

## Adiponectin in Type II Diabetes Mellitus

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### Abstract

**Background:** Diabetes mellitus is a chronic disorder characterized by impaired metabolism of glucose and lipids due to defect in insulin secretion or action. The association of obesity with development of type 2 diabetes may be partly mediated by altered secretion of adipokines by adipose tissues which may contribute to development of obesity. It has been reported that reduction in plasma adiponectin level may be related to the elevation of insulin resistance.

**Aim of Study:** This study aimed to evaluate the level of adiponectin in patients with type 2 diabetes mellitus.

**Subjects and Methods:** The current study examined sixty diabetic patients (type 2) with BMI from 30-40kg/m<sup>2</sup> and 20 age and sex matched healthy controls with BMI from 20-25 kg/m<sup>2</sup>.

**Statistical Analysis:** The data were tested for normality using the Anderson-Darling test and for homogeneity variances prior to further statistical analysis.

**Results:** Adiponectin level was significantly lower in all patients compared to controls. Lipid profile was altered in diabetic patients showing higher levels than in controls. In diabetic patients, adiponectin was significantly positively correlated with High Density Lipoprotein Cholesterol (HDL-C), while it was significantly negatively correlated with HbA<sub>1c</sub>, cholesterol, Low Density Lipoprotein Cholesterol (LDL-C), triglyceride and micro-albuminuria.

**Conclusion:** Adiponectin plays an important role in the patho-physiology of insulin resistance, diabetes, lipid metabolism. Reduction in adiponectin level may be related to the elevation of insulin resistance associated with diabetes mellitus type II. Adiponectin represents a very important step to understand the mechanism of obesity-induced insulin resistance and atherosclerosis. In contrast to other known adipocyte-derived hormones that are generally increased in obesity, adiponectin concentrations are that serum adiponectin levels were significantly inversely correlated with cholesterol, triglycerides and HbA<sub>1c</sub> in type 2 DM patients.

Decreased in obese individuals. This fact together with the promising results of experimental studies suggests the possibility that adiponectin replacement might become a new pharmacological approach to treatment of insulin resistance and/or atherosclerosis so our recommendations are monitoring

of adiponectin level in diabetic patients is a good predictor of glycemic control and should used in follow-up. Insulin serum level in diabetic patients should be measured to evaluate the effect of adiponectin on insulin level.

**Key Words:** Diabetes mellitus – Low density lipoprotein cholesterol – High density lipoprotein cholesterol – Body mass index

### Introduction

**THE** term diabetes mellitus describes a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. The global increase in obesity and greater physical inactivity has been suggested to underlie the alarming rise in the incidence of type 2 diabetes [1]. The association of obesity with development of type 2 diabetes may be partly mediated by altered secretion of adipokines by adipose tissues which may contribute to development of obesity [2]. It has been reported that reduction in plasma adiponectin level may be related to the elevation of insulin resistance [3]. The effects of diabetes mellitus include long-term damage, dysfunction and failure of various organs [4].

Adiponectin, an adipocyte-derived plasma protein, has been shown to play an important role in the regulation of fatty acid and glucose metabolism. Adiponectin enhances fatty acid oxidation both in skeletal and cardiac muscle as well as in the liver, thus reducing triglyceride content in these tissues [5]. Moreover, it stimulates glucose uptake by skeletal and cardiac muscle, and inhibits glucose production by the liver; consequently decreasing blood glucose levels. Adiponectin has effects on carbohydrate and lipid metabolism in skeletal muscle, cardiac muscle and liver. Adiponectin plays an important role in the pathophysiology of insulin resistance, diabetes and dyslipidemia. Reduced

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adiponectin level in plasma or level at baseline was shown to be associated with developing Type 2 Diabetes Mellitus (T2DM) and insulin resistance [5,6].

### Subjects and Methods

This work was carried out during the period from November 2015 to May 2016.

We examined samples of sixty diabetic patients (type 2DM) and 20 age and sex matched healthy controls were included in this study. The patients were selected from the outpatient clinic and inpatients of Internal Medicine Department of Assiut University Hospital. Formal consent was obtained from patients and controls. The study was approved by Ethical Committee of Faculty of Medicine, Assiut University.

Patients with the following conditions were excluded: Smoking habits, hypertension, liver or kidney disorders and those on lipid lowering drug, oral contraceptive pills.

Patients with the following conditions were included: Diabetic patients type II with Body Mass Index (BMI) from 30-40 kg/m<sup>2</sup>.

*The following investigations were done for all subjects:*

- 1- Random blood sugar.
- 2- Complete blood picture.
- 3- Kidney function test.
- 4- Micro-albumin in urine.
- 5- Liver function test.
- 6- Lipid profile.
- 7- Glycated hemoglobin (HbA<sub>1c</sub>).
- 8- Serum Adiponectin.

