

1-1-2020

## Adiponectin levels decrease independently of body mass index and diabetes type after the normalization of hyperglycemia

NALAN METİN AKSU

DUYGU YAZGAN AKSOY

MELTEM AKKAŞ

NEŞE ÇINAR

FATMA UÇAR

*See next page for additional authors*

Follow this and additional works at: <https://journals.tubitak.gov.tr/medical>

 Part of the [Medical Sciences Commons](#)

---

### Recommended Citation

AKSU, NALAN METİN; AKSOY, DUYGU YAZGAN; AKKAŞ, MELTEM; ÇINAR, NEŞE; UÇAR, FATMA; YILDIZ, OKAN BÜLENT; and USMAN, AYDAN (2020) "Adiponectin levels decrease independently of body mass index and diabetes type after the normalization of hyperglycemia," *Turkish Journal of Medical Sciences*: Vol. 50: No. 2, Article 5. <https://doi.org/10.3906/sag-1903-35>  
Available at: <https://journals.tubitak.gov.tr/medical/vol50/iss2/5>

This Article is brought to you for free and open access by TÜBİTAK Academic Journals. It has been accepted for inclusion in Turkish Journal of Medical Sciences by an authorized editor of TÜBİTAK Academic Journals. For more information, please contact [academic.publications@tubitak.gov.tr](mailto:academic.publications@tubitak.gov.tr).

---

## Adiponectin levels decrease independently of body mass index and diabetes type after the normalization of hyperglycemia

### Authors

NALAN METİN AKSU, DUYGU YAZGAN AKSOY, MELTEM AKKAŞ, NEŞE ÇINAR, FATMA UÇAR, OKAN BÜLENT YILDIZ, and AYDAN USMAN

## Adiponectin levels decrease independently of body mass index and diabetes type after the normalization of hyperglycemia

Nalan METİN AKSU<sup>1\*</sup>, Duygu YAZGAN AKSOY<sup>2</sup>, Meltem AKKAŞ<sup>1</sup>,  
Nese ÇINAR<sup>3</sup>, Fatma UÇAR<sup>4</sup>, Bülent Okan YILDIZ<sup>5</sup>, Aydan USMAN<sup>5</sup>

<sup>1</sup>Department of Emergency, Faculty of Medicine, Hacettepe University, Ankara, Turkey

<sup>2</sup>Department of Internal Medicine, Faculty of Medicine, Acıbadem Mehmet Aydınlar University, İstanbul, Turkey

<sup>3</sup>Department of Internal Medicine, Faculty of Medicine, Muğla Sıtkı Koçman University, Muğla, Turkey

<sup>4</sup>Department of Biochemistry, Yıldırım Beyazıt Dışkapı Research and Training Hospital, Ankara, Turkey

<sup>5</sup>Department of Internal Medicine, Faculty of Medicine, Hacettepe University, Ankara, Turkey

Received: 04.03.2019 • Accepted/Published Online: 02.01.2020 • Final Version: 09.04.2020

**Background/aim:** Acute hyperglycemia is generally a frequently encountered condition in the emergency department (ED), because it is seen as a complication of diabetes mellitus (DM). In this study, we aimed to detect the change in adiponectin levels during acute hyperglycemic states and after normalization of blood glucose with insulin treatment.

**Materials and methods:** Forty-eight patients over the age of 18 years who were admitted to the ED with acute hyperglycemia were included in the study. Serum samples were taken from patients on admission and 6 h after the normalization of blood glucose with insulin treatment, and adiponectin levels were measured in both samples.

**Results:** There were 21 female and 27 male patients with a median age of  $58.7 \pm 18$  years. All patients' blood glucose levels were normalized with insulin treatment according to international recommendations. Serum adiponectin levels decreased significantly after the normalization of blood glucose in the whole group. Adiponectin levels decreased from  $28.9 \pm 16.5$  to  $12.1 \pm 10.9$   $\mu\text{g/mL}$  ( $P < 0.0001$ ) in the whole group. This decrease was independent of diabetes type and body mass index.

