



## SERUM ADIPONECTIN AND INDICES OF CARDIOVASCULAR RISK IN YOUNG WOMEN WITH EXCESSIVE BODY MASS

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### Abstract

Adiponectin reduces oxidative stress, the release of C-reactive protein and influences on the process of atherogenesis reducing lipid accumulation in the blood vessels. The findings on the association of adiponectin with cardiovascular risk are contradictory. This study aimed to assess the relationship between adiponectin and indices of cardiovascular risk in women with excessive body mass.

Adiponectin, hsCRP and lipids were measured in blood samples obtained from normoglycemic women with excessive body mass (n=52; BMI $\geq$ 25 kg/m<sup>2</sup>) aged 25-40 yrs and age-matched healthy controls (n=36; BMI<25kg/m<sup>2</sup>). All subjects underwent blood pressure examination and anthropometric measurements.

Median concentration of adiponectin in the serum in women with excessive body mass was significantly lower than in women with normal weight (10,8 vs 15,5  $\mu$ g/ml; p<0,01). Similarly, median serum concentration of triglycerides, hsCRP and blood pressure values were significantly higher and HDL-cholesterol significantly lower in women with BMI $\geq$ 25 kg/m<sup>2</sup> in comparison to these with normal BMI, however only HDL-C and hsCRP were found to be beyond widely accepted cut-offs. Hypoadiponectinemia in women with excessive body mass (adiponectin concentration below the 5<sup>th</sup> percentile in the control group) was associated predominantly with abnormally increased median values of hsCRP and blood pressure. Concentrations of total cholesterol, non-HDL-C and LDL-C were also significantly higher in women with excessive body mass and hypoadiponectinemia, however still within the reference range.

Our results suggest that adiponectin may be used as a prognostic marker of cardiovascular risk in women with excessive body mass.

### INTRODUCTION

Adipose tissue plays a central role in the management of systemic energy stores as well as in many other processes [1]. This is in part due to its capacity to store triglycerides but is also a function of its ability to secrete many bioactive adipocytokines that have a major impact on energy homeostasis and several other processes [1, 2]. Adiponectin, secreted exclusively by adipose tissue, is one of the most important metabolically active cytokine in relation to its function in cardiovascular system [2,3,4]. Adiponectin has attracted much attention because of its anti-diabetic, anti-

atherogenic and anti-inflammatory effect [3,5,6]. Low-circulating levels of this adipokine are associated with multiple metabolic disorders including obesity, insulin resistance, type 2 diabetes, and cardiovascular disease [7,8,9,10]. Furthermore adiponectin reduces oxidative stress and the release of C-reactive protein [11,12]. It also influences on the process of atherogenesis reducing lipid accumulation in the blood vessels [13]. Recently, a few population-based studies presented results of adiponectin as a cardiovascular risk factor and its association with atherosclerosis, stable coronary artery disease and acute coronary syndromes [2,7,10,14]. Little is known about the association of adiponectin and such cardiovascular risk factors such as blood pressure. We aimed to investigate the relationship between serum adiponectin and indices of cardiovascular risk in young women with excessive body mass.

## **SUBJECTS**

The study group included 52 young women aged 20-40 yrs with abnormal body mass, recruited from patients of Department of Internal Diseases, E. Warminski City Hospital in Bydgoszcz. Study group consisted of 58 overweight and obese women (BMI $\geq$  25 kg/m<sup>2</sup>). The control group (BMI $<$ 25 kg/m<sup>2</sup>) consisted of 38 age-matched women (20-40 yrs) recruited on voluntary basis. Both groups were characterized by normoglycemia ( $<$  100 mg/dL). We have accepted the following cut-off values for lipids and hsCRP : TC $<$ 200 mg/dL, HDL-C  $>$ 50mg/dL, LDL-C $<$ 130mg/dL, TG $<$ 150 mg/dL, non-HDL-C  $<$ 160 mg/dL, hsCRP  $<$ 3mg/L. In each subject body weight and height were measured and BMI was calculated (kg/m<sup>2</sup>); also blood pressure was examined. Women included into the study had not taken any contraceptives, anti-inflammatory or other medicines known to affect lipid or carbohydrate metabolism. The written informed consent from each participant was obtained and the study was approved by the Bioethics Committee at Collegium Medicum, Nicolaus Copernicus University.

## **METHODS**

Fasting blood was drawn in the early morning (7.00-9.00 am). Serum was obtained within less than 1 hour to avoid proteolysis and stored deep-frozen (-80°C) in small aliquots until assayed but not longer than 8 months.

Serum was assayed for HDL-cholesterol (HDL-C), triglycerides (TG), total cholesterol (TC), and glucose (ARCHITECT ci8200, Abbott Diagnostics). LDL-cholesterol (LDL-C) and non-HDL-C values were calculated. Serum CRP (hsCRP) concentration was measured by a high-sensitivity method (BN II, Dade Behring) and adiponectin was assayed by ELISA (DRG MedTek, R@D).

The height (cm), weight (kg) were measured using standard methods. Systolic and diastolic blood pressure (BP) were measured according to standard procedures by trained personnel. The cut-off value of systolic BP was  $<$ 130 mmHg and  $<$ 85mmHg for diastolic BP.

