus with cardiovascular disease because these promote atheroma development in arteries (atherosclerosis). This disease process may leads to myocardial infarction (heart attack), stroke, and peripheral vascular disease.

**Table-1. Mean ± SD and P values of serum adiponectin, cholesterol, triacylglycerol, HDL, LDL, BMI, BF%, and age, in diabetic and non-diabetic subjects.**

| Parameters | Diabetic group N = 67 | Non-Diabetic group N = 43 | *P* value |
|---|---|---|---|
| Adiponectin (µg/ml) | 3.79 ± 3.16 | 7.06 ± 4.09 | 0.001 |
| Cholesterol (mg/dl) | 207.17 ± 45.92 | 177.20 ± 46.42 | 0.009 |
| Triacylglycerol (mg/dl) | 145.77 ± 67.93 | 132.88 ± 90.70 | 0.523 |
| HDL-C (mg/dl) | 45.33 ± 13.26 | 42.00 ± 14.32 | 0.321 |
| LDL-C (mg/dl) | 132.29 ± 44.01 | 111.80 ± 36.53 | 0.030 |
| BMI ($kg/m^2$) | 31.79 ± 6.31 | 28.93 ± 8.24 | 0.083 |
| BF% | 39.80 ± 9.94 | 31.55 ± 13.86 | 0.010 |
| Age (year) | 43 ± 9 | 40 ± 9 | 0.258 |

Adiponectin is exclusively secreted from adipose tissue into the bloodstream and in contrast to other adepokines; its level is inversely correlated with obesity and body fat percentage in adults [14]. A number of previous clinical studies showed a decrease in adiponectin levels in obese humans relative to lean subjects, and found a negative correlation between body mass index and plasma adiponectin levels in men and women [15], Our result demonstrate significant reduction of adiponectin level in obese group as compared with control ($p< 0.05$) as shown in **(Table-2)**.

Serum lipid profile levels show significant elevation of serum TG as shown in (table-2). Total cholesterol and LDL-C level elevated slightly but not significantly ($p> 0.05$, and there was no significant differences in HDL-C level as shown in (Table-2).

The presented data indicated that the mean value of body mass index (BMI) was significantly higher in obese group as compared with that found in control group ($p < 0.001$), while the mean value of body fat (BF%) percent was significantly higher in obese group as compared with control group ($P < 0.001$) as shown in **(table-2)**.

**Table-2. Mean ± SD and P values of serum adiponectin, cholesterol, triacylglycerol, HDL, LDL, BMI, BF%, and age, in obese and non-obese subjects.**

| Parameters | Obese group N = 65 | Non-obese group N = 45 | *P* value |
|---|---|---|---|
| Adiponectin (µg/ml) | 4.19 ± 3.74 | 6.06 ± 3.43 | 0.029 |
| Cholesterol (mg/dl) | 204.02 ± 48.54 | 185.16 ± 43.81 | 0.084 |
| Triacylglycerol (mg/dl) | 157.40 ± 74.22 | 103.56 ± 61.80 | 0.001 |
| HDL-C (mg/dl) | 43.15 ± 14.14 | 47.48 ± 11.73 | 0.148 |
| LDL-C (mg/dl) | 129.22 ± 43.71 | 119.52 ± 41.48 | 0.334 |
| BMI ($kg/m^2$) | 34.81 ± 3.71 | 21.30 ± 2.30 | < 0.001 |
| BF% | 42.99 ± 7.69 | 23.51 ± 7.91 | < 0.001 |
| Age (year) | 42 ± 8 | 42 ± 12 | 0.829 |

The mean value of serum adiponectin level was lowered significantly in diabetic obese group when compared with control group as shown in **(Table-3)**.

The mean value of total serum cholesterol, TG and LDL-C was elevated significantly in patients group as compared with control group, and there were no significant differences in HDL-C level as shown in **(Table-3)**.