**Conclusion:** Normalization of blood glucose in patients with hyperglycemia caused a decrease in adiponectin levels, independent of diabetes type and/or body weight in an acute emergency setting. Inhibited upregulation of adiponectin secretion and/or blunted suppressive effect of insulin due to hyperglycemia or exogenous insulin administration may have caused the decrease in adiponectin levels.

**Key words:** Hyperglycemia, adiponectin, body mass index

### 1. Introduction

Diabetes mellitus (DM) prevalence is increasing worldwide [1]. Hyperglycemia is a frequently encountered condition of patients with DM who are admitted to the Emergency Department (ED) [2].

Adiponectin is an adipokine which was initially thought to be secreted only from adipocytes, but it was later proven that adiponectin is also secreted from osteoblasts, liver parenchymal cells, myocytes, epithelial cells, and placental tissue [3,4]. Adiponectin is a major regulator of glucose metabolism with insulin-sensitizing properties; thus, low levels of adiponectin are associated with diabetes [5].

Adiponectin circulates in the concentration range of 3–30  $\mu\text{g/mL}$  in healthy individuals. The clearance of adiponectin is primarily mediated by the liver. It has a

surprisingly rapid turnover. The half-life of adiponectin is reported to be between 75 and 150 min. The serum half-life is reduced in patients with type 2 DM and it may be even shorter in patients with large fat cells and poor diabetes control [6,7]. Adiponectin levels are positively associated with insulin sensitivity. The glucose-lowering effect of adiponectin is primarily mediated by suppressing gluconeogenesis or glycogenolysis, and it may also be mediated by upregulation of Peroxisome proliferator activated receptor  $\alpha$  (PPAR $\alpha$ ) [4].

Adiponectin is also known as an antiinflammatory hormone [8]. It maintains metabolic homeostasis, and higher levels of adiponectin are associated with lower type 2 DM risk [9,10]. Adiponectin, with its insulin-sensitizing, antiatherogenic, antiapoptotic, and antiinflammatory

\* Correspondence: [nametaksu@yahoo.com.tr](mailto:nametaksu@yahoo.com.tr)

effects, may play a role in future therapies for obesity, type 2 diabetes, and atherosclerosis [4].

The effect of acute hyperglycemia on adiponectin levels is less studied [3,11]. We evaluated the effect of the normalization of blood glucose levels on adiponectin in patients admitted to the ED with acute hyperglycemia.

**2. Materials and methods**

**2.1. Patients**

This study was approved by the ethical board of Hacettepe University (HEK 09/177-107). Forty-eight adult patients admitted to the ED with hyperglycemia (blood glucose of  $\geq 300$  mg/dL) were included in the study. Written informed consent forms were obtained from all patients. Demographic features (age, sex), height, weight, and type of diabetes were recorded.

**2.2. Methods**

All patients were treated according to international recommendations for hyperglycemia, with appropriate amounts of intravenous fluid and intravenous crystalline insulin infusion. Euglycemia was reached within 6–12 h. Serum samples were taken from the patients on admission and at 6 h (which was chosen as an optimum time for half-life of adiponectin) after normalization of blood glucose to measure adiponectin levels. Adiponectin levels were measured by Biovendor Human Adiponectin ELISA. Results are given as  $\mu\text{g/mL}$ .

**2.3. Statistical analysis**

Statistical analyses were carried out using SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA). Numerical variables are shown as mean (range), and categorical

variables are shown as frequencies and percentages. The Mann–Whitney U test and Kruskal–Wallis test were used to determine differences in numerical variables between the groups, and the chi-square test was used to determine differences between categorical variables.  $P \leq 0.05$  was considered to be statistically significant.

**3. Results**

The study included 48 patients (21 female and 27 male), with a median age of  $58.7 \pm 18$  years. Clinical and laboratory parameters are presented in Table 1. Thirty-one patients had type 2 DM, 10 patients had type 1 DM, and 7 patients were diagnosed with diabetes at that particular admission.