*Statistical analysis:*

The data were tested for normality using the Anderson-Darling test and for homogeneity variances prior to further statistical analysis. Categorical variables were described by number and percent (N, %), where continuous variables described by mean and standard deviation (mean, SD). Chi-square and fisher exact tests used to compare between categorical variables where compare between continuous variables by unpaired *t*-test. Pearson correlation coefficient used to assess the association between continuous variables. A two-tailed *p*<0.05 was considered statistically significant. All analyses were performed with the IBM SPSS 20.0 software.

### Results

Table (1): Comparison between patients and control groups as regards random blood sugar, HbA<sub>1c</sub> & Adiponectin.

|                                     | Patients   | Control   | <i>p</i> -value |
|-------------------------------------|------------|-----------|-----------------|
| <i>Random blood sugar (mmol/L):</i> |            |           |                 |
| Mean ± SD                           | 12.02±2.33 | 6.48±0.85 | <0.001**        |
| Range                               | 8-17       | 5-7       |                 |
| <i>HbA<sub>1c</sub> %:</i>          |            |           |                 |
| Mean ± SD                           | 8.53±2.82  | 5.29±0.68 | <0.001**        |
| Range                               | 4.6-15.8   | 4.3-6.4   |                 |
| <i>Adiponectin (µg/ml):</i>         |            |           |                 |
| Mean ± SD                           | 3.89±1.19  | 8.56±0.4  | <0.001**        |
| Range                               | 1.25-8.3   | 7.9-9.3   |                 |

Random blood sugar level in patients ranged from 8-17mmol/L with mean ± SD 12.02±2.33. In the control it ranged from 5-7mmol/L with mean ± SD 6.48±0.85. HbA<sub>1c</sub> level in patients ranged from 4.6-15.8% with mean ± SD 8.53±2.82. In the control group it ranged from 4.3-6.4% with mean ± SD 5.29±0.68. Adiponectin level in patients ranged from 1.25-8.3µg/ml with mean ± SD 3.89±1.19. In the control group it ranged from 7.9-9.3 with mean ± SD 8.56±0.4.

Table (2): Correlation between adiponectin and different parameters in study and control groups.

|                   | Adiponectin |                 |          |                 |
|-------------------|-------------|-----------------|----------|-----------------|
|                   | Patients    |                 | Control  |                 |
|                   | <i>r</i>    | <i>p</i> -value | <i>r</i> | <i>p</i> -value |
| Cholesterol       | -0.367      | 0.004**         | -0.056   | 0.813           |
| Triglyceride      | -0.194      | 0.138           | 0.139    | 0.559           |
| HDL               | 0.107       | 0.414           | 0.385    | 0.094           |
| LDL               | -0.345      | 0.007**         | -0.269   | 0.251           |
| HbA <sub>1c</sub> | -0.576      | 0.001**         | 0.217    | 0.358           |
| Micro-Alb         | -0.276      | 0.033*          | 0.291    | 0.213           |

Adiponectin level was significantly lower in all patients compared to controls. Lipid profile was altered in diabetic patients showing higher levels than in controls. In diabetic patients, adiponectin was significantly positively correlated with High Density Lipoprotein Cholesterol (HDL-C), while it was significantly negatively correlated with HbA<sub>1c</sub>, cholesterol, Low Density Lipoprotein Cholesterol (LDL-C), micro-albumin and triglyceride.

There was statistically significant positive correlations between BMI and HbA<sub>1c</sub>, random blood sugar, cholesterol and LDL. There was statistically significant negative correlation between BMI and adiponectin.

Table (3): Correlation between blood sugar, HbA<sub>1c</sub>, Micro-Alb, cholesterol, triglyceride, HDL, LDL and adiponectin as regard BMI.

|                   | BMI kg/m <sup>2</sup>  |                 |                        |                 |
|-------------------|------------------------|-----------------|------------------------|-----------------|
|                   | 30-35kg/m <sup>2</sup> |                 | 35-40kg/m <sup>2</sup> |                 |
|                   | <i>r</i>               | <i>p</i> -value | <i>r</i>               | <i>p</i> -value |
| Blood sugar       | 0.076                  | 0.726           | 0.510                  | 0.001**         |
| HbA <sub>1c</sub> | 0.013                  | 0.951           | 0.687                  | 0.000**         |
| Micro-Alb         | 0.145                  | 0.500           | 0.234                  | 0.170           |
| Cholesterol       | 0.004                  | 0.987           | 0.459                  | 0.005**         |
| Triglyceride      | 0.133                  | 0.536           | 0.188                  | 0.271           |
| HDL               | 0.388                  | 0.061           | 0.090                  | 0.602           |
| LDL               | 0.090                  | 0.676           | 0.468                  | 0.004**         |
| Adiponectin       | -0.102                 | 0.635           | -0.461                 | 0.005**         |