The mean value of body mass index was significantly higher in diabetic obese group as compared with control group, while the mean value of body fat percent was significantly higher in patients group as compared with control group

as shown in **(Table-3)**. The risk of diabetes in self-reported weight and generally starts to increase at a BMI of 22 and is 40 times higher at a BMI over 35 [16-17].

increases by 9% for each kg gained

The current results demonstrate that diabetes mellitus when accompanied with obesity then the patient more liable to develop hyperlipidemia, and these results in consistence with previous reports.

**Table-3. Mean ± SD and P values of serum adiponectin, lipid profiles, BMI, BF%, and age, in diabetic obese and non-diabetic non-obese subjects.**

| Parameterss | Diabetic obese group N = 42 | Non-Diabetic non-obese group N = 20 | p value |
|---|---|---|---|
| Adiponectin (µg/ml) | 3.47 ± 3.27 | 7.97 ± 3.70 | 0.004 |
| Cholesterol (mg/dl) | 207.44 ± 48.08 | 153.40 ± 28.30 | < 0.001 |
| Triacylglycerol(mg/dl) | 155.36 ± 65.53 | 86.30 ± 48.31 | 0.001 |
| HDL-C (mg/dl) | 44.62 ± 13.35 | 44.40 ± 10.31 | 0.922 |
| LDL-C (mg/dl) | 132.15 ± 44.07 | 99.70 ± 25.72 | 0.005 |
| BMI ($kg/m^2$) | 34.83 ± 3.36 | 20.18 ± 1.98 | < 0.001 |
| BF% | 43.92 ± 6.37 | 18.89 ± 6.34 | < 0.001 |
| Age (year) | 42 ± 7 | 38 ± 10 | 0.238 |

To evaluate serum adiponectin and lipid profile in various subgroups of type-2 diabetic obese patients, subjects were categorized into three groups according to diabetes mellitus and obesity. Group B consist of 42 patients (diabetic obese), group C contained 25 patients (diabetic non-obese), and group D involved 23 subjects (non-diabetic obese), these three groups where compared with control group A which include 20 subjects (non-diabetic non-obese). The results of adiponectin, serum total cholesterol, serum TG, HDL-C, and LDL-C levels are shown in **(Table-4)**.

Significant decreases of serum adiponectin levels were obtained. Significant elevation for each of total serum cholesterol, TG and LDL-C were observed in diabetic obese group as compared with the control group. Serum HDL-C levels did not show significant variation.

On the other hand significant decrease of adiponectin levels were obtained in diabetic non-obese ($p < 0.05$), while a significant elevation were obtained for total cholesterol levels ($p<0.01$) as compared with the control group. Serum TG, LDL-C and HDL-C levels did not show significant variation between diabetic non-obese and control group.

Serum level of total cholesterol and TG show significant elevations ($p<0.05$) in non-diabetic obese group as compared with control group, other parameters remain within normal range when compared with the control group.

From these data, it was indicated that the effect of type-2 diabetes mellitus on adiponectin level was more pronounced than the effect of obesity and it is effect was potentiated by obesity.

**Table-4. ANOVA analysis of serum hormones (adiponectin, insulin), interleukin-8 (IL-8) and lipid profile level in various subgroups of type-2 diabetic obese and control.**

| Parameters | (A and B)* | (A and C) * | (A and D) * |
|---|---|---|---|
| Adiponectin | 0.001 | 0.026 | NS |
| Cholesterol | 0.001 | 0.005 | 0.035 |
| Triacylglycerol | 0.007 | NS | 0.009 |
| HDL-C | NS | NS | NS |
| LDL-C | 0.03 | 0.059 | NS |

***A: Control group N = 20 ; *B: Diabetic obese group N = 42**

***C: Diabetic non-obese group N = 25 ; *D: Non- diabetic obese group N = 23**

**NS: Not significant.**

Serum level of total cholesterol was influenced by both type-2 diabetes mellitus and obesity. Obesity has clear effect on the serum level of TG, whereas type-2 diabetes mellitus has no clear effect. On the other hand type-2 diabetes has clear effect on the serum level of LDL-C, whereas the obesity has no clear effect.