Serum adiponectin levels decreased significantly after the normalization of blood glucose in the whole group. Adiponectin levels decreased from  $28.9 \pm 16.5$  to  $12.1 \pm 10.9$   $\mu\text{g/mL}$  ( $P < 0.0001$ ) in the whole group. The decrease in adiponectin persisted when evaluated according to Body Mass Index (BMI) and type of DM (Tables 2 and 3).

**4. Discussion**

The results of the present study demonstrated that adiponectin levels decreased after the normalization of blood glucose in patients with hyperglycemia. This was not dependent on diabetes type and/or body weight. Studies that evaluate the effects of acute hyperglycemia are rare. This is the first study that has demonstrated a decrease in adiponectin levels after the correction of hyperglycemia.

Aso et al. investigated the effect of acute hyperglycemia after oral glucose load in healthy subjects on total and

**Table 1.** The distribution of the patients according to BMI, sex, and previous DM.

BMI (kg/m <sup>2</sup> )	Normal (<24.9)	Overweight (25–29.9)	Obese (>30)
N	16	20	12
Sex	3 F/ 13 M	9 F/11 M	9 F/3 M
Previous DM	11 (68.8%)	19 (95%)	11 (91.75%)

BMI: Body mass index; DM: diabetes mellitus.  
Data are presented as n (%) or mean  $\pm$  SD.

**Table 2.** The change in adiponectin levels before and after treatment according to BMI.

BMI (kg/m <sup>2</sup> )	Number (n)	Adiponectin ( $\mu\text{g/mL}$ )		P
		Before treatment	After treatment	
Normal (<24.9)	16	$26.4 \pm 17.5$	$13.3 \pm 13.0$	0.006
Overweight (25–29.9)	20	$34.6 \pm 14.2$	$13.3 \pm 11.9$	<0.001
Obese (>30)	12	$24.4 \pm 17.1$	$8.9 \pm 5.5$	0.005

**Table 3.** The change in adiponectin levels before and after treatment according to diabetes type.

Diabetes type	Adiponectin ( $\mu\text{g/mL}$ )		P
	Before treatment	After treatment	
Type 1	28.8 $\pm$ 17.3	10.5 $\pm$ 8.2	0.007
Type 2	26.3 $\pm$ 18.4	8.7 $\pm$ 7	<0.001

high-molecular-weight (HMW) adiponectin. HMW adiponectin decreased significantly at 120 min after oral glucose load [12]. In another study, after an acute glucose load test, HMW adiponectin decreased in patients with normal glucose tolerance tests and those with impaired fasting glucose (fasting blood glucose levels over 100 mg/dL), but there was no change in patients with impaired glucose tolerance (glucose levels of 140–200 mg/dL 2 h after glucose challenge) and diabetes (glucose levels over 200 mg/dL 2 h after glucose challenge). Percentage change in adiponectin was negatively correlated with serum insulin but not glucose levels. This change is explained by an increase in insulin levels, which were less prominent in patients with impaired glucose tolerance and diabetes [13].

Koniari et al. reported that glucose loading increased adiponectin levels in healthy and impaired glucose tolerant patients. This response was significantly lower in diabetic patients. They stated that acute hyperglycemia is a stress factor that upregulates adiponectin secretion. The absence of this upregulation in the diabetic group is explained by the presence of lower adiponectin levels in diabetics [14].

In a study by Siervo et al., after oral glucose tolerance tests, adiponectin levels decreased both in healthy patients and in those with metabolic syndrome [15]. Dullaart et al. evaluated the effects of insulin secretion on adiponectin levels with usage of a hyperinsulinemic clamp in type 2 diabetic patients and healthy subjects. Insulin lowered the adiponectin levels in patients with type 2 DM; however, it did not change the levels in healthy subjects [16]. Insulin receptor dysfunction is associated with increased circulating adiponectin. Insulin directly suppresses adiponectin secretion from the marrow's adipose tissue [17]. In another study, in which the separate and combined effects of hyperglycemia and hyperinsulinemia on different markers were evaluated, adiponectin increased by euinsulinemia-hyperglycemia clamp. Adiponectin decreased in the states of hyperinsulinemia-hyperglycemia, and with the hyperinsulinemia-euglycemia clamp. Hyperinsulinemia is thought to prevent the effect of hyperglycemia in increasing adiponectin [11].