### Discussion

Adiponectin is a collagen-like protein that is solely secreted by adipocytes. Accumulating evidence from animal and human studies demonstrated that Adiponectin played an important role in the pathophysiology of insulin resistance, diabetes, lipid metabolism (Kadowaki et al.) [5] the results of our study showed that all diabetic patients with high BMI (35-40kg/m<sup>2</sup>) have lower concentration of adiponectin and adiponectin is significantly inversely correlated with BMI and there is significant positive correlations between BMI and HbA<sub>1c</sub>, random blood sugar, cholesterol and LDL. This in agreement with Weyer et al., [7] Yamamoto et al., [8] and Wei-Siung et al., [9] who reported that adiponectin levels are strongly associated with obesity (increased BMI) and insulin resistance. The association of obesity with development of type 2 diabetes may be partly mediated by altered secretion of adipokines by adipose tissue. Greater adiposity down regulates the secretion of adiponectin [10]. Consequently attempts to reduce body weight to normalize serum adiponectin levels could be effective in preventing the development of diabetes mellitus [11]. In our study we found that Adiponectin level was significantly lower in all diabetic patients (type 2) compared to controls. Lipid profile was altered in diabetic patients showing higher levels than in controls. In diabetic patients, adiponectin was significantly positively correlated with High Density Lipoprotein Cholesterol (HDL-C), while it was significantly negatively correlated with glucose, HbA<sub>1c</sub>, Cholesterol, Low Density Lipoprotein Cholesterol (LDL-C) which is in agreement with Zurawska-klis et al., [12] who found that serum adiponectin levels were significantly inversely correlated with cholesterol, triglycerides and HbA<sub>1c</sub> in type 2 DM patients.

### Conclusion:

Adiponectin plays an important role in the patho-physiology of insulin resistance, diabetes, lipid metabolism. Reduction in adiponectin level may be related to the elevation of insulin resistance associated with diabetes mellitus type II. Adiponectin represents a very important step to understand the mechanism of obesity-induced insulin resistance and atherosclerosis. In contrast to other known adipocyte-derived hormones that are generally increased in obesity, adiponectin concentrations are decreased in obese individuals. This fact together with the promising results of experimental studies suggests the possibility that adiponectin replacement might become a new pharmacological approach to treatment of insulin resistance and/or atherosclerosis so our recommendations are monitoring of adiponectin level in diabetic patients is a good predictor of glycemic control and should used in follow-up. Insulin serum level in diabetic patients should be measured to evaluate the effect of adiponectin on insulin level.

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## الأديبونيكتين في داء السكري النوع الثاني

الأديبونيكتين هو بروتين يفرز بواسطة الخلايا الشحمية ووجد أنه يلعب دوراً مهماً في عمليات الأيض المتعلقة بسكر الجلوكوز والدهون حيث يقلل من مستويات سكر الدم والدهون الثلاثية.

أجريت هذه الدراسة لمعرفة العلاقة بين مستوى الأديبونيكتين في الدم ومستوى السكر والهيموجلوبين السكري والدهون في مرضى السكري من النوع الثاني وشملت الدراسة ستين مريضاً وعشرين من الأصحاء كمجموعة ضابطة وتم إجراء فحوصات معملية روتينية وقياس مستوى الأديبونيكتين في مصل الدم. وأظهرت الدراسة أن مستوى الأديبونيكتين في مصل الدم يكون أقل في المرضى مقارنة بالأصحاء وأن هناك علاقة طردية بين مستوى السكر في الدم ومستوى الدهون ومعامل كتلة الجسم كما أن هناك علاقة عكسية بين مستوى الأديبونيكتين ومستوى كل من السكر والدهون ومعامل كتلة الجسم. وجد كذلك أن مستوى الدهون في الدم والزلزال في البول يكون أعلى في المرضى ذوي أكثر من 8% هيموجلوبين سكري مقارنة بمن هم أقل من 8% بينما يكون مستوى الأديبونيكتين أقل.

وخلصت الدراسة إلى أن البدانة ومقاومة الأنسولين مرتبطة بإنخفاض مستويات الأديبونيكتين وإن استعمال الأديبونيكتين كعلاج قد يكون قادراً على تقليل مقاومة الأنسولين وضبط مستوى السكر بالدم وقد يكون الأديبونيكتين علامة جديدة للسيطرة الأيضية لدى الأشخاص الذين يعانون من مرض السكري النوع الثاني وهذا قد يجعل الأديبونيكتين أداة علاجية واعدة في المستقبل.