The spearman correlations and scatter plots were used to evaluate bivariate relationship of serum adiponectin level with lipid profile in patient and control groups. In diabetic group adiponectin significantly negatively correlated with TC [$r = -0.271$, $p = 0.026$], with serum TG, [$r = -0.389$, $p = 0.003$], and with serum LDL-C, [$r = -0.267$, $p = 0.043$], while there was significant positive correlation between adiponectin and HDL-C [$r = 0.346$, $p = 0.008$]. In contrast; in control group there was significant negative correlation between adiponectin and TG [$r = -0.327$, $p = 0.040$], and there was significant positive correlation between adiponectin and HDL-C [$r = 0.314$, $p = 0.030$], as shown in **(Table-5).**

Negative correlation of adiponectin with total cholesterol, serum TG and LDL-C and positive correlation with HDLC may suggest that decreased adiponectin levels may be associated with an atherogenic lipoprotein profile, similar associations between adiponectin and total cholesterol, TG, LDL-C, and HDL-C were observed by other authors among non-diabetic and diabetic subjects [18-19].

**Table-5. Correlation of serum adiponectin with serum lipid profile level in type-2 diabetic patients and control group.**

| Parameters | Diabetic patients | | Control | |
|---|---|---|---|---|
| | R | p | R | P |
| Cholesterol | -0.271 | 0.024 | -0.235 | NS |
| Triacylglycerol | -0.389 | 0.003 | -0.327 | 0.040 |
| HDL-C | 0.346 | 0.008 | 0.314 | 0.030 |
| LDL-C | -0.267 | 0.043 | -0.242 | NS |

The spearman correlations and scatter plots were used to evaluate bivariate relationship of serum adiponectin and lipid profile with the BMI in type-2 diabetic patients and in non-diabetic (control) subjects. In diabetic patients serum adiponectin show significant negative correlation with BMI [r = -0.314, p = 0.010], serum total cholesterol produce significant positive correlation with BMI [r = 0.266, p = 0.03], serum TG illustrate significant positive correlation [r = 0.397, p = 0.001], serum HDL-C demonstrate significant negative correlation with BMI [r = -0.276, p = 0.024], serum LDL-C show significant positive correlation with BMI [r = 0.257, p = 0.036]. Whereas in control group significant positive correlation of serum TG with BMI [r = 0.307, p = 0.036] as shown in **(Table-6)**.

Adiponectin secretion, in contrast to secretion of other adipokines, is paradoxically decreased in obesity, this may be attributable to inhibition of adiponectin gene transcription by inflammatory and angiogenic factors secreted by hypertrophic adipocytes [(20)]. These results demonstrate that adiponectin level decreased as BMI increased, but these reductions are significant and more pronounced in diabetic group, than in control group, which may be due to accumulation the effects of type-2 diabetes mellitus and obesity.

Significant positive correlations of BMI with TC, TG, LDL-C and significant negative correlation with HDL-C in diabetic group may be due to increase availability of glucose for VLDL synthesis and decrease in lipoprotein lipase activity leading to decrease of VLDL from peripheral circulation. An increased body fat was identified with higher levels of LDL-C/ HDL-C ratio and decreased HDL-C due to decrease in hepatic lipase activity resulting in decrease VLDL clearances which are metabolic abnormalities characterizing metabolic syndrome [(21)].

**Table-6. Correlation of serum adiponectin hormone and Lipid profile level with the body mass index (BMI) in type-2 diabetic patients and control group.**

| Parameters | Diabetic patients | | Control | |
|---|---|---|---|---|
| | R | P | r | P |
| Adiponectin | -0.314 | 0.010 | -0.207 | NS |
| Cholesterol | 0.266 | 0.03 | 0.189 | NS |
| Triacylglycerol | 0.397 | 0.001 | 0.471 | 0.009 |
| HDL-C | -0.276 | 0.024 | -0.040 | NS |
| LDL-C | 0.257 | 0.036 | 0.255 | NS |

## Conclusions

The major finding in the present study was demonstrated that a decreased serum adiponectin level was associated with obesity and type-2 diabetes mellitus, also decreased adiponectin level was associated with the elevation of lipid profile levels so adiponectin as hormone plays an important role in the prevention of hyperlipidemia, and consequently atherosclerosis and its complications.

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