## **STATISTICAL METHODS**

All data were presented as mean  $\pm$  standard deviation (Gaussian distribution of results) or median and the 25<sup>th</sup> and 75<sup>th</sup> percentile (non-Gaussian distribution). The student t-test and U-Mann-Whitney test were used to compare differences. Comparison of mean values between groups were done by ANOVA or Kruskal-Wallis test.  $P<$ 0,05 was considered statistically significant. Statistical analysis was performed using Statistica 8.0 for Windows (Stat Soft).

## **RESULTS**

Characteristics of study and control groups is presented in Table 1. Among measured biochemical parameters only median HDL-C and CRP concentrations were found to be below or over the accepted cut-offs. Median serum adiponectin in all women with excessive body mass (mean BMI 32,6  $\pm$ 6,1 kg/m<sup>2</sup>) was significantly lower than in normal weight women, however this was especially observed in a subgroup of obese women (BMI 36,9 $\pm$ 5,3; adiponectin 10,1 vs 15,5 $\mu$ g/mL;  $p<$ 0.02). In overweight women (BMI 27,5 $\pm$ 1,4) and controls adiponectin concentrations were similar.

Table.1 Characteristics of the study and control group.

	Study group BMI $\geq$ 25 (n=52)	Control group BMI < 25 (n=36)	P
<b>TC (mg/dl)</b>	174 (144-199)	164 (155-185)	ns
<b>HDL-C (mg/dl)</b>	48 (42-53)	54 (50-61)	0.00006
<b>LDL-C (mg/dl)</b>	101 (83-129)	99 (84-115)	ns
<b>TG (mg/dl)</b>	90 (65-122)	64 (51-73)	0.00002
<b>Non-HDL-C</b>	127 (93-149)	111 (96-130)	0.08
<b>hsCRP (mg/l)</b>	2.04 (1.12-4.45)	0.67 (0.30-1.02)	0.00001
<b>Adiponectin (<math>\mu</math>g/ml)</b>	10.8 (7.33-15.49)	15.5 (9.68-17.97)	0.014
<b>Systolic BP (mmHg)</b>	130 (120-140)	120 (114-120)	0.00003
<b>Diastolic BP (mmHg)</b>	85 (71.5-95)	76.5 (70-80)	0.0002

On the basis of the distribution of adiponectin concentration in the control group of clinically healthy normal weight women we have accepted the 5th percentile as the cut-off for the lowest adiponectin. Thus as hypoadiponectinemia the concentration of adiponectin  $\leq$  6,02  $\mu$ g/mL was regarded (Table 2). Among women with excessive body mass those with hypoadiponectinemia had abnormally increased median CRP and blood pressure values. Median concentrations of measured lipid variables such as TC, LDL-C and non-HDL-C were also significantly higher in hypoadiponectinemia, however still within the accepted reference range. This was not the case if similar comparison was performed in a study group in relation to serum CRP. The 95<sup>th</sup> percentile cut-off for hsCRP in the control group was found to be 1,4 mg/L . We have not found any significant differences between the values of measured variables in women with BMI  $\geq$ 25 kg/m<sup>2</sup> if their CRP concentrations were over or below the 95<sup>th</sup> percentile cut-off (results not shown).

Table.2 Concentration of analyzed variables in relation to adiponectin

Parameters	Study group		
	Adiponectin cut-off 5th percentile (6,02 µg/ml)		
	> 5th percentile	≤ 5th percentile hypoadiponectinemia	p
TC (mg/dl)	167 (141-199)	198 (192-244)	0,04
HDL-C (mg/dl)	48 (42-55)	47 (43-50)	ns
non- HDL-C (mg/dl)	122 (91-149)	159 (142-200)	0,03
LDL-C (mg/dl)	97 (77-126)	124 (116-164)	0,04
TG (mg/dl)	90 (62-122)	98 (82-107)	ns
hsCRP (mg/l)	1,9 (1,1-4,0)	3,6 (3,5-6,5)	0,04
Systolic BP (mmHg)	130 (120-135)	145 (135-150)	0,03
Diastolic BP (mmHg)	84 (70-90)	100 (93-102)	0,004

## DISCUSSION

In the present study we have investigated whether adiponectin is related to cardiovascular risk in women with excessive body weight by analyzing the association of its serum level with biochemical and clinical variables. Hypoadiponectinemia in women with excessive BMI was found to be associated with significantly increased values of blood pressure and hsCRP concentration, that exceeded the accepted cut-offs.

Recent data suggest that adiponectin has many defensive properties against obesity-related hypertension [15,16,17]. Chow et al demonstrated for the first time an inverse relation between adiponectin concentration and the future development of hypertension [18]. They suggested that low adiponectin levels may play an important role in the pathogenesis of human hypertension. Low adiponectin levels are associated with increased plasma concentration of free-fatty acids and hepatic fat content and have been linked to the development of insulin resistance, which might, in turn, represent a base for the development of hypertension [19]. Hypoadiponectinemia might influence blood pressure also through other mechanisms, including endothelial dysfunction and the activation of the inflammatory cascade [18,19].

Some studies suggested that adiponectin level measurements could be useful in identifying obese patients at high risk of dyslipidemia and cardiovascular disease [20]. Our results also confirm a close association of hypoadiponectinemia with increased cardiovascular risk related to hs-CRP level. Moreover, we may suggest that measuring adiponectin seems to offer additional value over hsCRP, used routinely as the inflammatory marker, in assessing cardiovascular risk in women with excessive body mass.

We are aware of the limitation of this study that includes a relatively small groups; however, our results suggest that adiponectin may be used as a prognostic marker of cardiovascular risk in women with excessive body mass.

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