In this study, we demonstrated a decrease in adiponectin levels after correction of hyperglycemia with insulin treatment. This is the first clinical study that has demonstrated the effect of correction of acute hyperglycemia on adiponectin levels. Adiponectin is known to inversely correlate with body weight and abdominal obesity [18]. The decreases in adiponectin levels were independent of BMI in our study. Although visceral obesity, which is a main contributor of type 2 diabetes, has a major role in the secretion of adipokines, adiponectin levels were also reported to change and affect outcomes in those with type 1 DM [19,20]. The decrease in adiponectin was not affected by diabetes type in our study.

This change may be due to an inhibited upregulation of adiponectin secretion and/or a blunted suppressive effect of insulin due to hyperglycemia or exogenous insulin administration may have caused the decrease in adiponectin levels.

The insulin-sensitizing action of adiponectin is primarily due to decreased hepatic gluconeogenesis and it increases glucose transport in the muscles. Adiponectin mediates antidiabetic effects via direct metabolic actions, by improving insulin sensitivity, and, as recently demonstrated, by playing an important role in the stimulation of autophagy [21,22].

Our sample size was limited in terms of patients with different background disease profiles. This might have influenced the adiponectin levels. Scientists still need to do further studies to address the puzzling cross-talk between adiponectin and other metabolic factors.

In conclusion, adiponectin decreased after the correction of hyperglycemia in an emergency setting. This decrease was independent of diabetes type and/or body weight. Acute hyperglycemia, which upregulates adiponectin secretion and/or exogenous insulin administration, may have caused the decrease in adiponectin levels. Adiponectin is a promising adipokine in the treatment of many diseases; however, perplexing factors in both secretion and metabolism mandate, before it can be confidently used as a marker and/or a therapeutic target.

#### Declaration of conflict of interest

The authors report no conflicts of interest.

#### Source of support

This work was supported by the Hacettepe University Scientific Research and Developmental Office (010D02101002).

## References

1. Centers for Disease Control and Prevention. National Diabetes Statistics Report. Prevent Type 2 Diabetes. Atlanta, GA, USA: CDC; 2019..
2. Gupta T, Hudson M. Update on glucose management among noncritically ill patients hospitalized on medical and surgical wards. *Journal of Endocrine Society* 2017; 1 (4): 247-259. doi: 10.1210/js.2016-1055
3. Faraj M, Beaugregard G, Tardif A, Loizon E, Godbout A et al. Regulation of leptin, adiponectin and acylation-stimulating protein by hyperinsulinaemia and hyperglycaemia in vivo in healthy lean young men. *Diabetes & Metabolism* 2008; 34 (4): 334-342.
4. Achari AE, Jain SK. Adiponectin, a therapeutic target for obesity, diabetes, and endothelial dysfunction. *International Journal of Molecular Sciences* 2017; 18 (6): E1321. doi: 10.3390/ijms18061321
5. Frankenberg ADV, Reis AF, Gerchman F. Relationships between adiponectin levels, the metabolic syndrome, and type 2 diabetes: a literature review. *Archives of Endocrinology and Metabolism* 2017; 61 (6): 614-622.
6. Andersson DP, Laurencikiene J, Acosta JR, Rydén M, Arner P. Circulating and adipose levels of adipokines associated with insulin sensitivity in nonobese subjects with type 2 diabetes. *Journal of Clinical Endocrinology and Metabolism* 2016; 101 (10): 3765-3771.
7. Halberg N, Schraw TD, Wang ZV, Kim JY, Yi J et al. Systemic fate of the adipocyte-derived factor adiponectin. *Diabetes* 2009; 58 (9): 1961-1970.
8. Jaganathan R, Ravindran R, Dhanasekaran S. Emerging role of adipocytokines in type 2 diabetes as mediators of insulin resistance and cardiovascular disease. *Canadian Journal of Diabetes* 2018; 42 (4): 446-456.e1.
9. Wang Y, Meng RW, Kunutsor SK, Chowdhury R, Yuan JM. Plasma adiponectin levels and type 2 diabetes risk: a nested case-control study in a Chinese population and an updated meta-analysis. *Scientific Reports* 2018; 8 (1): 406.
10. Adiyaman SC, Ozer M, Saydam BO, Akinci B. The role of adiponectin in maintaining metabolic homeostasis. *Current Diabetes Reviews* 2020; 16 (2): 95-103. doi: 10.2174/1573399815666190702155733
11. Perkins JM, Joy NG, Tate DB, Davis SN. Acute effects of hyperinsulinemia and hyperglycemia on vascular inflammatory biomarkers and endothelial function in overweight and obese humans. *American Journal of Physiology, Endocrinology and Metabolism* 2015; 309 (2): E168-176.
12. Aso Y, Terasawa T, Kato K, Jojima T, Suzuki K et al. The serum level of soluble CD26/dipeptidyl peptidase 4 increases in response to acute hyperglycemia after an oral glucose load in healthy subjects: association with high-molecular weight adiponectin and hepatic enzymes. *Translational Research* 2013; 162 (5): 309-316.
13. Ozeki N, Hara K, Yatsuka C, Nakano T, Matsumoto S et al. Serum high-molecular weight adiponectin decreases abruptly after an oral glucose load in subjects with normal glucose tolerance or impaired fasting glucose, but not those with impaired glucose tolerance or diabetes mellitus. *Metabolism* 2009; 58 (10): 1470-1476.
14. Koniari K, Tousoulis D, Antoniadis C, Nikolopoulou A, Voltrakis E et al. The effect of glucose loading on adiponectin levels in diabetes mellitus type 2. Implications for Endothelial Dysfunction. *Journal of Disease Markers* 2014; 1 (2): 6.
15. Siervo M, Corander M, Mander AP, Browning LM, Jebb SA. Acute effects of hyperglycaemia on asymmetric dimethylarginine (ADMA), adiponectin and inflammatory markers (IL-6, hs-CRP) in overweight and obese women with metabolic syndrome. *British Journal of Biomedical Science* 2010; 67 (4): 216-218.
16. Dullaart RPF, Riemens SC, Meinardi JR, Wolffenbuttel BHR, Sluiter WJ. Plasma adiponectin is modestly decreased during 24-hour insulin infusion but not after inhibition of lipolysis by Acipimox. *Scandinavian Journal of Clinical Laboratory and Investigation* 2005; 65 (6): 523-532.
17. Uchihashi K, Aoki S, Shigematsu M, Kamochi N, Sonoda E et al. Organotypic culture of human bone marrow adipose tissue. *Pathology International* 2010; 60 (4): 259-267.
18. Orlando A, Nava E, Giussani M, Genovesi S. Adiponectin and cardiovascular risk. From pathophysiology to clinic: focus on children and adolescents. *International Journal of Molecular Sciences* 2019; 20 (13): E3228. doi: 10.3390/ijms20133228
19. Ismail MM, Abdel Hamid TA, Ibrahim AA, Marzouk H. Serum adipokines and vitamin D levels in patients with type 1 diabetes mellitus. *Archives of Medical Sciences* 2017; 13 (4): 738-744.
20. Yazıcı D, Yavuz D, Ögünç AV, Şirikçi Ö, Toprak A et al. Serum adipokine levels in type 1 diabetic patients: association with carotid intima media thickness. *Metabolic Syndrome and Related Disorders* 2012; 10 (1): 26-31.
21. Ahlstrom P, Rai E, Chakma S, Cho HH, Rengasamy P et al. Adiponectin improves insulin sensitivity via activation of autophagic flux. *Journal of Molecular Endocrinology* 2017; 59 (4): 339-350.
22. Ruan H, Dong LQ. Adiponectin signaling and function in insulin target tissues. *Journal of Molecular Cell Biology* 2016; 8 (2): 101-109.